AWHONN

PROMOTING THE HEALTH OF WOMEN AND NEWBORNS

M. TERESE VERKLAN | MARLENE WALDEN

SHARRON FOREST

CORE CURRICULUM FOR

NEONATAL INTENSIVE CARE NURSING

6TH EDITION

With the Endorsements of

AMERICAN ASSOCIATION of CRITICAL-CARE NURSES

National Association of Neonatal Nurses

ELSEVIER

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Neonatal Intensive Care Nursing

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Neonatal Intensive Care Nursing

SIXTH EDITION

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To Mom, Cindy, Paul, and Theresa George—thank you
for showing me I have no boundaries. And in loving memory of my father.
MTV

In loving memory of my mother, Wanda, and my twin sister, Sharlene,
who taught me so much about love and caring for others.
Also to my professional colleagues who teach me so much;
but most important, to the babies and families who have taught me
the art of neonatal nursing.
MW

In loving memory of my mother, Monie—my nursing role model and
unwavering champion.
SF

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PREFACE

The provision of intensive care to the high-risk neonate challenges every neonatal care provider. Research and refinements in technology have made "high-tech" modalities such as extracorporeal membrane oxygenation (ECMO), nitric oxide, and hypothermia available to many more hospitals. The art and science of neonatal nursing are never stochastic. We learn from scientists; researchers; interprofessional colleagues; and, of course, our infants and their families. At a minimum, we are expected to enhance our application of clinical knowledge by utilizing an evidence-based approach to improve patient outcomes. The role of the nurse is frequently to bring together all the pieces of the puzzle to ensure comprehensive, clinically excellent, and compassionate care to sick newborns and their families.

The sixth edition of *Core Curriculum for Neonatal Intensive Care Nursing* is intended as a clinical resource and as an aid to prepare the nurse to take the high-risk neonatal nursing certification examination, whether it is the American Association of Critical Care Nurses Certification Examination (CCRN-neo) or the National Certification Corporation (RNC-NIC). The book is divided into sections and designed in an outline format so that it may be used as an easy reference. The first section, *Antepartum, Intrapartum, and Transition to Extrauterine Life*, addresses clinical issues related to factors that affect the fetus and the neonate's ability to successfully adapt to postnatal life. Information is also presented as to how we can assist in the recognition of the high-risk fetus/neonate and plan interventions that support the physiologic demands of the neonate during transition. *Cornerstones of Clinical Practice* presents concepts common to the delivery of quality care to all high-risk newborns and families. The third section, *Pathophysiology: Management and Treatment of Common Disorders*, provides a systems approach to the assessment and management of the disease processes high-risk neonates commonly present with. The last section, *Professional Practice*, focuses on the caregiver to strengthen competency with respect to research use, in addition to providing an overview of universal ethical and legal issues that may be encountered in the practice of neonatal nursing.

This text is the collaborative effort of the three major nursing specialty associations: the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN); the American Association of Critical-Care Nurses (AACN); and the National Association of Neonatal Nurses (NANN). The book brings together experts in the care of the high-risk neonate, all having the common goal of providing a comprehensive resource for the management and care of sick newborns. We are honored to be the editors of such an outstanding collaborative effort.

M. Terese Verklan
Marlene Walden
Sharron Forest

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PART 1
Antepartum, Intrapartum, and Transition to Extrauterine Life

CHAPTER 1
Uncomplicated Antepartum, Intrapartum, and Postpartum Care

Bonita Shviraga and Jennifer G. Hensley

OBJECTIVES

1. Identify normal physiologic changes of each system in pregnancy.
2. Describe parameters to assess gestational age and establish pregnancy dating.
3. Discuss genetic screening options for pregnancy.
4. Identify medications that may cause congenital malformations.
5. Outline components of prenatal care, including history, physical, laboratory, and diagnostic testing.
6. Explain tests of fetal lung maturity.
7. Identify six methods of antepartum fetal surveillance.
8. Discuss the normal stages of labor and delivery.
9. Describe low-risk labor management, including fetal monitoring guidelines.
10. Discuss normal immediate postpartum recovery and related postpartum nursing assessments and management.

Antepartum, intrapartum, and postpartum care are not usually included within the practice parameters of the neonatal nurse. Yet an understanding of the normal processes of pregnancy, birth, and postpartum recovery provides a framework for beginning to understand factors that affect the developing fetus and the high-risk neonate. This chapter discusses uncomplicated antepartum, intrapartum, and postpartum nursing care. In addition, an overview of the normal physiologic changes that can be expected in a healthy mother is included.

Terminology

A. **Calculation of gestation:** 280 days, 40 postmenstrual weeks, or 10 lunar months counted from the first day of the last menstrual period. (Actual duration of gestation from conception to estimated date of delivery is 38 weeks, assuming a 28-day cycle.)
B. **Trimesters:** division of gestation into three segments of approximately equal duration.
   1. First trimester: 0 to 12 weeks.
   2. Second trimester: 13 to 27 weeks.
   3. Third trimester: 28 to 40 weeks.
C. **Preterm, late preterm, term, and post-term pregnancy:** *preterm*, less than 37 completed weeks; *late preterm*, $34^{0/7}$ to $36^{6/7}$ weeks; *term*, 37 to 42 weeks; and *post-term*, greater than 42 weeks.

Normal Maternal Physiologic Changes by Systems

A. Alimentary tract and perinatal nutrition.
   1. During pregnancy, there is an increased caloric need of 300 kcal/day to support the growing fetus and increased maternal metabolic rate (Antony et al., 2017). Pregnant teenagers need an additional 100 to 200 kcal/day. According to the Institute of Medicine (IOM), now known as the National Academy of Medicine, the total recommended weight gain for women with a normal body mass index (BMI) is 25 to 35 pounds, and for underweight women a gain of up to 40 pounds may be recommended (American College of Obstetricians and Gynecologists [ACOG], 2016a). The IOM recommends limiting weight gain to 11 to 20 pounds for obese women; however, some experts feel this target is still too high (ACOG, 2016a; Antony et al., 2017) and that adverse pregnancy outcomes can be further decreased in obese women by further limiting pregnancy weight gain (Antony et al., 2017).
   2. An inadequate intake of folic acid has been associated with neural tube defects (NTDs) (U.S. Preventive Services Task Force, 2016). It is likely that the

functional mechanism for folate's effect on NTDs is its epigenetic role in DNA methylation and histones (Ross and Desai, 2017). Routine supplementation of folic acid 0.4 to 0.8 mg is recommended for women of childbearing age or for those planning a pregnancy to assist in the prevention of NTDs (U.S. Preventive Services Task Force, 2016). Women with a previously affected child should take folic acid 4 mg daily for 1 month prior to conception and throughout the first 3 months of gestation (Agency for Healthcare Research and Quality [AHRQ], 2017; West et al., 2017).

3. Approximately 50% of pregnancies are affected by morning sickness during the first trimester, which is associated with increased levels of human chorionic gonadotropin (hCG) and progesterone (West et al., 2017).
4. The stomach loses tone, has decreased motility, and may have delayed emptying time due to the smooth muscle relaxation effects of progesterone (King et al., 2015). Evidence regarding delayed gastric emptying is inconclusive; however, there is a delay during labor (Antony et al., 2017).
5. Relaxation of the pyloric sphincter and upward displacement of the diaphragm, in combination with increased intra-abdominal pressure from the enlarging uterus, can result in gastroesophageal reflux and heartburn (West et al., 2017).
6. The small bowel has reduced motility and hypertrophy of the duodenal villi to increase absorption of nutrients. Constipation is a problem because of mechanical obstruction from the uterus, reduced motility, and increased water absorption (King et al., 2015; West et al., 2017).
7. The gallbladder has decreased muscle tone and motility after 14 weeks as a result of the effects of progesterone. High levels of estrogen may decrease water absorption by the gallbladder's mucosa, leading to dilute bile, with resulting inability to sequester cholesterol. This increase in cholesterol may lead to gallstone formation during the second and third trimesters of pregnancy (Antony et al., 2017). Decreased gallbladder tone may also lead to increased retention of bile salts, resulting in pruritus and cholestasis gravidarum. Cholestasis gravidarum has been associated with increased risk of stillbirth and preterm deliveries (Cappell, 2017).
8. The liver is displaced upward by the enlarging uterus. Estrogen may cause altered production of plasma proteins, bilirubin, serum enzymes, and serum lipids. Alterations in laboratory values such as reduced serum albumin, elevated alkaline phosphatase, and elevated serum cholesterol may mimic liver disease. Serum levels of bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) are unchanged in normal pregnancy and may be used as an indicator of hepatic compromise during pregnancy. During labor, alkaline phosphatase levels may increase further, and AST, ALT, and lactate dehydrogenase levels may increase as a result of the stress of labor (Cappell, 2017).
9. The gut microbiome changes in pregnancy, with an altered bacterial load and composition. These changes resemble the gut microbiome found in proinflammatory and prodiabetogenic states and may promote energy storage and fetal growth (Antony et al., 2017).

B. Respiratory system.
   1. The increased vascularity and vascular congestion of the upper respiratory tract, resulting from increased levels of estrogen, causes hypersecretion of mucus from the nasopharynx, which may lead to nasal stuffiness, sinus congestion, and epistaxis (nosebleed) during pregnancy (Antony et al., 2017).
   2. Maternal oxygen requirements increase during 20% during pregnancy (Cunningham et al., 2014).
   3. The chest wall profile changes. Increased levels of estrogen and relaxin cause relaxation of intercostal ligaments with resulting increased chest expansion and chest circumference and an increase in the subcostal margin angle (Cunningham et al., 2014). The diaphragm is elevated by 4 cm in the third trimester (King et al., 2015).
   4. Respiratory changes during pregnancy include a 30% to 40% increase in tidal volume, a 15% to 20% decrease in expiratory reserve volume, a 20% to 25% decrease in residual volume, and a 20% decrease in functional residual capacity (Antony et al., 2017). Forced expiratory volume does not change in pregnancy and is a reliable indicator of respiratory illness, including asthma, in pregnant women (Antony et al., 2017). Increasing progesterone levels lead to chronic hyperventilation by 8 weeks, as reflected in the increase in tidal volume. Maternal $Paco_2$ levels decrease to 32 mm Hg and oxygen levels rise to 106 mm Hg early in pregnancy to allow fetal–placental exchange (Antony et al., 2017). As a result of these cumulative respiratory changes, pregnant women may experience physiologic dyspnea. To prevent the maternal acidosis due to the carbon dioxide levels from the fetus, mild hyperventilation occurs, which may cause a respiratory alkalosis. According to Cunningham et al. (2014), progesterone lowers the threshold and increases chemosensitivity to carbon dioxide; in response to the respiratory alkalosis, plasma bicarbonate levels decrease from 26 to 22 mmol/L, creating a slight increase in blood pH that shifts the oxygen dissociation curve to the left. Although pulmonary function is not impaired, respiratory diseases may be more serious during pregnancy (Cunningham et al., 2014).

C. Sleep.
   1. Pregnancy may increase sleep disorders and change sleep profiles, which may extend into the postpartum period. The majority of pregnant women (66% to 94%) report sleep alterations, which may begin as early as the first trimester and worsen as pregnancy progresses (Antony et al., 2017).
   2. There is a decrease in rapid eye movement (REM) sleep, which is important for cognition, and a decrease in stage 3 and 4 non-REM sleep, which is important for rest. By the third month postpartum, stage 3 and 4 alterations resolve; however, sleep disruption may occur due to nocturnal infant awakenings (Antony et al., 2017).
   3. Restless leg syndrome (RLS) onset or its worsening in pregnancy may also contribute to sleep disturbances and should be assessed (Antony et al., 2017).

D. Skin.
   1. Because of elevated levels of estrogen, spider angiomas are frequently seen on the neck, face, throat, and arms. Palmar erythema is common in two thirds of white women and one third of African American women (Antony et al., 2017; Cunningham et al., 2014).
   2. Striae gravidarum occurs in some women due to the thinning of the elastin fibers in the connective tissue under the skin (King et al., 2015).
   3. Increased pigmentation is due to increased levels of estrogen and melanocyte-stimulating hormone and occurs in approximately 90% of women. This is most marked on the nipples, areolas, perineum, and midline of the lower portion of the abdomen (commonly called the *linea nigra*) (Antony et al., 2017).
   4. Hyperpigmentation of the face, known as *chloasma* or *melasma* and also referred to as the *mask of pregnancy*, is caused by melanin deposits in the epidermis and macrophages. The resulting dark, blotchy appearance of the face, forehead, and upper lip occurs in up to 70% of women and is exacerbated by ultraviolet light (Wang and Kroumpouzos, 2017).
   5. During gestation, a greater percentage of the hair remains in the anagen (growth) phase, which decreases normal hair loss. Hair loss commonly occurs between 2 and 4 months after delivery due to an increase in the telogen (resting) phase of hair growth. The hair returns to a normal growth phase within 1 to 5 months (Wang and Kroumpouzos, 2017).
   6. Changes in secretory glands occur during pregnancy. Sebaceous gland activity alterations are variable, and the resulting changes in acne development are unpredictable (Wang and Kroumpouzos, 2017). Eccrine sweat gland activity increases as a result of increased thyroid activity, body weight, and metabolic activity and may result in miliaria and dyshidrotic eczema.
   7. Changes in the nails are uncommon but may occur beginning in the first trimester. Changes include brittleness, distal separation of the nail bed, subungual hyperkeratosis, whitish discoloration (leukonychia), and transverse grooving (Wang and Kroumpouzos, 2017). The cause is unknown.
   8. There is a change in the vaginal microbiome, with decreased diversity and decreased number of species present and a predominance of *Lactobacillus* species. One of the predominant neonatal gastrointestinal (GI) species, *L. johnsonii*, is increased in the vaginal microbiome and may be important in the establishment of the neonatal GI microbiome (Antony et al., 2017).

E. Urinary system.
   1. Structural renal changes begin during the first trimester and are a result of progesterone, pressure from the enlarging uterus, and increase in blood volume. The kidneys enlarge, the ureters dilate, hyperplasia of the smooth muscle walls of the ureters occurs, and the ureters elongate. Hydronephrosis occurs in 80% of pregnant women (Antony et al., 2017; Columbo, 2017).
   2. An increase in asymptomatic bacteriuria (ASB) may lead to cystitis and pyelonephritis in pregnancy. The most common pathogen for ASB is *Escherichia coli* (Columbo, 2017).
   3. The renal plasma flow increases by 75%, with a 25% decrease in the third trimester (Antony et al., 2017). The increased renal plasma flow is accompanied by an increase in the glomerular filtration rate of 50%, which leads to an increase in creatinine clearance and a decrease in nitrogen levels, as reflected by decreased blood urea nitrogen (BUN) and serum creatinine levels (Antony et al., 2017).
   4. Due to the expansion of plasma volume and water retention in pregnancy, even though sodium retention is increased by 900 mEq, serum levels of sodium decrease by 3 to 4 mmol/L (Antony et al., 2017).
   5. The reduced threshold for glucose reabsorption may result in glycosuria in pregnancy. Glycosuria can be detected in up to 90% of pregnant women with normal blood glucose. However, repetitive glycosuria warrants evaluation (Antony et al., 2017). Glucose measurements in the management of diabetes mellitus may be affected.
   6. A small amount of proteinuria may occur in pregnancy due to decreased protein reabsorption (King et al., 2015). Urinary protein excretion increases in pregnancy, with an upper limit of 300 mg in a 24-hour period (Antony et al., 2017). Greater than trace proteinuria may not indicate pathology, but warrants evaluation for urinary tract infection and preeclampsia.

F. Cardiovascular system.
   1. There is an increase in maternal blood volume by 40% to 50% from the end of the first trimester, peaking at 32 weeks (King et al., 2015). If the plasma volume increases faster than red blood cell (RBC) production, a physiologic anemia may result (King et al., 2015).
   2. There is an increase in maternal heart rate, which increases by 17% above the nonpregnant state by the third trimester. Stroke volume increases by 8 weeks' gestation until 20 weeks at 20% to 30% above prepregnancy levels. There is an increase in cardiac output beginning in the first trimester and peaking at 30% to 50% above prepregnancy levels, with most of the increase in cardiac output to the uterus, placenta, and breast (Antony et al., 2017).
   3. Because the heart is displaced leftward and upward by the enlarging uterus, the cardiac silhouette increases on x-ray films. It is important to confirm cardiomegaly with an echocardiogram and not rely solely on x-ray (Antony et al., 2017).
   4. Altered cardiac sounds in pregnancy include splitting of the first heart sound, an audible S_3 heart sound, systolic ejection murmurs (96% of pregnant women), and transient diastolic murmurs (up to 18% of pregnant women). Diastolic murmurs should be evaluated (Antony et al., 2017).
   5. Blood pressure (BP) remains at the prepregnancy level in the first trimester and drops during the second trimester at approximately 24 weeks of gestation by a mean arterial pressure (MAP) of 5 to 10 mm Hg. It returns to normal prepregnancy levels at the end of pregnancy. It is recommended in the ambulatory setting that BP be taken in the sitting position and that the fifth Korotkoff sound be used for diastolic BP measurement (Antony et al., 2017).
   6. Between 20 and 24 weeks of gestation, pressure on and resulting obstruction of the inferior vena cava may occur in the supine position. The resulting 10% to 30% fall in cardiac output, due to the decrease in stroke volume as a result of decreased blood in the heart, results in supine hypotension. Positioning the mother in a lateral position or with lateral displacement of the uterus with placement of a wedge under her hip assists in the prevention of supine hypotension (Antony et al., 2017).
   7. Blood stagnates in the lower extremities because of compression of the pelvic veins and the inferior vena cava, contributing to dependent edema and the development of varicosities (King et al., 2015).

G. Breasts.
   1. Early changes in the breasts during the first trimester include tenderness and paresthesia (Cunningham et al., 2014). The symptoms usually subside at the end of the first trimester.
   2. The areolas enlarge and darken. Sebaceous glands on the areolae increase activity in preparation for lactation and therefore become more prominent (Cunningham et al., 2014).
   3. Estrogen, progesterone, human placental lactogen (hPL), hCG, prolactin, and luteal and placental hormones cause hyperplasia of the breast tissue and development of lactiferous ducts and lobular alveolar tissue during the second and third trimesters (King et al., 2015). Physical examination may reveal palpable milk ducts and excretion of colostrum from the nipples.
   4. Colostrum, which is a high-protein precursor of breast milk, may be expressed toward the end of pregnancy (King et al., 2015).
   5. The breast begins lactogenesis with alveolar cells changing to a secretory epithelium toward the middle of pregnancy. After delivery, the second stage of lactogenesis, milk production, begins (King et al., 2015).

H. Skeletal changes.
   1. Compensating for the anteriorly positioned growing uterus, the lower portion of the back curves. This lordosis shifts the center of gravity backward over the lower extremities and causes low back pain, a common complaint in pregnancy (Antony et al., 2017; King et al., 2015).
   2. The sacroiliac and pubic symphysis joints loosen during pregnancy due to effects of the hormone relaxin and may result in pain localized to the symphysis pubis and radiating down the inner thigh (Antony et al., 2017).
   3. Alteration in the center of gravity, loosening of the joints, and an unsteady gait increase the risk of falls in pregnancy.
   4. Although serum calcium levels decrease during pregnancy, serum ionized calcium levels are unchanged. Maternal serum calcium levels are maintained, and fetal calcium needs are met through increased maternal intestinal absorption of calcium (Antony et al., 2017).
   5. Bone turnover is low in the first trimester and later increases in the third trimester when peak fetal calcium transfer occurs; however, osteoporosis is not associated with pregnancy bone turnover (Antony et al., 2017).

I. Hematologic changes.
   1. Plasma volume increases 15% by the end of the first trimester, undergoes a rapid expansion during the second trimester, peaks at 32 to 34 weeks, and then plateaus near term (Cunningham et al., 2014). Plasma volume at or near term is 50% above prepregnancy levels (Antony et al., 2017).
   2. The white blood cell (WBC) count rises progressively during pregnancy and labor. Prepregnancy levels range from 5000 to 12,000 cells/microliter

(mcL) and increases up to 20,000 to 30,000 cells/mcL in labor and the early postpartum period (Antony et al., 2017).

3. The RBC count begins to rise during the first trimester, with an average increase of 18% throughout pregnancy without iron supplementation (Antony et al., 2017). The increase in plasma volume changes the ratio of RBCs to plasma, causing a decreased hematocrit. This "physiologic anemia of pregnancy" reaches the lowest levels at 30 to 34 weeks. As the hematocrit begins to rise, a closer-to-normal ratio of RBCs to plasma results in a higher hematocrit near term (Antony et al., 2017).
4. Iron requirements for a pregnancy are 1000 mg (Antony et al., 2017; Cunningham et al., 2014). Fetal and placental requirements are 300 mg. Serum ferritin levels decline after midpregnancy (Cunningham et al., 2014).
5. Pregnancy has been called a *hypercoagulable state*. The platelet count decreases slightly as a result of increased destruction or hemodilution but remains within the normal range. About 8% of women have a gestational thrombocytopenia in the third trimester (Antony et al., 2017). Fibrinogen is increased by 50% to 80%, and factors I, II, VII, VIII, IX, and XII increase (Antony et al., 2017; King et al., 2015). Bleeding and clotting times remain normal (Antony et al., 2017). The incidence of thromboembolism increases five- to six-fold and is greatest during the postpartum period (Antony et al., 2017).
6. Pregnancy is known to result in altered immunologic function so that the "foreign fetus" is accommodated. Therefore, a decrease in cellular immunity may account for improvement of certain autoimmune diseases in pregnancy and an increased susceptibility to infection. The humoral immune system, characterized by antibody-mediated immunity, remains intact (King et al., 2015).

J. Endocrine and metabolic changes.

1. Thyroid.
   a. The thyroid remains unchanged or slightly enlarges during pregnancy, which is detected only by ultrasound. Suspected goiter should be evaluated during pregnancy (Antony et al., 2017).
   b. Thyroid-binding globulin (TBG) increases during the first trimester due to the effect estrogen has on the liver. TBG plateaus by 12 to 14 weeks' gestation and results in increases in total T_4 and total T_3 levels (Antony et al., 2017).
   c. Although there may be changes in laboratory indices, pregnant women remain euthyroid (Antony et al., 2017). Increased hCG levels are associated with decreased thyroid-stimulating hormone (TSH) levels in early pregnancy. There is a transient decrease in TSH during the first trimester, with a return to normal levels by the second trimester. The hormone hCG has thyrotropic activity and can activate TSH receptors and increase secretion of T_4 (Antony et al., 2017).
   d. Although T_4 and T_3 levels begin to increase in the first trimester and peak in the middle of pregnancy, serum portions of T_3 and T_4 are normal, unless a maternal iodine deficiency is present or there are abnormalities of the thyroid gland (Antony et al., 2017).
   e. TSH does not cross the placenta (Antony et al., 2017). There is transplacental transfer of T_4, which is necessary for fetal neurologic development in early gestation (Antony et al., 2017). The fetus is dependent on maternal transfer of thyroid hormones until 12 weeks' gestation and still has some reliance on maternal transfer after the fetal thyroid is functional (Antony et al., 2017).
   f. Additional research is in progress to evaluate maternal hypothyroidism and universal screening of mothers (Antony et al., 2017).
   g. Iodine crosses the placenta and is 75% of the maternal level (Antony et al., 2017). Also, radioactive iodine given to the mother crosses the placenta and can concentrate in the fetal thyroid after 12 weeks' gestation and cause adverse fetal affects (Antony et al., 2017).
2. Carbohydrate metabolism.
   a. Pregnancy is characterized by mild fasting hypoglycemia, postprandial hyperglycemia, and hyperinsulinemia (Antony et al., 2017; Cunningham et al., 2014).
   b. The basal metabolic rate is increased by 10% to 20% by the third trimester (Cunningham et al., 2014).
   c. Peripheral resistance to insulin is referred to as the *diabetogenic effect of pregnancy*. Its purpose is to ensure a sustained postprandial supply of glucose for the fetus. By term, there is a 45% to 70% reduction in the action of insulin. The hormones that may be responsible for this effect are hPL, progesterone, and estrogen. hPL may increase lipolysis, leading to increased free fatty acids, which increases tissue resistance to insulin (Cunningham et al., 2014).
   d. Glucose is actively transported to the fetus; however, insulin and glycogen do not cross the placenta. During pregnancy, hyperglycemic states rapidly change to fasting states, resulting in hypoglycemia. In this fasting state, there is an increase in levels of fatty acids, triglycerides, and cholesterol. This switch in fuels from glucose to lipids is referred to as *accelerated starvation,* and ketonuria rapidly occurs (Cunningham et al., 2014).

Antepartum Care

A. Initial antepartum visit.
   1. A thorough obstetric history is obtained.
      a. Gravidity (G), indicating the number of pregnancies, and parity (P), indicating the number of births. The obstetric history is often written as a *four-number parity* "G_ P_ [T-P-A-L]," with T-P-A-L representing the number of term-preterm-abortions (spontaneous or elective)-living births. Quick reference to G_P_ is *two-number parity*, used on the mother–baby unit.
         1) *G* indicates the number of times the woman has been pregnant, irrespective of the outcome of the pregnancy, including this pregnancy.
         2) In the *two-number parity*, *P* represents all births over 20 weeks.
         3) In the *four-number parity*, *P* represents the number of term deliveries; number of preterm deliveries; number of abortions up to $19^{6/7}$ weeks, including ectopic pregnancies; and number of living children.
         4) For example, G5P1120 indicates this is a woman's fifth pregnancy; she has had one term delivery, one preterm delivery, two abortions, and has no living child. It does not, however, indicate the etiology of the preterm birth, abortions, or causes of demises. This information is typically included in a table of past pregnancies, which includes the following: date of delivery, gestational age, length of labor, birth weight, gender, type of delivery, type of anesthesia, place of delivery, and complications.
      b. Information regarding course of pregnancy and delivery: weeks of completed gestation for each pregnancy, weight of newborn at birth, any maternal or neonatal complications, duration of labor in hours, type of delivery (vaginal, operative-assisted), and reason (forceps, vacuum, or cesarean), as well as any information known about uterine scarring and postoperative course.
      c. Medical history and review of systems, including infections (hepatitis, human immunodeficiency virus [HIV], herpes simplex virus [HSV], rubella, varicella, sexually transmitted infections, tuberculosis, group B streptococcus [GBS]), psychosocial assessment, substance use, recent travel, and family history.
      d. Genetic history: ethnicity; maternal age (>35 years); paternal age (>50 years); family history of genetic disorders, such as Down syndrome or fragile X syndrome; NTD; intellectual disability; and cystic fibrosis. Ethnic predispositions to certain genetic disorders are:
         1) African Americans: sickle cell anemia.
         2) Ashkenazi Jews: Tay–Sachs disease, Canavan disease, familial dysautonomia.
         3) Cajuns: Tay–Sachs disease.
         4) French Canadians: Tay–Sachs disease.
         5) Mediterranean descent: β-thalassemia and sickle cell disease.
         6) Southeast Asians: α-thalassemia (Gabbe et al., 2017).
      e. History of pregnancy loss or neonatal death (Gabbe et al., 2017).
      f. Exposure to teratogens (Gabbe et al., 2017).
      g. History of current pregnancy.
      h. Review of systems.
   2. Perform a complete physical examination, including a complete pelvic examination.
   3. Initial laboratory work (Table 1.1), including genetic screening blood work, such as screening for ethnically linked disorders.

ASSESSMENT OF GESTATIONAL AGE

A. **Last menstrual period (LMP)** to determine gestational age is a reliable method, provided the woman's cycles are regular; this method assumes a 28-day cycle with conception on day 14.
   1. A menstrual history should include frequency and duration of menstrual periods, heaviness of menstrual flow, menarche, and hormonal contraceptive use.
   2. The estimated date of delivery (EDD), or due date, may be determined by Nägele's rule: EDD = First day of LMP – 3 months + days + 1 year.

B. **Ultrasonography** (ACOG, 2017a).
   1. Ultrasound dating of the pregnancy is essential when the LMP is unknown, menstrual cycles vary more than 7 days, conception occurred while using hormonal contraception, or the size of the uterus on physical examination varies from that predicted by the LMP. Transvaginal sonography/ultrasound (TVS) is more accurate for determining gestational age in the first trimester; transabdominal sonography/ultrasound (TAS) uses biometric measurements as the fetus grows in the second trimester.
   2. Ultrasound dating of the pregnancy is most accurate once an embryo is visualized and a crown–rump length can be measured and up to $12^{6/7}$ weeks post-LMP (ACOG, 2016b). When the mean gestational sac diameter is ≥25 mm, an embryo should be visible via TVS, and when the embryo measures ≥7 mm, fetal cardiac activity (FCA) should be noted. The ACOG has developed parameters for redating the pregnancy when there is a discrepancy between the LMP and ultrasound measurements (Table 1.2).

Table 1.1

Routine Initial Prenatal Tests

Standard Test	Reason for Screening Test
Blood type and Rh status	Identify blood type and Rh status for postpartum hemorrhage and Rh incompatibility with fetus
Antibody screen	Identify fetuses at risk for hemolytic disease of the newborn/fetus
Complete blood count	Baseline laboratory studies Rule out maternal anemia or thalassemia Rule out thrombocytopenia; repeated between 24 and 28 weeks
Hemoglobin electrophoresis in patients with African/African American ethnicity	Screen at-risk populations to determine carrier status and determine if partner screening is indicated (*women with sickle cell trait have higher risk of bacteriuria in pregnancy*)
Cystic fibrosis carrier testing	Determine carrier status and determine if partner screening is indicated
Rubella antibody screen	Identify women susceptible to acquiring rubella during pregnancy (immunize *after* delivery)
MSQS (maternal serum for AFP, hCG, estriol, inhibin-A)	Genetic screening offered between 15 and 20 weeks AFP screens for neural tube defects Combination of serum markers sensitive in identifying Down syndrome
Diabetes screen on all women between 24 and 28 weeks; if high risk, do at initial obstetrics visit too	1-hour glucose screen to determine need for 3-hour GTT to rule out gestational diabetes
Mantoux TB test	Rule out need for immediate follow-up
Urine	
Urinalysis: Glucose, ketones, protein, nitrite, RBCs, WBCs, bacteria	Screen for diabetes, pregnancy-related hypertension, renal disease, possible urinary tract infection
Culture and sensitivity	Rule out asymptomatic bacteriuria (*GBS may be identified in heavily colonized women*)
Cervical Cancer Screening	
Papanicolaou smear; begin age 21; ≥30 years include high-risk HPV	Identify cytologic changes that could be precancerous
Sexually Transmitted Infections	
Neisseria gonorrhoeae and *Chlamydia* DNA by NAAT from cervix or urine	Identify treatable sexually transmitted diseases, most of which can cause fetal or neonatal morbidity
Hepatitis B surface antigen	Identify women whose offspring can be treated at birth to prevent hepatitis B infection with HBIg and HB vaccine
Human immunodeficiency virus 1 and 2	Identify women in need of treatment to decrease transmission to the fetus
Hepatitis C antibody	Screen at-risk women
Syphilis (VDRL, RPR, or treponemal test)	Identify women in need of treatment to reduce fetal/neonatal morbidity *(mandated by law in most states)*

AFP, α-fetoprotein; *DNA*, deoxyribonucleic acid; *GBS*, group B streptococcus; GTT, gamma-glutamyl transferase; *HB vaccine*, hepatitis B vaccine; *HBIg*, hepatitis B immune globulin; *hCG*, human chorionic gonadotropin; *HPV*, human papilloma virus; *MSQS*, maternal serum quadruple screen; *NAAT*, nucleic acid amplification testing; *RBCs*, red blood cells; *Rh*, Rhesus factor; *RPR*, rapid plasma reagin; *TB*, tuberculosis; *VDRL*, Venereal Disease Research Laboratory; *WBCs*, white blood cells.

From American Academy of Pediatrics (AAP) and the American College of Obstetricians and Gynecologists (ACOG). (2017). *Guidelines for Perinatal Care* (8th ed.). Elk Grove Village, IL: American Academy of Pediatrics.

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3. At 14 weeks' gestation, or with a crown–rump length of ≥84 mm, biparietal diameter (BPD) is more accurate and highly reproducible for fetal measurements. Four parameters are used to establish gestational age: BPD, head circumference (HC), abdominal circumference (AC), and femur length (FL).
4. In the absence of medical conditions or risk factors that could affect the pregnancy, and taking into consideration the cost and for what insurance will reimburse, the optimal time for one dating ultrasound examination is between 18 and 22 weeks' gestation (American Academy of Pediatrics [AAP] and ACOG, 2017).

C. Pelvic examination and fundal height.
1. Determination of the size of the uterus during an early examination (before 12 to 14 weeks) is relatively accurate if the mother is of normal height and not grossly obese.
2. Fundal height measurements in centimeters (McDonald's measurements) from the symphysis

Table 1.2

Perinatal Infections – TORCH Infections

Infection/ Incubation	Transmission	Detection	Maternal Effects	Neonatal Effects	Incidence and Prevention
Cytomegalovirus (CMV); incubation (CMV): 28 to 60 days MOST COMMON CONGENITAL INFECTION	Urine, breast milk, cervical mucus, semen, saliva, urine, transplacental; Organ transplantation Primary maternal infection associated with overall 30% to 40% transmission to fetus; Increasing risk as trimesters progress; Greatest risk third trimester	Rising IgM titer Viremia detected 2 to 3 weeks after initial infection	Clinically "silent" Only 1% to 5% acquire symptoms (low-grade fever, malaise, arthralgia, hepatomegaly)	90% infected Asymptomatic at birth 5% to 15% may have long-term sequelae, 5% with severe involvement at birth (IUGR, microcephaly, periventricular calcification, deafness, blindness, chorioretinitis, intellectual disability, hepatosplenomegaly)	0.2% to 3.2% newborns with congenital CMV Rigorous personal hygiene throughout pregnancy to prevent infection U.S. pregnant women first-degree infection 0.7% to 4%, second-degree infection 13.5%
Herpes simplex virus (HSV-1, HSV-2); incubation: 2 to 12 days	First-degree outbreak = 25% to 60% congenital transmission second-degree outbreak = less than 2% congenital transmission Mucocutaneous exposure, i.e., infected birth canal; ascending infection with rupture of membranes; Transplacental if initial infection occurs during pregnancy (rare)	Vesicles on cervix, vagina, or external genitalia; painful lesions; Confirm diagnosis by viral culture	Painful genital lesions; Primary infection associated with fever, malaise, myalgias; Lymphadenopathy; urinary retention	Transplacental has resulted in miscarriages (rare); Mortality rate 5% to 60% if neonate exposed and infected by active primary infection; Neurologic or ophthalmic sequelae; Disseminated infection in 70% of cases, with hepatic, respiratory, CNS involvement	1200 to 1500 neonatal cases/year in United States (not accurate; HSV not a reportable disease); Begin maternal antiviral prophylaxis every day at 36 weeks; Cesarean birth if lesions present in labor
Rubella virus; incubation: 12 to 23 days ELIMINATED in United States since 2004 due to routine vaccination begun in 1969; cases seen are from outside the United States or those who are underimmunized	Nasopharyngeal secretions; Transplacental	Rising IgM titer; Initial OB visit should confirm immunity to virus with rubella-specific IgG	Generalized erythematous maculopapular rash on face, neck, arms, and legs lasting 3 days; Lymphadenopathy, fever	Miscarriage, fetal death, CRS; mild to severe ocular, cardiac, auditory, neurologic involvement; 85% chance CRS infection in first trimester, 50% CRS 13 to 16 weeks; Rare CRS after 20 weeks	Vaccine contraindicated during pregnancy; Vaccinate nonimmune women postpartum
Toxoplasmosis protozoa, *Toxoplasma gondii*; Incubation: 5 to 18 days	Transplacental; Ingestion of contaminated foods or cysts in cat feces;	Serologic antibody titer testing for rising IgM	Asymptomatic with cervical lymphadenopathy, malaise;	Incidence of transmission increases with gestational age, but earlier fetal infection poses more catastrophic sequelae	Infection in the United States is 1:1000 to 8000

Table 1.2

Perinatal Infections – TORCH Infections—cont'd

Infection/ Incubation	Transmission	Detection	Maternal Effects	Neonatal Effects	Incidence and Prevention
PREGNANT WOMEN SHOULD AVOID SOFT CHEESES, RAW MILK, UNDERCOOKED MEATS, AND DELI MEATS	Impossible to transmit to others because the infecting organisms are tissue bound and are not secreted		Premature labor and delivery **"The cheese disease"**	Neurologic (hydrocephaly, microcephaly), ophthalmologic; IUGR	Reduce contact with cat feces during pregnancy (e.g., litter box and gardening)

CNS, Central nervous system; *CRS*, congenital rubella syndrome; *IgG*, immunoglobulin G; *IgM*, immunoglobulin M; *IUGR*, intrauterine growth restriction; OB, obstetrician; *TORCH*, *t*oxoplasmosis, *o*ther infections (e.g., congenital syphilis, Zika, parvovirus), *r*ubella, *c*ytomegalovirus infection, *h*erpes simplex.

From American College of Obstetricians and Gynecologists (ACOG). (2018a). *Management of herpes in pregnancy. Practice Bulletin No. 82.* June 2007 (reaffirmed 2018). *Obstetrics and Gynecology, 109,* 1489–1948.

From American College of Obstetricians and Gynecologists (ACOG). (2017f). *Cytomegalovirus, parvovirus B19, varicella zoster, and toxoplasmosis in pregnancy. Committee Opinion No. 151.* 2015 (reaffirmed 2017). *Obstetrics and Gynecology, 125,* 1510–1525.

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From Centers for Disease Control and Prevention. (2018). *Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB. Prevention HIV among pregnant women, infants, and children.* (Last updated: March 21, 2018). Retrieved 23 April 2018 from https://www.cdc.gov/hiv/group/gender/pregnantwomen/index.html.

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pubis to the top of the fundus are made from 20 weeks on to assess growth and approximate gestational age ±2 cm. The uterus is generally at the umbilicus at 20 weeks.

3. For mothers who have significantly increased BMIs, ultrasound is indicated to monitor fetal growth.

D. Quickening is the first feeling of fetal movement.
   1. Primigravida: quickening by 18 to 20 weeks.
   2. Multigravida: quickening by 16 to 18 weeks.

E. **Fetal heart tones:** Detected by an electronic Doppler device as early as 9 weeks and expected by 12 weeks; may be auscultated with a fetoscope by 19 to 20 weeks. Today, the fetoscope is rarely used in developed countries but may be used in the developing world.

GENETIC SCREENING

A. **Screening tests for aneuploidy** are available to all pregnant women in all trimesters, regardless of maternal age (ACOG, 2016c).

B. **Noninvasive screening for chromosomal abnormalities** (ACOG, 2016d).
   1. Cell-free DNA (cfDNA) testing by maternal venipuncture may be offered after 10 weeks' gestation to evaluate for trisomy 13, 18, and 21, as well as sex hormone abnormalities; therefore, fetal gender is also identified with cfDNA testing.
   2. First-trimester integrated screening between $10^{0/7}$ to $13^{6/7}$ weeks includes ultrasound measurement of fetal nuchal translucency (normal <3 mm) and/or biochemical markers. Biochemical markers include hCG and pregnancy-associated plasma protein A (PAPP-A) (ACOG, 2016c).
   3. When nuchal translucency cannot be performed (e.g., obesity), serum integrated biochemical marker screening can be performed in the first and second trimesters. Results are withheld until all screening is complete (ACOG, 2016c).
   4. All patients should be offered screening for cystic fibrosis; if carrier status is detected, the partner should be screened (ACOG, 2016d).
   5. Second-trimester ultrasound at 18 to 20 weeks for review of fetal systems, amniotic fluid, placental location, and cervical length. Ultrasound may also detect markers of chromosomal abnormalities.
   6. Second-trimester biochemical marker screening between 15 and 20 weeks for open NTD, Down syndrome, trisomy 13, and trisomy 18 with up to four markers—α-fetoprotein (AFP), estriol, hCG, and inhibin A. Irregularities in test values may be predictive of pregnancy compromise, such as intrauterine growth restriction.

C. Invasive genetic testing.
   1. Preimplantation genetic diagnosis using only a few cells; errors are possible, and follow-up chorionic villus sampling (CVS) or amniocentesis is recommended (ACOG, 2016c).
   2. CVS between 10 and 13 weeks: transabdominal or transvaginal aspiration of trophoblastic tissue with a catheter under ultrasound guidance (Driscoll et al., 2017). Risk of pregnancy loss is 0.5% (ACOG, 2016c). Maternal serum AFP level should be drawn between 15 and 20 weeks to check for fetal NTD.
   3. Amniocentesis at 15 to 20 weeks: aspiration of approximately 20 to 30 mL of amniotic fluid with a spinal needle inserted through the maternal

abdomen into the uterine cavity under ultrasound guidance. Direct chromosomal analysis of fluid and AFP measurement are performed. Risk of pregnancy loss is 0.1% to 0.3% (ACOG, 2016c).

ANTEPARTUM VISITS

A. **Frequency:** Traditional obstetric visits are recommended every 4 weeks until 28 weeks, then every 2 to 3 weeks until 36 weeks, and then weekly; however, for low-risk pregnancies, the number of visits can be reduced (AAP and ACOG, 2017).
B. **Routine assessments:** Weight, blood pressure, fundal height, fetal presentation, fetal heart tones, fetal movement, abnormal bleeding or discharge, signs of preterm labor, signs of preeclampsia, psychosocial state.
C. **Laboratory and diagnostic assessments.**
   1. 24- to 28-week visit:
      a. A 50-g oral glucose challenge test for gestational diabetes mellitus (GDM) is performed. A level greater than 130 to 140 mg/dL is abnormal and warrants a 3-hour oral glucose tolerance test. The diagnosis of GDM is made if two values are elevated on plasma values: fasting, 95 mg/dL; at 1 hour, 180 mg/dL; at 2 hours, 155 mg/dL; at 3 hours, 140 mg/dL (AAP and ACOG, 2017).
      b. Obtain repeat hemoglobin and hematocrit determinations to check for anemia. Repeat at 36 weeks if anemia is detected.
   2. 28-week visit: obtain a repeat antibody titer for Rh-negative mothers; administer Rh immunoglobulin, 300 mcg, if no anti-D antibody has been detected.
   3. Ultrasonography may be indicated as the pregnancy develops to evaluate fetal growth, amniotic fluid volume, Doppler flow, or assessment of placenta.
   4. 36-week visit: repeat HIV, syphilis, gonorrhea, and chlamydia cultures if indicated.
   5. 35- to 37-week visit: obtain vaginal/rectal swab for a GBS culture. If the woman is penicillin allergic, antibiotic sensitivities for erythromycin and clindamycin should be obtained if the culture is GBS positive (Centers for Disease Control and Prevention [CDC], 2010). The culture result is reliable for 5 weeks (CDC, 2010).

ANTEPARTUM FETAL SURVEILLANCE

A. Fetal movement counts or fetal kick counts.
   1. Fetal movement periods last approximately 40 minutes, and quiet periods last approximately 20 minutes. The longest quiet period observed by ultrasound is 75 minutes. Although prospective studies of fetal movement have not shown benefit to prevent perinatal mortality, fetal movement counts one to three times a day by the mother may show some benefit (Greenberg and Druzin, 2017).
   2. Various protocols have been utilized and various criteria have been used to define decreased fetal movement. A woman may be instructed to count fetal movements over a 2-hour period up to 10 movements. If the infant moves fewer than 10 times in 2 hours, there is cause for concern and further testing, such as nonstress test (NST), is indicated. This method is widely used but has received the most scrutiny and needs further evaluation (Greenberg and Druzin, 2017). Other criteria have been utilized; however, Greenberg and Druzin propose that maternal perception of sustained decreased fetal movement by the mother warrants evaluation.
B. **NST:** This is the most widely used screening method for fetal well-being. It is indicated for patients at risk of placental insufficiency and may be started as early as 28 weeks' gestation but is often utilized after 32 weeks' gestation.
   1. Some indications for NST include post-term pregnancy, diabetes mellitus, hypertension, previous stillbirths, intrauterine growth restriction, decreased fetal movements, and Rh disease (ACOG, 2016e).
   2. Testing is repeated once or twice weekly and classified as *reactive* or *nonreactive*. A *reactive* NST result is two fetal heart rate (FHR) accelerations, defined as a 15-beat rise from baseline lasting for at least 15 seconds, with return to baseline during a 20-minute period in a fetus 32 weeks or greater. In fetuses from 28 to 32 weeks, a threshold of a 10-beat rise from baseline for 10 seconds is utilized. A *nonreactive* test result is no FHR accelerations after 40 minutes (ACOG, 2016e). According to the ACOG (2016e), repetitive variable decelerations, defined as three in 20 minutes or FHR decelerations of 1 minute or more, are associated with increased risk of fetal compromise and cesarean delivery and require further evaluation.
C. Contraction stress test (CST).
   1. The CST evaluates the reserve function of the placenta. Indications for use are the same as for use of the NST. The CST is most often used after a nonreactive NST result (Greenberg and Druzin, 2017).
   2. Done by evaluating fetal heart tracing during three spontaneous or induced moderate contractions lasting 40 seconds or longer in a 10-minute period (ACOG, 2016e). Contractions can be induced through nipple stimulation (endogenous oxytocin) or intravenous oxytocin challenge test (exogenous).
   3. The CST simulates a labor pattern and allows the fetus to be stressed as in normal labor. The CST evaluates for FHR decelerations in relation to the onset of uterine contractions (ACOG, 2016e).
      a. A positive CST result is defined as late decelerations of the FHR that are present with greater than 50% of contractions in a 10-minute window.

Delivery should be considered with a positive CST result (Greenberg and Druzin, 2017).

b. Findings may also be considered suspicious or equivocal, unsatisfactory, or as showing tachysystole. These cases require retesting in the next 24 hours for adequate interpretation of fetal well-being (Greenberg and Druzin, 2017).

E. Biophysical profile (Greenberg and Druzin, 2017).

1. The biophysical profile (BPP) uses real-time ultrasonography to evaluate five parameters, each receiving either 0 or 2 points; the maximum score is 10 points, with management based on the assigned score. The five parameters are NST, fetal breathing, gross body/limb movements, fetal tone, and amniotic fluid. The BPP correlates well with fetal acid–base status. BPP scoring: 8 to 10, normal; 4 to 6, suspect chronic asphyxia and assess for delivery or further assessment, depending on gestational age; 0 to 2, strongly suspect chronic asphyxia and delivery indicated.
2. The false-negative rate of the BPP is less than 0.1%, or less than 1 fetal death/1000 within 1 week.
3. Modified biophysical profile (mBPP): NST/amniotic fluid index (AFI). Studies have revealed comparable predictive values for mBPP (0.8/1000 fetal death within 1 week) and BPP.
   a. NST is an indicator of present fetal condition.
   b. AFI is a marker of longer-term fetal status.

F. Amniotic fluid assessment.

1. Decreased amniotic fluid volume (oligohydramnios) is associated with uteroplacental insufficiency. It may also be indicative of fetal genitourinary or lung anomalies. There is an increased incidence of perinatal morbidity and mortality with oligohydramnios (Gilbert, 2017).
2. Polyhydramnios may be associated with chromosomal disorders, anatomic anomalies such as tracheoesophageal fistula, maternal diabetes, preterm delivery, and perinatal mortality (Gilbert, 2017).
3. Measurement of amniotic fluid: Single deep vertical pocket measurement of 2 cm is considered adequate (ACOG, 2016e), and although an AFI of 5 or greater has been used, randomized controlled trials support the use of the deepest vertical pocket to diagnose oligohydramnios (ACOG, 2016e).

LABORATORY ASSESSMENTS FOR DOCUMENTING FETAL LUNG MATURITY (GREENBERG AND DRUZIN, 2017)

A. Lecithin/sphingomyelin (L/S) ratio ≥2.0 indicates fetal lung maturity and occurs when fetal lung surfactant is present in amniotic fluid (at approximately 35 weeks). Positive predictive value is 98%. Blood or meconium in the fluid can affect results.

B. Phosphatidylglycerol (PG), a minor component of surfactant, is also present in amniotic fluid at approximately 35 weeks and increases rapidly at 37 weeks. PG is indicative of completed lung maturity. Measurement of PG is a more reliable test of lung maturity in mothers with diabetes than is measurement of the L/S ratio.

C. Fetal lung maturity assay measures surfactant/albumin ratio in amniotic fluid. It is less expensive, is easier to perform, and has fewer false-negative results than the L/S ratio or PG measurement.

D. Lamellar body counts are produced by type II pneumocytes and are a direct measurement of a storage form of surfactant (Greenberg and Druzin, 2017). The test is inexpensive and may be performed in 15 minutes with less than 1 mL of amniotic fluid. Values of 30,000 to 55,000/mcL are highly indicative of pulmonary maturity. Meconium and blood have a minimal effect on values.

MATERNAL INFECTIONS

A. TORCH infections (Table 1.3).

1. Acronym rarely used to refer to five infectious diseases: *t*oxoplasmosis, *o*thers (e.g., parvovirus, congenital syphilis), *r*ubella, *c*ytomegalovirus infection, and *h*erpes simplex; all cross the placenta and may adversely affect the fetus.

B. Sexually transmitted infections (Table 1.4).

C. Other communicable diseases (Table 1.5).

D. Chorioamnionitis (Gabbe et al., 2017).

1. An infection of the chorion, amnion, and amniotic fluid that may cause perinatal morbidity and mortality; usually associated with prolonged labor and rupture of membranes but can also be found in women with intact membranes.
2. Usually an ascending infection, commonly caused by *E. scherichia coli*, GBS, anaerobic streptococci, and *Bacteroides*.

E. Infection with GBS.

1. Approximately 10% to 30% of women are colonized with GBS (Gabbe et al., 2017). Colonization can be transient, chronic, or intermittent.
2. GBS may cause severe invasive disease in neonates. The majority of neonatal GBS infections occur in the first week of life and present as sepsis or pneumonia (CDC, 2010). There has been an 80% decline in neonatal GBS infection in the first week of life since universal screening of all women and administration of intrapartum antibiotics as prophylaxis was instituted (CDC, 2010); early-onset infection has decreased from 1.7/1000 live births to 0.24/1000 live births between 1993 and 2014 (CDC, 2016a).
3. All women should be screened at 35 to 37 weeks of gestation for vaginorectal GBS. Cultures done ≤5 weeks before delivery have a 95% to 98% negative predictive value; after 5 weeks, the negative predictive value declines (CDC, 2010). Any woman with positive culture results should be given intrapartum antibiotic prophylaxis (IAP) during labor according to CDC guidelines (2010).

Table 1.3

Perinatal Infections – Sexually Transmitted Infections

Infection/Incubation	Detection	Maternal Effects	Neonatal Effects	Incidence
Human immunodeficiency virus (HIV-1, HIV-2); incubation: variable, months to years	Antigen–antibody test; repeat if positive Follow-up with nucleic acid–based HIV test to distinguish between HIV-1 and HIV-2	Immunocompromise AIDS Co-infections	30% chance of transmission from infected mother Syndrome in up to 65% of infected infants within a few months after birth	8500 births annually to HIV+ women Antenatal antiviral therapy and neonatal dosing 4 to 6 weeks after birth decreases transmission to <1%
Chlamydia trachomatis bacteria; Incubation: variable but more than 1 week **MOST COMMON STI**	Endocervical, oral, or rectal NAAT, with >90% sensitivity and 99% specificity	Most cases asymptomatic Mucopurulent cervicitis Occasionally premature rupture of membranes, preterm labor, IUGR, infertility, chorioamnionitis Frequently associated with other STIs	25% to 50% of exposed have conjunctivitis within days to weeks 5% to 20% develop pneumonia	U.S. cases annually = 3 million 50% to 70% asymptomatic Treat with Zithromax in pregnancy Treat partner
Neisseria gonorrhoeae bacteria, gram-negative diplococcus; Incubation: 10 days	Endocervical, oral, or rectal NAAT, with >90% sensitivity and 99% specificity	60% to 80% infections asymptomatic Pelvic peritonitis, premature rupture of membranes, postpartum endometritis, chorioamnionitis Increased infertility and/or ectopic pregnancy	Purulent neonatal conjunctivitis Sepsis, meningitis	In United States may be 700,000 cases/year; Treat woman with third-generation cephalosporin If positive, also treat for *Chlamydia* Treat partner
HPV; incubation: unknown (3 months to years)	Visualization of tiny cauliflower-shaped, painless lesions in genital/perianal area DNA	Lesions enlarge during pregnancy, may block birth canal; Lesions may be friable during pregnancy; Associated with other STIs	Transmission to neonate has potential for juvenile laryngeal papillomatosis Very rare (<1:1000 to 1500 pregnancies)	Preconceptual vaccination Estimated 40 to 60 million people infected worldwide
Syphilis: *Treponema pallidum*, a spirochete; Incubation: 3 weeks on average	Nontreponemal test: VDRL, RPR; Treponemal test: FTA-ABS, TPPA, TPHA, EIA, DFA of lesions	Primary chancre: painless ulcerative lesion; Secondary syphilis: fever and malaise, red macules on palms or soles of feet, Generalized lymphadenopathy; Early latent (<1 year's duration) Late latent (>1 year's duration); Tertiary syphilis cardiovascular, CNS involvement	Transplacental migration of spirochete close to 100% at any gestational age Outcomes vary depending on gestation: Stillbirth, IUGR nonimmune hydrops, premature labor	Screen all pregnant women; Only maternal treatment is benzathine PCN G Sporadic outbreaks in United States, declined to 0.9 cases/100,000 by 2012
Trichomonas vaginalis: a protozoan; incubation: 4 to 20 days	"Wet prep" saline examination; DNA; Urinalysis	Malodorous, discolored vaginal discharge	Infant contact through infected vagina; Usually asymptomatic	Not reported to CDC but estimated in as many as 20% of pregnancies Estimates of 10% to 15% of all cases of vaginitis

AIDS, Acquired immune deficiency syndrome; *CDC*, Centers for Disease Control and Prevention; *CNS*, central nervous system; *DFA*, direct fluorescent antibody; *DNA*, deoxyribonucleic acid; *EIA*, enzyme immunoassay; *HPV*, human papilloma virus; *IUGR*, intrauterine growth restriction; *NAAT*, nucleic acid amplification test; *RPR*, rapid plasma reagin; *STI*, sexually transmitted infection; *TPHA, Treponema pallidum* hemagglutination; *TPPA, Treponema pallidum* particle agglutination assay; *VDRL*, Venereal Disease Research Laboratory.

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Table 1.4

Perinatal Infections – Other Communicable Diseases

Infection/ Incubation	Mode of Transmission	Maternal Effects	Neonatal Effects	Incidence and Prevention
Influenza virus; incubation: 24 to 72 hours	Respiratory secretions	Usually brief but incapacitating disease Death occurs from secondary bacterial pneumonia	Any risk of malformation has been confined to first trimester Most studies fail to support teratogenicity	Killed virus vaccine Vaccine safe during pregnancy
Mumps: Paramyxovirus; incubation: 16 to 18 days	Respiratory secretions	Spontaneous abortion rate is increased two-fold	Teratogenicity is unknown	Avoid pregnancy for 1 month after vaccination
Fifth disease: Parvovirus B19; incubation: 4 to 20 days; parvovirus preferentially invades rapidly dividing cells, i.e., fetal tissue	Respiratory secretions, blood, hand to mouth, perinatal	Facial rash ("slapped cheek") Elevated temperature Arthralgia 20% asymptomatic	Spontaneous abortions; aplastic anemia, heart failure, nonimmune hydrops; fetal death rare if maternal infection >20 weeks' gestation	65% pregnant women immune Avoid outbreaks
Hepatitis B virus	STI, blood, stool, saliva, transplacental; HBsAg determines exposure, and HBeAg determines infectivity	Fever, jaundice, malaise, hepatosplenomegaly Premature labor	Increased stillbirth rate Chronic HBV liver disease and 25% lifetime risk premature death	One third of infants born to HBsAg-positive mothers will have HBsAg/HBeAg positivity and anti-HBeAg negativity
Chickenpox: varicella-zoster virus (VZV); incubation: 14 days	Respiratory secretions Transplacental	Severe in adults Risk of premature labor as a result of high temperature Risk of varicella pneumonia appears to be increased during pregnancy Mortality 5%	Congenital varicella syndrome 2% of infants with maternal infection in first trimester have cutaneous scarring, eye abnormalities, and intellectual disability Severe disseminated neonatal disease may develop, and up to 30% die	90% of women are immune; In the United States occurs in less than 0.1% of pregnancies; administer antiviral to mother within 24 hours If maternal rash onset 5 days before to 2 days after delivery, administer VZIG to neonate
Zika virus	Bite of infected *Aedes* mosquito Sex	Fever, rash, headache, joint pain, red eyes, muscle pain	Congenital Zika syndrome: microcephaly, affected areas: brain, eyes, joints, muscles	2462 U.S. pregnant women with evidence of infection Avoid Zika-infested areas

HBeAg, hepatitis B "e" antigen; *HBsAg*, hepatitis B surface antigen; HBV, hepatitis B virus; *STI*, sexually transmitted infection; VZIG, varicella-zoster immune globulin; *VZV*, varicella-zoster virus.

From American Academy of Pediatrics (AAP) and the American College of Obstetricians and Gynecologists (ACOG). (2017). *Guidelines for Perinatal Care* (8th ed.). Elk Grove Village, IL: American Academy of Pediatrics.

From American College of Obstetricians and Gynecologists (ACOG). (2018a). *Management of herpes in pregnancy. Practice Bulletin No. 82.* June 2007 (reaffirmed 2018). *Obstetrics and Gynecology, 109,* 1489–1948.

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Normal Labor and Birth

A. **Stages and phases of labor:** There are three stages of labor.
   1. First stage: onset of contractions to complete dilatation; has three phases.
      a. Latent phase: onset of labor to time when the slope of cervical dilatation changes.
      b. Active phase: approximately 4 cm to complete cervical dilatation. Maximum slope is from 5 to 9 cm and is a time when labor progresses rapidly.

Table 1.5

Recommendations for Assessment and Documentation of Fetal Status During Labor

	WHEN USING INTERMITTENT AUSCULTATION[a,b]				
	Latent Phase (<4 cm)	**Latent Phase (4 to 5 cm)**	**Active Phase (>6 cm)**	**Second Stage (Passive Fetal Descent)**	**Second Stage (Active Pushing)**
Low-risk without oxytocin	At least hourly	Every 15 to 30 minutes	Every 15 to 30 minutes	Every 15 minutes	Every 5 to 15 minutes

[a]Frequency of assessment should always take into consideration maternal–fetal condition and at times will need to occur more often based on maternal–fetal clinical needs, for example, a temporary or ongoing change in maternal or fetal status.

[b]Summary documentation is acceptable, and individual hospital policy should be followed.

From Association of Women's Health and Obstetrical & Neonatal Nursing. (2015). Fetal heart monitoring. *Journal of Obstetric, Gynecologic, & Neonatal Nursing*, *44*(5), 683–686.

c. Transition: portion of the active phase from 8 to 10 cm with intense contraction and beginning of descent.

2. Second stage: complete dilatation to delivery of infant. Maximum fetal descent coincides with transition and second stage.
3. Third stage: time from delivery of infant to delivery of placenta.

B. Intrapartum labor management.

1. Admission.
   a. History, review of prenatal records, contractions, membrane status, bleeding, fetal movement, and nutritional status.
   b. Physical examination: vital signs, fetal heart tones, contraction pattern, abdominal examination (Leopold's maneuvers, estimated fetal weight, scars), extremities, vaginal examination (dilatation, effacement, station), pelvis examination if history warrants to assess for ruptured membranes. Nitrazine, pooling, and ferning are nonspecific tests for detection of ruptured membranes. PAMG-1 (AmniSure) is an immunoassay test that is more specific and sensitive for ruptured membranes.
2. FHR monitoring (ACOG, 2017b).
   a. The patient should be identified as being low or high risk on the basis of available data. The ACOG (2017) recommends that low-risk patients have auscultation of FHR every 30 minutes in the first stage and every 15 minutes in the second stage.
   b. Intermittent auscultation or electronic fetal monitoring may be utilized in low-risk pregnancies to assess fetal status (Table 1.6).
   c. Use of electronic fetal monitoring has not been associated with a decrease in cerebral palsy and has a false-positive rate of 99%. Electronic fetal monitoring has poor interobserver and intraobserver reliability and is associated with an increased risk of operative vaginal delivery and cesarean sections for abnormal fetal heart tracings or acidosis or both (ACOG, 2017).
   d. High-risk patients should have FHR evaluated every 15 minutes in the first stage and every 5 minutes in the second stage. ACOG (2017c) recommends the use of continuous fetal monitoring for high-risk patients.
   e. Electronic fetal monitoring—Eunice Shriver Kennedy National Institute of Child Health and

TABLE 1.6

Recommendations for Assessment of Fetal Status During Labor

	WHEN USING ELECTRONIC FETAL MONITORING[a,b]				
	Latent Phase (<4 cm)	**Latent Phase (4 to 5 cm)**	**Active Phase (>6 cm)**	**Second Stage (Passive Fetal Descent)**	**Second Stage (Active Pushing)**
Low-risk without oxytocin	At least hourly	Every 30 minutes	Every 30 minutes	Every 15 minutes	Every 15 minutes
With oxytocin or risk factors	Every 15 minutes with oxytocin; every 30 minutes without	Every 15 minutes	Every 15 minutes	Every 15 minutes	Every 5 minutes

[a]Frequency of assessment should always take into consideration maternal–fetal condition and at times will need to occur more often based on maternal–fetal clinical needs, for example, a temporary or ongoing change in maternal or fetal status.

[b]Summary documentation is acceptable, and individual hospital policy should be followed.

From Association of Women's Health and Obstetrical & Neonatal Nursing. (2015). Fetal heart monitoring. *Journal of Obstetric, Gynecologic, & Neonatal Nursing*, *44*(5), 683–686.

Human Development terminology is currently recommended. FHR patterns are described according to their baseline, variability, accelerations, and decelerations (Macones et al., 2008):

1) **FHR baseline** evaluated over a 10-minute segment. Normal baseline is 110 to 160 beats per minute (bpm). It is determined by approximating the FHR to increments of 5 bpm. There must be at least 2 minutes of identifiable baseline.
   a) Bradycardia is less than 110 bpm for 10 minutes or greater.
   b) Tachycardia is greater than 160 bpm for 10 minutes or greater.
2) **FHR baseline variability** is fluctuations in FHR over a 10-minute window that are determined by the peak to trough in bpm. Variability is classified as:
   a) Absent variability: amplitude range undetectable.
   b) Minimal variability: amplitude greater than undetectable but less than 5 bpm.
   c) Moderate variability: amplitude 6 to 25 bpm.
   d) Marked variability: greater than 25 bpm.
3) **Accelerations** are an abrupt increase in FHR to the peak in less than 30 seconds by at least 15 beats and lasting at least 15 seconds. A prolonged acceleration is ≥2 minutes but less than 10 minutes. In fetuses less than 32 weeks, an FHR acceleration is ≥10 beats lasting ≥10 seconds.
   d) **Decelerations** are decreases in FHR and are classified in relationship to their occurrence relative to the contractions, as well as based on various characteristics of the deceleration. They are classified as early, late, or variable. Recurrent decelerations occur ≥50% of the time in a 20-minute window, and intermittent decelerations occur less than 50% of the time in a 20-minute window.
   e) **Sinusoidal FHR patterns** are undulating sine wave patterns with a cycle of 3 to 5 per minute that persists for ≥20 minutes.

f. FHR patterns are classified by category (Macones et al., 2008):
   1) Category I: Normal FHR reflecting normal acid–base balance and can be followed in routine manner, without intervention.
   2) Category II: Indeterminate FHR not predictive of abnormal fetal acid–base balance. These tracings require continued surveillance and re-evaluation.
   3) Category III: Abnormal FHR tracing predictive of abnormal fetal acid–base balance. Requires prompt evaluation and possible intervention to resolve the abnormal pattern or delivery.

g. A category II or category III FHR detected by auscultation is an indication for continuous electronic fetal monitoring: bradycardia, tachycardia, or FHR decelerations.

h. **Uterine activity** monitoring may be measured by external palpation, external tocodynamometer, or intrauterine pressure catheter to assess frequency, duration, and intensity of contractions. Uterine activity is classified as follows:
   1) Normal: ≤5 contractions in 10 minutes averaged over 30 minutes.
   2) Tachysystole: greater than 5 contractions in 10 minutes averaged over 30 minutes.

C. First-stage management (ACOG, 2017c; Neal et al., 2015).
   1. Latent phase of first stage: Period of time from onset of regular contractions to rapid progress of dilation of cervix.
   2. Active phase of first stage of labor: From time of increase in rate of cervical dilation to complete dilation (10 cm), which marks the beginning of the second stage. Mean time for nulliparas is 3.7 hours, and for multiparas is 2.2 hours. Recent studies indicate that active labor does not begin for many women until 6 cm.
   3. Slope of labor curve is not linear, but rather hyperbolic. Physiologic labor encourages watchful waiting. Primiparas may dilate at a rate of 0.5 cm/hr and still be within normal limits.
   4. Amniotomy does not significantly affect the length of labor or cesarean rates.
   5. The ACOG and the Society for Maternal-Fetal Medicine (2016) define arrest of labor in a woman who is 6 cm or more dilated with ruptured membranes and with 4 hours or more of adequate contractions (200 Montevideo units) or 6 hours or more of inadequate contractions and no cervical change. Oxytocin augmentation may be indicated.

D. Second-stage management (ACOG, 2017c; Low et al., 2015).
   1. Fetal descent/pushing.
      a. The ACOG and the Society for Maternal-Fetal Medicine (2016) recommend allowing pushing for at least 3 hours for primiparas and 2 hours for multiparas, and possibly longer if the woman has an epidural. Research has shown no significant relationship between second-stage duration and perinatal mortality, 5-minute Apgar scores less than 7, neonatal seizures, or admission to a neonatal intensive care unit (ACOG, 2017c; ACOG & Society Maternal-Fetal Medicine, 2016; Low et al., 2015).
      b. Current recommendations state that a critical factor is time of duration of active pushing

rather than overall duration of the second stage (Roberts and Hanson, 2007); therefore, passive descent and evaluation of fetal descent relative to time spent actively pushing is advised, and the ACOG (2017) supports a period of 1 to 2 hours of "laboring down" without active pushing at the onset of the second stage.

E. Third stage—time from the birth of the baby to the delivery of the placenta (Schorn and King, 2017).
   1. Normal duration ranges from 0 to 30 minutes. By 15 minutes, 90% of term placentas deliver.
   2. There is increased risk of postpartum hemorrhage with increased duration. If duration of the third stage is greater than 30 minutes, risk of postpartum hemorrhage increases six-fold.
   3. Two management approaches.
      a. Physiologic management or "hands off": prophylactic uterotonics not administered, delayed cord clamping, and placenta delivered by maternal effort.
      b. Active management: routine administration of uterotonics before placenta delivery, delayed cord clamping of 1 to 3 minutes, gentle controlled cord traction, and external uterine massage after placental delivery.

F. Fourth stage of labor (Schorn and King, 2017).
   1. Fourth stage of labor is the first hour after birth.
   2. Importance of bonding and initiation of breastfeeding.
   3. Skin-to-skin contact with mother and infant advised.

Puerperium: The "Fourth Trimester"

The period from delivery through the sixth week after birth is considered the postpartum period. Under the Newborns' and Mothers' Health Protection Act of 1996, minimum federal standards mandate health plans to provide coverage for 48 hours after a normal vaginal birth and 96 hours after a cesarean birth unless the attending health care provider and mother agree on early discharge (United States Department of Labor, 2016).

A. Uterine involution.
   1. Involution begins immediately after delivery and takes about 6 weeks to complete (Fahey, 2015). The fundus is generally firm at the level of the umbilicus and generally decreases by one finger breadth daily. It is not palpable abdominally by 2 weeks.

B. Breasts/breastfeeding.
   1. Lactogenesis stage 1: Occurs during pregnancy as a result of progesterone, prolactin, and hPL and is completed at delivery with a decrease in progesterone (Newton, 2017).
   2. Lactogenesis stage 2: During the first 2 to 3 postpartum days, high-protein colostrum secretion provides the infant with nutrition (Newton, 2017). It also has high concentrations of protein, immunoglobulin A, and lactoferrin and a lower fat content than more mature milk (Newton, 2017). On the second or third postpartum day, milk secretion begins and breast engorgement may occur. Engorgement generally resolves spontaneously within 24 to 36 hours. In non-breastfeeding mothers, lactation ceases within 1 week.
   3. Lactogenesis stage 3: Mature milk is established by the end of the first or second week. Milk production is based on supply–demand, and stimulation of the nipple and areola by suckling provides a sensory nerve stimulus to secrete prolactin and oxytocin, important hormones for milk production (Newton, 2017).
   4. Establishment of breastfeeding is facilitated by continuous labor support, skin-to-skin contact of mother and infant, early initiation of breastfeeding within the first hour of life (Wright, 2015), rooming-in, breastfeeding on demand, not using pacifiers, and not providing formula supplementation unless medically indicated. Postpartum breastfeeding support contributes to successful initiation and continuation of breastfeeding.
   5. Lactogenesis stage 4: According to Newton (2017), this stage involves involution and cessation of breastfeeding when frequency of feeds is less than 6 in 24 hours and volume of milk is less than 400 mL in 24 hours. If there is a decrease in nipple stimulation, prolactin levels fall and milk production decreases or ceases. In addition, if there is not transfer of milk for 24 to 48 hours, the intraductal pressure increases and causes an inhibition of lactation (Newton, 2017).

C. Sleep postpartum.
   1. Women have difficulty getting sufficient sleep during the postpartum period (Kantrowitz-Gordon, 2015).
   2. Women slept an average of 7.2 hours per night during the first 4 months postpartum; however, the sleep was fragmented, with awake time of 2 hours in the middle of the night (Kantrowitz-Gordon, 2015).

D. Preventive immunizations and Rh_o(D) immune globulin.
   1. **Rubella vaccination** in the form of the measles, mumps, rubella (MMR) vaccine should be administered in the immediate postpartum period to all women who are not immune (Kantrowitz-Gordon, 2015).
   2. **Rh_o(D) immune globulin** (300 mcg given intramuscularly) is administered prophylactically to Rh-negative women during antepartum at 28 weeks and within 72 hours of bleeding, injury, trauma, and amniocentesis. After delivery, it is administered to Rh-negative women with an Rh-positive fetus to prevent sensitization from fetal–maternal

transfusion of Rh-positive fetal erythrocytes (ACOG, 2017d; Kantrowitz-Gordon, 2015). Rh_o(D) immune globulin may be withheld if delivery occurred within 3 weeks of the antepartal dose and no significant maternal–fetal hemorrhage occurred. According to the ACOG (2017d) anti-D immune globulin remains in most patients for 12 weeks, and consensus guidelines do not recommend administering a repeat dose if the woman delivers beyond 40 weeks' gestation, as long as the antepartum dose was given at 28 weeks or beyond.

3. **Tetanus, diphtheria, and acellular pertussis (Tdap):** It is recommended that all pregnant women receive Tdap at 27 to 36 weeks of gestation. Women who have not previously received a dose of Tdap, including breastfeeding women, should receive one immediately postpartum (ACOG, 2017e; CDC, 2012). Family members or persons in close contact with infants should also receive the vaccine (ACOG, 2017e). The rationale for the vaccine is to decrease pertussis infection risk in adults with close contact with the infant prior to the infant's immunizations and thus decrease infant morbidity and mortality (ACOG, 2017e).
4. **Influenza vaccine:** It is recommended that women be offered the seasonal flu vaccine if it is during influenza season and she has not received it (Kantrowitz-Gordon, 2015).
5. **Varicella vaccine:** According to the CDC the Advisory Committee on Immunization Practices (ACIP) recommends antenatal screening for varicella immunity; mothers who do not have evidence of immunity should receive the first dose of varicella vaccine before postpartum discharge and the second dose 4 to 8 weeks later (Marin et al., 2007).

E. Emotional changes postpartum.
1. Postpartum blues may occur from birth to 14 days postpartum. Mild, transient symptoms of emotional lability may be caused by hormonal changes, sleep deprivation, role adjustment, and physiologic changes. Symptoms may be more intense if there are neonatal problems.
2. Postpartum depression may occur from birth throughout 6 months postpartum, and evaluation includes diagnostic criteria for depression. There are various screening tools, such as the Beck or Edinburgh Postpartum Depression scales or the Center for Epidemiological Studies Depression Scale (CES-D) (Kantrowitz-Gordon, 2015). If risk is identified, it is important to inquire about self-harm and suicidal or homicidal ideation (Kantrowitz-Gordon, 2015). A rare, severe form of postpartum depression is postpartum psychosis, which may encompass suicidal thoughts or delusional behaviors.
3. Postpartum thyroiditis may cause symptoms of fatigue and depression. Women with postpartum depression should be evaluated for thyroiditis (Fahey, 2015).

F. Postpartum care.
1. The ACOG (2018b) recommends postpartum care be an ongoing process, not a single visit.
2. Postpartum contact with the mother is advised within the first 3 weeks, and a comprehensive postpartum visit is recommended no later than 12 weeks (ACOG, 2018b).
3. According to the ACOG (2018b) the comprehensive visit should include physical, social, and psychological well-being, including screening for postpartum depression; an atherosclerotic cardiovascular disease (ASCVD) risk assessment should be done if there is a history of preterm birth, gestational diabetes, or hypertensive disorders in pregnancy. Follow-up of chronic medical diseases should be coordinated with care providers. Contraception and pregnancy spacing should be discussed.

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CHAPTER 2

Antepartum–Intrapartum Complications

Helen M. Hurst

OBJECTIVES

1. Identify the physiology and functions of the placenta.
2. Identify maternal risk factors before and during pregnancy.
3. Discuss the effects of select antepartum/intrapartum conditions and complications in the mother and fetus/neonate.
4. Identify the effects of selected medications on the mother and fetus/neonate.
5. List maternal/fetal/neonatal complications associated with select obstetric interventions.
6. Identify the effects of obstetric analgesia/anesthesia on the fetus/neonate.

An understanding of maternal risk factors and complications enhances the ability of the nurse to anticipate and recognize neonatal complications and intervene appropriately. The purpose of this chapter is to provide a review of maternal risk factors and selected antepartum/intrapartum complications, conditions, and interventions, along with the associated assessment management and treatment and potential fetal/neonatal complications. These risk factors may exist before the pregnancy or develop during the antepartum and intrapartum periods (Table 2.1).

Anatomy and Physiology (Baschat and Seravalli, 2017; Burton et al., 2017; London et al., 2017)

A. **The fetus.** The fetus is a part of the maternal–placental–fetal complex.

B. **Functions of the placenta.** The placenta is the connection between the maternal and embryonic circulatory systems, facilitating metabolic and nutrient exchange. The maternal side (basal plate) attaches to the uterine wall, and the fetal side (chorionic plate) is the surface where the umbilical cord attaches. Functions of the placenta include fetal nutrition, respiration, and excretion. It also has immunologic properties and has some endocrine function. Placental development begins at implantation, with the maternal–placental–embryonic circulation complete at approximately 17 days; it becomes a discrete organ by 14 weeks of gestation (London et al., 2017). Conditions and substances that affect the pregnant woman have the potential to affect placental functions of respiration, nutrition, excretion, and hormone production. As a selective barrier, the placenta prevents the passage of certain substances. Decreased placental function can in turn adversely affect the fetus.

C. **Placental transport mechanisms.** Transport mechanisms include simple diffusion and bulk/flow solvent drag (hydrostatic and osmotic pressures, endocytosis/exocytosis, and transporter protein–mediator processes) (Burton et al., 2017). These mechanisms are influenced by multiple factors:

1. Placental area.
   a. To supply the increased growth needs of the fetus, the placenta normally increases in size as the pregnancy advances.
   b. A placenta not growing at the same rate as the fetus or that has decreased functional area resulting from an infarct or separation (placenta abruptio) prevents the optimal transport of materials between the fetus and the mother.
   c. Decreased functional placental area can result in a decrease in fetal growth, fetal or neonatal distress, and even fetal or neonatal death.
2. Concentration gradient.
   a. Passive and facilitated diffusion of unbound substances dissolved in maternal and fetal plasma occurs in the direction of lesser concentration.
   b. The greater the concentration gradient, the faster the rate of diffusion.
   c. Concentration gradients exist when dissolved substances are removed from the plasma by metabolism, cellular uptake, or excretion.

Table 2.1

Prenatal High-Risk Factors

Factor	Maternal Implications	Fetal/Neonatal Implications
Social-Personal		
Low income level and/ or low educational level	Insufficient or later antenatal care ↑ Risk preterm birth Poor nutrition ↑ Risk preeclampsia	Low birth weight Prematurity IUGR/SGA
Poor diet	↑ Inadequate nutrition/inadequate weight gain ↑ Risk of preterm labor/birth ↑ Risk anemia ↑ Risk preeclampsia	Fetal malnutrition Prematurity IUGR/SGA
Living at high altitude	↑ Hemoglobin	Prematurity IUGR ↑ Hemoglobin (polycythemia)
Multiparity greater than three	↑ Risk antepartum or postpartum hemorrhage	Anemia Fetal death
Weight less than 45.5 kg (100 lb)	Poor nutrition Cephalopelvic disproportion Prolonged labor	IUGR Hypoxia associated with difficult labor and birth
Weight greater than 91 kg (200 lb)	↑ Risk hypertension ↑ Risk cephalopelvic disproportion (CPD) ↑ Risk diabetes	↓ Fetal nutrition/perfusion ↑ Risk macrosomia
Age less than 16	Poor nutrition Insufficient/late antenatal care ↑ Risk preeclampsia ↑ Risk CPD	Low birth weight ↑ Fetal demise
Age older than 35	↑ Risk preeclampsia ↑ Risk cesarean birth Psychosocial issues	↑ Risk congenital anomalies ↑ Chromosomal abnormalities
Smoking one pack per day/more	↑ Risk hypertension ↑ Risk cancer	↓ Placental perfusion → ↓ O_2 and nutrients available Low birth weight IUGR/SGA Preterm birth
Use of addicting drugs	↑ Risk poor nutrition ↑ Risk infection with intravenous (IV) drugs ↑ Risk HIV, hepatitis C ↑ Risk abruptio placentae	↑ Risk congenital anomalies ↑ Risk low birth weight Neonatal withdrawal Lower serum bilirubin
Excessive alcohol consumption	↑ Risk poor nutrition Possible hepatic effects with long-term consumption	↑ Risk fetal alcohol spectrum disorders
Preexisting Medical Disorders		
Diabetes mellitus	↑ Risk preeclampsia, hypertension Episodes of hypoglycemia and hyperglycemia ↑ Risk cesarean birth	Low birth weight Macrosomia Neonatal hypoglycemia ↑ Risk congenital anomalies ↑ Risk respiratory distress syndrome
Cardiac disease	Cardiac decompensation Further strain on mother's body ↑ Maternal death rate	↑ Risk fetal death ↑ Perinatal mortality ↑ Risk of cardiac disease
Anemia: Less than 11 g/dL hemoglobin, less than 32% hematocrit	Iron-deficiency anemia Low energy level ↓ Oxygen-carrying capacity	Fetal death Prematurity Low birth weight
Hypertension	↑ Vasospasm ↑ Risk of central nervous system (CNS) irritability ↑ Risk convulsions ↑ Risk cerebrovascular accident (CVA) ↑ Risk renal damage	↓ Placental perfusion Low birth weight Preterm birth

Continued

Table 2.1

Prenatal High-Risk Factors—cont'd

Factor	Maternal Implications	Fetal/Neonatal Implications
Thyroid disorder Hypothyroidism	↑ Infertility ↓ Basal metabolic rate (BMR), goiter, myxedema ↑ Risk miscarriage ↑ Risk preterm labor/birth ↑ Risk preeclampsia	↑ Spontaneous abortion ↑ Risk congenital goiter ↑ Risk IUGR/SGA ↑ Risk anemia ↑ Risk stillbirth
Hyperthyroidism	↑ Risk postpartum hemorrhage ↑ Risk preeclampsia Danger of thyroid storm	Developmental delay ↑ Incidence congenital anomalies ↑ IUGR/SGA ↑ Risk neonatal hyperthyroidism
Renal disease (moderate to severe)	↑ Risk renal failure	↑ Risk IUGR/SGA ↑ Risk preterm birth
Diethylstilbestrol (DES) exposure	↑ Infertility, spontaneous abortion ↑ Cervical incompetence ↑ Risk breech presentation	↑ Risk preterm birth
Obstetric Considerations		
Previous Pregnancy		
Stillborn	↑ Emotional/psychologic distress	↑ Risk IUGR/SGA ↑ Risk preterm birth
Recurrent abortion	↑ Emotional/psychologic distress	↑ Risk abortion
Cesarean birth	↑ Possibility repeat cesarean birth Risk of uterine rupture	↑ Risk preterm birth ↑ Risk respiratory distress
Rh or blood group sensitization		↑ Risk erythroblastosis fetalis Hydrops fetalis Neonatal anemia Kernicterus Hypoglycemia
Current Pregnancy		
Large for gestational age (LGA)	↑ Risk cesarean birth ↑ Risk gestational diabetes ↑ Risk operative birth	↑ Risk birth injury Hypoglycemia
Gestational diabetes mellitus	↑ Risk operative birth ↑ Risk preeclampsia ↑ Risk extensive lacerations ↑ Risk primary pulmonary hypertension (PPH) ↑ Risk shoulder dystocia	Macrosomia Hyperbilirubinemia ↑ Risk birth injury
Rubella (first trimester)		Congenital heart disease Cataracts Nerve deafness Bone lesions Prolonged virus shedding
Rubella (second trimester)		Hepatitis Thrombocytopenia
Cytomegalovirus		Retinochoroiditis Seizures, coma, microcephaly IUGR Encephalopathy
Herpes virus type 2 (HSV type 1 also has 10% risk)	Severe discomfort Concern about possibility of cesarean birth, fetal infection	Neonatal herpesvirus type 2 Hepatitis with jaundice Neurologic abnormalities
Syphilis	↑ Incidence abortion	↑ Fetal demise Congenital syphilis
Urinary tract infection	↑ Risk preterm labor Uterine irritability	↑ Risk preterm birth

Table 2.1

Prenatal High-Risk Factors—cont'd

Factor	Maternal Implications	Fetal/Neonatal Implications
Abruptio placentae and placenta previa	↑ Risk hemorrhage Bed rest Extended hospitalization	Fetal/neonatal anemia Intrauterine hemorrhage ↑ Fetal demise
Preeclampsia/eclampsia	See Hypertension	↓ Placental perfusion Low birth weight
Multiple gestation	↑ Risk postpartum hemorrhage ↑ Risk gestational diabetes ↑ Risk preeclampsia ↑ Risk placenta previa	↑ Risk preterm labor/birth ↑ Risk stillbirth ↑ Risk fetal demise ↑ Risk IUGR/SGA ↑ Risk malpresentation
Elevated hematocrit (greater than 41%)	Increased viscosity of blood	Fetal death rate five times normal rate
Spontaneous premature rupture of membranes	↑ Uterine infection	Preterm birth Fetal demise

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IUGR, intrauterine growth restriction; *SGA,* small for gestational age.

For example, the excretion of CO_2 from the maternal lungs maintains the concentration gradient for CO_2, permitting fetal plasma CO_2 to cross from fetal plasma to maternal plasma. Inefficient maternal excretion of CO_2 may lead to maternal respiratory acidosis and fetal acidosis.

3. Diffusing distance.
   a. The greater the distance between maternal and fetal blood in the placenta, the slower the diffusion rate of substances.
   b. Any edema that develops in the placental villi increases the distance between the fetal capillaries within the villi and the maternal arterial blood in the intervillous spaces, thus slowing the diffusion rate of substances between the maternal and fetal circulations. Edema of the villi may occur in:
      1) Maternal diabetes.
      2) Transplacental infections.
      3) Erythroblastosis fetalis.
      4) Twin-to-twin transfusion syndrome.
      5) Fetal congestive heart failure.
   c. Thinning of the placental membrane in the second half of pregnancy decreases diffusing distance, thus increasing the functional efficiency of the placenta. However, this change also facilitates the passage of drugs in pregnancy and the intrapartum period.
4. Uteroplacental blood flow.
   a. At term, uterine blood flow is 750 mL/min or more, representing 10% to 15% of the maternal cardiac output.
   b. Decreased blood flow to the uterus or within the intervillous spaces will decrease the transport of substances to and from the fetus.
   c. Causes of decreased uteroplacental blood flow include:
      1) Maternal vasoconstriction caused by hypertension, cocaine abuse, diabetic vasculopathy, and smoking.
      2) Maternal vasodilatation caused by vasodilators, antihypertensives, and regional anesthetics with sympathetic blockade actions.
      3) Decreased maternal cardiac output in supine hypotension.
      4) Decreased maternal blood flow in intervillous spaces resulting from edema of the placental villi.
      5) Tachysystole (>5 contractions in 10 minutes, averaged over 30 minutes) (American College of Obstetricians and Gynecologists [ACOG], 2017).
      6) Increased uterine resting tone.
      7) Severe maternal physical stress.
      8) Degenerative placental changes near term.
5. Fetal factors.
   a. Fetal tachycardia, often seen with fetal hypoxia, is analogous to an adult's "blowing off CO_2"; the increased heart rate increases the delivery of CO_2 to the placenta for diffusion to the maternal circulation. Fetal tachycardia represents a chronic decrease in oxygen.
   b. Conversely, fetal bradycardia resulting from hypoxia or anoxia leads to an increased CO_2 level. Fetal bradycardia in the absence of congenital

heart disease represents an acute decrease in oxygen.
c. Umbilical cord compression leads to CO_2 accumulation and acidosis.
d. Fetal pH during labor is usually 0.1 to 0.15 unit less than the maternal pH; this difference increases the transport of acidophilic substances from the mother to the fetus and reduces albumin binding of drugs, resulting in more free drug availability in the fetal bloodstream.

Conditions Related to the Antepartum Period

PREECLAMPSIA AND ECLAMPSIA (ACOG, 2013; SIBAI, 2017; WEBSTER AND WAUGH, 2017)

Hypertensive disorders in pregnancy, including gestational hypertension, preeclampsia and eclampsia, chronic hypertension, and chronic hypertension with superimposed preeclampsia, are a major cause of maternal–fetal morbidity and death in the United States and worldwide. The main pathophysiologic events in preeclampsia are vasospasm, hematologic changes, and endothelial damage, leading to tissue hypoxia and multiple organ involvement.

A. **Incidence:** The incidence of hypertensive disorders is 5% to 10% of all pregnancies, with the incidence of preeclampsia at 5% to 8% of all pregnancies.
B. **Etiology/predisposing factors (Sibai, 2017; Webster and Waugh, 2017).**
   1. The exact cause(s) of preeclampsia and eclampsia are still being researched; current theories involve an immunologic maladaptation, imbalance in angiogenesis, genetic predisposition, endothelial cell activation, increased oxidative stress, abnormal trophoblast invasion or poor implantation, alterations in coagulation, damage to vascular endothelium, and cardiovascular maladaptation.
   2. Preeclampsia and eclampsia are associated with nulliparity, extremes of maternal age (teenagers and age >40 years), preexisting medical/genetic conditions, interpregnancy interval more than 7 years, family history of preeclampsia, preeclampsia in a previous pregnancy, obesity, pregnancy with assisted reproduction, maternal small for gestational age, chronic inflammatory conditions (lupus, rheumatologic disease), a history of gestational diabetes or type 1 diabetes mellitus, chronic hypertensive or renal disease, thrombophilias (factor V Leiden mutation, antiphospholipid syndrome), multifetal gestation, or large fetus. Other predisposing factors include poor outcomes in a previous pregnancy, such as placental abruption, fetal death, and fetal growth restriction (FGR) in previous pregnancies.
C. Clinical presentation of preeclampsia.
   1. Systolic blood pressure (BP) of ≥140 mm Hg and less than 160 mm Hg, or a diastolic of ≥90 mm Hg and less than 110 mm Hg, after 20 weeks of gestation in a woman with previously normal BP. BP measurements must be on at least two occasions, 4 hours apart, and no more than 7 days apart. Severe preeclampsia is a systolic BP of ≥160 or diastolic ≥110 mm Hg (ACOG Practice Bulletin #202, ACOG, 2019).
   2. Proteinuria (≥300 mg/dL in a 24-hour urine collection), or a protein/creatinine ratio ≥0.3, or a urine dipstick reading of 1+ on two occasions when other blood or urine testing is unavailable. These changes are due to decreased renal perfusion resulting in the development of glomerular capillary endotheliosis.
   3. Edema is not a relevant factor in the diagnosis of preeclampsia, as more than one third of preeclamptic patients may not exhibit edema. However, if a pregnant woman demonstrates a rapid increase in generalized edema, screening for preeclampsia should be initiated (Webster and Waugh, 2017).
   4. Other signs and symptoms include headache, hyperreflexia with clonus, visual and retinal changes, irritability, nausea and vomiting, epigastric pain, dyspnea, and oliguria.
D. Potential complications.
   1. The earlier the preeclampsia occurs, the greater the risks to both the mother and fetus. Early recognition of symptoms and prompt diagnosis can lead to improved maternal/fetal outcomes.
   2. Maternal.
      a. Eclampsia.
      b. Cardiopulmonary failure and pulmonary edema.
      c. Hepatic failure, hemorrhage, or rupture.
      d. Cerebrovascular accident.
      e. Renal cortical necrosis.
      f. Disseminated intravascular coagulation.
      g. HELLP syndrome (i.e., *h*emolysis, *e*levated *l*iver enzymes, and *l*ow *p*latelets).
      h. Retinal detachment.
      i. Stroke or death (rare).
      j. Long-term cardiovascular morbidity.
   3. Placental/fetal.
      a. Fetal effects result from placental insufficiency due to vasoconstriction that may lead to fetal growth restriction, abruption leading to hypoxia, and the subsequent sequela of preterm birth.
         1) Premature placental aging, placental infarction, and decrease in amniotic fluid.
         2) Abruptio placentae in 1% to 4% of cases, depending on the severity of the disease (Webster and Waugh, 2017).

3) Fetal growth restriction.
4) Low birth weight infant.
5) Fetal hypoxia and neurologic injury.
6) Prematurity.

E. Assessment and management (Sibai, 2017; Webster and Waugh, 2017).
1. Preeclampsia.
a. In women with mild gestational hypertension and preeclampsia, the objectives are maternal/fetal safety and the birth of an infant that does not require prolonged neonatal intensive care unit (NICU) and/or neonatal care. The rate of eclampsia in women who reach 37 weeks' gestation is 1:500. Initial diagnostic workup includes 24-hour urine, complete blood count (CBC), platelet count, liver enzymes, and serum creatinine.
b. Fetal evaluation: Weekly/biweekly ultrasound for estimated fetal weight (EFW) and amniotic fluid index (AFI), weekly/biweekly nonstress test (NST). A biophysical profile (BPP) should be conducted after a nonreactive NST.
c. Weekly prenatal visits.
d. Education on signs and symptoms to report (persistent headache, visual disturbances, abdominal pain).
e. Daily fetal movement (kick) counting.
f. Induction of labor is recommended at $37^{0/7}$ weeks' gestation if signs of severe preeclampsia and/or fetal compromise are not present before that time.
2. Severe preeclampsia.
a. Primary goals of management include prevention of seizures (via limitation of stimuli and drug therapy), prevention of complications, and birth of a live infant. In women presenting with severe preeclampsia before the point of fetal viability ($23^{0/7}$ weeks), delivery should occur after the mother is stabilized. Women at less than $34^{0/7}$ weeks and greater than $23^{0/7}$ weeks who are stable, along with a stable fetal condition, should be cared for at facilities with maternal and neonatal intensive care capabilities. Due to the increased risk of maternal morbidity and mortality and the inherent risks to the fetus, delivery is recommended if severe preeclampsia presents after 34 weeks of gestation.
b. Seizure precautions.
c. Placental–fetal evaluation: continuous electronic fetal monitoring; fetal movement counting; ultrasonography to determine fetal growth and AFI; serial NSTs, BPP, and/or umbilical artery Doppler studies; and amniocentesis to determine fetal lung maturity.
d. Medications.
1) Intravenous (IV) magnesium sulfate may be initiated in women who have preeclampsia with evidence of severe symptoms (visual disturbances, headaches, clonus, right upper quadrant pain, altered mental state) as a central nervous system (CNS) depressant to prevent seizures, with therapy continued at least 24 hours postpartum. A transient decrease in BP may occur. Use in all women who have preeclampsia without severe symptoms is not recommended (ACOG, 2013).
a) Fetal/newborn effects: Decreased fetal heart rate (FHR) variability and weakness, lethargy, hypotonia, flaccidity, and poor suck in the newborn.
2) Antihypertensives for sustained systolic BPs of at least 160 mm Hg or diastolic BPs of at least 110 mm Hg (ACOG, 2013):
a) Labetalol hydrochloride, nifedipine, and hydralazine are first-line agents. Adverse effects, contraindications, and provider experience are considered when determining choice and route (IV or oral) of the medication. Nifedipine is often the preferred choice due to ease of use and lack of fetal side effects. Contraindications include severe bradycardia, moderate to severe asthma, and congestive heart failure (labetalol); aortic stenosis (nifedipine); and idiopathic systemic lupus erythematosus, severe tachycardia, heart failure, and acute porphyria (hydralazine).
b) Fetal/newborn effects: Transient fetal bradycardia (labetalol); tachycardia, bradycardia, and late decelerations (hydralazine); no noted side effects with nifedipine.
3) Corticosteroids to increase fetal lung maturity when birth can be delayed for 24 to 48 hours and the woman is $\leq 34^{0/7}$ weeks of gestation.
a) Fetal/newborn effects: Positive effects include reduced incidence of respiratory distress syndrome, intraventricular hemorrhage, and neonatal death.
e. Delivery.
1) Gestational age of the fetus, fetal presentation, cervical status, and the condition of both the mother and fetus should be considered when determining whether birth will be vaginal or by cesarean section. Maternal wishes should be considered in any decision regarding mode of delivery. Severe preeclampsia is not an indication for cesarean section, and the vaginal route is preferred.
2) Neuraxial anesthesia (spinal/epidural) is the preferred method of anesthesia. General anesthesia has the risk of aspiration and

potential difficulty with intubation due to airway edema.

3. Eclampsia (Sibai, 2017; Webster and Waugh, 2017).
   a. Eclampsia is a seizure or unexplained coma with signs and symptoms of preeclampsia that are unrelated to other cerebral conditions. Clinical symptoms that may indicate impending eclampsia include persistent occipital/frontal headaches, blurred vision, photophobia, right upper quadrant and/or epigastric pain, and alterations in mental status.
   b. Immediate notification of physician or certified nurse-midwife.
   c. Continuation or initiation of IV magnesium sulfate; continued at least 24 hours postpartum.
   d. Safety measures for women during and after seizures to prevent injury.
   e. Support of respirations with airway, oxygen, and suctioning and the correction of hypoxemia and/or acidemia.
   e. FHR changes: Bradycardia, transient late decelerations, decreased variability, and compensatory tachycardia. FHR changes usually resolve within 30 minutes, and a decision to rush delivery should not be made based on FHR changes within this period. If FHR changes last more than 30 minutes, a cause other than the seizure should be considered.
   f. Continuous maternal assessment, including assessment for uterine contractions and signs of placental abruption.
   g. Diagnostic workup: CBC, clot observation, serum creatinine, liver enzymes, fibrinogen, arterial blood gases, and electrolytes.
   h. Maternal stabilization before delivery.
   i. Emotional support of mother and family members.
   j. Assessment of newborn infant for:
      1) FGR.
      2) Preterm gestational age.
      3) Hypoxia and acidosis.
      4) If the mother received magnesium sulfate, observe 24 to 48 hours for respiratory depression and neuromuscular depression (weakness, lethargy, hypotonia, flaccidity, and poor suck) (Davidson et al., 2016).
      5) With maternal administration of labetalol, observe for hypotension, bradycardia, hypoglycemia, respiratory depression, and transient tachypnea.

DIABETES IN PREGNANCY
(ACOG, 2018; LANDON ET AL., 2017; SOH ET AL., 2017)

Women with insulin-dependent diabetes who become pregnant and pregnant women in whom gestational diabetes mellitus (GDM) or type 1 diabetes develops are at risk during the antepartum period due to altered carbohydrate metabolism. Optimal control of maternal blood glucose concentration and anticipatory management of the newborn are important elements of perinatal care, with optimal glycemic control a pivotal factor in the prevention of perinatal morbidity. Currently, 30% to 50% of perinatal mortality results from congenital anomalies in pregnancies in which the mother has type 1 or type 2 diabetes.

A. **Incidence:** 3% to 5% of all pregnancies are complicated by diabetes mellitus and 7% by GDM, the most common type of diabetes in pregnancy.
B. **Etiology and predisposing factors in gestational diabetes.**
   1. In the second half of pregnancy, the secretion of human placental lactogen increases cellular resistance to insulin. Additionally, cortisol and glycogen levels increase. The pancreas of the woman who is predisposed to diabetes cannot meet the increased demand for insulin, which leads to hyperglycemia.
   2. Risk factors for GDM include maternal obesity, previous history of gestational diabetes, a family history of diabetes, age greater than 25 years, member of an ethnic group at risk for diabetes (Native North American, Hispanic, African American, Pacific Islanders, and South or East Asian Americans), and prior obstetric history (infant weighing >4500 g, congenital anomaly, stillbirth, or hydramnios).
C. Screening for gestational diabetes (ACOG, 2018).
   1. All pregnant women should be screened via a 50-g 1-hour glucose challenge test at 24 to 28 weeks of gestation. If this test is abnormal, a 3-hour 100-g oral glucose tolerance test (OGTT) should be conducted (two-step approach).
   2. Early screening, preferably during the first prenatal visit, should be performed on women who are obese or overweight (body mass index [BMI] >25 [>23 in Asian Americans]) and who have other risk factors (first-degree relative with diabetes, physical inactivity, high-risk race or ethnicity, previous GDM, previous infant >4000 g, polycystic ovarian syndrome, hypertension [140/90 or on therapy for hypertension], high-density lipoprotein [HDL] <35 md/dL, triglycerides >250 mg/dL, history of cardiovascular disease, and any other conditions associated with insulin resistance). The two-step process may also be used for early screening and should still be repeated at 24 to 28 weeks of gestation.
   3. Women who had GDM should also be screened for diabetes and prediabetes between 4 and 12 weeks' postpartum.
D. Potential complications.
   1. Stillbirth is more frequent after 36 weeks' gestation in women with poor glycemic control and in pregnancies with hydramnios, fetal macrosomia, vascular disease, and preeclampsia.

2. Maternal.
   a. Hypoglycemic reactions in the first trimester.
   b. Ketoacidosis.
   c. Progression of vasculopathy, nephropathy, and retinopathy with preexisting diabetes.
   d. Hydramnios.
   e. Preeclampsia and eclampsia.
   f. Asymptomatic bacteriuria leading to pyelonephritis.
   g. Dystocia.
   h. Urinary tract infections and monilial vaginitis.
3. Fetal/neonatal: Improved outcomes are demonstrated with careful attention to pre-pregnancy and pregnancy glycemic control.
   a. Macrosomic (weight >4000 g) or large-for-gestational-age (LGA) infant, with possible traumatic vaginal birth, such as with shoulder dystocia, and birth trauma.
   b. Fetal death.
   c. Respiratory distress syndrome.
   d. Hypoglycemia, hypocalcemia, and hypomagnesemia.
   e. Polycythemia and hyperbilirubinemia.
   f. Cardiomyopathy.
   g. Congenital malformations, a consequence of poorly controlled preexisting diabetes, may include anencephaly, open spina bifida, holoprosencephaly, ventricular septal defects, transposition of the great vessels, sacral agenesis, or caudal dysplasia.

E. Assessment and management.
1. In preexisting diabetes:
   a. Preconception counseling is recommended, with a focus on the optimal control of blood glucose levels before future pregnancies. Insulin is considered the therapy of choice for women whose blood glucose cannot be controlled by diet and exercise, but oral hypoglycemics are now offered as a suitable alternative for women who cannot, or who prefer not to, take insulin. Both glyburide and metformin can be used in pregnancy; glyburide is superior to metformin, as it does not cross the placenta with a subsequent decreased incidence of neonatal hypoglycemia. Although metformin crosses the placenta, there is no evidence of teratogenicity; however, women may also need insulin supplementation with this medication. Supplementation should begin with 0.4 mg of folic acid daily and be continued through the first trimester to reduce the risk for neural tube defects.
   b. Glycosylated hemoglobin tests may be performed before conception and during the pregnancy to assess glucose control during the previous 1 to 2 months, with an acceptable hemoglobin A_{1c} goal of 5% to 6%.
   c. Home blood glucose monitoring, diet, exercise, and either insulin pump therapy or several daily injections of insulin are prescribed to maintain euglycemia (fasting <95 mg/dL; <140 mg/dL 1 hour postprandial; <120 mg/dL 2 hours postprandial). Optimal control is associated with a decreased risk of macrosomia, respiratory distress syndrome, congenital anomalies, and perinatal death, as well as preterm labor (PTL) and maternal urinary tract infections.
   d. Early evaluation in pregnancy for evidence of diabetic retinopathy and nephropathy.
   e. In the first trimester, screening for nuchal translucency, free β-human chorionic gonadotropin (β-hCG), and pregnancy-associated plasma protein A (PAPP-A) may be offered.
   f. At 16 weeks of gestation, maternal serum α-fetoprotein (MSAFP) testing is offered, with a comprehensive ultrasound performed at 18 to 21 weeks to assess for the presence of neural tube defects or other anomalies. An alternative may include the triple screen (MSAFP, maternal serum unconjugated estriol, and β-hCG) or the quad screen (between 15 and 18 weeks), which includes inhibin A in addition to the three elements of the triple screen.
   g. Monthly ultrasounds for fetal growth between 28 and 36 weeks of gestation to monitor fetal growth. Umbilical artery Doppler velocimetry is recommended in women with hypertensive disease or nephropathy.
   h. Weekly prenatal visits after 28 weeks. Additional fetal assessments include twice-weekly NSTs between 28 and 32 weeks' gestation, with a BPP for nonreactive NSTs. Daily fetal movement counting is recommended in the third trimester.
   i. Timing and mode of delivery are based on the clinical presentation of both the woman and the fetus. Delivery is recommended before 37 weeks in the woman with vascular disease and worsening hypertension or fetal problems, between 37 and 39 weeks in the woman with vascular disease, and at 39 weeks in the woman with well-controlled blood glucose and the absence of vascular disease. Birth should take place in a facility with a NICU.
   j. IV Insulin may be required during labor to maintain blood glucose within normal physiologic range. Hourly monitoring of glucose levels to ensure optimum titration of insulin to decrease the risk of neonatal rebound hypoglycemia.
   k. Before the decision for the induction of labor, amniocentesis is performed to determine the lecithin/sphingomyelin (L/S) ratio and the presence of phosphatidylglycerol (PG). Delivery is

conducted before term gestation if maternal or fetal complications develop.

2. In gestational diabetes (ACOG, 2018; Landon et al., 2017):
   a. A 2000- to 2500-calories-per-day diet, comprising 33% to 40% complex carbohydrates.
   b. Self-monitoring of blood glucose, with fasting and three 2-hour postprandial glucose levels daily. If good control is achieved on diet therapy, blood glucose can be monitored at less frequent intervals.
   c. Although insulin is considered the first-line agent for GDM, in women unwilling or unable to use insulin therapy, metformin may be used as an alternative. Although not approved by the U.S. Food and Drug Administration for use in GDM, even though it crosses the placenta, it does not appear to be teratogenic.
   d. Fetal surveillance beginning at 32 weeks' gestation, earlier if other risk factors are present, especially if the woman has poor glycemic control.
3. Neonatal assessment:
   a. Assess for gestational age and size (LGA or FGR).
   b. Assess for:
      1) Respiratory distress.
      2) Hypoglycemia, hypocalcemia, and hypomagnesemia.
      3) Polycythemia and hyperviscosity.
      4) Complications resulting from decreased blood flow, erythrocyte hemolysis, and thrombosis.
      5) Congenital malformations.
      6) Signs/symptoms of cardiomyopathy or congestive heart failure.
      7) Birth injuries: Fractured clavicle, intracranial bleeding, facial nerve paralysis, brachial palsy, and skull fractures.

Conditions Related to the Intrapartum Period

PRETERM LABOR
(HEZELGRAVE AND SHENNAN, 2017)

PTL is labor occurring after 20 weeks and before 37 completed weeks of gestation. PTL is generally defined as the presence of uterine contractions and documented cervical change. Threatened PTL is the presence of uterine contractions without cervical change. The prognosis for the fetus improves with each week of pregnancy gained.

A. **Incidence:** In 2016, 9.85% of live births in the United States were preterm. Complications from prematurity are the leading cause of perinatal morbidity and mortality (March of Dimes, 2017).

B. **Etiology/predisposing factors.**
   1. The exact cause of PTL is unknown, although inflammation, infections (e.g., chorioamnionitis, periodontitis, urinary tract infections, and bacterial vaginosis), uterine distension, and cervical insufficiency have been implicated.
   2. A number of maternal factors are associated with an increased incidence of spontaneous PTL/spontaneous preterm birth:
      a. Socioeconomic effects: Advanced maternal age, lower income/social status or educational level, African American race, poor nutrition, and inadequate prenatal care.
      b. Medical/obstetric past history and current problems: Use of assisted reproductive technologies, bleeding of unknown origin during pregnancy, anemia, preexisting or gestational hypertension or diabetes, previous preterm birth, prior stillbirth, previous uterine surgery, pregnancy termination, short interpregnancy interval, uterine anomalies and cervical insufficiency, multifetal pregnancy, systemic and genitourinary tract infections, hydramnios, immunologic factors, placental abruption, and placenta previa. A history of a spontaneous preterm birth continues to be the most significant risk factor for preterm birth (Davidson et al., 2016; Simhan et al., 2017).
      c. Lifestyle factors: Use of alcohol, cigarette smoking, and substance abuse; intimate partner violence; and high levels of stress.
   3. Fetal factors contributing to the development of PTL/preterm birth may include fetal congenital anomalies and complications from multifetal gestation.
   4. Risk scoring systems, designed to screen women during pregnancy, have low sensitivity. Many women who give birth before term do not have any known risk factors, and half of all preterm births have no known cause.

C. Clinical presentation.
   1. Painless or painful persistent uterine contractions.
   2. Low, dull, intermittent, or constant backache.
   3. Menstrual-like cramping.
   4. Pelvic pressure.
   5. Abdominal cramps, which may be accompanied by diarrhea.
   6. Increased vaginal discharge, which may be mucoid, watery, or slightly bloody.
   7. Spontaneous premature rupture of membranes.
   8. Progressive cervical effacement and dilatation.
   9. The clinical presentation most often associated with preterm birth includes cervical dilation of 3 cm, 80% effacement, ruptured membranes, bleeding, and six or more contractions per hour.

D. Potential complications.
   1. Maternal.
      a. Side effects from tocolytic agents.
      b. Emotional stress, depression, anxiety, and financial issues.
   2. Fetal/neonatal.
      a. Preterm birth with an increase in neonatal morbidity and mortality.
      b. Risks associated with prematurity, such as respiratory distress syndrome, necrotizing enterocolitis, intracranial hemorrhage, seizures, septicemia, and sequelae of FGR.
      c. Side effects from pharmacotherapeutics (tocolytic agents, antibiotics, corticosteroids).

E. Assessment and management.
   1. Assessment for the presence of PTL risk factors at the first and subsequent prenatal visits.
   2. Patient education regarding the signs and symptoms of PTL at every prenatal visit, along with assessment for these symptoms at each visit.
   3. Encouraging the reduction/elimination of modifiable risk factors (smoking, substance and alcohol abuse, nutrition, treat infections, stress reduction, and other behavioral factors).
   4. The use of the fetal fibronectin (fFN) testing, performed on vaginal secretions in symptomatic women, and transvaginal ultrasounds to assess cervical effacement and length may help prevent a false-positive diagnosis of PTL and eliminate unnecessary and potentially harmful pharmacologic treatment.
   5. The Society for Maternal-Fetal Medicine (SMFM) recommends that women with a singleton pregnancy who have had a previous spontaneous preterm birth (20 to $30^{6/7}$ weeks) should receive progesterone supplementation (17α-hydroxyprogesterone caproate) intramuscularly each week, from 16 to 20 weeks' gestation, until 36 weeks or delivery (SMFM Publications Committee, 2017).
   6. Although episodes of suspected PTL are widely treated with bed rest, there is little evidence that this intervention is effective (Davidson et al., 2016).
   7. Interventions demonstrated to decrease neonatal morbidity and mortality include:
      a. Transfer of the mother antenatally to an appropriately equipped facility.
      b. Antibiotic administration to prevent infection of the neonate with group B Streptococcus (GBS).
      c. Administration of antenatal glucocorticoids to promote lung maturation and decrease the incidence of respiratory distress syndrome and intraventricular hemorrhage.
      d. Magnesium sulfate administration for preterm delivery before 32 weeks to decrease incidence of cerebral palsy. Data do not support the use of this medication as a tocolytic, as research has not demonstrated that its use prolongs pregnancy.
   8. When appropriate and not contraindicated, tocolytic therapy may be initiated to delay birth for 24 to 48 hours to allow time for antenatal corticosteroid therapy and maternal transport to a tertiary care facility. Tocolytic therapy has not been shown to decrease rates of preterm birth.
      a. Nifedipine (Procardia), a calcium channel blocker given orally, is the primary choice for tocolysis, as it is selective in inhibiting uterine contractility and is easily administered orally. Contraindications include cardiac disease, hypertension, cardiovascular compromise, and intrauterine infection. Nifedipine should not be administered concurrently with magnesium sulfate and β-mimetics. Maternal side effects include headache, flushing, hypotension, and tachycardia. Studies have no noted fetal/neonatal effects.
      b. Prostaglandins (cyclooxygenase inhibitors) mediate contractions and are as effective as tocolytics. Indomethacin is given before 32 weeks' gestation, and its use is restricted to 2 to 3 days. Maternal side effects include nausea, vomiting, and dyspepsia. Maternal contraindications include coagulation disorders, drug-induced asthma, renal or hepatic insufficiency, and peptic ulcer disease. Fetal contraindications include oligohydramnios, chorioamnionitis, renal anomalies, twin-to-twin transfusion syndrome, and ductal-dependent cardiac defects. Fetal/neonatal side effects include oligohydramnios, premature closure of the ductus arteriosus, and primary neonatal pulmonary hypertension.
      c. Terbutaline (Brethine), a β-mimetic, has commonly been used as a tocolytic; its use should be limited to a single 0.25-mg dose subcutaneously. This may be used while a therapy with a slower onset of action is being started or to stop contractions during the initial evaluation of the patient to assist in the diagnosis of PTL. Maternal contraindications include severe preeclampsia or eclampsia, suspected or known heart disease, hyperthyroidism, pregestational diabetes requiring insulin, fever, and signs and/or symptoms of chorioamnionitis. Maternal side effects include tachycardia, hypotension, palpitations, hyperglycemia, shortness of breath, chest discomfort, and pulmonary edema. Fetal/neonatal effects include tachycardia and neonatal hypoglycemia.
   9. If labor progresses, the following measures are important:
      a. Notification of the NICU team and communication of patient history, management, and any other pertinent information.

b. The head is delivered in a slow, controlled fashion, especially in a precipitous delivery.
c. Although cesarean section is not indicated for all preterm deliveries, it may be considered for the preterm fetus with a breech presentation because of the risk of cord prolapse and the potential risk of difficulty controlling the birth of the head.
d. Delayed cord clamping (30 seconds to 5 minutes) may have the neonatal benefit of need for less resuscitation and higher initial hematocrits, circulating blood volume, and higher diastolic BP.

ABRUPTIO PLACENTAE
(FRANCOIS AND FOLEY, 2017; DAVIDSON ET AL., 2016)

In abruptio placentae, the placenta separates prematurely and in varying degrees from the uterine wall during pregnancy or labor, and is a common cause of bleeding in the second half of pregnancy. The abruption may be marginal (hematoma at margin of placenta), central, or complete.

A. **Incidence:** Placental abruption occurs in 1 in 100 pregnancies. One third of all bleeding in pregnancy results from placental abruption.
B. **Etiology/predisposing factors.**
   1. Although the cause of placental abruption has not been definitively established, maternal hypertensive disorders are the most common precipitating factor. Other risk factors include history of previous abruption, substance abuse (cocaine use, cigarette smoking), trauma, uterine/placental factors (anomalies, fibroids, abnormal formation of the placenta, chronic ischemia, previous cesarean scar), maternal diseases (asthma, hypothyroidism, thrombophilias), rapid uterine decompression associated with polyhydramnios and multifetal pregnancy, increased parity and maternal age, and premature rupture of membranes.
C. Clinical presentation.
   1. Maternal signs and symptoms.
      a. Dark or bright red vaginal bleeding (mild to severe). Bleeding may be concealed behind the placenta, so may not be obvious.
      b. Abdominal or lower back pain.
      c. Persistent cramping or sharp, continuous abdominal pain.
      d. Board-like and tender abdomen.
      e. Uterine irritability.
      f. Elevated uterine resting tone.
      g. Tachysystole.
      h. Increasing abdominal girth as the uterus enlarges with the accumulation of blood.
      i. Signs of hypovolemic shock as blood loss increases.
   2. FHR abnormalities.
      a. Loss of fetal heart tones.
      b. Tachycardia.
      c. Late or variable decelerations.
      d. Decreased FHR variability.
D. Potential complications.
   1. Maternal (Francois and Foley, 2017; Navti and Konje, 2017).
      a. Anemia.
      b. Hypovolemic shock.
      c. Couvelaire uterus (blood forced between the muscle fibers of the uterus).
      d. Disseminated intravascular coagulation (DIC).
      e. Postpartum hemorrhage.
      f. Fetomaternal hemorrhage.
      g. Acute renal failure.
      h. Death.
   2. Fetal/neonatal.
      a. Anemia.
      b. Preterm birth and sequelae associated with prematurity.
      c. Hypoxia.
      d. Hypovolemia.
      e. Increased risk of long-term neurobehavioral problems.
      f. Risk for sudden infant death syndrome and hypoxia-associated periventricular leukomalacia.
      g. FGR.
      h. Perinatal death.
E. Assessment and management.
   1. Close monitoring and ongoing assessment are key in the care of the woman presenting with active vaginal bleeding.
      a. Accurate quantification of blood loss (Association of Women's Health Obstetric and Neonatal Nurses [AWHONN], 2014).
      b. Pain.
      c. Frequent assessment of maternal vital signs (BP, pulse, respirations).
      d. Frequent assessment of the FHR.
      e. Uterine contractions, tone, and tenderness.
      f. Signs/symptoms of shock (restlessness; cold, clammy skin; poor perfusion).
   2. Management, timing, and mode of delivery decisions are based on the severity of the abruption, gestational age and well-being of the fetus, and maternal–fetal status.
      a. If the fetus is stable and maternal hematologic status can be maintained, ultrasonography is needed to locate the placenta and determine the degree of placental separation and location of hematoma.
      b. Insertion of large-gauge IV catheters (16- to 18-gauge) for administration of fluids and blood products.
      c. CBC, coagulation studies, and type and crossmatch for blood.

d. Urine drug screen if substance abuse suspected.
e. Notification of the NICU and neonatologist/pediatrician.
f. Emotional support of woman and family.
g. Any episode of bleeding during pregnancy in an Rh-negative woman requires a Kleihauer–Betke test and the administration of Rh immunoglobulin (RhoGAM) (Davidson et al., 2016).

PLACENTA PREVIA
(DAVIDSON ET AL., 2016; FRANCOIS AND FOLEY, 2017; NAVTI AND KONJE, 2017)

Placenta previa is implantation of the placenta in the lower part of the uterus near or over the cervical os, and is described as low-lying, marginal, partial, or complete. Placenta previa is a common cause of bleeding in the second half of pregnancy, when the lower uterine segment stretches and thins.

A. **Incidence:** The incidence is 1 in 200 births in the United States.
B. **Etiology/predisposing factors.**
   1. The precise cause of placenta previa is unknown, but risk factors include advanced maternal age, previous placenta previa, increasing parity, prior cesarean birth or uterine surgery, living in higher altitudes, infertility treatments, cigarette smoking, cocaine use, maternal race, multifetal gestation, history of abortion, male fetus, and prior curettage.
C. Clinical presentation.
   1. Bright red, painless vaginal bleeding, with most patients experiencing at least one episode.
   2. Uterine contractions occur in 10% to 20% of cases, but otherwise the uterus is usually soft and nontender, with many women being asymptomatic.
   3. If an ultrasound is performed at less than 20 weeks of gestation, a low-lying placenta may be noted. However, at this gestational age, the lower uterine segment is not yet fully developed, and the placenta may migrate away from the cervical os as the pregnancy progresses.
   4. High presenting part or abnormal lie (e.g., transverse, breech).
D. Potential complications.
   1. Maternal.
      a. Anemia.
      b. Hypovolemic shock.
      c. Endometritis.
      d. Postpartum hemorrhage.
      e. Abnormal placental implantation (placenta accreta, percreta, and increta).
      f. Air embolism.
      g. Risk of recurrence in a future pregnancy.
   2. Fetal/neonatal.
      a. Perinatal mortality.
      b. Fetal anemia.
      c. Malpresentation.
      d. FGR.
      e. Prematurity and subsequent sequelae.
      f. Congenital malformations (cardiovascular, gastrointestinal, respiratory, CNS) (Navti and Konje, 2017).
E. Assessment and management.
   1. Treatment, timing, and mode of delivery decisions are based on the amount of bleeding, placental location, gestational age, cervical status, grade of previa, and condition and presentation of fetus. Any episode of bleeding during pregnancy in an Rh-negative woman requires a Kleihauer–Betke test and the administration of RhoGAM to Rh-negative, unsensitized women.
   2. Marginal or partial placenta previa with minimal bleeding is managed conservatively.
      a. Serial ultrasounds to confirm diagnosis, placental location, and monitor fetal growth.
      b. No vaginal examinations.
      c. Activity restrictions at home or in the hospital as determined by clinical presentation.
      d. Nutritional supplements and dietary management to prevent anemia.
      e. Antenatal corticosteroid therapy may be considered (if <34 weeks).
      f. Avoidance of intercourse.
      g. Time of delivery is based on the clinical picture, but is generally recommended at 37 weeks when fetal lung maturity is documented.
   3. Partial or total placenta previa and/or greater amounts of bleeding require more intensive assessment and management, in addition to what is noted earlier.
      a. Frequent assessment of vaginal bleeding, with accurate estimation of blood loss.
      b. Frequent assessment of maternal vital signs and continuous monitoring of the FHR and uterine contractility.
      c. Insertion of large-gauge IV catheters (16- to 18-gauge) for administration of fluids and blood products.
      d. Diagnostic workup: CBC, type, and cross-match for possible blood transfusion.
      e. If uterine contractions occur, tocolysis may be considered.
      f. If bleeding stops, expectant management may be reinstituted.

UMBILICAL CORD PROLAPSE
(DAVIDSON ET AL., 2016; STEER AND CHANDRAHARAN, 2017)

Umbilical cord prolapse is life threatening to the fetus and requires immediate and effective management by the nurse. It occurs when the cord falls below the presenting part (overt) or is compressed between the presenting part and the pelvis or cervix (occult).

A. **Incidence:** Varies from 1 to 3 in 1000 births, with an incidence in vertex presentations of 3% and in breech presentations of 3.7%.
B. **Etiology/predisposing factors.**
   1. The fetal presenting part does not fill the pelvic inlet completely, and the cord slips past it, often when the membranes rupture.
   2. Predisposing factors include fetal malpresentations (breech, transverse lie, shoulder), obstetric manipulations (e.g., amniotomy, external cephalic version, intrauterine pressure catheter [IUPC] insertion), abnormally long cord (>80 cm), PTL, low birth weight fetus, multiple gestation, polyhydramnios, lack of engagement of the presenting part, and multipara (more than five previous births).
C. Clinical presentation.
   1. The cord is protruding from the vagina or the cord is palpable on vaginal examination.
   2. In an occult prolapse, the cord may not be visible or palpable but is located between the presenting part and the pelvis or cervix.
   3. FHR changes may include an abrupt occurrence of persistent, severe variable decelerations and/or bradycardia.
D. Potential complications.
   1. Maternal.
      a. Emotional distress for mother and family due to the need for rapid and unexpected interventions.
      b. If general anesthesia is used for surgery, may result in uterine atony with subsequent postpartum bleeding.
      c. Blood loss from cesarean birth.
   2. Fetal/neonatal.
      a. Fetal/neonatal complications are directly related to compression of the umbilical cord, and perinatal mortality increases as increased time elapses between cord prolapse and birth.
      b. Fetal hypoxia leading to long-range neurologic complications.
      c. Fetal death.
E. Assessment and management.
   1. Assessments on admission to labor and delivery.
      a. Presenting part and its station.
      b. Dilation of cervix.
      c. Status of membranes.
      d. Evaluation of the FHR.
   2. Assessment for risk factors for cord prolapse, including presence of polyhydramnios or lack of engagement of presenting part. Ambulation during labor and artificial rupture of membranes may be contraindicated if either of the other conditions noted is present.
   3. Assessment after artificial or spontaneous rupture of membranes.
      a. Monitor FHR for changes as indicated earlier.
      b. Perform vaginal examination to detect prolapse if indicated.
   4. If prolapse has occurred (Steer and Chandraharan, 2017):
      a. Keep the examining hand in the vagina to elevate the presenting part away from the cord and to relieve cord compression until birth of the fetus. An alternative measure is to insert an indwelling catheter to fill the mother's bladder with sterile saline solution to elevate the fetal presenting part so that it is off the cord. Replacement of the cord into the uterus (funic reduction) is not recommended, as this may result in spasm of the umbilical vessels, resulting in further fetal compromise.
      b. Place the mother in the knee–chest position or steep Trendelenburg's.
      c. Continuous monitoring of the FHR.
      d. Administration of oxygen, insertion of IV lines if not already present, and notification of the anesthetist and NICU.
      e. If the cervix is fully dilated and the fetal station is below the ischial spines, vaginal birth may be expedited. However, emergency cesarean delivery may be preferable, especially if the cervix is not fully dilated and the fetus exhibits signs of potential compromise.

SHOULDER DYSTOCIA
(CROFTS AND DRAYCOTT, 2017; LANNI ET AL., 2017)

Shoulder dystocia is an acute obstetric emergency in which the provider is unable to deliver the shoulders of the infant by the usual maneuvers (downward traction) after birth of the head.

A. **Incidence:** Incidence is 0.2% to 3% of vaginal births. As this is a major obstetric emergency that must be acted upon quickly and occurs infrequently, multidisciplinary simulation drills should be instituted in the facility (Lanni et al., 2017).
B. **Etiology/predisposing factors.**
   1. There is a relative or absolute discrepancy between the pelvic inlet and the shoulders of the fetus.
   2. Factors associated with shoulder dystocia, although not good predictors, include maternal obesity, increased maternal age, prolonged second stage of labor, GDM, previous birth of an infant more than 4000 g, excess maternal weight gain, male fetus, and post-term.
C. Clinical presentation.
   1. Prolonged deceleration phase of labor (8 to 10 cm).
   2. Prolonged second stage of labor.
   3. After birth of the head, it recoils against the perineum and restitution does not occur (turtle sign). The usual traction from below is not successful in delivering the neonate.
   4. Delivery of the head to delivery of the shoulders is more than 60 seconds.

D. Complications.
   1. Maternal.
      a. Third- or fourth-degree lacerations.
      b. Postpartum hemorrhage.
      c. Psychological distress.
   2. Fetal/neonatal.
      a. Birth injuries (brachial plexus palsy, Erb's palsy, facial nerve palsy, or fractured clavicle or humerus).
      b. Hypoxic injury.
      c. Permanent brain/spinal cord injury.
      d. Intrapartum or neonatal death.

E. **Assessment and management** (Crofts and Draycott, 2017; Lanni et al., 2017).
   1. If risk factors are present and/or the provider anticipates a possible shoulder dystocia, the neonatal team should be present for delivery.
   2. Anticipate shoulder dystocia if descent of the head is slow and estimated weight is large. Make sure the woman's bladder is empty before birth occurs.
   3. If shoulder dystocia occurs, the provider should immediately state "shoulder dystocia" and attempt additional obstetric maneuvers.
      a. Maternal pushing should stop to prevent further impact of the shoulder.
      b. Use the McRoberts maneuver (maternal hip flexion; an exaggerated lithotomy position).
      c. Apply suprapubic pressure (not fundal) to attempt to release the anterior shoulder; the pressure may be directly downward or lateral.
      d. Perform an episiotomy to make manipulation easier.
      e. Turn the woman onto her side or pull the hips off the bed to free the sacrum.
      f. Turn the woman on "all fours" facing downward to widen the pelvic outlet if this can be easily accomplished (Gaskin's maneuver).
      g. Manually rotate the shoulders from the anteroposterior to the oblique diameter.
      h. Use the Woods' corkscrew maneuver, in which both hands are inserted internally to rotate the posterior shoulder to the anterior position for delivery under the pubic bone, with the maneuver repeated for the other side.
      i. Deliver the posterior arm.
      j. The provider must not apply quicker, harder, or more downward traction.
      k. A last resort would be the attempted replacement of the fetal head into the vagina (Zavanelli maneuver) and subsequent emergency cesarean section.

BREECH PRESENTATION
(CLUVER AND HOFMEYR, 2017; LANNI ET AL., 2017)

A. **Incidence:** Incidence is dependent on gestational age, as high as 25% in gestations of less than 28 weeks, and overall may be seen in 3% to 4% of all labors. A breech presentation may be frank, complete, or footling.

B. **Etiology/predisposing factors.**
   1. Maternal.
      a. Polyhydramnios or oligohydramnios.
      b. Uterine abnormalities (e.g., bicornuate uterus).
      c. Contracted pelvis.
      d. Use of anticonvulsant medications.
      e. Lax abdominal wall.
   2. Placental/fetal.
      a. Fetal anomalies (trisomy 13, 18, and 21; myotonic dystrophy; Potter syndrome).
      b. Preterm fetus.
      c. Fetal asphyxia or death.
      d. Multiple pregnancy

C. Clinical presentation.
   1. Woman feels fetus kicking in the lower abdomen.
   2. Fetal heart sounds are loudest above the umbilicus.
   3. Use of Leopold's maneuvers indicates head is in the fundal area and the breech is in the pelvis.
   4. On vaginal examination, the presenting part is soft, no fontanelles are felt, and the genitalia may be identified.

D. Complications.
   1. Maternal.
      a. Complications associated with cesarean section.
      b. Potential for obstructed delivery if birth is vaginal.
   2. Fetal/neonatal complications resulting from vaginal birth.
      a. Prolapsed/compressed cord.
      b. Asphyxia (from fetal head entrapment, cord compression, or slow delivery).
      c. Genital damage in the male infant.
      d. CNS injuries such as intracranial hemorrhage, brachial plexus injury, and severed spinal cord, especially if fetal head is hyperextended.

E. Assessment and management.
   1. Assess for presentation at each prenatal visit; some breech presentations may resolve spontaneously.
   2. Postural exercises, in which the woman assumes either the knee–chest or an elevated-hip posture several times a day to help the fetus turn from breech to cephalic presentation.
   3. External cephalic version (ECV) between 36 and 37 weeks' gestation to rotate the fetus. Greatest success is noted with double footling breech, posterior placenta, and 37 weeks' gestation. Tocolytics may be used before the procedure.
   4. Assessments on admission to labor and delivery:
      a. Perform Leopold's maneuvers and vaginal examination to determine presentation.
      b. Report clinical findings immediately to the physician or midwife.
      c. Ultrasonography may be ordered to confirm breech presentation, determine degree of flexion of fetal head, evaluate size of fetal head, estimate

fetal weight, diagnose fetal anomalies, and locate placenta.

5. The mode of delivery should be based on the experience level of the provider, with the majority choosing elective cesarean delivery. If the provider is experienced in breech delivery, he or she may plan a delivery as long as specific guidelines are followed and the woman is provided with informed consent regarding maternal and neonatal risks (ACOG, 2016).
6. Assessment of the neonate who was in the breech presentation may reveal:
   a. Edema of the external genitalia.
   b. A continuation of the frank breech position for a period after the birth.

Obstetric Analgesia and Anesthesia

(Davidson et al., 2016; Hawkins and Bucklin, 2017; Nutter, 2019; Tsen, 2017)

Both pharmalogic and nonpharmalogic pain management can be effective for women in labor. Side effects of medication, pain, and stress can all affect the fetus to some degree. Nonpharmacologic methods of pain management (e.g., labor support, freedom of movement, hypnosis, acupressure and acupuncture, application of heat or cold, listening to music, breathing techniques, massage, hydrotherapy, and transcutaneous electrical nerve stimulation) can be important and useful for the laboring woman if she desires a nonmedicated birth, or until she is ready for pharmacologic pain management or an epidural.

OBSTETRIC ANALGESIA

Obstetric analgesia (systemic medication) is given by either the intramuscular (IM) or the IV route and in as small a dose as possible. Any use of analgesia in the laboring woman should consider the potential effects on the mother/fetus, effects on contractions and the progress of labor, and the medical condition of the mother. Narcotic analgesics such as butorphanol tartrate (Stadol) and nalbuphine hydrochloride (Nubain) are commonly used for pain relief in labor, with sedation being the primary mechanism of action.

A. Potential side effects or complications.
   1. Maternal.
      a. Respiratory depression.
      b. Nausea and vomiting.
      c. Hypotension.
      d. Drowsiness and dizziness.
      e. Clammy skin and sweating.
   2. Fetal/neonatal.
      a. Decreased variability of the FHR, transient sinusoidal pattern.
      b. Neonatal respiratory depression.

B. Assessment and management.
   1. Assess for pain/discomfort, well-established labor pattern, and maternal request.
   2. Avoid administration of analgesics close to birth if possible.
   3. Administer IV analgesics slowly; give during a uterine contraction to minimize amount of drug transferred to the fetus.
   4. Observe the woman for side effects and monitor the FHR with the electronic fetal monitor or via intermittent auscultation.
   5. With maternal hypotension, turn the woman onto her left side, increase IV infusion of fluids, and closely monitor the FHR and maternal BP.
   6. Have naloxone (Narcan), oxygen, and ventilatory equipment available to manage potential newborn respiratory depression.
   7. Document use of analgesic and relay information to the nursery/neonatal team.
   8. Observe the neonate for potential side effects of maternal analgesia.

INHALED ANALGESIA

(NUTTER, 2019; TSEN, 2017)

The use of inhaled analgesia (nitrous oxide 50%/oxygen 50%) is becoming more frequent in the United States and is used extensively in Europe and Canada. In the doses used for labor, it provides both an anxiolytic and analgesic effect. Self-administered, it places the woman in control of her own pain relief, and users have high levels of satisfaction. Specific machines are available that deliver the correct mixture for use in labor analgesia, along with scavenging systems to remove exhaled gases. This method can also be useful during a manual removal of the placenta, during perineal suturing, or in other instances where the woman has a high degree of anxiety.

A. Potential side effects.
   1. Maternal.
      a. Dizziness, nausea, and vomiting.
      b. Dysphoria.
   2. Fetal/neonatal.
      a. No adverse fetal/neonatal effects have been noted.

B. Assessment and management.
   1. The woman must be able to hold the mask herself (it must not be attached to her face), making a seal. She must inhale and exhale into the mask, beginning 30 seconds before a contraction is expected. As the analgesia takes effect, the mask will fall away and prevent the continuous inhalation of the gas.
   2. Contraindications include impaired oxygenation or hemodynamic instability, or if she cannot hold the mask herself.
   3. If other sedating medications are being used, caution must be exercised.
   4. Inform significant other or visitors that she must hold the mask herself and not to hold it for her.

OBSTETRIC ANESTHESIA (GENERAL, NEURAXIAL, REGIONAL)

(DAVIDSON ET AL., 2016; HAWKINS AND BUCKLIN, 2017; NUTTER, 2019; TSEN, 2017)

Several types of anesthesia are used in labor and delivery. Neuraxial anesthesia includes the epidural and spinal (also provides analgesia), the most common mode of analgesia/anesthesia for labor and birth in the United States. A less frequently used regional anesthesia method is the pudendal block, which may be used for repair of lacerations, birth, and instrumented vaginal births. Local anesthesia involves perineal infiltration with a local anesthetic agent before episiotomy, birth, and/or perineal repair. General anesthesia is primarily reserved for emergency cesarean section when an epidural/spinal is ineffective or contraindicated, or in complicated vaginal births when it is not possible to have immediate and effective neuraxial/regional anesthesia.

A. Potential complications with general anesthesia.
   1. Maternal (Davidson et al., 2016).
      a. Vomiting and aspiration of gastric contents, with acid pneumonitis (Mendelson's syndrome).
      b. Respiratory depression.
      c. Hypotension or hypertension.
      d. Tachycardia.
      e. Laryngospasm.
      f. Uterine atony.
      g. Initiation of breastfeeding may be slower.
   2. Fetal/neonatal.
      a. Neonatal respiratory depression and hypotonicity.
      b. Fetal depression in proportion to the amount of anesthesia, with the anesthetic reaching the fetus approximately 2 minutes after induction.

B. Assessment and management with general anesthesia.
   1. The woman must have nothing by mouth while in labor if there is a strong possibility that she will receive general anesthesia. Note the time of her last meal.
   2. Administration of antacid prophylactically before general anesthesia to increase the pH of the stomach contents in case of aspiration.
   3. Place a wedge under the right hip to cause displacement of the uterus and prevent compression of the vena cava.
   4. Have the neonatal team present at birth and ready for potential resuscitation.
   5. Monitor the newborn infant after surgery for side effects of anesthesia.

C. Potential complications with neuraxial, regional, and local anesthetics.
   1. Maternal.
      a. Spinal or epidural anesthesia/analgesia (Hawkins and Bucklin, 2017).
         1) Hypotension (nausea/vomiting, dizziness, decreased baseline BP).
         2) Allergic reaction to the injected anesthetic.
         3) Toxic reaction to overdose, intravascular injection (metallic taste, ringing in the ears, slurred speech, numbness of tongue/mouth, seizures, respiratory depression), or intrathecal injection (respiratory depression, severe hypotension, loss of consciousness).
         4) Respiratory paralysis from "high spinal" anesthesia (breast numbness, inability to breathe).
         5) Postdural puncture headache.
         6) Failure of anesthetic to be effective.
         7) Urinary retention during labor and/or postpartum.
         8) Hematoma formation compressing the spinal cord, with potential for permanent damage.
         9) Paralysis.
         10) Prolonged second stage and potential increase in instrumented vaginal delivery (forceps/vacuum).
         11) Increase in the use of oxytocin.
         12) Increased maternal temperature.
      b. Pudendal block (Davidson et al., 2016).
         1) Sciatic nerve trauma.
         2) Perforated rectum.
         3) Anesthetic toxicity.
         4) Broad-ligament hematoma.
      c. Local infiltration.
         1) Few, if any, complications.
         2) Anesthetic toxicity from intravascular injection or use of large amounts of local anesthetic agent.
   2. Fetal/neonatal.
      a. Complications primarily result from the sequelae of maternal complications (e.g., hypotension, respiratory depression, toxic/allergic reactions, etc.) and the resulting physiologic effects on the maternal–placental–fetal unit.
         1) Fetal compromise, evidenced by late decelerations, bradycardia, increased or decreased variability, prolonged decelerations.
         2) Newborn bradycardia, apnea, hypotonia, seizures (with maternal toxic reaction).
         3) Side effects of medications used to resolve maternal complications (e.g., ephedrine for hypotension may lead to newborn tachycardia, increased muscular activity, jitteriness).

D. Assessment and management.
   1. Note history of allergies to local anesthetics, history of major anesthesia complications, and family history of anesthesia complications.
   2. Assess for contraindications (allergy to local anesthetic agents, infection at needle placement site, coagulopathies, hemodynamic instability, inability/refusal to consent or cooperate).

3. Prehydrate with 500 to 1000 mL IV fluid before spinal or epidural anesthesia/analgesia to minimize hypotensive effects from sympathetic blockade.
4. Uterine displacement with roll under right hip to prevent vena caval compression after epidural/spinal placement.
5. Frequent monitoring of BP after administration of spinal or epidural anesthetic; monitoring of FHR after any type of regional anesthesia/analgesia.
6. Monitor bladder distention and catheterize if necessary.

CESAREAN DELIVERY
(BERGHELLA ET AL., 2017; ROBSON AND BERGHOLT, 2017)

A. **Incidence:** The cesarean birth rate in the United States was 31.9% in 2016, with non-Hispanic black women having the highest rate at 35.9%. The primary cesarean section rate in 2016 was 21.8%, and the vaginal birth after cesarean section (VBAC) rate was 12.4% (Martin et al., 2018). Although the rates of cesarean delivery have been declining since 2009, possible reasons for the increases seen between 1996 (20.7%) and 2009 (32.9%) include an increase in the numbers of women with comorbidities (obesity, multiple gestation, diabetes), increased number of labor inductions with failure of induction, decline in vaginal breech birth and limited offering of trial of labor after cesarean (TOLAC), decreased operative vaginal deliveries, repeat cesareans, increases in numbers of women over age 35, maternal request for elective cesarean, and physician fears of litigation (Berghella et al., 2017; Martin et al., 2018; Robson and Bergholt, 2017).

B. **Indications.**
   1. Maternal.
      a. Previous uterine surgeries.
      b. Cephalopelvic disproportion.
      c. Cesarean delivery at maternal request.
      d. Maternal medical conditions.
      e. Placental issues (e.g., abruptio placentae, previa, placenta accrete).
      g. Active maternal herpes.
      h. Dystocia
   3. Fetal.
      a. Suspected fetal compromise/nonreassuring FHR status.
      b. Breech or other malpresentation.
      c. Congenital anomalies such as neural tube defects and hydrocephalus.
      d. Suspected fetal macrosomia.

C. Potential complications.
   1. Maternal.
      a. Infection (endomyometritis, wound infections).
      b. Anesthesia complications.
      c. Uterine atony and subsequent hemorrhage.
      d. Morbidity and mortality from anesthesia.
      e. Inadvertent operative injuries (e.g., lacerations to bladder or bowel, ureteral injury, and injury to adjacent organs).
      f. Venous thromboembolism (VTE).
      g. Septic pelvic thrombophlebitis.
   2. Fetal/neonatal (Murray and McKinney, 2014).
      a. Fetal compromise from reactions to anesthesia or mode of anesthesia (general).
      b. Preterm birth and complications associated with prematurity.
      c. Transient tachypnea of the newborn.
      d. Persistent pulmonary hypertension.
      e. Anemia from blood loss caused by incision of placenta and lack of full placental transfusion.
      f. Inadvertent operative injuries (e.g., lacerations, bruising, trauma).

D. Assessment and management.
   1. Perform usual interventions to prepare the woman for a surgical procedure (e.g., VTE prophylaxis, antibiotic prophylaxis, surgical consents, history and physical by provider).
   2. Notify neonatology/newborn team and pediatrician.
   3. Remove fetal scalp electrode before surgery if present.
   4. Left lateral tilt for uterine displacement.
   5. Follow neonatal resuscitation program protocols for neonatal care after birth.

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CHAPTER 3
Perinatal Substance Abuse

Karen D'Apolito

OBJECTIVES

1. Identify the incidence and risk factors associated with substance use disorder in pregnancy.
2. Identify maternal, fetal, neonatal, and child outcomes related to substance use disorder.
3. Describe the factors associated with breastfeeding and maternal substance use dependence.
4. Describe the physical and behavioral signs of neonatal abstinence syndrome (NAS).
5. Identify the pharmacologic and nonpharmacologic treatment of NAS.
6. Describe future strategies for the improvement of care for infants with NAS.

Overview

Substance abuse has been an issue for society over the past decades. Almost all drugs consumed by a mother are known to cross the placenta and have effects on the fetus. The most frequent drugs used in pregnancy include tobacco, followed by alcohol, cannabis, and illicit substances (Forray and Foster, 2015); however, much recent attention has been given to the misuse of prescription drugs by pregnant women. Overall, in 2016, the nonmedical use of prescription drugs in the United States was reported to be 54% of citizens 18 to 25 years of age (Substance Abuse and Mental Health Services Administration [SAMHSA], 2017). In one study of 9000 pregnant women, 5% reported the use of prescription drugs in 2016 (Kozhimannil et al., 2017). All pregnant women with a substance use disorder should be encouraged to attend a medication-assisted treatment (MAT) program that also addresses the medical, mental, and emotional needs of not just pregnant women but all women with a substance use disorder (National Institute on Drug Abuse [NIDA], 2018a). The success of treatment depends on social support, the rapport the client has with her health care provider, and treatment availability (Krans and Patrick, 2016).

Infants born to mothers who have a substance use disorder may have an increased risk of birth defects, fetal growth restriction, increased risk of premature birth, signs of neonatal abstinence syndrome (NAS) or toxicity and late-onset behavioral and developmental problems (Forray and Foster, 2015). Infants hospitalized for NAS have increased health care costs. Between 2000 and 2001 it was estimated that one baby was born every 25 minutes with NAS (NIDA, 2015). One study examined the cost of care for 137,000 infants with NAS and reported a 10-times increase in average hospital cost for these infants compared with infants without NAS ($38,000 vs. $4000), for a total expenditure of $5.2 billion over a 3-year period (2013-2016) (Milliren et al., 2018). Seventy percent of these infants required pharmacologic treatment at a cost of $45,000, which added to the baseline cost per infant in addition to a prolonged hospital stay (22 vs. 11 days) (Milliren et al., 2018). Consistency with standard nonpharmacologic and pharmacologic approaches, as well as strict weaning protocols, are important to decrease length of stay (LOS), length of treatment (LOT), and overall costs associated with NAS. The future requires health care providers to study alternative places to treat infants with NAS to determine the best assessment practices and the best medications to manage infants with NAS.

It is important to remember that addiction resulting in substance use disorder is a chronic disease that can be treated successfully. It is defined as a chronic relapsing brain disease that is the result of drug seeking and use despite harmful consequences (NIDA, 2016). Considering the intrauterine drug exposure infants receive, they are not born addicted to drugs. They are passively exposed to drugs; therefore, these infants should not be labeled as drug-addicted infants.

A. Incidence of substance use during pregnancy.
   1. Many different classes of drugs are abused in the United States. These include opioids, central nervous system (CNS) stimulants, CNS depressants, and hallucinogens (Table 3.1). As reported in 2017, substance dependence was lower among pregnant women between the ages of 18 and 25 compared with nonpregnant women (1.5% vs. 3.9%). Similar results were found for pregnant women between the ages of 26 and 34 (0.5% vs. 2.3%) (Smith and Lipari, 2017).

Table 3.1

Common Drugs of Abuse

Opioids	CNS Stimulants	CNS Depressants	Hallucinogens
Codeine	Cocaine	Alcohol	Ecstasy
Demerol			Ketamine
Fentanyl	Ecstasy	Barbiturates (Nembutal)	LSD
Heroin			Marijuana
Hydrocodone (Vicodin)	Methamphetamine	Benzodiazepines (Xanax,	PCP
Hydrocodone (Oxycontin)	Nicotine	Librium, Valium, Ativan)	
Methadone		*Gabapentin (Neurontin)	
Morphine		Marijuana	
Oxycodone (Percocet)			

LSD, ; PCP,

* Vestal (2018)

From NIH (2018).

2. Polysubstance abuse is still prevalent among 50% of pregnant women (Forray, 2016).
3. There is a strong association between substance use disorder and mental health conditions, especially anxiety and depression (Loree et al., 2019).

B. Misuse of prescription drugs.
1. There has been an increase in the misuse of many different drugs in the United States (see Table 3.1). In 2013, 4.6 million women (3.8%) ages 18 or older have misused prescription drugs (SAMHSA, 2014).
2. It was reported that over the last 10 years the nonmedical use of prescription opioids has nearly doubled (Kozhimannil et al., 2017).

Risk Factors Associated With Substance Use Disorder in Women

A. Individuals who experience four or more types of childhood abuse had a 4 to 12 times increase in alcohol or drug abuse. This abuse included emotional, physical, and sexual abuse (LeTendre and Reed, 2017).
B. Adults who experienced emotional, physical, and sexual abuse had a 34% higher incidence of developing an alcohol use disorder, 47% a cannabis use disorder, and 41% a drug use disorder (LeTendre and Reed, 2017). Substance use disorder is four times higher in women with a history of sexual abuse as an adult (Rakesh et al., 2015).
C. There is a significant association between substance use and major depression, especially in women. The development of alcohol abuse or dependence is twice as great in women compared with men (Rakesh et al., 2015).
D. Women who are at high risk for depression are more likely to abuse drugs, and women who are sexually abused are at higher risk of depression.
E. Genetics and environmental factors play a role in addiction. Fifty percent of individuals with addiction have a genetic predisposition, and 50% are addicted due to poor coping skills (Melemis, 2018).

Pregnancy Outcomes for Substance Use Disorder Associated With Common Drugs of Abuse

A. **Alcohol** (Popova et al., 2017).
1. In the United States alcohol use among women 18 to 44 years of age is 54%, and 18% of these women binge drink (binge drinking is >3 drinks per occasion in women or a blood alcohol level of 0.08% or above) (Dejong et al., 2019).
2. About 15 out of 10,000 babies born to women who drink during pregnancy will have fetal alcohol spectrum disorder (FASD) (Popova et al., 2017).
3. Alcohol crosses the placenta readily, and fetal blood alcohol levels reach maternal levels 2 hours after maternal consumption (Dejong et al., 2019).
4. Alcohol consumption during pregnancy can result in miscarriage, preterm labor, stillbirth, spontaneous abortion, and preterm delivery (Dejong et al., 2019; Popova et al., 2017).

B. **Benzodiazepines** (Shyken et al., 2019).
1. Benzodiazepines are sedatives prescribed for anxiety and insomnia.
2. Easily cross the placenta.
3. The self-report of anxiety symptoms during the first trimester of pregnancy is 18%, 19% in the second semester, and 25% postpartum. Women were reported to be treated for depression (25%) and anxiety (24%).
4. Benzodiazepines, when taken with methadone, have demonstrated an increased risk of overdose morbidity and mortality (71% lethargy, 29% respiratory depression, 22% coma, 5% respiratory failure, and 2% cardiac arrest).

5. Increased incidence of cesarean delivery.
6. Common drugs typically prescribed are alprazolam (Xanax), chlordiazepoxide (Librium), lorazepam (Ativan), and diazepam (Valium).

C. **Cocaine** (Smid et al., 2019).
1. Cocaine easily crosses the placenta and the blood–brain barrier by simple diffusion, causing generalized vasoconstriction by directly affecting maternal and fetal blood vessels. This vasoconstriction can result in teratogenic effects on the developing fetus.
2. Pregnant women who use cocaine and crack tend to be older, African American, and of low socioeconomic status.
3. Some effects of using cocaine during pregnancy can include hypertension, myocardial infarction, renal failure, placenta abruption, miscarriage, stillbirth, and uterine rupture.

D. **Marijuana** (Stickrath, 2019).
1. Marijuana is the most commonly used illicit substance during pregnancy.
2. The main chemical in marijuana, tetrahydrocannabinol (THC), crosses the placenta readily (Metz and Borgelt, 2018).
3. In the United States 4% of pregnant women reported using marijuana within the last month and 7% within the last year. With the legalization of marijuana in some states, the risk of use has declined. In 2005, 5% of women reported no risk compared with 19% in 2015.
4. The data are inconclusive regarding the negative effects of marijuana use during pregnancy. There is evidence to suggest that marijuana use in conjunction with smoking may contribute to maternal asthma. There may also be a high association of stillbirth in women who consume marijuana and nicotine during pregnancy.
5. The American College of Obstetricians & Gynecologists (ACOG Committee Opinion #637, 2017) recommends:
   a. Women who are pregnant or planning to become pregnant should be encouraged to discontinue marijuana use, including medical marijuana (safer alternative therapies are available).
   b. Women should be counseled about potential health consequences if marijuana is used during pregnancy.

E. **Methamphetamine** (Smid et al., 2019).
1. More than 30 million users worldwide use methamphetamine (United Nations Office on Drugs and Crime [UNODC], 2017). From 2005 to 2015 the percentage of people using methamphetamine increased from 2% to approximately 30%.
2. It is one of the most common drugs used during pregnancy, with prevalence rates ranging from 0.7% to 4.8% (Wright et al., 2015). Among students (9th to 12th grade), lifetime use of methamphetamine is approximately 7%, which is a significant risk factor for adolescent pregnancy (Smid et al., 2019).
3. Pregnant women using methamphetamine are typically white (64%), unemployed, and less than 24 years of age.
4. Use during pregnancy can result in premature delivery, cesarean delivery, fetal death, and hypertension.

F. **Nicotine** (Crume, 2019).
1. Smoking during pregnancy is the most preventable cause of infant morbidity and mortality.
2. It has been documented that between 2000 and 2010, there has been a 2.5% decrease in smoking among pregnant women (13.2% in 2000 and 10.7% in 2010). Additionally, during this period, 11% of women who smoked 3 months before pregnancy stopped smoking by the third trimester of pregnancy (43% to 54%, respectively).
3. Nicotine readily crosses the placenta and the blood–brain barrier.
4. Pregnant women have an increased risk for placenta previa, placental abruption, and premature rupture of membranes (Crume, 2019) and possibly ectopic pregnancy (Cnattingius, 2014).
5. Smoking can make it difficult for a woman to become pregnant (Centers for Disease Control and Prevention, 2017).

G. **Opioids** (Sanjanwala and Harper, 2019).
1. Combined data from three national organizations (2007 to 2012) found an average of 21,000 pregnant women aged 15 to 44 misused opioids over the past month (0.9%) compared with nonpregnant women (2.6%) (Smith and Lipari, 2017) (Fig. 3.1).
2. Opioids cross the placenta readily, and neonates may exhibit NAS.
3. Opioid use is a leading cause of pregnancy-related deaths in the United States.
4. Untreated opioid use during pregnancy is associated with:
   a. Preterm delivery.
   b. Placental abruption.
   c. A 16-fold increase in stillbirth.
   d. Prostitution and an increase in sexually transmitted diseases (ACOG Committee Opinion #524, 2017).

H. Selective serotonin reuptake inhibitors (SSRIs) (Tran and Adelaide, 2015).
1. Psychiatric disorders are present in up to 14% of pregnant women.
2. Prevalence rates of major and minor depression during pregnancy are between 13% and 18%.
3. Use of antidepressants during pregnancy is estimated to be between 2% and 6%.
4. SSRIs are commonly used to treat depression among pregnant women.

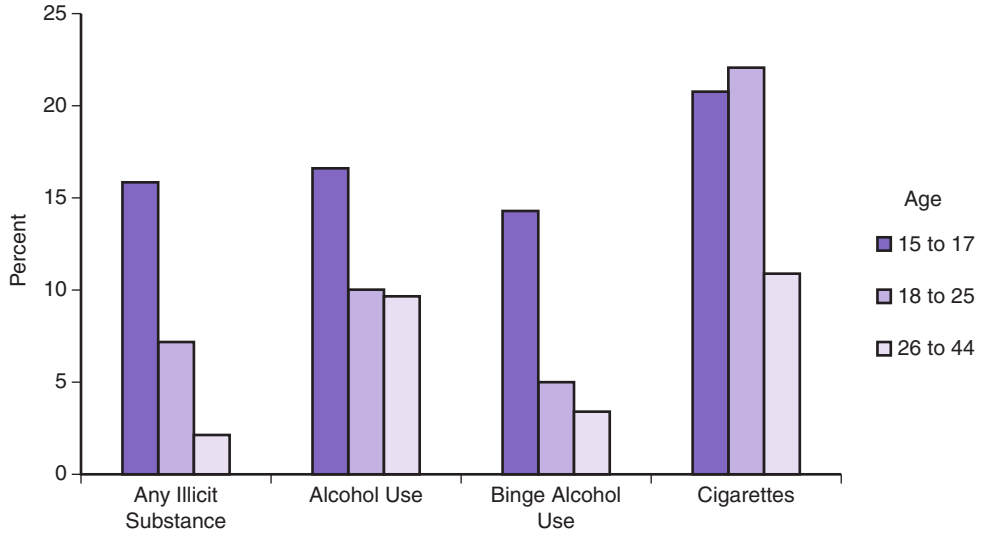

Fig. 3.1 Past Month Opioid Misuse Among Women Aged 15 to 44 by Pregnancy Status and Age 2007–2012. *(From Smith, K., & Lipari, R., [2017]. SAMHSA; The CBHSQ Report. Women of Childbearing Age and Opioids.)*

Fetal and Neonatal Outcomes for Common Drugs of Prenatal Substance Dependence

A. **Alcohol** (Mamluk et al., 2017).
   1. Prematurity.
   2. Small for gestational age (SGA).
   3. FASD.
   4. These outcomes can occur based on the amount of alcohol consumed during pregnancy (based on 32 g or 3.2 standard drinks—one standard drink is 10 g of pure alcohol).

B. **Benzodiazepines** (Shyken et al., 2019).
   1. Preterm delivery and low birth weight.
   2. Poor muscle tone, poor feeding, drowsiness, low Apgar scores requiring ventilation, poor suck, and hypothermia.
   3. When used with opioids, increased incidence of NAS.

C. **Cocaine** (Smid et al., 2019).
   1. Information is inconclusive, but structural malformation such as urinary tract, limb reduction, and intestinal atresia may occur.
   2. Preterm delivery and low birth weight.

D. **Marijuana** (Hennessy, 2018).
   1. There is controversy regarding the effects of prenatal exposure of marijuana on the fetus. Some report that prematurity can occur with heavy use (at least weekly) compared with women who used less freely (10% vs. 6%) (Mark et al., 2016).
   2. Decreased birth weight by an average of 109 g has been reported.
   3. No decrease in body length, head circumference, Apgar scores, neurobehavioral changes, or days spent in the hospital have been reported with maternal marijuana use during pregnancy.

E. **Methamphetamine** (Smid et al., 2019).
   1. Premature delivery, lower birth weight, smaller head circumference.
   2. Neonatal death.
   3. Cardiac defects, gastroschisis, limb reduction, biliary atresia, neural tube defects, cleft lip and palate.

F. **Nicotine** (Crume, 2019).
   1. Premature delivery, restricted fetal growth.
   2. Sudden infant death syndrome (SIDS).
   3. Cardiovascular and heart defects, musculoskeletal defects, limb reduction defects, missing or extra digits, clubfoot, craniofacial defects, eye defects, orofacial clefts, gastroschisis, anal atresia, and undescended testicles.
   4. It is estimated that 5% to 8% of preterm deliveries, 13% to 19% of term low birth weight deliveries, 23% to 34% of SIDS, and 5% to 7% of preterm-related deaths are related to prenatal smoking in the United States.

G. **Opioids** (Sanjanwala and Harper, 2019).
   1. An increased risk for spina bifida (2.2-fold increase), hydrocephalus, eye chamber defects, and gastroschisis have been attributed to fetal exposure to opioids during the first and third month after conception.
   2. Low birth weight and decreased length were found for neonates exposed to high doses of buprenorphine (dose not specified) (Jansson et al., 2017).

3. Thirty percent to 80% of neonates will develop NAS and require treatment (McCarthy et al., 2015).

H. SSRIs (Shyken et al., 2019).
   1. NAS is possible if used during the second and third trimester of pregnancy.

Childhood Outcomes for Common Drugs of Prenatal Substance Dependence

A. **Alcohol** (Dejong et al., 2019).
   1. The IQ level of children with alcohol exposure can be variable. Some children exposed to low levels of alcohol have not exhibited deficiencies in cognitive functioning at 12 months of age (McCormack et al., 2018); however, others have reported inattention, mental health problems, and problems with short-term memory.
   2. With heavy exposure, some children develop FASD. This disorder is associated with reduced intelligence (decreased IQ, poor reasoning and judgment skills, learning disabilities, and speech delay), attention disorders, neuropsychological defects (hyperactivity, poor coordination), and physical abnormalities including facial dysmorphology (smooth philtrum) (DeJong et al., 2019).
   3. No cure; however, early intervention from birth to 3 years of age can improve child development.

B. Benzodiazepines.
   1. Increased internalizing behaviors (anxiousness, emotional reactivity, somatic complaints) and externalizing behaviors (aggression, attention problems) were seen at 1.5 and 3 years of age (Brandlistuen et al., 2017).
   2. Other reports state there are not enough data to suggest psychomotor developmental delays (Shyken et al., 2019).
   3. Children prenatally exposed to benzodiazepines scored higher on tests for oppositional-defiant disorder and aggression; however, similar results were found with children whose mothers had anxiety but were not treated (Shyken et al., 2019).

C. **Cocaine/methamphetamine** (Smid et al., 2019).
   1. Heavy prenatal methamphetamine exposure (≥3 days/week) was associated with anxiety, depression, and attention problems in children 3 to 5 years of age. At 7 years of age some children had poor cognitive functioning.
   2. Studies of long-term outcomes of infants with intrauterine cocaine exposure remain difficult to find. In children less than 6 years of age, there are reports of problems with growth, inhibitory control, attention, poor language and motor skills, and abstract reasoning.

D. **Marijuana** (Stickrath, 2019).
   1. Congenital anomalies are not associated with marijuana exposure.
   2. The amount of abnormality seems to be associated with dose and timing of exposure.
      a. No changes in intellectual testing were present in children aged 3.
      b. Children heavily exposed to marijuana (≥1 joint/day) during the first trimester had decreased verbal reasoning skills.
      c. Children at the age of 10 who were exposed during the first and second trimester of pregnancy demonstrated more hyperactivity, impulsivity, and decreased attention.
      d. At the age of 14, children had lower reading, math, and spelling scores.
   3. No NAS signs in the newborn period, and follow-up studies do not show any effect in children 5 to 6 years of age (Hamdan, 2017).

E. **Methamphetamine** (Smid et al., 2019).
   1. Long-term studies are limited.
   2. Heavy prenatal methamphetamine exposure (≥3 days/week) was associated with anxiety, depression, and attention problems at 3 years of age.
   3. At 3 to 4 years of age, no report of poor cognitive functioning until the child was 7 years of age; however, the younger children did have difficulties with visual motor processing.
   4. Brain neuroimaging at 7 to 15 years of age suggests alterations in the striatum (motor and reward system) and frontal lobes with gender differences. These differences may be due to rewiring of the cortical pathways in the frontal lobe.

F. **Nicotine** (Crume, 2019).
   1. Smoking during pregnancy affects fetal lung development that may result in altered pulmonary functioning through the first years of life, possibly leading to a lifelong reduction in lung function.
   2. It has been reported that smoking during pregnancy may increase childhood obesity by 55%.
   3, Maternal smoking during pregnancy has also been associated with early menarche in female children.

G. Opioids.
   1. Little is known about the long-term effects of children who were exposed to methadone or buprenorphine in utero. It has been reported that children 48 to 57 months of age ($n = 66$) born with intrauterine exposure to both of these drugs were found to function lower on tasks involving short-term memory, inhibition, and low scores on executive function (Konijnenberg and Melinder, 2015).

H. SSRIs (Rotem-Kohavi, 2017).
   1. Some studies suggest that children prenatally exposed to SSRIs can exhibit the following:
      a. An increase in internalizing behaviors and anxiety in 36-month-old children.
      b. Possible increased risk of autism spectrum disorder (ASD).
      c. Shift in language perception (unable to notice differences between vowel and consonant sounds).
      d. Executive functioning (inhibitions and behavioral regulation) difficulties in 4-year-olds.
      e. Important to remember that all the risks may be influenced by genetics and maternal mood.

Breast Milk and Drugs

A. Factors that determine whether a drug will enter breast milk include:
   1. Drug properties such as low molecular weight, volume of distribution, maternal serum protein binding, and high lipid solubility and drugs with a long half-life (more likely to accumulate in breast milk, which are more easily absorbed by the infant) (Hale, 2019).
   2. A milk to plasma (M/P) ratio (amount of drug in breast milk) and the relative infant dose (RID) (division of the infant's dose [150 mg/kg/day] by maternal dose in mg/kg/day) determine how much drug the baby receives. An M/P ratio of less than 1 is low (limited drug in breast milk) and an RID less than 10% of maternal dose is safe to use and suggests a small amount of drug is transferred to the milk. A level greater than 1 suggests a large amount of drug is in the breast milk (Hale, 2019).
   3. Breastfeeding is contraindicated only if the mother is taking illicit drugs, has polydrug abuse, or is infected with HIV (Kocherlakota, 2014).
   4. The highest alcohol levels in breast milk occur 30 to 60 minutes after consumption (Lactmed, 2018).

B. Cocaine/methamphetamine.
   1. Not recommended in breastfeeding women (Hale, 2019; Smid et al., 2019).
   2. If ingested, a minimum of pump and dump for 24 hours is recommended before breastfeeding (Hale, 2019).

C. Marijuana.
   1. There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding. Because of this lack of data, marijuana use is discouraged (ACOG Committee Opinion #637, 2017).

D. **Methadone** (SAMHSA, 2015).
   1. Mothers taking methadone can breast-feed despite maternal dose (Hale, 2019).
   2. The benefits of breastfeeding outweigh the small amount of methadone that enters the breast milk.

E. Buprenorphine (Hale, 2019).
   1. The amount of buprenorphine in human milk is small, and no short-term negative effects have been seen in infants.
   2. RID is 0.09% to 1.9%.

F. **SSRIs** (Hamdan, 2017).
   1. SSRIs are the most commonly used antidepressant in postpartum mothers.
   2. The type of SSRI can influence whether breastfeeding is recommended.
   3. Sertraline (Zoloft) and paroxetine (Paxil) have minimal transfer into breast milk and have no adverse effects on the infant; however, fluoxetine (Prozac) is not recommended when the mother is breast-feeding because it produces significant plasma concentrations in some breastfed infants and has a long half-life.

Preconception Counseling and Screening

A. The goal of preconception counseling and screening is to provide health promotion, physical assessment, risk screening, vaccinations, and counseling for women of reproduction age to reduce risk factors that might affect future pregnancies (WellCare Health Plans, 2014).

B. Both ACOG and the World Health Organization (WHO) agree that universal screening with brief intervention, followed by referral to appropriate treatment, should be the standard of care (Sanjanwala and Harper, 2019).

C. Methods of screening include:
   1. SBIRT (Screening, Brief Intervention, and Referral Treatment) is a brief intervention approach to the treatment of people with substance use disorder or who are at risk of future dependence on alcohol and other substances (SAMHSA, 2017).
   2. The four Ps (asks patient about substance use) (Center for Adolescent Substance Abuse Research [CEASAR], 2016) and NIDA Quick Screen (an online screening tool for substance abuse filled out by the patient) (Sanjanwala and Harper, 2019).
   3. Women should have access to postpartum psychosocial support services, including substance use disorder treatment and relapse prevention programs (ACOG, 2017b).
   4. Contraceptive counseling and access to contraceptive services should be a routine part of substance use disorder treatment, and women who smoke tobacco or use e-cigarettes should be counseled to quit (ACOG, 2017a).

Treatment Approaches for Pregnant Women

A. MAT is the most common recommended treatment for an opioid use disorder in pregnancy (ACOG, 2017b).
B. Methadone.
   1. Methadone, a full mu receptor agonist (does not activate the mu receptor), changes how the brain and nerves respond to pain (SAMHSA, 2015).
   2. Methadone is used in MAT to help people reduce or eliminate their use of heroin and other opioids (SAMHSA, 2015).
   3. During pregnancy metabolism fluctuates. If dosing during pregnancy was increased, efforts should be made to return the patient to prepregnancy dosing. Methadone may be dosed 3 times per day (Sanjanwala and Harper, 2019).
   4. Methadone for the treatment of opioid use disorder can only be dispensed as a part of a federally licensed outpatient treatment program (Sanjanwala and Harper, 2019).
C. Buprenorphine (Subutex).
   1. Subutex is a partial agonist (mixed agonist–antagonist activity) that can be used, like methadone, to mitigate the effects of opioid withdrawal (Sanjanwala and Harper, 2019).
   2. The effects of Subutex increase with each dose; however, when at a moderate dose the effects level off, even with increasing doses. This leveling off decreases the risk of misuse, dependency, and side effects (SAMHSA, 2016).
   3. Subutex treatment does not require a federally regulated clinic. Therapy can be office based; however, infrequent visits can increase the risk of relapse, therefore, licensed providers are required to have a referral system for psychosocial intervention (Sanjanwala and Harper, 2019).
   4. Buprenorphine and naloxone (Suboxone). It is given to limit the abuse of Subutex. Although naloxone is not orally or sublingually absorbed, attempts to inject or snort Suboxone will produce severe adverse effects (nausea, vomiting, drug withdrawal, sweating, irregular heartbeat) (Sanjanwala and Harper, 2019).
D. Recidivism is common. Some triggers for drug relapse may include loss of insurance and access to treatment, demands of caring for a new baby, sleep deprivation, and threat of loss of child custody (ACOG, 2018).
E. Cognitive behavioral therapy is based on the idea that our thoughts cause our feelings and behaviors, not external things like people, situations, or events. The goal is to help people change the way they feel or act, even if the situation does not change (National Association of Cognitive-Behavioral Therapies, 2018).
F. Motivational interviewing is a patient-centered method for helping people use intrinsic motivation to change health behaviors by exploring and resolving ambivalence. Strategies include being nonjudgmental, empathetic, and supportive (Academy of Pediatrics, 2018).

Barriers to Treatment

A. Policy makers have a misguided understanding of the chronicity of addiction and the need to provide quality treatment programs that meet the medical and psychosocial needs of this vulnerable population (Krans and Patrick, 2016).
B. The incarceration of pregnant women for substance abuse disorder can compromise the health of the woman and her fetus. The threat of incarceration has driven women away from seeking prenatal care or continuing to engage in care, leading to worse outcomes for the mother and fetus (Angelotta et al., 2016; Guttmacher Institute, 2017).
C. Fear of being reported by health care professionals to child protective services (Polak et al., 2019).
D. Limited number of treatment programs in the United States that accept pregnant women.
E. The stigmatism associated with substance dependence during pregnancy is a barrier to women getting treatment as early as possible (Krans and Patrick, 2016).

Comorbidities Associated With Substance Use Disorders

A. Polysubstance use in pregnancy is common, as well as psychiatric comorbidity (Forray, 2016).
B. People with mental illness may turn to alcohol or other drugs as a form of self-medication to improve mental health symptoms. Similarly, alcohol and drugs worsen the symptoms of mental illness (National Alliance on Mental Illness, 2017).
C. Pregnant women with opioid use disorder often have co-occurring mental health conditions, in particular, depression, history of trauma, posttraumatic stress disorder (PTSD), and anxiety (ACOG Committee Opinion, 2017a).

Screening Methods to Identify Potential Substance Users

A. Mother.
   1. Self-report is a practical and inexpensive way to obtain a history of prenatal substance use; however, many women are reluctant to discuss substance use because of the social and legal consequences.

Clinicians should establish respectful, empathic, and collaborative relationships with patients (McQueen and Murphy-Oikonen, 2016).

2. Urine is a biological specimen used for screening. It can detect metabolites for opioids, nicotine, cocaine, and amphetamines. Maternal permission is required. Universal urine screening (all women in labor) can increase sensitivity and specificity of the test; however, targeted urine testing identifies women at high risk and is more cost-effective than universal screening (McQueen and Murphy-Oikonen, 2016).
3. Hair sampling is second to urine testing. Hair is easy to collect and can have a wider window of detection, enabling the assessment of chronic drug use (Newman, 2016).
4. Breast milk can be sent for screening. The test requires 5 mL of breast milk placed in a leakproof sterile container. The specimen can last at room temperature for 72 hours, refrigerated for 14 days, and frozen for 1 year. When transported to the laboratory, the milk should be kept cold using ice packs (Quest Diagnostics, 2019).

B. Infant.

1. Urine screening of the newborn will have a high false-negative rate because only results for infants with recent exposure will be positive (Botash, 2018). Alcohol can be detected in the urine from 3 to 10 hours; opioids, amphetamines, benzodiazepines, and cocaine metabolites are detected within 1 to 4 days, and barbiturates and marijuana 2 to 6 weeks.
2. Meconium is the most common specimen sent for drug screening. Drug metabolites are present in the meconium from 20 weeks gestational age (GA) to term. For maximum sensitivity, the sample should be 3 g (1 tsp) of meconium (United States Drug Testing Lab, 2018). Meconium is more likely to identify infants with intrauterine drug exposure than urine (Botash, 2018).
3. Umbilical cord tissue is a more recent screening method. Umbilical cord toxicology can detect amphetamines, cocaine, opioids, barbiturates, and cannabinoids along with their metabolites. It is easy to collect, and samples can be refrigerated for 21 days in case later testing is needed (O'Reilly, 2018). Collection involves cutting a 6-inch section of the umbilical cord. Further information about the collection process can be found at http://www.usdtl.com/assets/Umbilical_Cord_Collection_Instructions.pdf.

Neonatal Abstinence Syndrome

A. Definition.

1. NAS is a postnatal drug withdrawal syndrome exhibited by some opioid-exposed infants during pregnancy. It is characterized by hyperactivity of the central and autonomic nervous system and gastrointestinal (GI) system (Sanlorenzo et al., 2018).

B. The incidence of NAS per hospital births increased from 1.2 to 7.5 among rural infants and from 1.4 to 4.8 among infants born in urban communities (Sanlorenzo et al., 2018).

1. Maternal use of opioids is the major cause of NAS; however, NAS can occur with exposure to other drugs (Asti et al., 2015).
2. Drug withdrawal is self-limiting. Severe cases will require pharmacologic management (Asti et al., 2015).
3. When considering gender differences, male infants were more likely to be diagnosed and treated for NAS than female infants (Charles et al., 2017).

C. Cost and LOS (Corr and Hollenbeak, 2017).

1. U.S. hospital admissions related to NAS increased more than four-fold with a cost of approximately $316 million between 2003 and 2012.
2. LOS was 3.5 times longer for infants with NAS than for a baby without NAS (17 hospital days vs. 5 days).
3. It has been documented that Medicaid covered the cost for 82% of infants diagnosed with NAS in 2014 compared with 74% in 2004 (Winkelman et al., 2018).
4. Total hospital costs for infants with NAS covered by Medicaid increased by 5% between 2004 and 2014 ($65 million in 2004 to $462 million in 2014) (Winkelman et al., 2018).

Clinical Signs of Neonatal Abstinence Syndrome

A. NAS will occur in 55% to 94% of infants exposed to opioids in utero (Asti et al., 2015).

B. NAS will lead to several signs and behaviors related to neurologic irritability, poor feeding, and GI dysfunction (Corr and Hollenbeak, 2017).

C. Infants at risk for NAS should be monitored in the hospital for signs and symptoms. If mother was on a low-dose prescription opioid with a short half-life (e.g., hydrocodone) and no signs of withdrawal occur within 3 days, the infant can be discharged. If an infant is born to a mother on an opioid with a long half-life (methadone), the neonate should be observed for a minimum of 5 to 7 days (Hamdan, 2017).

D. General clinical signs can include:

1. Disturbances in the infant's CNS, metabolic, vasomotor, respiratory, and GI systems. (Hamdan, 2017).
2. GI signs such as poor feeding, regurgitation, vomiting, and diarrhea, leading to dehydration and poor weight gain (Hamdan, 2017).

3. CNS signs typically appear first such as irritability, jitteriness, tremors, and decreased or excessive crying. Hyperirritability is the hallmark sign of NAS and can lead to agitation, difficulty sleeping, inconsolable crying, and seizures. Seizures occur in 2% to 11% of neonates with NAS and are a serious sign that requires immediate treatment (Kocherlakota, 2014).

Clinical Signs Associated With Some Drugs

A. Exposure to cocaine and methamphetamine can produce signs of irritability, jitteriness, drowsiness, and respiratory distress (Smid et al., 2019).
B. Methadone can be associated with more severe signs of NAS; however, buprenorphine seems to produce mild signs of NAS, less treatment time, and decreased LOS (Tolia et al., 2018).
C. No clinical signs of NAS have been reported for intrauterine exposure to marijuana (Raffaeli et al., 2017); however, in one study signs of NAS were increased in infants whose mothers were on maintenance buprenorphine for substance abuse disorder and did or did not smoke marijuana during the third trimester of pregnancy (28% vs. 16%). This finding suggests that prenatal exposure to marijuana may influence the immediate postnatal period by worsening an infant's withdrawal signs (O'Connor et al., 2017).
D. Exposure to SSRIs does not exhibit signs of NAS. The signs observed, such as irritability, tremors, and agitation, are drug effects rather than signs of withdrawal. These infants are experiencing neonatal adaptation syndrome, which is self-limiting and resolves by 2 weeks (Hamdan, 2017).
E. It has been documented that the risk of NAS increases with co-exposure to antidepressants, benzodiazepines, and gabapentin. Marijuana combined with opioid exposure did not have an effect on the infant's need for pharmacologic treatment or LOS (Sanlorenzo et al., 2018).

Assessment of Neonatal Abstinence Syndrome

A. The Finnegan Scoring Tool (FANST) is the most widely used assessment tool for NAS. This comprehensive tool assigns a cumulative score based on the internal observation of 21 items relating to signs of neonatal abstinence (Hamdan, 2017) (Fig. 3.2).
B. It is important to maintain a 90% or greater interobserver reliability when using the FNAST (two nurses independently score during an examination and compare the signs scored). This should be done at least once a shift for infants hospitalized for NAS (D'Apolito, 2014).

Onset of Signs of Neonatal Abstinence Syndrome

A. Manifestations of NAS depend on the drug of exposure, the dose, the frequency of maternal use, and the infant's own metabolism and excretion of the active drug compounds. Withdrawal is a function of the drug's half-life: the longer the half-life, the later the onset of withdrawal signs. A longer half-life is also associated with a decreased likelihood of NAS in the infant (Hamdan, 2017). Infants prenatally exposed to short-acting drugs such as morphine require in-hospital observation for a minimum of 3 days compared with infants exposed to opioids with a long half-life (methadone and heroin) who require a minimum of 5 to 7 days of observation (Sanlorenzo et al., 2018) (Table 3.2).
B. Genetic testing has begun to determine which infants may or may not develop NAS. Those full-term infants with the *COMPT* (catechol-o-methyltransferase) and *ORPM1* (mu-opioid receptor) genes may help to predict which infants may or may not develop more severe signs of NAS (Cole et al., 2017).
C. Premature infants (<35 weeks GA) have a lower risk of developing NAS. This is due to their immature CNS, different total drug exposure, and lower fat deposits. Many drugs such as methadone, marijuana, heroin, cocaine, and benzodiazepines are lipid soluble; therefore, they accumulate less in premature infants (Hale, 2019).

Differential Diagnosis

A. Signs of NAS can mimic other neonatal conditions such as infection, hypoglycemia, hypocalcemia, hyperthyroidism, intracranial hemorrhage, hypoxic-ischemic encephalopathy, and hyperviscosity syndrome. If none of these diagnoses are present, a detailed interview with the mother, partner, friends, and family about their drug use is warranted (Hamdan, 2017).

Nonpharmacologic Treatment of Neonatal Abstinence Syndrome

A. All infants with NAS should receive nonpharmacologic care. The goal is to create a gentle, soothing environment with minimal stimulation (Stover and Davis, 2015).

NEONATAL ABSTINENCE SCORING SYSTEM

System	Signs and Symptoms	Score	AM						PM						Comments
Central Nervous System Disturbances	Excessive high-pitched (or other) cry Continuous high-pitched (or other) cry	2 3													Daily weight:
	Sleeps <1 hour after feeding Sleeps <2 hours after feeding Sleeps <3 hours after feeding	3 2 1													
	Hyperactive Moro reflex Markedly hyperactive Moro reflex	2 3													
	Mild tremors disturbed Moderate-severe tremors disturbed	1 2													
	Mild tremors undisturbed Moderate-severe tremors undisturbed	3 4													
	Increased muscle tone	2													
	Excoriation (specific area)	1													
	Myoclonic jerks	3													
	Generalized convulsions	5													
Metabolic/Vasomotor/Respiratory Disturbances	Sweating	1													
	Fever <101° (99°–100.8° F/37.2°–38.2° C) Fever >101° (38.4° C and higher)	1 2													
	Frequent yawning (>3 or 4 times/interval)	1													
	Mottling	1													
	Nasal stuffiness	1													
	Sneezing (>3 or 4 times/interval)	1													
	Nasal flaring	2													
	Respiratory rate >60/min Respiratory rate >60/min with retractions	1 2													
Gastrointestinal Disturbances	Excessive sucking	1													
	Poor feeding	2													
	Regurgitation Projectile vomiting	2 3													
	Loose stools Watery stools	2 3													
		Total Score													
		Initials of Scorer													

Fig. 3.2 FNAST. *(From D'Apolito, K., & Finnegan, L. (2010).* Assessing signs & symptoms of neonatal abstinence using the Finnegan scoring tool: An inter-observer reliability program *(2nd ed., p. 30). Retrieved from NeoAdvances.com.)*

Some methods to achieve this include (Mangat et al., 2019):

1. Quiet environment (decreased light and noise).
2. Swaddling.
3. 1:2 nurse–patient ratio.
4. Use of guidelines for skin care.
5. Adequate nutrition to decrease weight loss. Calories may need to be increased to 150 to 215 kcal/kg/day. Provide more frequent feedings and a lactose-free formula to help with reflux, diarrhea, and vomiting (Wiles et al., 2014).
6. Music therapy, nonoscillating water beds (Edwards and Brown, 2016).
7. Volunteers to cuddle infants (Holmes et al., 2016).
8. Ear laser acupuncture along with pharmacologic treatment (Raith et al., 2015), acupuncture with

Table 3.2

Onset of Clinical Signs of Neonatal Abstinence

Heroin	With 24 hours of birth
Methadone	42 to 72 hours after birth
Buprenorphine	40 hours; most severe signs 70 hours
Alcohol (ethanol)	3 to 12 hours
Barbiturates	Median onset 4 to 7 days; range 1 to 14 days
SSRI (neonatal adaptation syndrome)	Hours to days and resolve in 1 to 2 weeks

From Hudak, M., & Tan, R. (2012). Neonatal drug withdrawal. Academy of Pediatrics Committee on Drugs and the Committee on Fetus and Newborn. *Pediatrics, 129*(2), e540–e560.

tiny needles inserted into three or four points on the outer ear (Boucher, 2017), or pressure acupuncture when pressure is applied to areas of the head and limbs (Edwards and Brown, 2016).

9. Breastfeeding and prone vs. supine positioning (Edwards and Brown, 2016).
10. Rooming-in may improve breastfeeding, maternal satisfaction, and more maternal involvement in the care of her newborn (Holmes et al., 2016).

Pharmacologic Treatment of Neonatal Abstinence Syndrome (Raffaeli et al., 2017)

A. The goal of treatment is to control mild and severe signs of withdrawal and avoid possible complications such as seizures, weight loss, and dehydration.
B. Optimal treatment has not been established.
C. In the case of NAS to opioid exposure, opioids should be the first line of treatment.
D. Primary therapy can be supplemented with additional drugs if needed.
E. Pharmacologic management is typically provided in an inpatient setting; however, outpatient strategies have been described, such as discharge home on maintenance therapy with subsequent ambulatory care visits. This practice is not currently recommended because of safety. More studies are required to examine the efficacy of home detoxification programs for infants.

Drugs Used to Treat Neonatal Abstinence Syndrome

A. The most common drugs used to start therapy for opioid exposure is an opioid followed by phenobarbital or clonidine as adjunct therapy (Hamdan, 2017).
B. Oral morphine is the first-choice drug to treat NAS (Raffaeli et al., 2017). Nationally 80% of nurseries use oral morphine to treat NAS (Mangat et al., 2019). It has a short half-life (9 hours), making it easy to titrate to clinical signs, but requires frequent administrations (every 3 to 4 hours). There can be an increased risk of sedation and respiratory depression using oral morphine; therefore, close monitoring is required. The maximum dose for treatment of NAS with oral morphine is 0.2 mg/kg/dose (NeoFax Essentials, 2017).
C. Methadone is also used to treat NAS. Methadone has a longer half-life (26 to 30 hours), allowing more stable blood level over time and resulting in less frequent dosing (Raffaeli et al., 2017). One study suggested methadone was superior to oral morphine; however, the methadone used in that trial was a special formulation not currently used in practice (Davis et al., 2018).
D. Sublingual buprenorphine for NAS seems to be associated with shorter duration of opioid treatment and hospitalization compared with oral methadone therapy; however, little is known about the pharmacokinetics and pharmacodynamics. More research is needed (Raffaeli et al., 2017).
E. Clonidine is a nonnarcotic medication that is used as a secondary treatment. Limited data suggest that clonidine alone or with an opioid may be effective in decreasing adverse effects and treatment time (Streetz et al., 2016). When clonidine was compared with oral morphine ($n = 16$ and 15, respectively), LOT was significantly less with clonidine (28 days vs. 30 days) ($p = 0.02$) (Bada et al., 2015).
F. Phenobarbital can be used as adjunct therapy with an opioid. Phenobarbital is typically added when the maximum opioid dose is reached (Mangat et al., 2019). Phenobarbital has no effect on the GI signs of withdrawal such as diarrhea; therefore, it should be used in conjunction with an opioid (Kraft et al., 2017).
G. Oral sucrose should not be used to treat NAS. Infants with NAS have poorly functioning endogenous opioid systems due to intrauterine exposure to methadone or other opioids. Therefore, oral sucrose is ineffective in calming opioid-exposed infants displaying symptoms of NAS (Pediatric Care Online, 2017).

Standardization of Pharmacologic Management

A. It has been recommended that the type of drug used to treat NAS is not as important as strict adherence to a treatment protocol (standardization). Standardization is more effective in decreasing LOS (Hall et al., 2015).
B. Each nursery that cares for infants with NAS should develop a protocol regarding comprehensive treatment for infants who are at risk for NAS or have NAS (McQueen and Murphy-Oikonen, 2016).

		TIME													
Signs & Symptoms	**Score**	**AM**						**PM**							**Comments**
CNS Disorders															
Crying: Excessive High Pitched Crying: Cont. High Pitched	**2** **3**														
Sleeps <1 hr after feeding Sleeps <2 hr after feeding Sleeps <1 hr after feeding	**3** **2** **1**														
Hyperactive Moro Reflex Markedly Hyperactive Moro Reflex	**2** **3**														
Mild Tremors: Disturbed Mod-Severe Tremors: Disturbed	**1** **2**														
Mild Tremors: Undisturbed Mod-Severe Tremors Undisturbed	**3** **4**														
Increased Muscle Tone	**2**														
Excoriation (specific area)	**1**														
Myoclonic Jerk	**3**														
Generalized convulsions	**5**														
Metabolic, Vasomotor, and Respiratory Disturbance															
Sweating	**1**														
Fever ≤101 (37.2° to 38.3° C) Fever >101 (38.4° C)	**1** **2**														
Frequent Yawning (>3)	**1**														
Mottling	**1**														
Nasal Stuffiness	**1**														
Sneezing (>3)	**1**														
Nasal Flaring	**2**														
Respiratory rate (>60/min) Respiratory rate (>60/min with retractions	**1** **2**														
Gastrointestinal Disorders															
Excessive Sucking	**1**														
Poor Feeding	**2**														
Regurgitation Projectile Vomiting	**2** **3**														
Loose Stools Watery Stools	**2** **3**														
Total Score															
Initials of Scorer 1															
Initials of Scorer 2															
Interobserver Reliability %															
Average daily score															

Adapted from Finnegan, L. (1990). Neonatal abstinence syndrome. In N. Nelson (Ed.), *Current therapies in neonatal-perinatal medicine* (pg. 317). Philadelphia, PA: B. C. Decker.

Environment to Care for Infants with Neonatal Abstinence Syndrome

A. There is no evidence that infants with NAS require treatment in the neonatal intensive care unit (NICU). The environment in some NICUs may impose barriers to implementing nonpharmacologic care (Grossman et al., 2017).
B. Rooming-in is another option. This allows mothers and infants to stay together on a pediatric floor for observation and treatment. It has been reported that rooming-in can decrease the infant's LOT by 5.7 days and LOS by more than 5 days (Howard et al., 2017).
C. Opening a special unit with private hospital rooms can provide a better environment to implement environmental changes, meet developmental needs, and minimize neurobehavioral signs of NAS (Saunders et al., 2014).

Discharge and Follow-Up

A. Discharge should occur when the following criteria are met:
   1. The infant is taking oral feedings and is adequately gaining weight.
   2. The infant is physiologically stable.
   3. The infant is showing neurobehavioral recovery (can reach full alert state, appropriately responds to social stimuli, can be consoled with appropriate measures) (Hamdan, 2017).
B. The risk of readmission is inversely related to the length of birth hospitalization (the longer the initial hospitalization, the less incidence of hospital readmission) (Patrick et al., 2015).
C. Provide follow-up care in the first few weeks to months of life to assess growth, behavioral characteristics, and motor ability (Raffaeli et al., 2017).
D. Prolonged follow-up care is important to detect short- and long-term problems. The focus should be on neurodevelopmental, nutritional, psychobehavioral, and social adjustments (Raffaeli et al., 2017).
E. Prognosis widely varies and depends on the family, socioeconomic variables, and whether either or both parents continue to use illicit drugs (Hamdan, 2017).
F. Assess family support (Kocherlakota, 2014).

The Future (Hamdan, 2017)

A. Rooming-in is a promising strategy when managing infants with NAS; however, there are drawbacks, such as lack of funding, lack of personnel, and lack of appropriately designed hospital units. More research is needed in this area.
B. Additional studies are needed to evaluate the efficacy of caring for infants with NAS outside the NICU (Loudin et al., 2017).
C. Studies to determine the best medications to treat NAS are needed. Whether short-acting drugs, such as morphine, or longer-acting drugs, such as methadone or buprenorphine, will provide better outcomes for infants who require pharmacologic therapy is not currently known (Hamdan, 2017).
D. More pharmacogenetic studies are needed to determine if a prediction can be made regarding which infants will and will not develop NAS.
E. More research on the use of antiaddiction vaccines that may block the pharmacologic effects of drugs (Horton, 2015).

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CHAPTER 4

Adaptation to Extrauterine Life

M. Terese Verklan

OBJECTIVES

1. Identify the primary features of fetal circulation.
2. Identify physiologic changes that occur during the transition to extrauterine life.
3. Identify routine care considerations for a newborn infant during the transition period.
4. Identify signs and symptoms of common problems in the transition period.
5. Define the methods and intervention times for parental teaching.

The transition period is considered to be the first 6 to 10 hours of life, but more than a period of time, it is a process of physiologic change in the newborn infant that begins in utero as the child prepares for the transition from intrauterine placental support to extrauterine self-maintenance. The fetus prepares for transition during the course of gestation in such ways as storing glycogen, producing catecholamines, increasing surfactant reserves, and depositing brown fat. The neonate's ability to accomplish the transition to extrauterine life will depend on gestational age and the quality of placental support during gestation, as well as any physical defects or anomalies that may affect major organ systems.

Anatomy and Physiology

CHARACTERISTICS OF PLACENTAL–FETAL CIRCULATION

A. Placenta.
   1. Blood oxygenation and elimination of waste products of metabolism. Transfer of O_2 and Co_2 across the placenta is by simple diffusion.
   2. High rate of metabolism. The placenta uses one third of all the oxygen and glucose supplied to it by the maternal circulation for its own metabolic needs.
   3. Low-resistance circuit. The placenta receives approximately 50% of fetal cardiac output.
   4. Characteristics of uterine venous blood as it enters the intervillous space: Pco_2 of 38 mm Hg, Po_2 of 40 to 50 mm Hg, and pH of 7.36.

B. **Fetal shunts/blood flow (Fig. 4.1)** (Moore et al., 2015)**.**
   1. Umbilical vein (Po_2 32 to 35 mm Hg). It carries oxygenated blood from the placenta to the fetus.
   2. Ductus venosus. Forty percent to 60% of the umbilical venous blood bypasses the liver through the ductus venosus to the inferior vena cava (IVC). It is a low-resistance channel that allows a significant portion of relatively well-oxygenated blood to enter the heart directly; the other half passes through the liver and enters the IVC via the hepatic veins. This mixing of blood slightly lowers the Po_2.
   3. IVC blood and the blood from the coronary sinuses (Po_2 = 25 to 28 mm Hg). This blood is largely deflected across the right atrium, through the foramen ovale, and into the left atrium. In contrast, most of the blood from the superior vena cava (SVC), also returning to the right atrium, is deflected to the right ventricle (see item 6, later). The crista dividens (lower edge of the septum secundum) separates the flow of blood from the IVC into two streams, with 50% to 60% of the blood from the IVC being diverted across the foramen ovale into the left atrium (Blackburn, 2018) and the remainder of blood from the IVC remaining in the right atrium and mixing with poorly oxygenated blood from the SVC and coronary sinus.
   4. Left atrium. Blood is received from the right atrium via the foramen ovale and mixes with a small amount of blood returning from the lungs via the pulmonary veins.
   5. Left ventricular blood (Po_2 = 25 to 28 mm Hg). Virtually all this blood is from the IVC by way of the right atrium–foramen ovale–left atrium pathway. Left ventricular blood is pumped out through the aorta to the brain from the upper part of the aortic arch. Approximately 90% of the blood from the ascending aorta feeds the coronary, carotid, and

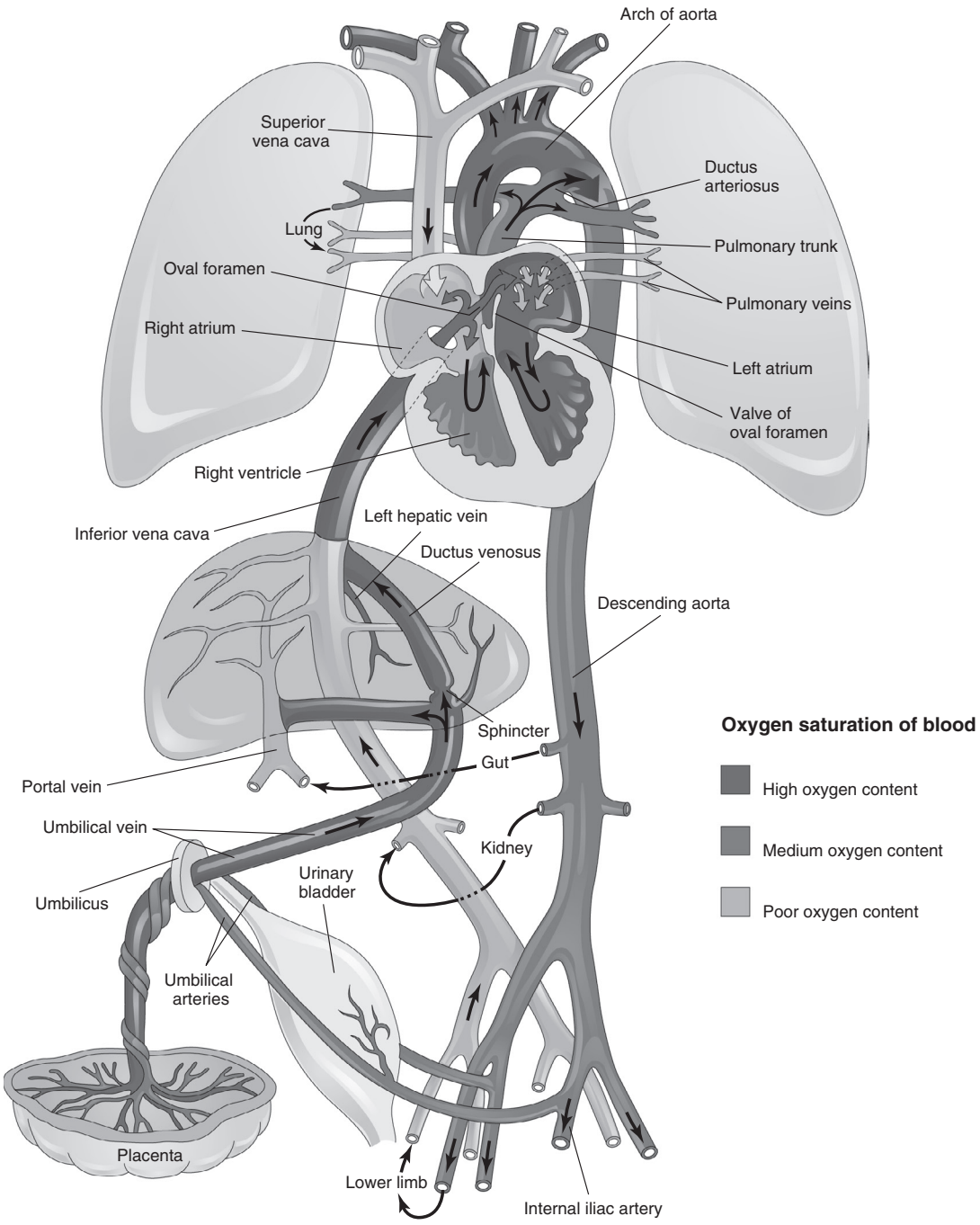

Fig. 4.1 Simplified scheme of fetal circulation. *Shaded areas* indicate oxygen saturation of the blood; *arrows* show course of fetal circulation. Organs are not drawn to scale. *(From Moore, K. L., Persaud, T. V. N., & Torchia, M. G. [2013].* The developing human: Clinically oriented embryology *[9th ed.]. Philadelphia, PA: Elsevier Saunders.)*

subclavian arteries and thus the brain and upper extremities.

6. The SVC. Unoxygenated blood returning from the brain and upper extremities is received by the SVC. Ninety-seven percent enters the right atrium and flows to the right ventricle through the tricuspid valve; only 3% flows to the left atrium via the foramen ovale.
7. Right atrium. Some mixing occurs here between the unoxygenated SVC blood and the oxygenated IVC blood not shunted directly into the left atrium via the foramen ovale.
8. Right ventricle. The dominant ventricle (Po_2 = 19 to 22 mm Hg) ejects about 66% of the total cardiac output. Most of the blood is shunted across the ductus arteriosus, away from the lungs, and into

the descending aorta to supply the kidneys and intestines. It then divides into two arteries, which subsequently return back to the placenta.

9. Ductus arteriosus. Equal in size to the aorta, it connects the pulmonary artery to the descending aorta. The blood flows right to left (pulmonary artery to aorta) across the ductus arteriosus because of high pulmonary vascular resistance and low placental resistance. Patency is maintained by the low oxygen tension in utero and by the vasodilating effect of prostaglandin E_2.
10. Low pulmonary blood flow (only 10% to 12% of the right ventricular output). This results from high pulmonary vascular resistance (Blackburn, 2018).
11. Descending aorta. It supplies the kidneys and intestines, divides into two arteries, and returns blood to the placenta for oxygenation.

FETAL LUNG CHARACTERISTICS

A. **Decreased blood flow.** In part, the decrease is caused by compression of the pulmonary capillaries by the fetal lung fluid.
B. **Pulmonary arteries.** The small pulmonary arteries of the fetus have a thick, muscular medial layer; they are very reactive and are actively constricted by the low Po_2 normally present during fetal life. Pulmonary vascular resistance increases throughout fetal life.
C. **Lung fluid secretion.** Fetal lungs actively secrete fluid, which decreases near term. At term, the lungs contain 30 mL of plasma ultrafiltrate per kilogram of body weight. This is comparable to a postnatal thoracic gas volume of 25 mL/kg. An adequate fluid volume is necessary for lung development. Fluid moves into and out of the lungs through the trachea.
D. **Fetal breathing.** In-utero fetal breathing movements have been detected as early as 11 weeks of gestation. They contribute to lung development.
E. **Surfactant.** Surfactant is secreted into the amniotic fluid by the fetal lung before 20 weeks of gestation. The absolute quantity of surfactant increases throughout gestation in both the lung and amniotic fluid and can support extrauterine respiration at approximately 34 weeks of gestation.

FETAL METABOLISM AND HEMATOLOGY

A. **Glucose.** Fetal blood glucose concentrations are 70% to 80% of maternal blood glucose concentrations. Glucose is exchanged via the placenta by facilitated diffusion.
B. **Glycogen**. Large glycogen stores (2 to 10 times that of an adult) provide large energy reserves to sustain the newborn infant through the transition period.
C. **Hemoglobin.** Fetal hemoglobin has an increased affinity for oxygen. Fetal hemoglobin is progressively replaced by adult hemoglobin from weeks 32 to 36 of gestation and is approximately 80% of the total hemoglobin at term.

LABOR

A. **Placenta.** Maternal placental perfusion ceases with uterine contractions.
B. **Stress hormones**. High concentrations of stress hormones (predominantly norepinephrine) are released as a direct effect of the resultant hypoxia on the adrenal medulla.

DELAYED CORD CLAMPING

If feasible, delay clamping the cord for 30 to 60 seconds, especially in preterm neonates, to provide an adequate placental transfusion (Katheria and Finer, 2018; Raju, 2012).

CARDIOPULMONARY ADAPTATION AT BIRTH

A. Cardiovascular adaptation (Fig. 4.2) (Blackburn, 2018; Moore et al., 2015).
   1. Umbilical cord is clamped.
      a. Placenta is separated from the circulation, and the umbilical arteries and veins constrict.
      b. As the low-resistance placental circuit is removed, there is a resultant increase in systemic blood pressure; the systemic vascular resistance then exceeds the pulmonary vascular resistance.
   2. The three major fetal shunts (ductus venosus, foramen ovale, and ductus arteriosus) functionally close during transition (Blackburn, 2018).
      a. Ductus arteriosus. The lungs now provide more efficient oxygenation of the blood, and the arterial oxygen tension rises. This rise in Po_2 is a potent stimulus to constriction of the ductus arteriosus. Increased pulmonary blood flow increases the metabolism of circulating prostaglandins, and the loss of prostaglandins contributed by the placenta enhances the constrictive effects of oxygen on the ductus.
      b. Foramen ovale. The fall in pulmonary vascular resistance results in a drop in right ventricular and right atrial pressure, and the increased systemic vascular resistance results in an increase in left atrial and left ventricular pressures, causing the foramen ovale to close against the atrial septum.
         1) The foramen ovale becomes sealed by the deposit of fibrin and cell products during the first month of life.
         2) Until the foramen ovale is anatomically sealed, anything that produces a significant increase in right atrial pressure can reopen the foramen ovale and allow a right-to-left shunt.
      c. Ductus venosus. Absent umbilical venous return leads to closure of the ductus venosus. It functionally closes within 2 to 3 days and becomes the ligamentum venosum.

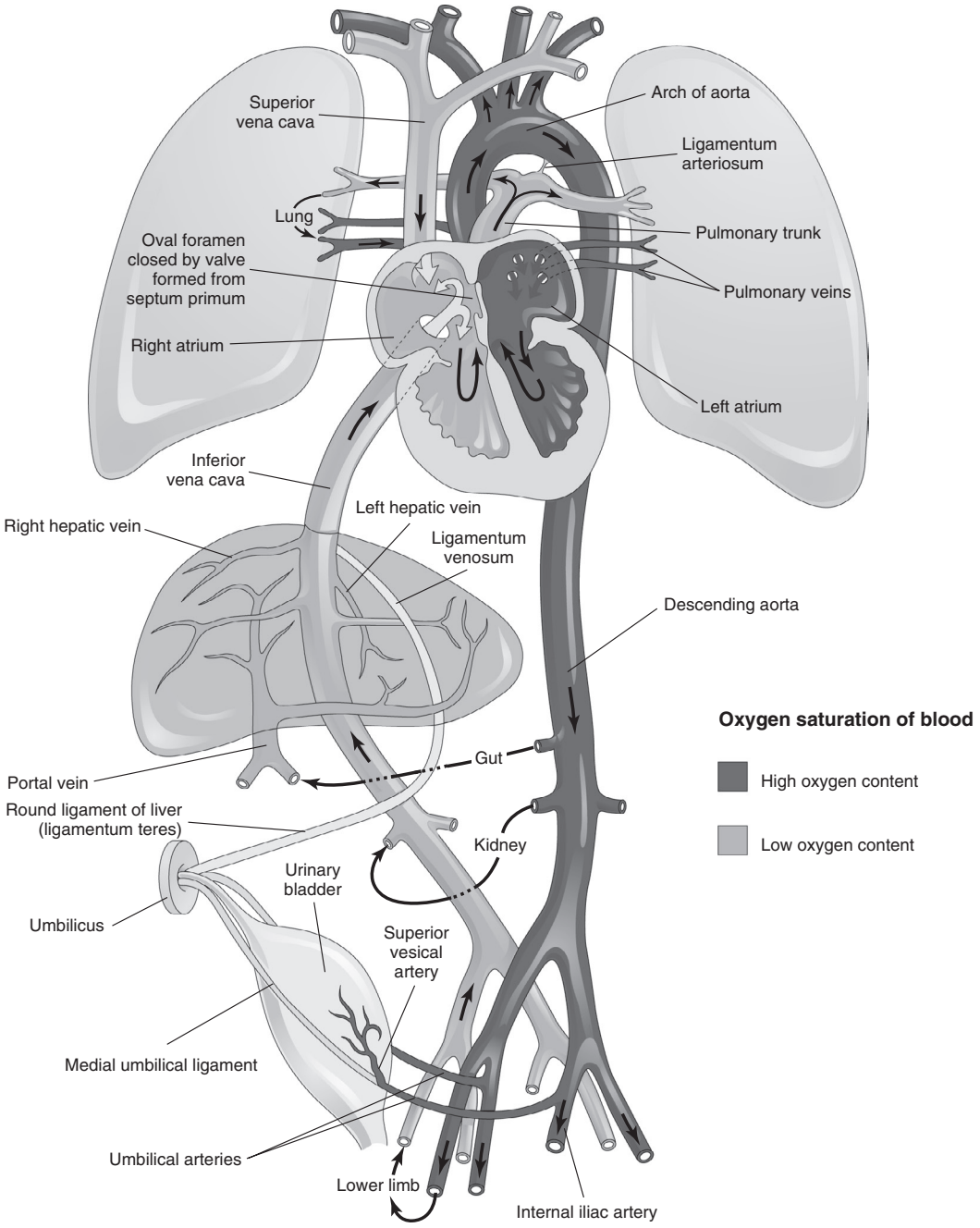

Fig. 4.2 Simplified representation of circulation after birth. Adult derivatives of fetal vessels and structures that become nonfunctional at birth are also shown. *Arrows* indicate course of neonatal circulation. Organs are not drawn to scale. *(From Moore, K. L., Persaud, T. V. N., & Torchia, M. G. [2013].* The developing human: Clinically oriented embryology *[9th ed.]. Philadelphia, PA: Elsevier Saunders.)*

3. Postnatal circulation (see Fig. 4.2) (Blackburn, 2018; Moore et al., 2015).
   a. Systemic venous blood enters the right atrium from the SVC and the IVC.
   b. Poorly oxygenated blood enters the right ventricle and passes through the pulmonary artery into the pulmonary circulation for oxygenation.
   c. The oxygenated blood returns to the left atrium through the pulmonary veins.
   d. This blood passes through the left ventricle and into the aorta to supply the systemic circulation with oxygenated blood.

B. Pulmonary adaptation (Blackburn, 2018; Hanson et al., 2018).
   1. The lungs as the organ of gas exchange. Intermittent breathing begins in utero long before delivery and, after birth, is a continuation of movements and reflexes that have been well established.

2. Stimuli for initiating respiration. The mild hypercapnia, hypoxia, and acidosis that result from normal labor are due partially to the intermittent cessation of maternal–placental perfusion with contractions. The decreased pH stimulates the respiratory center directly; the low Po_2 and high Pco_2 stimulate the respiratory center by means of central and peripheral chemoreceptors (Gauda and Martin, 2018). Other stimuli include cold, light, noise, and touch.
3. Entry of air into lungs with the first breath.
   a. Aeration of the lungs drives fluid into the interstitium; it is then absorbed through the lymphatic and pulmonary circulation. The rate at which this process occurs is variable, and fine crackling rales may be audible throughout the lungs until this process is completed.
   b. The pulmonary vessels respond to the increase in Po_2 with vasodilation. Pulmonary vascular resistance progressively decreases until adult levels are reached by 6 to 8 weeks of age (Blackburn, 2018).
4. Inspiration of air and expansion of lungs. The thoracic squeeze (during labor and vaginal delivery) empties the lungs of approximately one third of the fetal lung fluid; the subsequent recoil of the chest wall causes inspiration of air and expansion of the lungs. Negative intrathoracic pressures generated with the first breath may be as high as 20 to 70 cm H_2O because of the mechanical advantage created by the high resting level of the diaphragm in the nonaerated lung (Niermeyer et al., 2016). Subsequent breaths in the normal newborn infant require 15 to 20 cm H_2O pressure.
5. Establishing the functional residual capacity (FRC) is essential to maintaining lung mechanics and gas exchange (Hanson et al., 2018).
   a. The newborn chest wall is very compliant and prone to collapse at the end of exhalation.
   b. Maintenance of a normal FRC depends on increased expiratory resistance through glottic narrowing (laryngeal adduction), continuing inspiratory muscle activity throughout expiration, and increased rates of breathing to limit expiratory time.
6. The work of inspiration is predominately related to overcoming the surface tension of the walls of the terminal lung units at the gas–tissue interface. On expiration, the ability to retain air depends on surfactant (Hanson et al., 2018).
   a. Surfactant is a complex of phospholipids, neutral lipids, and proteins produced and secreted by type II alveolar pneumocytes.
   b. Dipalmitoyl phosphatidylcholine (DPPC) is the surface active component that decreases the surface tension of the alveoli to almost zero at the air–liquid interface.
   c. Surfactant production is developmentally regulated and induced by glucocorticoids and factors that increase intracellular cyclic adenosine monophosphate (AMP), such as terbutaline and β-adrenergic agonists.
   d. As the surfactant lowers the surface tension in the alveolus at end expiration, it stabilizes the alveoli and prevents collapse.

Routine Care Considerations During Transition (Gardner and Hernandez, 2016; Taylor et al., 2018; Walker, 2018)

A. Initial newborn evaluation should include:
   1. History: prenatal, intrapartum, postpartum, family.
   2. Complete physical examination.
      a. Close attention to significant high-risk factors and complications.
   3. Evaluate need for additional diagnostic testing and follow-up.
   4. Education and counseling to family.

B. **Assessment/observation.** Within 2 hours of birth, the neonate's health status should be evaluated and the neonate assessed for risks that may complicate the transition to extrauterine life (American Academy of Pediatrics [AAP] and American College of Obstetricians and Gynecologists [ACOG], 2017; Taylor et al., 2018; Walker, 2018).
   1. Body measurements. Head circumference, length, and weight are recorded.
   2. Vital sign assessment. Vital signs recorded on admission will include heart rate, respiratory rate, and axillary temperature. Universal blood pressure screening in the well newborn infant is not warranted (AAP, 1993).
   3. Gestational age assessment. Weight, head circumference, and length are graphed against the assessed gestational age and medical record (refer to Chapter 7).
   4. Clinical changes. During the first hours of life, vital signs stabilize and the newborn proceeds through sleep–wake cycles associated with readiness-to-feed behaviors. The time sequence of changes is altered in infants with low Apgar scores, immaturity, maternal medications, and intrinsic disease (refer to Chapter 5).
   5. Head-to-toe physical examination (refer to Chapter 7). The following findings seen during transition are within normal limits as the infant progresses through the physiologic changes described under "Cardiopulmonary Adaptation at Birth" earlier.
      a. Skin.
         1) Acrocyanosis. Vasoconstricted peripheral vessels result in a mottled appearance; peripheral

pulses are decreased initially. (These findings are sequelae of catecholamine release, mild acidosis, and cold stress.)
2) Petechiae of the face and facial bruising. A vertex presentation, a rapid second stage of labor, or a tight nuchal cord may result in these skin changes. (With severe facial bruising, central color may be assessed by looking at the mucous membranes in the mouth.)

b. Head.
1) The neonate's head is large relative to the body. During a vaginal delivery, considerable molding of the skull bones may take place to facilitate passage through the birth canal. Molding resolves during the first hours and days.
2) Caput succedaneum (edema of the presenting part of the scalp, caused by pressure that restricts the return of venous and lymph flow during vaginal delivery) may be present.

c. Respirations/breath sounds.
1) Initially, coarse rales and moist, tubular breath sounds. These breath sounds may continue until clearing of lung fluid is complete.
2) Prolonged expiratory phase.
3) Respiratory rate of 30 to 60 breaths per minute.
4) Grunting and retracting (intercostal and substernal). These findings may be present during the first hours of life as lung fluid is cleared.

d. Heart sounds.
1) Second heart sound may be loud during the first 2 hours; splitting of the second heart sound is usually detectable at 2 to 4 hours of age and increases during the next 12 hours (pulmonic ahead of aortic component).
2) Soft grade 2/6 systolic murmur may be present; represents a left-to-right shunt across the ductus arteriosus before its closure.

e. Heart.
1) Normal heart rate 120 to 160 beats per minute (bpm); increased initially, with a mean peak of 180 bpm, and then decreased or irregular.
2) Consistently high or low heart rate suggests a pathologic condition.

f. Intestines.
1) Blood flow is reduced initially.
2) As the bowel begins to fill with air, normal motility and bowel sounds are present within 15 minutes.
3) The normal term neonate passes meconium within the first 24 hours after birth. If a term neonate has not passed meconium by 48 hours after birth, the lower gastrointestinal (GI) tract may be obstructed (refer to Chapter 29).

g. Urinary function.
1) Urine is normally passed within the first 24 hours after birth.
2) Failure to void within the first 24 hours may indicate genitourinary obstruction or abnormality (refer to Chapter 33).

h. Extremities. Findings may include deformities resulting from the intrauterine position.

C. **Thermoregulation considerations in the nursery** (Gardner and Hernandez, 2016). The admission assessment and observation should be done in a controlled environment, such as a radiant warmer or incubator. These heat sources provide warmth and prevent heat loss so that the infant maintains a normal temperature without increasing oxygen consumption, using glucose stores, or exceeding brown fat stores in the process of nonshivering thermogenesis (mediated by norepinephrine released by cold stress). Normal axillary ranges are 97.7° to 99.5° F (36.5° to 37.5° C) for the term neonate and 97.3° to 98.6° F (36.3° to 36.9° C) for the preterm neonate. Hypothermia and hyperthermia occur when the infant's attempts to maintain a normal temperature fail, which has serious metabolic consequences for the newborn infant (refer to Chapter 6).

1. Monitor temperature. Check axillary temperature every 30 minutes to 1 hour during transition while the infant is under a radiant warmer. Avoid hyperthermia (skin temperature greater than 37° C or axillary temperature greater than 37.5° C). Note: Monitoring the axillary temperature allows time for successful intervention before a fall in core temperature indicates failure of the body's heat-regulation mechanism.
2. Check temperature at least every 4 hours until the infant's condition is stable and then every 8 hours until discharge.
3. Environmental temperature (incubator or warmer). Record environmental temperature with temperature checks of the infant to monitor his or her environmental requirements. Note: These requirements can be checked against the normal ranges of neutral thermal environmental temperature needs as a tool in evaluating an infant's condition.
4. If the high-risk neonate is stable, thermoregulatory needs may be met by placing the infant skin-to-skin with the mother's naked chest and covering both with a blanket. The neonate's axillary temperature still needs to be monitored at the appropriate intervals.
5. First bath. Delay bath until body temperature has stabilized and is within normal limits. Check temperature 30 minutes after the bath and 1 hour after transfer to open crib. It may not be feasible to bathe a high-risk neonate displaying difficulties with transition until days after birth.

D. Transition nursery medications (AAP and ACOG, 2017; Taylor et al., 2018).
   1. Eye care. Administered to both eyes before 1 hour of age in all neonates, regardless of type of delivery.
      a. Recommendation. Apply a 1- to 2-cm ribbon of sterile ophthalmic ointment containing 0.5% erythromycin or 1% tetracycline, or an ophthalmic solution of 2.5% povidone–iodine for prophylaxis of ophthalmia neonatorum due to *Neisseria gonorrhoeae*. Prophylaxis for *Chlamydia trachomatis* requires erythromycin or tetracycline.
      b. Procedure. Instill medication into conjunctival sac within 1 hour of birth; however, this may be delayed until after the first breastfeeding. The medication should not be flushed from the eye after application. A new tube is used for each infant.
   2. Vitamin K_1 (phytonadione). Administer vitamin K within 1 hour of birth.
      a. Recommendation. Every neonate should receive a single parenteral dose of natural vitamin K (phytonadione). Administer 0.5 mg if the infant weighs less than 1.5 kg and 1 mg if the infant weighs more than 1.5 kg.
      b. Risk of deficiency. Maternal dietary inadequacy of vitamin K, hepatic immaturity, reduced liver stores, and absence of intestinal flora predispose the infant to deficiency of vitamin K; gut bacteria are a substantial source. Vitamin K is needed to promote the hepatic biosynthesis of vitamin K–dependent clotting factors, including prothrombin (factor II), proconvertin (factor VII), plasma thromboplastin component (factor IX), and Stuart factor (factor X). Deficiency results in hemorrhagic disease of the newborn (HDN), now referred to as *vitamin K–dependent bleeding* (refer to Chapter 31).
   3. Hepatitis vaccine and hepatitis B immunoglobulin (HBIG) (Pammi et al., 2016).
      a. Rate of hepatitis B virus (HBV) infection. If the mother is hepatitis B surface antigen (HBsAg) and hepatitis B "e" antigen (HBeAg) positive, the infant has a 90% risk of HBV infection in the first 12 months if treatment is not received. There is a 20% risk of HBV infection if the mother is positive for HBsAg only.
      b. Chronicity. In the absence of treatment, the neonate will likely become a carrier and will eventually develop primary hepatocellular carcinoma.
      c. Maternal HBsAg-positive treatment recommendations.
         1) Child is bathed as soon as temperature is stable.
         2) Hepatitis B vaccine (Engerix-B 10 mcg or Recombivax-HB 5 mcg) and HBIG 0.5 mL intramuscularly (prepared from plasma to contain a high titer of antibody against HBsAg) should be administered before 12 hours of age; may be given concurrently at different sites; 85% to 95% effective in preventing both HBV infection and the chronic carrier state.
         3) Remaining doses of hepatitis B vaccine are given at 1 and 6 months of age.
      d. Maternal HBsAg-negative treatment recommendations.
         1) Hepatitis B vaccine should be administered to all infants, including those born to HBsAg-negative mothers.
         2) Hepatitis B vaccine (Engerix-B 10 mcg or Recombivax-HB 5 mcg) is administered before discharge from the hospital. The second dose is administered at 1 to 2 months of age, and the third dose at 6 to 18 months of age.
      e. Unknown maternal HBsAg status at delivery. Follow the schedule for maternal HBsAg-positive status. Additional HBIG administration will depend on the results of maternal serologic screening done within 12 hours after delivery.
      f. Premature infants with birth weight less than 2 kg born to HBsAg-negative mothers should receive the vaccine just before hospital discharge if the infant weighs more than 2 kg, or the dose is delayed until 2 months of age when other routine immunizations are given. All premature infants born to HBsAg-positive mothers should receive immunoprophylaxis (HBIG) and vaccine beginning as soon as possible after birth, followed by appropriate postvaccination testing.

E. Glucose needs/first feeding (Blackburn, 2018; Rozance et al., 2016; Taylor et al., 2018).
   1. The stress of delivery causes increased conversion of fats and glycogen to glucose for the increased energy needs of temperature maintenance, skeletal muscles, and breathing and crying. Breakdown products of this conversion are glucose, free fatty acids, and glycerol.
   2. Hepatic glycogen is mobilized immediately after birth in response to the increased catecholamines to provide a continuing source of glucose to the brain in the absence of placental supply; in a healthy term infant, up to 90% of the hepatic glycogen stores may be consumed by 3 hours of life.
   3. Blood glucose concentration at birth is about 85% of the maternal level. The last maternal meal, the duration of labor, the mode of delivery, the type and amount of intravenous (IV) fluids administered to the mother, and medications given to the mother all influence the actual concentration of glucose. The glucose level then falls for 1 to 2 hours, followed by an increase and stabilization at

mean levels of approximately 70 mg/dL by the age of 3 hours in healthy, nonstressed infants.

4. A screening blood glucose test (on capillary whole blood) should be performed in infants with risk factors at 30 minutes to 1 hour of age. A glucose level less than 40 mg/dL at any time in any newborn infant is an indication for evaluation and treatment. The goal is to maintain the glucose value at greater than 40 to 45 mg/dL in the first 72 hours of life and greater than 40 to 50 mg/dL thereafter. After 72 hours of life, plasma glucose concentrations should approximate that of older children and adults. Note: The whole-blood glucose level on the screening test is usually 10% to 15% lower than the corresponding serum or plasma level because the erythrocytes will continue to metabolize the glucose in the sample. Risk factors include:
   a. Asphyxia, cold stress, increased work of breathing, and sepsis, which lead to an increased metabolic response and increased use of glucose.
   b. Reduced stores of glucose in premature and small-for-gestational-age infants.
   c. Hyperinsulinemia in infants of mothers with diabetes or gestational diabetes and in large-for-gestational-age infants, resulting in rapid removal of glucose from the circulation.
   d. Any symptoms of a low blood glucose level. An infant may have jitteriness, irritability, seizures, hypothermia, temperature instability, lethargy, poor feeding, emesis, apnea, pallor, cyanosis, and weak or high-pitched cry (see also "Common Problems and Clinical Presentation," item D: Metabolic problems). Note: Capillary samples from an unwarmed heel may lead to a falsely low glucose value because of stasis of blood and ongoing transfer of glucose to the cells (refer to Chapter 9).
5. If the high-risk neonate is able to safely tolerate enteral feedings, early, frequent feedings should be given on demand; frequency is not to exceed 4 hours between feedings (maximum of 3 hours between feedings for infants weighing <2.5 kg). Allow the infant to begin cue-based feeding when he or she is demanding nutrition and when evaluation findings are within normal limits; nursing or formula feeding can be used (type of formula is by family's or physician's choice). Several infant-driven feeding scales can help determine the neonate's readiness for oral feeding, the quality of the feeding, and techniques used to assist the neonate to orally feed.
   a. Evaluation before feeding.
      1) Physical examination. Bowel tones are normal, and abdomen is soft and nontender. Sucking reflex is normal, with no excessive mucus. Passage of an orogastric tube is indicated before feeding if questions exist regarding esophageal patency. Anus and nares are patent. The respiratory rate is less than 60 breaths per minute, and the pattern of breathing is normal.
      2) Contraindications to nippling the feeding or to breastfeeding (consider gavage feeding for these infants, if general condition permits).
         a) Choanal atresia.
         b) Respiratory rate greater than 60 breaths per minute without other signs of respiratory distress.
         c) Weak suck.
         d) Absent coordination of suck and swallow.
      3) Contraindications to any enteral feedings.
         a) Cyanosis.
         b) Severe birth asphyxia.
         c) Shock.
         d) Increased work of breathing and oxygen requirement.
         e) Suspicion of GI obstruction.
   b. Guidelines for feeding in case of transient asymptomatic hypoglycemia.
      1) May breastfeed or be offered formula (by nipple or gavage) if there are no contraindications to enteral feedings (see "Contraindications," item a(3), earlier) and the infant is active and vigorous.
      2) Check glucose level 30 minutes to 1 hour after feeding is given.
   c. Although dextrose gel may improve maternal–infant bonding and improve the rate of exclusive breastfeeding after discharge, the effectiveness of 40% dextrose gel administered to the buccal mucosa for the treatment of neonatal hypoglycemia remains unclear (Chandrasekharan and Lakshminrusimha, 2017; Weston et al., 2016). However, if given along with the feeding, hypoglycemia may be decreased in at-risk term and late preterm infants in the first 48 hours after birth (Harris et al., 2013; Newman and Bunch, 2017).
   d. Indications for IV glucose infusion (see "Initial Stabilization of the Sick Newborn Infant").
      1) Hypoglycemia is persistent and symptomatic.
      2) Enteral feedings are contraindicated.
      3) Oral feedings do not maintain normal glucose levels.
      4) Initial glucose screening level is less than 40 mg/dL.

F. Ongoing teaching during transition.
   1. Discuss with family the infant's ability to see and hear, with a preference for black–white contrast initially and the sound of a higher-pitched voice.
   2. Demonstrate or point out infant's response to stimuli (tactile, visual, auditory): self-consolability, body movements, gaze, head turning.

3. Discuss physical findings.
   a. Transient: head molding, acrocyanosis, birth trauma, positional deformities.
   b. Permanent: congenital anomalies, birthmarks.
4. A stable infant may stay with the family from birth through recovery to the postpartum period with appropriate observation and teaching provided by all staff members in contact with the family unit.

G. If newborn transitioned in a nursery, he or she may be transferred when the following are stable.
1. Temperature, heart rate, respiratory rate.
2. Glucose level.
3. Normal physical assessment findings or abnormal findings that do not require continuous observation or immediate intervention or treatment.

Recognition of the Sick Newborn Infant

REVIEW OF PERINATAL HISTORY (REZAEE ET AL., 2013)

A. **Ultrasonographic–biophysical profile:** estimated date of confinement, evidence of congenital anomalies, twins, breech, preterm, and intrauterine growth restriction.
B. **Medications or history of substance abuse:** alcohol, nicotine, cocaine, opiates, marijuana, amphetamines, tocolytics, anticonvulsants, anticoagulants, and analgesics/anesthetics.
C. **Maternal illnesses:** pregnancy-induced hypertension, diabetes, intrapartum fever/infection (e.g., with group B streptococcus, genital herpes simplex virus, human immunodeficiency virus, and varicella), HBsAg positive, thyroid disease, inherited disorders, and cardiac disease.
D. **Perinatal fetal distress, delivery complications:** abnormal fetal heart rate pattern, meconium staining of the amniotic fluid, rapid delivery, difficult delivery, rupture of membranes more than 18 hours before delivery.
E. **Cesarean delivery and indications:** breech presentation, fetal distress, placenta previa, abruptio placentae, cephalopelvic disproportion, failure to progress in labor.

PHYSICAL ASSESSMENT (REFER TO CHAPTER 7)

A. Skin.
1. Cyanotic.
2. Pale.
3. Mottled.
4. Cool to touch.
5. Poor perfusion.

B. Respiratory system.
1. Poor color.
2. Tachypnea.
3. Decreased air entry.
4. Increased work of breathing: grunting, flaring, and retracting.
5. Apnea.
6. Unequal breath sounds.
7. Oxygen requirement.

C. Cardiovascular system.
1. Abnormal heart sounds such as murmur.
2. Weak, absent, or unequal pulses.
3. Hepatosplenomegaly.

D. Central nervous system (CNS).
1. Hypertonic or hypotonic.
2. Jitteriness, tremors.
3. Lethargy.
4. Bulging fontanelle (record baseline head circumference).
5. Seizures.
6. Irritability, high-pitched cry.

E. Morphologic features.
1. Congenital anomalies (e.g., abdominal wall defects, imperforate anus).
2. Severe birth trauma.
3. Absent or decreased limb movement.
4. Asymmetry.

F. GI tract.
1. Abdominal distention (measure baseline abdominal girth).
2. Increased gastric contents on aspiration.
3. Inability to pass an orogastric tube.
4. Excessive mucus.
5. Emesis soon after birth or after first feeding.

DIAGNOSTIC TOOLS (BRADSHAW AND TANAKA, 2016)

A. Pulse oximetry (peripheral monitoring of oxygen saturation).
1. Oxygen saturation (Sao_2) of blood is that percentage of the total hemoglobin concentration that is chemically combined with oxygen.
2. A baseline Pao_2 value should be obtained to confirm the infant's oxygen level.

B. **Arterial blood gas determinations.** If oxygen requirement persists, pulse oximetry saturations in room air are decreased, and cyanosis is present, an arterial blood gas should be performed.
C. **Chest x-ray examination.** Anteroposterior and lateral views are needed if respiratory distress is present or cardiac disease is suspected.
D. **End-tidal carbon dioxide ($EtCO_2$).** To detect carbon dioxide levels at the end of expiration. Is useful to determine correct placement of the endotracheal tube. Note: When using colorimetric $EtCO_2$ monitoring, it may take several breaths before a color change is detected.
E. **Transillumination.** Use a high-intensity light placed over the side of the chest in question if pneumothorax or pneumomediastinum is suspected.

F. **Whole-blood glucose screening test or serum glucose determination if indicated by history or assessment results:** see "Routine Care Considerations During Transition," item E: Glucose needs/first feeding.
G. **Hematocrit determination (refer to Chapter 31).**
   1. History of blood loss.
   2. Plethoric or pale infant.
   3. Twins (to rule out twin-to-twin transfusion).
   4. Heel-stick (capillary) samples tend to have higher results by approximately 10%.
   5. Hematocrit variations. Highest hematocrit is at 2 to 4 hours of age and then progressively falls as a result of the beginning of red blood cell breakdown and the cessation of erythropoiesis in response to a comparatively oxygen-enriched environment.
H. Complete blood cell count with differential examination of the white blood cells (refer to Chapter 32).
   1. As part of a sepsis diagnostic evaluation.
   2. To screen for normal and abnormal hematologic indices.
I. Blood culture as part of a diagnostic evaluation for sepsis (refer to Chapter 32).
J. Urine sample collection (refer to Chapter 33).
   1. Urinalysis.
   2. Screening test for drugs of abuse.
K. **Lumbar puncture:** performed at the discretion of the physician/advanced practice nurse as part of a diagnostic evaluation for sepsis (refer to Chapter 32).
L. **Ultrasonography, computed tomography, and magnetic resonance imaging (refer to Chapters 33 and 34).**
   1. Cranial evaluation for abnormal CNS findings.
   2. Abdominal examination if history of two-vessel cord to rule out renal anomalies.
M. **Echocardiography and electrocardiography:** as part of a diagnostic study for a congenital cardiac defect (refer to Chapter 28).
N. **Passage of orogastric tube (refer to Chapter 10).**
   1. To check patency of esophagus in infants with excessive pooling of mucus in the oropharynx.
   2. To decompress a distended abdomen.
   3. To measure and assess gastric contents (>25 mL and/or significant bile in the stomach indicates obstruction).

COMMON PROBLEMS AND CLINICAL PRESENTATION

A. Birth trauma (refer to Chapter 2).
B. Perinatal hypoxia–ischemia (refer to Chapter 34) (Blackburn, 2018; McQuillen et al., 2017; Volpe, 2018).
   1. Birth asphyxia is defined as interference with gas exchange resulting in compromised oxygen delivery, accumulation of CO_2, and a switch to anaerobic metabolism.
   2. Fetal distress is indicated by an abnormal fetal heart rate pattern, meconium staining of the amniotic fluid, scalp pH less than 7.20, and Apgar scores less than 5 at 1 minute of age and less than 7 at 5 minutes of age.
   3. Pathophysiologic sequelae include the following:
      a. Decreasing Po_2. The tissue hypoxia that ensues leads to anaerobic metabolism with release of lactic acid into the circulation.
      b. Respiratory acidosis from elevated levels of carbon dioxide.
      c. Metabolic acidosis.
         1) Results in high pulmonary vascular resistance.
         2) Leads to decreased surfactant release.
      d. Hypoxic–ischemic damage to less vital organs such as kidney and gut after redistribution of blood to vital organs.
      e. The myocardium depends on its stored reserves of glycogen for energy as its supply of oxygen falls. Eventually, this reserve is consumed and the myocardium is simultaneously exposed to progressively lower Po_2 and pH levels. The combined effects lead to reduced myocardial function with decreased blood flow to vital organs.
   4. All newborn infants have some degree of respiratory acidosis and hypoxia during labor and vaginal delivery; a healthy term infant has increased tolerance and reserves. The asphyxiated newborn infant has more prolonged hypoxia and respiratory acidosis and may have additional metabolic acidosis, hypothermia, and hypoglycemia.
   5. Clinical findings.
      a. Mild to moderate perinatal hypoxia–ischemia.
         1) Extended awake, alert state (45 minutes to 1 hour).
         2) Dilated pupils.
         3) Normal muscle tone.
         4) Active suck.
         5) Regular or slightly increased respiratory rate.
         6) Normal or slightly increased heart rate.
      b. Moderate to severe perinatal hypoxia–ischemia.
         1) Hypothermia.
         2) Hypoglycemia.
         3) Pupils constricted.
         4) Respiratory distress manifested by grunting, flaring, retracting, tachypnea, and oxygen requirement.
         5) Seizures (subtle and multifocal clonic; 12 to 24 hours of age).
         6) Acute tubular necrosis after reduced blood flow to the kidneys.
         7) Hypotonia initially, lethargy.
         8) Bradycardia.
      c. Severe perinatal hypoxia–ischemia requires constant monitoring in a level III/IV (intensive care) nursery.
         1) Pale skin, poor perfusion, hypotension.
         2) Cerebral edema.

3) Seizures.
4) Apnea.
5) Intracranial hemorrhage.

C. Pulmonary problems (refer to Chapters 24 to 26) (Jackson, 2018; Wilson and Fitzgerald, 2019., 2013; Parker and Kinsella, 2018).
1. Air leak: 2% to 10% of healthy term neonates develop spontaneous air leak, as do 16% to 36% of neonates who require ventilatory support, including continuous positive airway pressure.
a. Tachypnea, unequal breath sounds, shift of heart tones, and distant heart tones.
b. Transillumination of chest is positive for free air.
2. Retained lung fluid, respiratory distress syndrome (because of prematurity or birth asphyxia), and pneumonia.
a. Decreased air entry with respiratory distress syndrome and pneumonia.
b. Increased work of breathing: grunting, flaring, and retracting.
c. Tachypnea, apnea.
d. Decreased saturations (Sao_2), cyanosis, continued oxygen requirement.
3. Aspiration syndromes (meconium, blood).
a. Coarse rales.
b. Tachypnea.
c. Barrel chest.
4. Upper airway obstruction (e.g., choanal atresia or micrognathia).
5. Extrapulmonary (e.g., phrenic nerve injury with resultant diaphragmatic paralysis or eventration of the diaphragm).

D. Cardiovascular problems (refer to Chapter 28) (Hoffman et al., 2019; Scholz and Reinking, 2018).
1. Congenital heart disease.
a. To improve detection of newborns with critical congenital heart defects, the AAP recommends pulse oximetry screening of all healthy newborn infants in the newborn nursery. Infants with a positive screening result should have a diagnostic echocardiogram performed (AAP, 2012).
b. Acyanotic lesions.
1) Patent ductus arteriosus with a left-to-right shunt.
2) Ventricular septal defect.
3) Atrial septal defect.
4) Endocardial cushion defect or atrioventricular canal defects.
c. Obstructive lesions.
1) Aortic stenosis.
2) Coarctation of the aorta.
3) Pulmonary valve stenosis or atresia.
4) Hypoplastic left heart syndrome.
d. Admixture of lesions.
1) Normal or increased pulmonary blood flow.
a) Complete transposition of the great vessels.
b) Truncus arteriosus.
c) Anomalous venous connections of the pulmonary veins.
2) Decreased pulmonary blood flow.
a) Tetralogy of Fallot.
b) Tricuspid valve atresia.
2. Persistent fetal shunts.
a. Patent ductus arteriosus with right-to-left shunt.
b. Persistent pulmonary hypertension.
3. Clinical findings.
a. Cyanosis with or without increased work of breathing, decreased oxygen saturations. Note: Absence of any signs of abnormal respiratory function in the presence of cyanosis suggests congenital heart disease.
b. Unequal or absent pulses, bounding pulses, decreased blood pressure in the lower extremities, and decreased perfusion.
c. Increased precordial activity, shift of point of maximal impulse of heart tones to right, murmur.
d. Congestive heart failure, indicated by tachypnea, moist breath sounds, tachycardia, peripheral edema, cardiomegaly, and hepatomegaly.

E. Hemodynamics (Noori et al., 2018).

ACUTE HYPOVOLEMIC SHOCK

A. Internal hemorrhage resulting from birth trauma; intracranial hemorrhage.
B. External hemorrhage resulting from placenta previa or abruptio placentae, cord accident, or fetal–maternal or twin-to-twin transfusion.
C. Respiratory distress, pallor, poor perfusion, hypotension, weak or absent pulses, anemia.
1. Polycythemia.
a. Plethoric, cyanotic, or excessively flushed with crying.
b. Hypoglycemia.
c. CNS symptoms, including jitteriness, hypotonia, lethargy, and seizures.
2. Anemia.
a. Acute or chronic blood loss.
b. Hemolysis from sepsis or ABO/Rh blood group incompatibilities.
c. Reduced red blood cell production, manifested by severe asphyxia, sepsis, and aplastic anemia.
d. Pale skin, murmur, tachypnea, normal arterial blood pressure, signs of congestive heart failure, including hepatosplenomegaly and increased vascular markings on x-ray film.

D. Metabolic problems.
1. Hypoglycemia (Werny et al., 2018).
a. Observed in infants who are large or small for gestational age; infants of diabetic mothers; premature infants; and stressed infants, such as those with sepsis, cold stress, or respiratory distress.

b. Clinical findings.
1) Jitteriness, irritability.
2) Seizures.
3) Hypothermia, temperature instability.
4) Lethargy.
5) Poor feeding, emesis.
6) Apnea.
7) Cardiorespiratory distress, cyanosis, oxygen requirement.
8) Pallor.
9) Tachycardia.
10) Weak or high-pitched cry.

2. Adverse effects of maternal medications; maternal use of illicit drugs (refer to Chapters 2 and 3).
a. Magnesium sulfate: infants present with respiratory depression, decreased muscle tone, and decreased serum calcium concentration.
b. Tocolytics: infants may present with hypoglycemia.
c. Narcotics: infants present with apnea, respiratory depression, and periodic breathing.
d. Cocaine: infants may present with apnea, poor muscle tone initially and then irritability and agitation, tremors, and feeding difficulties.
e. Marijuana or methadone: infants present with hyperthermia, agitation, and diarrhea.
f. Alcohol: infants have fetal alcohol syndrome with dysmorphic and behavioral abnormalities.

E. **Infection (see also** Chapter 32) (Ferrieri and Wallen, 2018).
1. Generalized bacterial or viral disease; acquired in utero or nosocomial.
2. Clinical findings. Note: Nearly 90% of neonates with early-onset group B streptococcus have signs of infection within 12 hours of birth (median age is 8 hours).
a. Temperature instability.
b. Tachypnea, apnea.
c. Respiratory distress, cyanosis.
d. Tachycardia.
e. Cool, mottled skin; weak pulses; capillary refill lasting longer than 2 seconds; and hypotension.
f. Disseminated intravascular coagulation.
g. Hepatosplenomegaly.
h. Unexplained jaundice.
i. Purpura, petechiae.
j. Hypoglycemia or hyperglycemia.
k. Poor feeding, emesis, and abdominal distention.
l. Lethargy, poor muscle tone.
3. In-utero viral infection: infant may be small for gestational age with microcephaly.

F. Congenital anomalies (frequently obvious on gross examination) (refer to Chapter 35).
1. Diaphragmatic hernia.
a. Immediate onset at birth of significant respiratory distress.
b. Shift in heart tones, decreased or unequal breath sounds, bowel tones heard in chest, scaphoid abdomen, and cyanosis.
2. Esophageal atresia with or without tracheoesophageal fistula.
a. Excessive amniotic fluid.
b. Increased pooling of secretions in the oropharynx, respiratory distress, unable to place orogastric tube.
3. Abdominal wall defects: omphalocele and gastroschisis.
4. Limb anomalies: amniotic banding, talipes equinovarus, polydactyly, and syndactyly.
5. Neural tube defects.
6. Intestinal obstructions.
7. Chromosomal abnormalities such as trisomy 21 or trisomy 18.
8. Urogenital abnormalities: exstrophy of bladder, hypospadias, epispadias, and ambiguous genitalia.

INITIAL STABILIZATION OF THE SICK NEWBORN INFANT

A. Short-term observation in transition nursery or intermediate nursery to monitor trends before the infant's transfer to a neonatal intensive care unit (NICU).
1. The infant may be capable of resolving the problem on his or her own if given time (e.g., correction of mild acidosis from asphyxia, clearing of lung fluid, stabilization of blood glucose concentration, and stabilization of blood pressure).
2. Monitor and record trends (i.e., improvement of respiratory rate toward normal, improved perfusion, and normal glucose screens).

B. Avoid excessive handling.
1. Organize care and interventions to avoid frequent, unnecessary stimulation of an already stressed infant.
2. Use pulse oximeter and cardiorespiratory monitor to reduce hands-on determination of vital signs.
3. Reduce background stimulation such as loud noises or bright lights.
4. Use nonnutritive sucking to lower activity levels and reduce energy needs.
a. Infant may be more comfortable in a prone position.
b. Crying can be stressful and is similar to a Valsalva maneuver, with prolonged exhalation, obstructed venous return, quick inspiratory gasp, and right-to-left shunting at the foramen ovale.
c. Crying depletes energy reserves and increases oxygen consumption.

C. Provide a neutral thermal environment (refer to Chapter 6).
1. Observe infant for apnea and hypotension during warming.
2. Avoid hyperthermia.

D. Supply glucose (refer to Chapter 9).
1. Oral administration of glucose for a blood glucose level of less than 40 mg/dL in an otherwise healthy

asymptomatic neonate; early, frequent feedings by nipple, gavage, or nursing.
   a. Give at least 0.5 to 1 ounce of formula by nipple or gavage if there are no contraindications to enteral feedings and the infant is free of symptoms (see "Routine Care Considerations During Transition"). If condition is stable, infant may be allowed to nurse 5 to 10 minutes on each breast.
   b. Begin maintenance formula at 50 to 70 kcal/kg/day, or breast-feed on demand every 2 to 3 hours.
   c. Check blood glucose 30 minutes to 1 hour after feeding.
   d. Consider giving a formula designed for premature infants when treating hypoglycemia orally.
      1) These formulas provide 50% of carbohydrate in the form of glucose polymers that are easily absorbed; salivary amylase retains its activity in the infant's stomach because of increased gastric pH and is effective in the digestion of glucose polymers (Blackburn, 2018).
      2) Approximately 50% of the fats are provided as medium-chain triglycerides (MCTs). As MCTs are absorbed from the stomach, they may also increase the level of plasma ketones, which can be used as an alternative substrate to glucose for brain metabolism (Blackburn, 2018).
      3) The process of absorbing fat (fatty acid oxidation and ketogenesis) spares glucose for brain energy needs; free fatty acids and ketones promote glucose production by providing essential gluconeogenic cofactors.
      4) Healthy newborn infants respond to a protein meal by preferentially increasing glucagon, which elicits a glycemic response.
   e. Consider administering 40% dextrose gel to the buccal mucosa for the treatment of low blood sugars in healthy newborns along with feedings.
2. IV administration of glucose for hypoglycemia (see "Routine Care Considerations During Transition," item D: Glucose needs/first feeding) is as follows:
   a. Provide bolus (2 mL/kg) of 10% dextrose in water ($E_{10}W$), followed by an infusion of 4 to 6 mg/kg/min; $D_{10}W = 100$ mg/mL.
   b. Monitor therapy with frequent glucose checks, and titrate the infusion rate and concentration to meet the infant's needs. Note: Do not administer an IV bolus of glucose greater than $D_{10}W$ because of reactive hypoglycemia and hypertonicity of the solution. Always follow a glucose bolus with a continuous infusion of glucose.

E. **Supply oxygen:** Assess needs with a pulse oximeter or with arterial blood gas determinations and close observation.
   1. Extended oxygen use in the transition nursery requires notification of the physician and transfer to a level II or III setting.
   2. Provide warmed, humidified oxygen by oxygen hood, continuous positive airway pressure by nasal prongs, or assisted ventilation by endotracheal tube according to the infant's needs (refer to Chapter 26).
   3. Monitor oxygen provided with an oxygen analyzer. Oxygen should be provided via a blender to provide the least Fio_2 required. The percentage and liters per minute should be recorded. Record blow-by oxygen in liters per minute and as distance from the infant's face.

F. Supply volume expanders, including blood and normal saline solution.
   1. For hypotension and blood loss.
   2. Requires IV line placement and transfer to level II or III nursery for continued management and observation, including cardiorespiratory monitoring and blood pressure checks to adjust therapy as necessary.

G. Antibiotics.
   1. As indicated by history, current status of the infant, and initial results of sepsis evaluation.
   2. Administer via peripheral IV or heparin-lock IV line.

Parent Teaching

BEFORE DELIVERY

A. **History.** Review obstetric history; anticipate needs of the infant at delivery.
B. **Complications**. If there are expected complications (preterm delivery, congenital anomalies) and time permits, discuss the anticipated plan of care with the family.
   1. Discuss plans for managing the infant, including plans for transfer to a level II, III, or IV nursery and any special equipment that may be used (oxygen hood, incubator, ventilator, monitors).
   2. Allow the parents to tour the NICU if possible.
C. **Parental support.** Encourage parents to express their feelings, fears, and misgivings; involve support people.

AT DELIVERY

A. **After drying the neonate, place on the mother's naked chest when possible with uncomplicated deliveries.** A warm blanket should be placed over the infant's back. Use the family's birth plan as much as possible.
B. **After delivery room assessment, return the infant to the family if the infant's condition is stable.**
C. **Answer questions regarding acrocyanosis, Apgar scores, and morphologic findings.**
D. **Allow parents time to visit, breast-feed, and see extended family.**

DURING TRANSITION

A. "Introduce" the newborn to the family by noting unique features (dimples, long eyelashes, hair color).

B. Encourage the support person to touch and talk to the infant.
C. Discuss physical findings such as caput succedaneum, head molding, positional deformities, and birthmarks.
D. Discuss the infant's sensory capabilities, including sight, hearing, and smell.
E. Listen to the parents. Allow them to express their reactions as they compare their "dream" infant with the real infant they now have (too tiny, not the right sex, deformed, or premature).
F. After completion of admission procedures, the infant is returned to the family for feeding and visiting.
G. Allow the family to participate in the infant's care as permitted by the neonate's condition.

POSTPARTUM PERIOD (EARLY DISCHARGE)

A. **Parental involvement.** Involve the parents in evaluation of their learning needs; begin teaching as soon as delivery occurs.
B. **Short hospital stays and family instruction.** With shorter hospital stays, there is less time available for teaching and an increased importance of teaching. This may be the only information many families receive on the care of a newborn infant.
   1. Classes; videotaped lectures.
      a. Cardiopulmonary resuscitation; safety.
      b. Breastfeeding.
      c. Developmental milestones.
   2. Follow-up visits by the nurse to the home and phone calls from postpartum nurses. Encourage families to call the nursery if they have questions about their newborn's care.
   3. Follow-up visit with the primary care provider within 48 to 72 hours. Encourage the family to select a primary care provider and assist in making an appointment for the first visit.
   4. Return visit for newborn screening or hyperbilirubinemia check if needed.

TRANSFER TO LEVEL II, III, OR IV SETTING

A. Provide prenatal teaching—if possible, with visits to the NICU.
B. Provide information booklets with location, phone numbers, visiting regulations, parent-to-parent groups, and necessary support personnel.
C. Bring the mother to the infant's bedside if the infant is unable to return to the mother after delivery. Allow family members to be near the infant as much as possible, and encourage them to see past the equipment to the infant and his or her special needs (gentle touch, stroking, soft voice, a familiar person).
D. When the infant is stable, allow family members to visit in the privacy of their postpartum room or a parent room if the neonate's condition warrants; for example, an infant with a heparin lock for antibiotics can be taken to the mother's room to nurse.
E. Provide a picture and footprints of the infant for the family. This is especially important if transfer to a level II, III, or IV nursery will be to another facility.
F. Facilitate the family in keeping in contact with the receiving facility, and be available to explain information given to the family.

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CHAPTER 5

Neonatal Delivery Room Resuscitation

Barbara Elizabeth Pappas and Deanna Lynn Robey

OBJECTIVES

1. Review the components of neonatal resuscitation as outlined by the Neonatal Resuscitation Program of the American Heart Association/American Academy of Pediatrics.
2. Compare three physiologic characteristics of the neonate that make neonatal resuscitation different from adult resuscitation.
3. Recognize the antepartum, intrapartum, and newly born period factors that indicate the neonate may be at risk for requiring resuscitation at birth.
4. Identify the equipment needed for neonatal resuscitation.
5. Recognize the importance of skin-to-skin care after resuscitation in the transition period of the neonate.
6. Define the characteristics of the various oxygen delivery systems.
7. Discuss the postresuscitative needs of the neonate.
8. Describe the potential complications of neonatal resuscitation.
9. Recognize three neonatal disease states, congenital malformations, or special situations that may alter the resuscitation process.
10. Discuss ethical considerations surrounding resuscitation of periviable or marginally viable neonates or those with unpredictable life expectancy.

Few neonates require resuscitation at birth. In approximately 85% of term newborns, spontaneous respirations are initiated within 10 to 30 seconds of life, with an additional 10% responding to drying and tactile stimulation. Approximately 5% will require some assistance at birth, but less than 1% will require full resuscitative measures (Perlman et al., 2015). Most neonates only require basic stabilization, including thermal and airway management. In those neonates who require advanced resuscitation, it is more likely to be caused by a respiratory problem, as the majority have a healthy heart.

Neonates at risk for resuscitation benefit from prompt, organized, and efficient interventions tailored to their needs and response. High-functioning resuscitation teams are optimal. Formalized education, hands-on performance in simulated scenarios with equipment, frequent periodic review, and mock codes are all beneficial in promoting the skills necessary for a smooth and coordinated resuscitation.

The risk for cardiopulmonary arrest does not stop once the neonate leaves the delivery environment. Physical and physiologic vulnerabilities continue to place the neonate at risk. Preparation for anticipated needs of the neonate is key in any situation. Effective teamwork, leadership, and communication are essential for the successful resuscitation of the neonate.

Definitions

Newly born: time of the infant's life from birth to the first hours after birth.

Neonate: refers to the first 28 days of the infant's life.

Infant: neonatal period extending through the first 12 months of life.

Anatomy and Physiology

Normal characteristics specific to the neonate differ from those of the adult, leaving the neonate at significant risk for compromise. A thorough understanding of the uniqueness of the neonate often allows anticipation and intervention before the neonate is compromised to the point of cardiac failure. Unknown physical variations make resuscitation and stabilization challenging. The lack of adequate perinatal information (i.e., ultrasound, genetic testing) and availability of only the gross physical assessment at birth can make resuscitation difficult. Unique characteristics specific to the neonate include the following:

A. Physiologic and anatomic characteristics.
   1. Large head in proportion to body size.
      a. Increased insensible water loss (IWL).
      b. Heat loss related to little or no insulating fat layer.

c. Minimal insulation and moisture retention from hair.
2. Short neck.
a. Lack of clarity in identifying landmarks contributes to difficulty in intubation.
b. Tendency for hyperextension and flexion of the neck.
3. Glottis positioned anteriorly in the hypopharynx.
a. Intubation may be difficult.
b. The neonate is predisposed to airway compromise from positioning.
4. Preferential nasal breathing.
a. Anatomic patency must be confirmed.
b. Increased airway resistance with edema from nasal suctioning.
5. Large surface area/body size ratio.
a. Increased IWL.
b. Hypothermia from heat loss.
6. Decreased muscle mass.
a. Increased potential for heat loss through external gradient.
b. Decreased ability to flex body to conserve heat, causing increased surface area in premature or ill neonate.
c. Decreased ability to generate heat.
7. Decreased subcutaneous fat (premature birth, intrauterine growth restriction).
a. Decreased heat production (from brown fat metabolism).
b. Increased heat loss (from lack of insulation and decreased flexion).
8. Thin epidermal layer.
a. Increased IWL; the more premature, the greater the loss.
b. Decreased support of internal gradient to maintain heat.
c. Increased risk for breakdown and injury can contribute to increase in IWL.

B. Immature systems.
1. Central nervous system.
a. Diminished ability to regulate vasomotor stability, resulting in impaired perfusion.
b. Poor autoregulation of blood pressure.
c. Poor temperature regulation.
2. Respiratory system.
a. Decreased absorption of lung fluid if cesarean section without trial of labor.
b. Decreased surface area for gas exchange.
c. Decreased availability of surfactant.
d. Increased risk for aspiration from gastric distention.
3. Neuromuscular system.
a. Decreased ability to shiver.
b. Decreased ability to generate heat.
4. Liver.
a. Decreased ability to metabolize drugs.
b. Decreased ability to mobilize glucose stores.
5. Kidneys.
a. Risk for decreased perfusion with compromise.
b. Decreased ability to excrete drugs and fluids.
6. Gastrointestinal system.
a. Gastric distention and respiratory compromise related to decreased gastrointestinal motility and forced air entry with positive pressure ventilation (PPV).
7. Metabolism.
a. Decreased glucose stores.
b. Decreased ability to convert stored glucose.
c. Inefficient energy production from stored glucose.
d. Increased utilization of glucose leading to hypoglycemia.
8. Immune system.
a. Increased predisposition to infection.
b. Immature immune response despite adequate cell counts.

C. Vascular access.
1. Small, fragile, and superficial veins making access difficult.
2. Vasoconstriction associated with acidosis, hypothermia, hypoglycemia, and shock.
3. Umbilical access. Normal cord includes two arteries and one vein. Inadvertent cannulization of the portal vein with umbilical vein catheterization can lead to liver damage with chemical resuscitation.

Risk Factors

Risk factors are warning signs that alert the perinatal team to the possibility of an emergency and the need for anticipatory preparation of neonatal resuscitation (Table 5.1).

Antepartum and intrapartum period conditions predispose the mother and fetus to stress and can interfere with the fetus tolerating labor and/or the successful transition to extrauterine life. Newly born period conditions in the delivery room or during the transitional period indicate the neonate is having difficulty making all the physiologic changes needed for successful adaptation to extrauterine life.

Anticipation of and Preparation for Resuscitation

Anticipation of and preparation for resuscitation requires an evidence-based multidisciplinary approach. Internationally, the Neonatal Resuscitation Program (NRP) is recognized as the "gold standard" for neonatal resuscitation. Program content is based on the American Academy of Pediatrics and American Heart Association's "Neonatal Resuscitation: 2015 American Heart Association Guidelines

Table 5.1

Perinatal Risk Factors Increasing the Likelihood of Neonatal Resuscitation

Antepartum Period	Intrapartum Period	Newly Born Period
Maternal age less than 16 years or more than 35 years	Abnormal fetal positioning or presentation (e.g., breech position)	Congenital malformations (e.g., cardiac, respiratory, gastrointestinal, neurologic, genitourinary)
Maternal diabetes	Cesarean delivery	Cardiac arrhythmia or murmur (e.g., tachycardia or bradycardia)
Hemorrhage, anemia	Fetal heart rate abnormalities (e.g., bradycardia, tachycardia)	Extreme color change (e.g., cyanosis, plethora, pallor, mottling)
Maternal substance abuse	Nonreassuring fetal heart rate patterns (category 2 or 3)	Prolonged or delayed capillary refill time
Maternal drug therapy such as magnesium sulfate, adrenergic-blocking agents, over-the-counter or herbal medications	Maternal or fetal intrapartum blood loss (e.g., abruptio placentae, placenta previa)	Respiratory distress (e.g., apnea, tachypnea, grunting, altered breath sounds, excessive secretions)
Maternal infection	Maternal sedation, anesthesia, or analgesia (e.g., narcotics in the previous 4 hours)	Temperature instability
No or late entry to prenatal care	Maternal fever or infection (e.g., chorioamnionitis)	Hypertonia/hypotonia
Polyhydramnios or oligohydramnios	Premature labor	Hypotension
Maternal cardiac, renal, pulmonary, thyroid, endocrine, gastrointestinal or neurologic disease	Prolonged labor (>24 hours or second stage >2 hours)	Seizures
Premature rupture of membranes	Precipitous delivery	Hypoglycemia
Anatomic abnormalities of the uterus	Prolonged rupture of membranes (>18 hours)	Prematurity
Isoimmunization, Rh, or ABO (blood group) incompatibilities	Instrument-assisted delivery (e.g., vacuum or forceps)	Postmaturity
Hypertension (pregnancy-induced or chronic)	Fetal malformations	Anemia or polycythemia
Multiple gestation	Meconium-stained amniotic fluid	Feeding difficulty or intolerance
Post-term gestation	Uterine hyperstimulation and/or tachysystole with fetal heart rate pattern changes	Seemingly well, then clinically deteriorates
Discrepancy in size and dates	Prolapse of the umbilical cord	
Previous pregnancy complication or fetal loss	Macrosomia	
Diminished or absent fetal activity		
Fetal malformations or anomalies (i.e., fetal hydrops)		

Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" (Wyckoff et al., 2015). The guidelines are based on the International Liaison Committee on Resuscitation (ILCOR) (2015) Consensus on Science statement regarding treatment recommendations for neonatal resuscitation (Perlman et al., 2015). All units and facilities caring for neonates must be adequately staffed, prepared, and equipped to deliver resuscitative care when anticipated or unexpected resuscitation needs arise.

A. Education and competency development.
   1. Completion of an educational program on neonatal resuscitation (e.g., NRP) does not equate to competency or confidence.
   2. Hands-on skill stations and simulation scenarios provide additional practice.
   3. Development and implementation of regular mock code system for education and quality improvement.
   4. Annual competency evaluation and review are recommended.
   5. Establish a quality improvement process for reviewing neonatal codes (e.g., effectiveness of call system, response times, and drug doses).

B. General preparation.
   1. Promote development of effective teams. Effective teams demonstrate clear communication and strong leadership and management.
   2. Consider the development and utilization of a rapid response team.
   3. Evaluate and update equipment frequently.

4. Arrange for periodic evaluation and maintenance of electrical equipment by the biomedical engineering department on a regularly scheduled basis.
5. Schedule periodic evaluations and maintenance of all respiratory equipment.
6. Formulate supply replacement procedures. Evaluate and replace supplies as quickly as possible after use.
7. Serial tests of alerting system for rapid, consistent response of personnel.

C. Delivery room preparation.
1. Position the NRP Flow Diagram (Fig. 5.1) easily within view of the resuscitative area.
2. Anticipate the needs of the neonate by evaluation of gestational age, risk factors, and immediate status at birth.
   a. Formulate a plan before anticipated need, if possible (e.g., endotracheal tube size, drug doses, concentrations, and handling equipment).
   b. Promote effective communication between personnel, departments, and institutions that encourages identification and notification of high-risk situations and preparedness.
3. Prewarm birthing room to minimize thermal losses in the neonate. Use a polyethylene plastic wrap or bag for the neonate less than 32 weeks of gestation.
4. Preheat warmer, hat, blankets, and nest (blanket rolls or bendable positioning device). Approximately 15 to 30 minutes (heat output set on high) is required to thoroughly warm the mattress on a radiant warmer bed. Assemble alternative heat sources (i.e., warming pad) at bedside as needed.
5. Assemble equipment in an organized, easily available system. Check function of equipment routinely and before each use.
6. Ensure safety of team members and utilization of standard precautions.
7. Identify and assemble available team members and designate roles.
8. Promote family-centered care through active family communication and involvement in decision making.

D. Questions to ask at every birth.
1. Communication between the obstetric and neonatal teams is essential to provide optimal resuscitative efforts. The four prebirth questions to ask are (Weiner, 2015):
   a. What is the expected gestational age?
   b. Is the amniotic fluid clear?
   c. How many babies are expected?
   d. Are there any additional risk factors?

E. Personnel roles.
1. Personnel roles should be defined by institutional policies and job descriptions, in addition to state laws, license regulations, and scope of practice definitions. The "resuscitative team" with identified member roles and expectations should be determined before delivery. A preresuscitation team briefing should consist of acknowledged perinatal risk factors; identification of a team leader; task delegation, including documentation; determination of supplies and equipment needed; and how to obtain additional help.
2. Preparedness for resuscitation should exist at every delivery. Every delivery should be attended by at least one person skilled in neonatal resuscitation who is immediately available and solely responsible for initiating resuscitation and stabilization of the neonate. If any perinatal risk factors are present (see Table 5.1), then at least two persons skilled in neonatal resuscitation should be present to solely manage the neonate. A fully qualified team should be available for more complex situations. For multiple births, separate teams for each neonate should be present.
3. A family-centered approach should include a designated support and communication liaison to the family. Family support should not be left unassigned. Family presence during resuscitation has not been shown to be detrimental to the outcome of the neonate.

F. Behavioral skills of resuscitative team.
1. Teamwork, leadership, and communication are essential skills of a successful resuscitation. Team members may consist of a variety of provider levels and experience. Key behavioral skills of an effective and efficient team include the following:
   a. Knowledge of your environment.
   b. Anticipation and planning.
   c. Identify team leader role.
   d. Effective communication.
   e. Optimal workload delegation.
   f. Wise attention allocation.
   g. Using all available information.
   h. Using available resources.
   i. Recruiting additional help when needed.
   j. Professional behavior.

G. Documentation.
1. Equally as important is clear, concise documentation of the resuscitation. A single person should be identified as the "documenter" during the entire event. Verbal announcement of assessments and interventions assists in a concise record. It is important to use a single time reference to prevent confusion. Use of a paper form or electronic template is helpful.

H. Postresuscitation team debriefing.
1. A quick debriefing shortly after the resuscitation creates good teamwork and assesses opportunities for improvement.

I. Non–delivery room preparation.
1. As with delivery room resuscitation, being prepared for unforeseen events throughout the neonate's

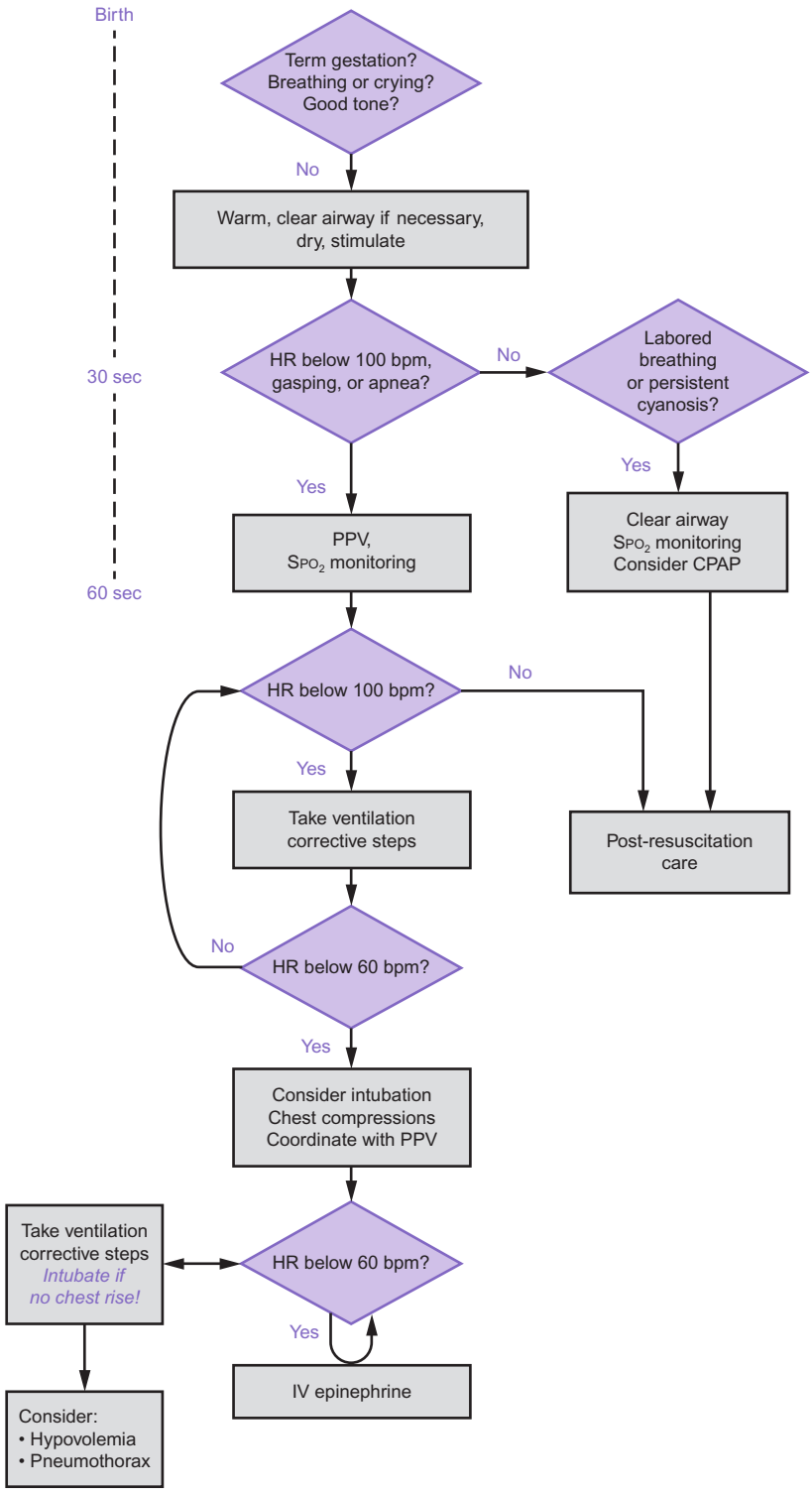

Fig. 5.1 NRP Flow Diagram. *bpm*, Beats per minute; *CPAP*, continuous positive airway pressure; *HR*, heart rate; *IV*, intravenous; *PPV*, positive pressure ventilation. *(From Weiner, G. M. [Ed.]. [2016]. Textbook of neonatal resuscitation [7th ed.]. Elk Grove Village, IL: American Academy of Pediatrics and American Heart Association).*

entire hospitalization can facilitate success in a time of crisis. Unlike delivery room events, non–delivery room resuscitation is often unpredictable and risks ill preparedness. The following events may precipitate respiratory or circulatory compromise:

a. Apnea.
b. Choking or aspiration (i.e., secretions, feedings).
c. Unwitnessed cardiac arrest.
d. Seizure.
e. Hypoxia or airway obstruction.
f. Infection.
g. Postoperative period.
h. Air leak syndromes.
i. Severe anemia (i.e., subgaleal hemorrhage, abruption).
j. Shock.

Equipment for Neonatal Resuscitation

Not every item on the supply list (Box 5.1 and Box 5.2) will be used, but it is important to have appropriate sizes and supply quantities to support a prolonged effort. Ensuring that equipment is functional and up to date is vital to a successful resuscitation. It is important that staff members be familiar with the equipment they will be using and practice with it frequently.

Apgar Scoring System

The Apgar score (Table 5.2) is a descriptive tool for documenting the status of the newborn after birth.

Box 5.1

Essential Supplies and Equipment Needed for Most Resuscitations

Warm	• Preheated warmer
	• Warm towels or blankets
	• Temperature sensor and sensor cover for prolonged resuscitation
	• Hat
	• Plastic bag or plastic wrap (<32 weeks' gestation)
	• Thermal mattress (<32 weeks' gestation)
Clear airway	• Bulb syringe
	• 10 Fr or 12 Fr suction catheter attached to wall suction, set at 80 to 100 mm Hg
	• Meconium aspirator
Auscultate	• Stethoscope
ventilate	• Flowmeter set to 10 L/min
	• Oxygen blender set to 21% (21% to 30% if <35 weeks' gestation)
	• Positive-pressure ventilation (PPV) device
	• Term- and preterm-sized masks
	• 8 Fr feeding tube and large syringe
Oxygenate	• Equipment to give free-flow oxygen
	• Pulse oximeter with sensor and cover
	• Target oxygen saturation table
Intubate	• Laryngoscope with size-0 and size-1 straight blades (size 00, optional)
	• Stylet (optional)
	• Endotracheal tubes (sizes 2.5, 3.0, 3.5)
	• Carbon dioxide (CO_2) detector
	• Measuring tape and/or endotracheal tube insertion depth table
	• Waterproof tape or tube-securing device
	• Scissors
	• Laryngeal mask (size 1) and 5-mL syringe
Medicate	• Access to:
	• 1:10,000 (0.1 mg/mL) epinephrine
	• Normal saline
	• Supplies for placing emergency umbilical venous catheter and administering medications
	• Electrocardiogram (ECG) monitor leads and ECG monitor

Box 5.2

Neonatal Resuscitation Supplies and Equipment List

Suction Equipment

Bulb syringe
Mechanical suction and tubing
Suction catheters, 5 Fr or 6 Fr, 10 Fr, 12 Fr, or 14 Fr
8 Fr feeding tube and large syringe
Meconium aspirator

Positive-Pressure Ventilation Equipment

Device for delivering positive-pressure ventilation
Face masks, newborn and preterm sizes
Oxygen source
Compressed air source
Oxygen blender to mix oxygen and compressed air with flowmeter (flow rate set to 10 L/min) and tubing
Pulse oximeter with sensor and cover
Target oxygen saturation table

Intubation Equipment

Laryngoscope with straight blades, No. 0 (preterm) and No. 1 (term)
Extra bulbs and batteries for laryngoscope
Endotracheal tubes, 2.5-, 3.0-, 3.5-mm internal diameter (ID)
Stylet (optional)
Stethoscope
Measuring tape and/or endotracheal tube insertion depth table
Scissors
Waterproof tape or tube-securing device
Alcohol pads
Colorimetric CO_2 detector
Laryngeal mask (or similar supraglottic device) and 5-mL syringe
5 Fr or 6 Fr orogastric tube if insertion port present on laryngeal mask
Suction setup with various catheter sizes: 6 Fr, 8 Fr, 10 Fr

Medications

Epinephrine 1:10,000 (0.1 mg/mL)—3-mL or 10-mL ampules
Normal saline for volume expansion—100 or 250 mL
Dextrose 10%, 250 mL (optional)
Normal saline for flushes
Syringes (1-mL, 3-mL, or 5-mL, 20- to 60-mL)

Umbilical Vessel Catheterization Supplies

Sterile gloves
Antiseptic prep solution
Umbilical tape
Small clamp (hemostat)
Forceps (optional)
Scalpel
Umbilical catheters (single lumen), 3.5 Fr or 5 Fr
Three-way stopcock
Syringes (3 to 5 mL)
Needle or puncture device for needleless system
Normal saline for flushes
Clear adhesive dressing to temporarily secure umbilical venous catheter to abdomen (optional)

Miscellaneous

Gloves and appropriate personal protection
Radiant warmer or other heat source
Temperature sensor with sensor cover for radiant warmer (for use during prolonged resuscitation)
Firm, padded resuscitation surface
Timer/clock with second hand
Warmed linens
Hat
Stethoscope (with neonatal head)
Tape, ½ or ¾ inch
Electrocardiogram (ECG) monitor leads and ECG monitor
Intraosseous needle (optional)

For Very Preterm Babies

Size-00 laryngoscope blade (optional)
Food-grade plastic bag (1-gallon size) or plastic wrap
Thermal mattress
Transport incubator to maintain baby's temperature during move to the nursery

Generally scored during or after resuscitation and stabilization at 1 and 5 minutes, it describes the neonate's physiologic condition in five categories: color, heart rate, reflex irritability, muscle tone, and respiratory effort. When the 5-minute score is less than 7, the Apgar score should be determined every 5 minutes until 20 minutes of age. The scores are not used for decision making during resuscitation. The scores are influenced by interventions, gestational age, maternal medications, and cardiorespiratory and neurologic conditions (e.g., malformations, hypoglycemia).

Decision-Making Process

Decision making during resuscitation requires quick and frequent assessment, intervention, and evaluation. The initial steps to resuscitation should be preceded by three

Table 5.2

Apgar Scoring System

Apgar Scoring System			
Indicators	2	1	0
Appearance	Completely pink	Acrocyanosis (body pink, extremities blue)	Pale or blue all over
Pulse Rate	More than 100 bpm	Less than 100 bpm	Absent
Grimace	Pulls away when stimulated; sneezes, coughs, good, strong cry	Facial grimace, feeble cry when stimulated	No response with stimulation
Activity	Active movement, well-flexed extremities	Some flexion of extremities	No movement (flaccid, limp)
Respiration	Good, strong cry	Slow, irregular Weak cry	Absent

Adapted from Apgar, V. A. (1953). Proposal for a new method of evaluation on the newborn infant. *Current Researches in Anesthesia and Analgesia*, July–August, 260–267.

questions that facilitate determination of whether resuscitation measures are required. Ask the following three questions (Weiner, 2015):

- Is the baby term gestation?
- Is the baby breathing or crying?
- Is there good muscle tone?

A. Timing of cord clamping (Mascola et al., 2017; Mercuri, 2016).
   1. Starting the timer after the complete birth of the neonate marks the time of birth. Delaying clamping of the cord allows the blood that remains in the placenta to infuse into the neonate via the umbilical vein. Studies have shown that cord clamping should be delayed for at least 30 to 60 seconds in vigorous term and preterm neonates. During this time, the neonate should be placed skin-to-skin on the mother's chest or abdomen and dried and swaddled with warmed linen. Assessment of the neonate's breathing effort and tone should occur while on the mother's chest or abdomen.
   2. Evidence has shown that benefits of delayed cord clamping include increased blood pressure and blood volume, decreased need for blood transfusions after birth, decreased brain hemorrhages, decreased necrotizing enterocolitis, and decreased mortality. Adverse effects may include delay in resuscitation of compromised neonates, increased risk for polycythemia, and early jaundice.

INITIAL STEPS OF RESUSCITATION

At most deliveries, the following steps are the only interventions necessary. These initial steps should be initiated within a few seconds and completed within 30 seconds of birth. Although these are noted as initial steps, they may be applied in coordination and at any time during the process.

A. Provide warmth.
   1. Prevent hypothermia and hyperthermia, which may increase metabolic requirements and contribute to respiratory distress, metabolic acidosis, and hypoglycemia. If severe asphyxia is suspected, caution should be taken to not overheat the neonate. Temperature should be kept between 36.5° C and 37.5° C.
      a. Place and keep the neonate in a preheated environment (radiant warmer and/or other heat source).
      b. Stable neonates should be placed skin-to-skin on the maternal chest, if possible.
      c. Supplement environmental support with warmed hat and linens.
      d. Avoid drafts, for example, sidewalls up on radiant warmer; keep bed away from ventilation drafts, and outside walls and windows.
   2. Open airway.
      a. Position the neonate supine with the head midline and neck slightly extended. The neonate's head should be in the "sniffing" position.
      b. Care should be taken to avoid hyperextension or flexion of the neck.
      c. A shoulder pad may help maintain the correct airway position, especially for neonates with a large occiput.
   3. Clear secretions.
      a. Clearing of oral secretions may be necessary if secretions are blocking the airway, making it difficult for the neonate to breathe, or if the neonate is gasping, has meconium-stained amniotic fluid, or PPV is anticipated.
         1) Use the least invasive method possible. Wipe the nose and mouth with towel, suction with bulb syringe, or use suction catheter attached to mechanical suction. The suction catheter should be no larger than 10 Fr, with negative pressure approximately 80 to 100 mm Hg.
         2) Suction the mouth before the nose to prevent aspiration should the neonate gasp.
         3) With copious secretions, it is wise to turn the neonate's head to the side, allowing

secretions to collect in the cheek area for easier removal.

4) Vigorous or prolonged deep catheter suctioning can result in trauma, bradycardia, or apnea induced by stimulation of the posterior pharynx and vagus nerve.

4. Dry.
   a. Place the neonate on prewarmed linen (blankets or towels) and dry gently to prevent evaporative heat loss.
   b. Remove damp hat and linens and replace with dry, prewarmed hat and linen to continue drying.
   c. Provide additional heat source as necessary. Do not use warm-water gloves or microwaved heat source (e.g., blankets, saline bag).
5. Stimulate.
   a. If the neonate does not respond to the previous actions, tactile stimulation to the back, trunk, and extremities may be necessary to stimulate breathing.
   b. Never shake a neonate.
   c. If after a period of tactile stimulation, sustained respirations are not achieved, then PPV will be required. If a diaphragmatic hernia is suspected, intubate the trachea and ventilate the neonate through the endotracheal tube with the resuscitation device.
6. Evaluate respirations and heart rate.
   a. To determine the effectiveness of the earlier initial steps, evaluate the neonate's respirations and heart rate. This should take no longer than 30 seconds. It is essential to remember that the most important and effective action during resuscitation is ventilation.
      1) If respirations are not effective or sustained, PPV should be started.
      2) If heart rate is less than 100 within the first minute of birth, PPV should be started.
7. Pulse oximetry.
   a. A pulse oximeter or electronic cardiac monitor should be available for all deliveries and used to confirm cyanosis, to provide supplemental oxygen, or if PPV is required. If the neonate's heart rate is low or has poor perfusion, the pulse oximeter may not function, and thus the cardiac monitor is recommended as the preferred technique. Recent evidence has shown the electrocardiogram (ECG) monitor will trend heart rate and oximeter quicker and more accurately than a pulse oximeter (Katheria et al., 2012; van Vonderen et al., 2015).
      1) Placement of the oximeter should be preductal (right upper extremity), and trending levels may take more than 10 minutes to rise to 90% or more in the full-term, stable neonate (Table 5.3).

Table 5.3

Preductal Target SpO_2 After Birth

Targeted Preductal SpO_2 After Birth (in Percentage by Minutes)	
1 minute	60% to 65%
2 minutes	65% to 70%
3 minutes	70% to 75%
4 minutes	75% to 80%
5 minutes	80% to 85%
10 minutes	85% to 95%

Adapted from Mariani, G., et al. (2007). Pre-ductal and post-ductal O_2 saturation in healthy term neonates after birth. *Journal of Pediatrics*, 150, 418–421.

      2) Allow 1 to 2 minutes for an accurate trend of heart rate or oxygen saturation after placing the pulse oximeter.
      3) Occasional dips in oxygen saturation (SpO_2) to a high 80% range may be considered normal in the first few days of life when unaccompanied by other changes in status.
8. Supplemental oxygen.
   a. Begin at any time if central cyanosis is present with a heart rate greater than 100 beats per minute (bpm) and adequate respirations.
      1) Use oxygen with a flowmeter set at 10 L/min and a blender that can provide a gas mixture of 21% to 100%. Start oxygen at 30% and adjust accordingly to achieve the target oxygen saturation. Deliver oxygen by mask, cupped hand holding the tubing over the neonate's face, flow-inflating bag and mask, or T-piece resuscitator. The closer the oxygen source to the face, the higher the oxygen concentration delivered.
      2) Be sure to allow some space between the mask and neonate to prevent continuous positive airway pressure (CPAP).
      3) Continue oxygen delivery until the neonate's color pinks and then slowly withdraw the oxygen per pulse oximeter and status, ensuring adequate delivery for the neonate to maintain the oximeter at target saturations.
9. Frequently and simultaneously evaluate the following:
   a. Airway for alignment and secretions.
   b. Respiratory rate, breath sounds, work of breathing (grunting, flaring, retracting, depth), symmetry of chest movement.
   c. Heart rate by counting for 6 seconds and multiplying by 10. Obtain heart rate by:
      1) Palpation at the base of the umbilical cord stump.
      2) Auscultation of the apical heartbeat with a stethoscope.

10. Meconium-stained fluid.
    a. Meconium-stained amniotic fluid may be an indication of fetal distress and should prompt the delivery room team to be prepared for possible resuscitative measures.
        1) A vigorous neonate with sustained respirations and good muscle tone may receive routine care with the initial steps of NRP. Place the neonate skin-to-skin with the mother, if possible. A bulb syringe may be used to clear the meconium-stained secretions from the mouth first and then the nose.
        2) If the neonate has depressed respirations or decreased muscle tone, suction with a bulb syringe to clear secretions from mouth and nose. After clearing the airway, if the neonate is gasping, not breathing, or has heart rate less than 100 bpm, begin PPV.
        3) Routine intubation for meconium-stained fluid is not recommended. A recent review of evidence by ILCOR has determined that there is insufficient evidence to continue the practice of routine intubation and tracheal suctioning of nonvigorous neonates (Perlman et al., 2015). As these neonates are still at risk for requiring resuscitation, at least two skilled people should be present at delivery.

B. Ventilation.
1. PPV should be initiated when the neonate has apnea or gasping respirations, a heart rate less than 100 bpm, or saturation levels (SpO_2) continue below the target range despite supplemental oxygen. Call for additional help if you are alone.
    a. Preparing for PPV.
        1) Clear airway of secretions.
        2) Place head and neck in neutral position (i.e., the "sniffing" position).
        3) The team member providing airway support and PPV should be at the neonate's head of the bed.
2. Resuscitation bags should not be larger than 750 mL and should be connected to oxygen and air source with blender attached.
    a. Self-inflating bags must have a reservoir to deliver high concentrations of oxygen, a pressure gauge, and a pressure-release valve. Bag cannot be used to deliver free-flow oxygen or CPAP.
    b. Flow-inflating (anesthesia) bags must have a gas source, pressure gauge, and flow control valve and can deliver free-flow oxygen of 21% to 100%. Positive end-expiratory pressure (PEEP) is controlled by the adjustable control valve.
    c. The T-piece resuscitator requires a compressed gas source and allows manual setting of inspiratory pressure and PEEP; can deliver 21% to 100% oxygen.
3. Mask of proper size should be used to obtain an adequate seal. Appropriate sizing should have the mask covering the chin, mouth, and nose but not the eyes.
4. PPV procedure.
    a. Assemble, set, and test the equipment before each delivery.
    b. Set the flowmeter at 10 L/min.
    c. Initial oxygen to be set at 21% for neonates ≥35 weeks' gestation. Set oxygen at 21% to 30% for neonates less than 35 weeks' gestation.
    d. Position and open airway as in "Open Airway."
    e. Assure airway is clear of secretions.
    f. Apply mask and ensure proper seal. Be careful not to apply too much pressure to the neonate's face or neck. Ensure avoiding the eyes with the mask.
    g. Place pulse oximeter or ECG monitor, and observe for improvement of heart rate and oximeter saturation. Adjust oxygen to maintain saturation trend within target range for age in minutes (see Table 5.3).
    h. Rate of ventilation is 40 to 60 breaths per minute, with initial inspiratory pressure (PIP) of 20 to 25 cm H_2O and end pressure (PEEP) of 5 cm H_2O. After initial inflating breaths and attaining a gentle chest rise, the PIP may be able to be decreased.
    i. Effective ventilation and signs of improvement include increasing heart rate, improving oximeter saturations, spontaneous breathing, and improving breath sounds and chest movement.
5. Initial heart rate assessment.
    a. After 15 seconds of initial ventilation, pause to check 6-second heart rate. With heart rate increasing, continue PPV and recheck heart rate after an additional 15 seconds.
    b. If after the initial 15 seconds of PPV, the heart rate is not increasing, check for chest movement with ventilation. If the chest is moving, continue PPV and recheck the heart rate after another 15 seconds (total of 30 seconds PPV).
    c. If after the initial 15 seconds of PPV, the heart rate is not increasing and the chest is not moving, perform the corrective actions listed next until chest movement is achieved. Once chest movement is achieved, provide 30 seconds of effective ventilation.
6. Corrective actions.
    a. Use the acronym **MR. SOPA** to assist in assessing and correcting ineffective ventilation.
        1) **M**ask adjustment on face.
        2) **R**eposition airway to "sniffing" position.
        3) **S**uction mouth and nose for secretions.
        4) **O**pen mouth slightly with jaw lifted forward.
        5) **P**ressure increase gradually.
        6) **A**irway alternative with intubation or laryngeal mask airway.

7. Second heart rate assessment.
   a. If the heart rate is ≥100 bpm, gradually decrease the rate of PPV and adjust oxygen to maintain SpO_2 within target range. PPV may be discontinued when the heart rate is sustained over 100 bpm and the infant is spontaneously breathing.
   b. If the heart rate is 60 to 100 bpm, continue PPV at 40 to 60 breaths per minute as long as the neonate is showing improvement. Monitor SpO_2 to maintain within target range. If the heart rate is not improving, assess lung sounds, chest movement, and perform the corrective actions noted earlier.
   c. If the heart rate is less than 60, reassess for chest movement and bilateral lung sounds, and perform the corrective actions as indicated. Provide oxygen to provide SpO_2 at target ranges. Inserting an alternative airway or endotracheal intubation is indicated. Increase oxygen to 100% and begin chest compressions.
8. Administering CPAP.
   a. If the neonate is breathing spontaneously with a heart rate over 100 bpm but has labored breathing and a low SpO_2 despite oxygen blow-by, CPAP may be helpful.
   b. CPAP helps keep the lungs inflated and allows for easier work of breathing for the neonate in distress.
   c. Endotracheal intubation may be avoided by using CPAP early.
   d. CPAP may be administered via a flow-inflating bag or a T-piece resuscitator. Test the amount of CPAP before placing the mask on the neonate's face. Set the PEEP on the manometer at 5 cm H_2O pressure. The CPAP pressure may be adjusted according to the neonate's work of breathing and oxygen requirement to maintain target SpO_2.
   e. It is wise to be cautious when providing CPAP, as this places the neonate at risk for air leaks (e.g., pneumothorax).
9. Oral gastric tube placement.
   a. Ventilation for more than several minutes (with or without compressions) can cause air to accumulate in the stomach.
   b. Place the oral gastric tube through the mouth rather than the nose to maximize ventilation through the nose.
   c. Aspirate gastric contents, secure in place, and leave open to air.

C. Alternative airways.
1. Indications.
   a. The neonate does not respond to face mask PPV, as evidenced by inadequate clinical improvement (heart rate, chest movement, breathing effort, color, SpO_2, muscle tone).
   b. Stabilizes the airway in situations such as diaphragmatic hernia, need for surfactant administration, and airway obstruction due to head and neck anomalies or copious, thick secretions.
   c. Prolonged ventilation is required.
   d. If chest compressions are necessary, facilitate coordination with compressions.
2. Endotracheal intubation (see Chapter 15).
   a. Obtain and prepare equipment (see Box 5.2).
   b. Should be a clean procedure.
   c. Perform intubation procedure.
   d. Confirm placement of endotracheal tube as evidenced by increase in heart rate, improvement in oximeter saturation, breath sounds over both lung fields, mist or "fogging" in endotracheal tube, and evidence of exhaled CO_2 on colorimetric CO_2 detector.
   e. Secure tube.
   f. Obtain chest x-ray to confirm endotracheal tube placement.
   g. Monitor for clinical deterioration after endotracheal intubation. Situations to consider include dislodgement of endotracheal tube (e.g., central cyanosis, oximeter desaturation, bradycardia, decreased or asymmetrical chest movement, breath sounds absent or diminished, CO_2 detector does not indicate presence of CO_2, distended abdomen, air noises audible over stomach, or no mist or "fogging" in tube), tube obstruction with secretions, pneumothorax, or equipment failure.
3. Laryngeal mask airway (LMA) (see Chapter 15).
   a. Alternative airway device useful when face mask PPV is ineffective and endotracheal intubation is not feasible or unsuccessful.
   b. May be helpful in neonates with congenital anomalies of the mouth, lip, palate, tongue, pharynx, or neck. May be necessary in neonates with extremely small mandible and large tongue such as Pierre Robin syndrome or trisomy 21.
   c. Soft, inflatable mask inserted into mouth and guided along hard palate until mask covers larynx. Once the mask is completely inserted, the cuff is inflated with air. The pilot balloon monitors the cuff's inflation. It is essential to deflate the cuff before removal of the LMA to prevent injury to the oropharynx.
   d. Limitations of the LMA include inability to use for suctioning secretions from airway, air leak may occur with high pressures, and may be ineffective with chest compressions.
   e. Evidence is insufficient to recommend use for administering endotracheal medications.

D. Chest compressions.
1. Chest compressions should be initiated when the heart rate remains less than 60 bpm after at least 30 seconds of effective PPV. Ideally, this should be

after 30 seconds of effective ventilation via a properly placed endotracheal tube or LMA.

2. The provider starting chest compressions should be standing at the side of the bed, as the team member providing coordinated ventilation is at the head of the bed.
3. It is most likely that when chest compressions are required, an umbilical catheter will need to be inserted for vascular access. Once the neonate is intubated, the team member providing chest compression should move to the head of the bed alongside the team member providing PPV, to provide space for the umbilical catheter insertion procedure.
4. Two-thumb technique.
   a. Place both thumbs side-by-side or, on a small neonate, one over the other. Location is on the sternum just below the imaginary nipple line. Take care to avoid the ribs and the xiphoid process.
   b. Encircle the neonate's chest with your hands and provide support for the back with your fingers (it is not required for fingers to touch in the back).
   c. Thumbs should remain in constant contact with the chest, yet allow the chest to fully rise during the release phase.
5. Compression depth is approximately one third the neonate's chest circumference.
6. Compression rate is 90 compressions per minute, with a compression/ventilation ratio of 3:1, equaling 120 events per minute.
7. Once chest compressions are initiated, increase the oxygen to 100%, as circulation is poor and oxygenation is decreased. Optimally, the neonate's trachea should be intubated during compressions.
   a. Reevaluate heart rate after 60 seconds of coordinated chest compressions and ventilation.
   b. ECG monitoring is preferred for assessing heart rate and saturation once chest compressions are started.
   c. A stethoscope or pulse oximeter may not be as accurate during resuscitation.
8. When the heart rate is 60 bpm or greater, stop chest compressions and continue PPV at a rate of 40 to 60 breaths per minute.
9. If the heart rate is less than 60 bpm despite 60 seconds of effective ventilation with coordinated, quality chest compressions, reassess for chest movement and equal lung sounds. Ensure that 100% oxygen is used and that depth of compressions is adequate with appropriate rate and coordinated with ventilation. Epinephrine administration and vascular access will be required at this time.

E. Medications.

1. Most neonatal resuscitations do not require medications or volume expanders. When medications are required, an umbilical venous catheter may be the fastest and most direct route. Intravenous (IV) administration of resuscitation medications is preferable whenever available. A peripheral IV line may also be used to administer medications or volume expanders (see Chapter 15). If unable to place an umbilical venous catheter or IV line, intraosseous access may be an acceptable alternative.
   a. Epinephrine is a cardiac stimulant that increases the heart rate and strength of contractions, causes peripheral vasoconstriction, and increases blood flow through the coronary arteries to the heart.
      1) Indication: Heart rate is less than 60 bpm **after** at least 30 seconds of effective assisted ventilation **and** another 60 seconds of coordinated chest compressions and airway ventilation with 100% oxygen.
      2) Dose: Only use 1:10,000 (0.1 mg/mL) concentration in neonates. IV route is preferred, although intraosseous may be used. IV or intraosseous dose is 0.1 to 0.3 mL/kg given rapidly. Endotracheal route is an option while vascular access is established, yet is the least effective. Endotracheal dose is 0.5 to 1 mL/kg.
      3) Response: Assess the heart rate 1 minute after administration; it should increase to greater than 60 bpm. If heart rate remains less than 60 bpm, dosing may be repeated every 3 to 5 minutes. If a lower dose range was used, consider increasing subsequent doses. The endotracheal dose may take longer to elicit a response, or no response may occur; repeat dose should be given once IV access is acquired.
   b. Volume expanders are fluids that increase the neonate's circulating blood volume to correct hypovolemia and facilitate tissue perfusion. Normal saline is the preferred fluid.
      1) Indication: When there is suspected shock (pallor, delayed capillary refill, weak peripheral pulses, persistent bradycardia, and no improvement in respiratory status) or a history of acute blood loss **and** the neonate is not responding to resuscitative efforts.
      2) Dose: 10 mL/kg given over 5 to 10 minutes intravenously. May be repeated if no signs of improvement.
      3) Response: Improvement in color, capillary refill time, peripheral pulses, muscle tone, and increased heart rate and saturation levels.
   c. O-negative packed red cells. Uncross-matched O-negative packed cells should be used in **emergency situations** when hypovolemia is suspected from fetal blood loss.

Postresuscitation Care

The goal of postresuscitation care is to evaluate the neonate's condition for complications, avoid intensifying conditions that may impair outcome (i.e., hypothermia, hypoglycemia), and help diagnose and treat underlying disease.

A. Assess oxygenation, ventilation, and acid–base balance.
   1. Check blood gas concentrations (capillary, arterial, and venous).
   2. Correlate findings with the neonate's clinical condition.
   3. Correlate findings with pulse oximetry and/or transcutaneous monitoring devices.
   4. Adjust the neonate's respiratory and oxygen support as needed. Assess for increase or return of respiratory distress, especially pulmonary hypertension and pneumonia.
   5. Avoid unnecessary suctioning.
   6. Consider surfactant therapy.
   7. Delay bathing.

B. Monitor glucose concentrations to ensure normoglycemia.
   1. Serial screening of blood glucose.
   2. Oral glucose gel may be used if neonate's vital signs are stable.
   3. Treat hypoglycemia and adjust maintenance dextrose infusion if IV fluids are required. Bolus infusions ($D_{10}W$, 2 mL/kg) may be required to elevate serum glucose in addition to maintenance infusion (see Chapter 9).
   4. Feeding may not be recommended, depending on neonate's status.

C. Volume and electrolyte support.
   1. Assess perfusion and evaluate for anemia, polycythemia, and hypovolemia.
   2. Calculate the fluid volume received during resuscitation and estimate volume deficiencies.
   3. Determine the amount needed (in milliliters per kilogram per day).
   4. Adjust IV rate as needed. Include all fluids in fluid calculations.
   5. Monitor the urine output. Keep an accurate account of the intake.

D. Chest and abdominal x-ray examination for pneumothorax, pneumomediastinum, pneumopericardium, and pneumoperitoneum.
   1. Assess endotracheal tube position.
   2. Assess the position of umbilical catheters.
   3. Evaluate for lung and cardiac disease.
   4. Rule out fractures and anomalies.

E. Central nervous system assessment.
   1. Assess neurologic status and reflexes.
   2. Monitor for seizure activity, unexplained apnea.
   3. Provide sedation as needed.
   4. Avoid hyperthermia.
   5. Consider induced therapeutic hypothermia once neonate meets protocol, if available.
   6. Consider delayed initiation of feedings and use of IV fluids.

F. Monitor vital signs and provide thermal support.
   1. Provide a neutral thermal environment to prevent the sequelae of hypothermia or hyperthermia. Placing the neonate skin-to-skin with mother after resuscitation may be considered based on the neonate's stability and mother's wishes. Skin-to-skin care in the initial hours after birth provides respiratory, temperature, and glucose stability, along with decreased crying and earlier breastfeeding (Phillips, 2013).
   2. Continue the assessment of perfusion and capillary refill time.
   3. Monitor the blood pressure, preferably arterial.
   4. Continuous cardiorespiratory monitoring is recommended. Assess the heart rate and respiratory rate as needed.

G. Screen for infection.
   1. Evaluate maternal history: titers, cultures, pretreatment, and risk factors.
   2. Obtain a complete blood cell count, differential cell count, platelet count, and C-reactive protein.
   3. Obtain blood and tracheal samples for cultures and for sensitivity testing as indicated.
   4. If the index of suspicion is high and the neonate's condition is stable, lumbar puncture may be performed for cerebrospinal fluid analysis.
   5. Provide broad-spectrum antibiotic coverage if suspicion for infection is high and/or cultures are positive.

H. Support family.
   1. Provide a family-centered approach to care. Actively collaborate with family regarding decision making.
   2. Provide skin-to-skin care as neonate's condition allows and mother wishes.
   3. Report the neonate's condition to the mother and significant others.
   4. Make appropriate referrals to ancillary support services.

I. Documentation.
   1. Accurate charting, including descriptive and often minute-by-minute documentation, reveals the events, interventions, and neonate's responses to the resuscitative efforts.
   2. Include pertinent perinatal factors, physical findings, procedures, and care performed; neonate's response; and team communication.
   3. Vital signs, medications, laboratory findings, and other factual data should also be included.
   4. Developmental support and the neonate's behavioral response to care should be integrated into resuscitation and stabilization documentation.

J. Safety.
   1. Ensure the neonate is accurately identified.
   2. Ensure the neonate is in a safe bedding situation. When not being held, the neonate should be placed in bed (crib, incubator, radiant warmer).
   3. Provide developmentally appropriate supportive care based on gestational age.
   4. Nurse-to-nurse communication should include a thorough history of resuscitation and stabilization.
   5. Reconcile medications if the neonate is transferred to another unit or another hospital.

Complications of Resuscitation

A. Trauma.
   1. Skin: bruises and abrasions from chest compressions, handling, and tape application and removal.
   2. Mucosa: laryngoscopy and intubation can cause trauma to and bleeding of the gums, lips, pharynx, and trachea.
   3. Internal organ damage from chest compressions.

B. Respiratory.
   1. Persistent pulmonary hypertension.
   2. Pneumonia.
   3. Pulmonary air leaks, including pneumothorax, pneumomediastinum, and pneumopericardium.
   4. Surfactant deficiency or deactivation.
   5. Meconium aspiration syndrome.

C. Neurologic.
   1. Hypoxic–ischemic encephalopathy.
   2. Apnea.
   3. Poor tone.
   4. Seizures.
   5. Intracranial hemorrhages such as subarachnoid, subgaleal, periventricular, and intraventricular.

D. Metabolic/hematologic.
   1. Hypothermia.
   2. Hypoglycemia.
   3. Electrolyte imbalance, especially calcium, sodium, and potassium.
   4. Anemia.
   5. Thrombocytopenia.
   6. Disseminated intravascular coagulopathy (DIC).
   7. Pallor, bruising, and petechiae.

E. Gastrointestinal.
   1. Ileus.
   2. Feeding intolerance.
   3. Necrotizing enterocolitis.

The Premature Neonate

The premature neonate is at higher risk for requiring resuscitative efforts compared with a full-term neonate (see Chapter 22). The late preterm neonate (34 weeks to $36^{6/7}$ weeks) is also at risk for requiring greater assistance (see Chapter 23).

A. Risk factors.
   1. Multisystem immaturity.
   2. Weak chest muscles and flexible ribs.
   3. Fragile skin, especially with very low birth weight (VLBW) neonates.
   4. Susceptible to trauma from resuscitative intervention.
   5. Susceptible to infection.
   6. Susceptible to hypovolemia.
   7. Increased thermal instability.

B. Warmth.
   1. Increase the temperature of the delivery room to 74° F to 77° F (23° C to 25° C).
   2. Use additional heat sources to maintain a neutral thermal environment.
   3. Preheat radiant warmer to 100% output well before expected birth.
   4. Place prewarmed hat on neonate's head.
   5. For neonates less than 32 weeks of gestation:
      a. Thermal wrapping with polyethylene plastic wrap or bag immediately after birth. Drying the body is not necessary.
      b. Portable thermal mattress placed below layers of warm linen.
   6. Monitor temperature closely and maintain the neonate's axillary temperature between 36.5° C and 37.5° C.
   7. Use a prewarmed transport unit during transfer.
   8. Maintain neutral thermal environment with neonate in heated, humidified incubator on servo-control.

C. Respiratory support.
   1. Oxygen.
      a. Use a blender at 21% to 30% oxygen for neonates less than 35 weeks' gestation and titrate oxygen to achieve appropriate SpO_2 range, using the same parameters as for term neonates.
      b. Monitor blood gases to adjust ventilation and oxygen concentration gradually and appropriately.
      c. Maintain SpO_2 with target range for gestational age.
      d. Monitor for apnea and bradycardia events.
   2. Ventilation.
      a. If PPV is needed, the lowest pressures possible should be used to achieve adequate responses, starting with 20 to 25 cm H_2O.
      b. Consider CPAP if heart rate greater than 100 bpm, spontaneous respirations with respiratory distress, decreased pulse oximetry, and cyanosis.
      c. Noninvasive positive pressure ventilation (NIPPV) is an additional alternative in attempting to prevent the need for endotracheal intubation.
      d. If endotracheal intubation is necessary, use initial PEEP of 5 cm H_2O.

3. Surfactant (see Chapter 24).
   a. Administration of surfactant is shown to be beneficial in neonates less than 30 weeks of gestation, even without signs of respiratory distress.
   b. CPAP immediately after birth should be considered as an alternative to routine intubation.
   c. In some cases of neonates who fail CPAP, surfactant administration and removal of endotracheal tube back to CPAP may be successful (Intubate–SURfactant–Extubate, or "INSURE") (Kandraju et al., 2013). Prophylactic surfactant is still recommended for extremely premature neonates (less than 26 weeks' gestation) because the likelihood of failing CPAP is relatively high.

D. Neuroprotection.
1. Be as gentle as possible with the tiny neonate (i.e., drying, ventilating, and cardiopulmonary resuscitation).
2. Maintain head in the midline position, preferably for the first 72 hours of life.
3. Do not position the neonate's legs higher than the head.
4. Maintain a dark, quiet environment.
5. Cluster routine care.
6. Infuse all IV fluids slowly and cautiously.
7. Avoid delivering excess ventilatory pressures during PPV or CPAP.
8. Avoid endotracheal suctioning as much as possible.
9. Consider delayed cord clamping for at least 30 to 60 seconds, based on the neonate's status immediately after birth, as this may delay resuscitative efforts. Evidence has shown that premature neonates benefit from delayed cord clamping by increasing blood volume and therefore decreasing hypotension, decreasing blood transfusions, and decreasing the risk of intraventricular hemorrhage and necrotizing enterocolitis (Chapman et al., 2016; Rhoades et al., 2017).

E. Infection prevention.
1. Wear gloves with all care and procedures.
2. Implement strategies to reduce nosocomial infections (e.g., ventilator-associated pneumonia, catheter-related bloodstream infections).
3. Use sterile supplies (e.g., sterile water) when possible for VLBW neonates.
4. Minimize use of tape and adhesives to reduce transepidermal stripping.

Special Situations

A. Choanal atresia/upper airway obstruction (see Chapter 24).
1. Definition and characteristics.
   a. Bony or soft tissue obstruction of the posterior nares; may be unilateral or bilateral.
   b. Respiratory distress may be present immediately after birth because of blockage of the primary airway, the nose.
   c. May present with cyanosis when quiet or at rest, pinks with crying.
   d. Inability to pass small-gauge suction catheter or nasogastric tube through each nare may be an indicator of choanal atresia.
2. Management.
   a. Stimulate neonate to cry, thereby using the secondary airway (mouth) for ventilation.
   b. Insert an oral airway or endotracheal tube as an oral airway into the posterior pharynx.
   c. Neonates with more complicated craniofacial malformations may require endotracheal intubation.

B. Pierre Robin syndrome.
1. Definition and characteristics.
   a. Small mandible and posteriorly set in relation to upper jaw.
   b. Displacement of the tongue posteriorly into the pharynx, causing partial or complete airway obstruction.
   c. Cleft palate is commonly associated.
2. Management.
   a. Maintain patent airway by turning the neonate onto the stomach (prone), which should cause the tongue to fall forward and open the airway.
   b. If this is not effective, insert an oral airway, a large catheter (12 F), or small endotracheal tube (2.5 mm) nasally to the posterior pharynx. If these procedures are unsuccessful, placement of an LMA may also be effective.

C. Pulmonary hypoplasia (see Chapter 24).
1. Definition and characteristics.
   a. Underdeveloped lungs resulting from insufficient space within the thoracic cavity for normal development.
   b. Associated with the Potter sequence, dysplastic renal conditions, chronic oligohydramnios, phrenic nerve absence, vertebral and chromosomal anomalies, and congenital diaphragmatic hernia.
   c. Deterioration may be rapid and acute with descending Apgar scores.
   d. Inability to ventilate the lungs adequately exhibited by poor chest movement, decreased breath sounds, and cyanosis.
   e. Very high pressures may be required to ventilate small, stiff lungs that place the neonate at high risk for pulmonary air leaks.
   f. May demonstrate poor perfusion and flaccid muscle tone related to respiratory and/or metabolic acidosis.
2. Management.
   a. Intubate.

b. Ventilate with as much pressure and oxygen as necessary to expand the lungs (i.e., adequate chest rise and fall).
c. Transilluminate and auscultate chest frequently, assessing for pulmonary air leaks. Be prepared for emergency evacuation of air leak.
d. Inhaled nitric oxide and/or extracorporeal membrane oxygenation (ECMO) treatment.

D. **Congenital diaphragmatic hernia** (see Chapter 29).
1. Definition and characteristics.
a. Herniation of the abdominal contents into the chest cavity during gestational development.
b. Pulmonary hypoplasia arises secondary to compression from abdominal organs and limited capacity for growth in the thoracic cavity.
c. Severity of symptoms is associated with the amount of lung compression and pulmonary hypoplasia. May present with respiratory distress shortly after birth and descending Apgar scores, or with late-onset respiratory distress.
d. Most commonly occurs on the left side.
e. May present with a scaphoid abdomen.
f. Lung sounds absent or decreased on the side of the defect.
g. Bowel sounds audible in the chest.
h. Heart sounds may be audible on the right side if left-sided defect.
i. Prenatal diagnosis possible through ultrasound. Polyhydramnios often present.
2. Management.
a. Consider immediate endotracheal intubation and ventilation to minimize overdistention of the stomach resulting from bag-and-mask ventilation.
b. Provide gastric decompression per 10 Fr orogastric tube, preferably Replogle (double-lumen Salem sump).
c. Systemic hypotension and respiratory or metabolic acidosis commonly occur. Aggressive management necessary to minimize pulmonary hypertension.
d. Inhaled nitric oxide may be used for neonates not responding to conventional therapies.

E. Persistent respiratory depression.
1. After PPV has restored a normal heart rate and target saturation; this respiratory depression or decreased muscle activity may be related to:
a. Brain injury such as hypoxic–ischemic encephalopathy, severe acidosis, or a central nervous system or neuromuscular abnormality.
b. Sedation related to a history of maternal narcotic administration within the 4 hours before delivery.

F. Multiple gestation.
1. Characteristics.
a. May be small for gestational age or intrauterine growth restricted.
b. Compression deformations may be present.
c. Distress may be related to placental abnormalities, compromise of cord blood flow, or mechanical complications during delivery.
2. Management.
a. Delivery of multiples may be unexpected.
b. Twin-to-twin transfusion may require volume resuscitation of donor twin.
c. Premature delivery common.
d. Provide a separate resuscitation team for each neonate. A systematic and planned approach for mobilizing extra resuscitative teams is necessary to ensure appropriate resuscitation of unexpected multiples.
e. Ensure adequate supplies and equipment are available, in addition to backup supplies, to manage multiple prolonged resuscitative efforts.

Resuscitation Outside the Hospital or Beyond the Immediate Neonatal Period

A. Temperature management.
1. Turn up the heat in the room.
2. Place the neonate skin-to-skin with mom.
3. Dry the neonate with blankets, towels, or anything available.
4. Avoid drafts and outside walls and windows.

B. Clearing the airway.
1. Wipe the mouth and nose with a cloth wrapped around your finger.
2. Use bulb syringe.

C. Ventilation.
1. Mouth-to-mouth or mouth-to-nose resuscitation can be used if no resuscitation bag and mask is available.

D. Chest compressions.
1. Apply NRP recommendations and proceed with 3:1 compression-to-ventilation ratio.

E. Vascular access.
1. Peripheral IV access is preferred.
2. Intraosseous needle into the tibia is an effective alternative.

Ethics

Collaboration with the family is essential with all decision making. Support the parents by providing options of caring

for their neonate during the dying process. Most importantly is minimizing suffering for the neonate.

A. Noninitiation of resuscitation may be appropriate in the delivery room when:
   1. Confirmed less than 22 weeks of gestation.
   2. Anencephaly.
   3. Confirmed lethal chromosomal anomaly or congenital malformation.
   4. Conditions associated with extremely high index of mortality or severe morbidity.

B. Discontinuation of support may be appropriate when it is determined that life-sustaining treatment is no longer in the neonate's best interest. At this point, it may be appropriate to switch from curative to palliative care. Gestational age, reason for arrest, involvement of other complications, whether therapeutic hypothermia is possible, and the expressed feelings and expectations of the parents need to be considered.

C. A strong predictor of mortality and morbidity is an Apgar score of 0 at 10 minutes. If after 10 minutes of complete and effective resuscitative efforts, the heart rate remains undetectable, it is reasonable to stop the resuscitation. However, each situation must be individually decided, including predisposing factors around the birth, availability of advanced neonatal care, and family's wishes.

D. Information at or around the time of delivery is often incomplete. Resuscitative options may include initiation of therapy and reevaluation of treatment decision making after more information is available.

E. Involve resource supports, such as clergy, social services, and palliative care team.

F. Consult hospital ethics committee or legal counsel if needed.

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CHAPTER 6

Thermoregulation

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OBJECTIVES

1. Discuss the importance of thermoregulation in the care of newborn infants.
2. Compare mechanisms of heat transfer involved in newborn thermoregulation.
3. Identify newborns at increased risk for thermal instability.
4. Recognize symptoms of hypothermia and hyperthermia in neonates.
5. Describe the physiologic processes involved in thermoregulation.
6. Apply strategies for managing the thermal environment.

Introduction

Neonates are the most vulnerable population in regard to temperature control. The smallest and most premature are unable to protect themselves against fluctuations in environmental temperature. Nurses are the first line of defense for this population. Thus, it is important that nurses understand the physiology and management of thermoregulation and use their skill and expertise to provide the best environment for these at-risk patients.

A. Background.
   1. Adverse consequences are associated with both hypothermia and hyperthermia. Hypothermia is the major temperature abnormality in neonates. An increase in mortality and morbidity associated with hypothermia is well documented and is recognized as a problem worldwide.
      a. In Europe during the mid to late 1800s, the use of an early crude form of incubator increased the survival rate of small babies.
      b. Pierre Budin documented the increased risk and morbidity of hypothermia in premature and low birth weight infants in "The Nursling" (Budin, 1907).
      c. In the early 1900s, premature babies displayed in incubators at world fairs and expositions showed increased survival of small babies cared for in warm environments (Silverman, 1979).
      d. In the 1950s, Silverman demonstrated that hypothermia increased morbidity and mortality (Silverman et al., 1958).
      e. The World Health Organization (WHO) recognizes hypothermia as a major threat to the health of newborns throughout the world ("Thermal protection of the newborn," WHO, 1997).
      f. The term *golden hour* refers to the first hour after a critical event, which is considered the most important for successful intervention. The term has been adopted by neonatology to describe an evidence-based approach to care during the first hour of life. A major focus during the "golden hour" is prevention of heat loss. Golden hour improvement projects have resulted in improved neonatal intensive care unit (NICU) admission temperatures (Ashmeade et al., 2016; Bissinger and Annibale, 2010; Castrodale and Rinehart, 2014).

B. Mechanisms of heat transfer.
   1. The transfer of heat moves from warm to cool. Four mechanisms of heat transfer affect neonates: conduction, convection, radiation, and evaporation (Fig. 6.1). Understanding these mechanisms and developing strategies to prevent both heat loss and heat gain are important in thermoregulation in the neonate.
      a. Conduction is the transfer of heat via direct contact.
         1) Heat is lost when the neonate comes in contact with a cold surface such as a mattress, x-ray plate, or scale.
         2) Heat is gained when the neonate comes in contact with a warmer surface such as a chemical warming mattress or warm blankets.
         3) The rate of heat transfer varies with the temperature gradient and the amount of skin in contact with the surface. Heat is transferred more readily from the skin to a metal object than from the skin to a cloth surface.

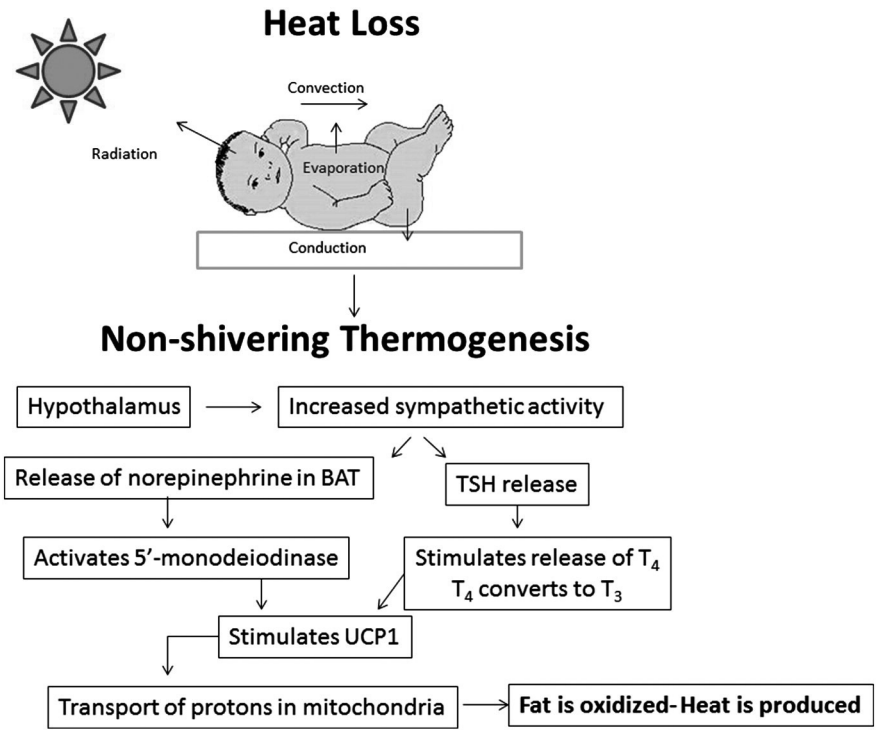

Fig. 6.1 Diagram of heat loss and nonshivering thermogenesis. *BAT*, Brown fat of adipose tissue; *TSH*, thyroid-stimulating hormone; T^3, triiodothyronine; T^4, thyroxine; *UCP1*, uncoupling protein-1. *(From Knobel, R. [2014]. Fetal and neonatal thermal physiology.* Newborn & Infant Nursing Reviews, *14:45–49.)*

b. Convection is heat transfer due to air currents or drafts.
   1) Incubators transfer the heat to infants through the circulation of warm air.
   2) Heat loss will occur when an infant is exposed to cool air, such as air conditioning, or is placed into an incubator that has not been prewarmed.
   3) Heat transfer increases with the temperature gradient between skin and air, with increased airflow, and with increased skin exposure.

c. Radiation is the transfer of heat from a warm object to a cooler object that is not in direct contact through infrared energy transfer. Think of standing near a sunny window in summer (heat gain) or a frosty window in winter (heat loss).
   1) Radiant warmers provide heat by this method.
   2) Heat transfer is affected by the temperature gradient and the distance and angle between the heat source and the skin surface.
   3) Radiant heat transfer is not affected by ambient air temperature.

d. Evaporation is heat transfer due to water vaporizing from the skin. This is known as *transepidermal water loss* (TEWL). Evaporation also occurs in the respiratory tract as moisture is lost into the drier surrounding air.
   1) In the delivery room, TEWL occurs due to the evaporation of amniotic fluid and accounts for 25% of neonatal heat loss (Dahm and James, 1972).
   2) High total body water, immature skin, and a relatively large body surface area result in increased evaporative losses in premature infants. This is more significant in very low birth weight infants (VLBW) and even more so in extremely low birth weight (ELBW) infants.

C. Thermal instability.
   1. Nurses caring for neonates should be able to identify infants who are at high risk for thermal instability. Prevention, early detection, and management of hypothermia and hyperthermia are essential to the well-being of neonates (Table 6.1).
      a. Hypothermia.
         1) Decreased brown fat, decreased glycogen stores, high TEWL, and poor muscle tone place neonates at increased risk for hypothermia (Box 6.1).
            a) Prematurity.
            b) Intrauterine growth restriction.
            c) Critically ill, sedated, or neurologic conditions.
            d) Open skin defects.
         2) Symptoms of thermal stress include a broad range of clinical, physiologic and behavioral changes (Box 6.2).
            a) Cardiorespiratory.

Table 6.1

Mechanisms of Heat Transfer and Strategies for Prevention

Mechanism	Heat Transfer	Situation	Strategies for Prevention
Conduction	Loss	Cold mattress	Prewarm bed or cover with several layers of warm blankets
		Weighing scale	Cover scale with a prewarmed blanket
		Extended posture	Position infant in a flexed/nested position
	Gain	Chemical mattress	No direct heat due to burn risk; place a blanket over mattress Follow manufacturer's recommendations
		Hot water bottle	Limit use due to inability to control temperature No direct heat due to burn risk; place a blanket over bottle
		Too many layers of clothing/blankets	Educate parents in thermoregulation
Convection	Loss	Cold air	Increase temperature in delivery room Move away from air conditioning vents Use radiant warmer
	Gain	Incubator	Monitor temperature frequently until neutral thermal conditions are established
Evaporation	Loss	Amniotic fluid	Place skin-to-skin with mother if condition allows Dry with warm blankets Wrap with warm blankets VLBW: place in polyethylene bag
		Bathing	Warm room Warm water Bathe quickly Dry and dress
		Vasodilation	Avoid overheating Avoid rapid rewarming
	Gain	Humidified incubator	Maintain prescribed humidity
		Vasoconstriction	Maintain neutral thermal environment Avoid situations that contribute to cold stress
Radiation	Loss	Cold incubator wall	Prewarmed incubator Double-walled incubator
		Cold window	Move away from window or cover window Radiant warmer with servo-control
	Gain	Direct sunlight	Position away from windows or close blinds
		Radiant warmer	Always use in servo-control mode
		Heat lamp	Use only as a last resort and monitor infant's temperature frequently

VLBW, Very low birth weight.

b) Behavioral.
c) Neurologic.

3) Poor weight gain may be a symptom of chronic hypothermia due to increased caloric use to maintain a normal temperature.
4) Coagulopathy may occur when hypothermia is severe.

b. Hyperthermia.
1) Neonates are at risk for hyperthermia because of the inability to dissipate heat (see Box 6.1).
a) Hypermetabolism due to sepsis.
b) Cardiac problems.
c) Drug withdrawal.
d) Dehydration.
e) Central nervous system (CNS) injury and malformation.
f) Drug side effects (prostaglandins).
2) Iatrogenic hyperthermia may occur when a radiant warmer is used on manual control.
3) Severe hyperthermia may be associated with seizures and death.

c. Monitoring temperature.
1) Frequent temperature measurements and observation are key to early detection of thermal instability.
2) It is important to measure the neonate's temperature accurately to ensure the temperature is within the normal range and to document the temperature in the medical record to provide data for following temperature trends.
3) Axillary temperatures are easy to obtain, are minimally invasive, and correlate well with core temperature.
a) Normal temperature range is 97.7° to 99.5° F (36.5° to 37.5° C) (*Guidelines for*

Box 6.1

Infants at Risk for Hypothermia and Hyperthermia

Hypothermia

- Cardiorespiratory abnormalities
- Central nervous system (CNS) abnormalities
- Critically ill
- Endocrine disorders
- Hypoglycemia
- Infection
- Large abdominal wall defects
- Large neural tube defects
- Premature
- Sedated infants/neuromuscular blockade
- Small for gestational age/growth restriction

Hyperthermia

- Cardiac defect
- CNS injury or malformation
- Dehydration
- Drug withdrawal
- Iatrogenic overheating
- Infection
- Maternal epidural anesthesia
- Maternal fever
- Medication side effects (prostaglandin)

Data from American Academy of Pediatrics and American College of Obstetricians and Gynecologists. (2007). *Guidelines for perinatal care* (6th ed.). Elk Grove Village, IL, and Washington, DC: American Academy of Pediatrics and American College of Obstetricians and Gynecologists; Baumgart, S. (2008). Iatrogenic hyperthermia and hypothermia in the neonate. *Clinics in Perinatology*, 35(1):183–197, ix–x; Blackburn, S. (2013). *Maternal, fetal, & neonatal physiology* (4th ed.). St. Louis, MO: Elsevier Saunders; Knobel, R., and Holditch-Davis, D. (2007). Thermoregulation and heat loss prevention after birth and during neonatal intensive-care unit stabilization of extremely low-birthweight infants. *JOGNN: Journal of Obstetric, Gynecologic and Neonatal Nursing*, 36(3):280–287; Lieberman, E., Lang, J., Richardson, D. K., et al. (2000). Intrapartum maternal fever and neonatal outcome. *Pediatrics*, 105(1 Pt. 1):8–13; and Mance, M. J. (2008). Keeping infants warm: Challenges of hypothermia. *Advances in Neonatal Care*, 8(1):6–12.

Box 6.2

Symptoms of Thermal Stress in Newborns

Hypothermia

- Apnea
- Bradycardia
- Central cyanosis
- Central nervous system (CNS) injury
- Coagulation defects (i.e., pulmonary hemorrhage)
- Death
- Hypoglycemia
- Hypotension/decreased cardiac output
- Hypotonia
- Hypoxia
- Feeding intolerance (abdominal distention, emesis, increased residuals)
- Increased metabolic rate
- Irritability
- Lethargy
- Metabolic acidosis
- Peripheral vasoconstriction (pallor, decreased capillary refill time)
- Poor weight gain (chronic hypothermia)
- Pulmonary vasoconstriction (persistent pulmonary hypertension of the newborn)
- Respiratory distress (decreased surfactant synthesis and activity)
- Shivering (mature neonates in presence of severe hypothermia)
- Weak cry or suck

Hyperthermia

- Apnea
- CNS depression/injury
- Death
- Dehydration (increased insensible water loss)
- Flushed/red skin
- Hypernatremia
- Irritability
- Lethargy/weak cry
- Poor feeding
- Seizures
- Sweating (term neonates)
- Tachycardia
- Tachypnea
- Vasodilation
- Warm to touch

Data from Baumgart, S. (2008). Iatrogenic hyperthermia and hypothermia in the neonate. *Clinics in Perinatology*, 35(1):183–197, ix–x; Blackburn, S. (2013). *Maternal, fetal, & neonatal physiology* (4th ed.). St. Louis, MO: Elsevier Saunders; Knobel, R., and Holditch-Davis, D. (2007). Thermoregulation and heat loss prevention after birth and during neonatal intensive-care unit stabilization of extremely low-birthweight infants. *JOGNN: Journal of Obstetric, Gynecologic and Neonatal Nursing*, 36(3):280–287; and Mance, M. J. (2008). Keeping infants warm: Challenges of hypothermia. *Advances in Neonatal Care*, 8(1):6–12.

Perinatal Care, Kilpatric et al., 2017; *Textbook of Neonatal Resuscitation (NRP)*, Weiner and Zaichkin, 2016; "Thermal protection of the newborn: a practical guide," WHO, 1997; Wyllie et al., 2015).

b) The WHO (1997) classifies hypothermia as:
   (1) Mild: 96.8° to 97.7° F (36° to 36.5° C).
   (2) Moderate: 89.6° to 96.8° F (32° to 36° C).
   (3) Severe: less than 89.6° F (<32° C).

c) Use electronic and digital thermometers according to the manufacturer's specifications.

4) Skin temperatures provide continuous temperature monitoring and a feedback mechanism when servo-controlled equipment is in use.
   a) Attach the thermistor securely to an exposed area of skin with an insulated cover, avoiding bony areas.
   b) Desired skin temperatures range from 97.2° to 99° F (36.2° to 37.2° C) (Knobel, 2014a).
   c) Skin temperatures on the abdomen, flank, and axilla have been found to correlate closely in hemodynamically stable infants (Joseph et al., 2017; Schafer et al., 2014).
   d) The use of clothing, wraps, or positioning devices inside a servo-controlled incubator may affect the skin temperature and require adjustment of the servo-control to maintain the axillary temperature in the desired range (Boyd et al., 2017; Schafer et al., 2014).
   e) If both central (abdominal) and peripheral skin temperatures are monitored, the expected difference is 0.5° to 1° C (Turnbull and Petty, 2013).
   f) A difference of 2° C or greater between central and peripheral skin temperatures is associated with cold stress resulting in peripheral vasoconstriction in infants beyond the first day of life. (Horns, 2002; Knobel et al., 2009; Lyon et al., 1997; Mok et al., 1991).
   g) A temperature of 98.2° to 98.4° F (36.8° to 36.9° C) might be optimal during transition in ELBW infants due to a decreased ability for vasoconstriction on the first day of life (Knobel, 2014b).
   h) Responding to decreases in skin and axillary temperatures at the first sign of cold stress may prevent hypothermia.

5) Rectal temperatures with a thermometer pose the risk of intestinal perforation and are not recommended.
   a) The core temperature may not decrease until the neonate has totally decompensated.
   b) Rectal thermistors are soft, flexible probes and provide continuous monitoring during therapeutic cooling for hypoxic–ischemic encephalopathy (HIE) (see Chapter 34).

6) Esophageal temperatures provide core temperature monitoring during therapeutic cooling for HIE or during surgery (see Chapter 34).

7) Ear thermometers are fast and easy to use but may be too large for premature infants. If the probe is placed incorrectly, the surface temperature may be measured rather than an approximation of core temperature.

8) Infrared thermometers, also called *temporal artery thermometers,* measure the surface temperature without touching the infant by capturing heat radiated from the skin surface (Sim et al., 2016).
   a) May be useful in newborn nurseries and in the more chronic infants in the NICU because they do not disrupt an infant's sleep pattern.
   b) They work best with infants in open cribs (Sim et al., 2016).
   c) More study is needed before using these thermometers routinely in neonatal units.

Physiology of Thermoregulation

Understanding the physiology of thermoregulation will provide the nurse with a knowledge base for temperature control in this population. It is important to distinguish between environmental, iatrogenic, and infectious causes of abnormal temperatures.

A. In utero.
   1. The maternal temperature is the ambient environmental temperature for the fetus (Blackburn, 2018; Knobel, 2014a).
   2. The neonate's temperature at birth reflects the intrauterine temperature.
      a. If the mother has a fever, it is common for the neonate's temperature to be elevated.
      b. Maternal temperature increases as labor progresses and may increase by an average of 1° C during labor due to physical activity and stimulation of the thermoregulatory center in the hypothalamus (Blackburn, 2018).
      c. Epidural anesthesia may also increase the maternal temperature. Temperatures as high as 99.5° to 100.4° F (38° C) have been reported (Blackburn, 2018).
      d. Increased maternal temperature is associated with lower Apgar scores, tachycardia, hypotonia, hypoxia, and an increased need for resuscitation and oxygen at birth (*Textbook of Neonatal Resuscitation (NRP)*, Weiner and Zaichkin, 2016).

B. After birth.
1. Physiologic conditions affect thermal stability, including physical characteristics of the neonate, metabolic processes, and physical activity.
   a. Thermal receptors in the skin affect the infant's response to cold stimuli (Blackburn, 2018).
      1) The most prominent and sensitive skin receptors are in the trigeminal area of the face (Blackburn, 2018).
      2) Stimulation of thermal receptors leads to vasoconstriction as a measure to conserve heat (Knobel, 2014a).
      3) ELBW infants are unable to respond to hypothermia with vasoconstriction during the first 12 hours after birth (Knobel, 2014a).
   b. The large surface area–to–body mass ratio in neonates affects thermoregulation.
      1) In term neonates, it is 3 times greater than that of an adult (Blackburn, 2018).
      2) In the preterm infant, it is 5 to 6 times greater than that of an adult and increases as gestation decreases.
   c. Premature infants have very thin skin, allowing greater loss of water and heat than seen in term neonates.
      1) Thin, permeable skin allows water to evaporate from the skin surface (TEWL) (Agren et al., 2006; Sedin and Agren, 2006).
      2) At 25 weeks of gestation, premature infants can lose 15 times more water through their skin than term neonates do (Agren et al., 2006; Sedin and Agren, 2006).
      3) The loss of water, and therefore heat, is inversely proportional to gestational age until about 33 weeks of gestation, when TEWL is similar to that of a term infant (Agren et al., 2006; Sedin and Agren, 2006).
   d. Posture can affect body temperature by decreasing or increasing the surface area for heat loss.
      1) Term neonates may lie in a tucked position to conserve heat or extend their arms and legs to dissipate heat.
      2) Preterm infants lack the muscle tone to maintain a flexed position and rely on caregivers to position them appropriately.
   e. Thermoregulation in neonates is affected by the type and amount of accumulated fat, which in turn is affected by both gestational age and birth weight.
      1) Infants have less insulating subcutaneous fat than adults do. Term neonates have only 16% of body fat compared with 30% to 35% in adults; preterm infants have even less.
      2) Brown fat or brown adipose tissue (BAT) generates more energy than any other tissue in the body and is important in heat production through nonshivering thermogenesis (NST) (see Fig. 6.1) (Aherne and Hull, 1966; Knobel, 2014a).
         a) NST, the major method of heat production in the neonate, is triggered when skin temperature decreases to less than 95° to 96.8° F (35° to 36° C).
         b) Heat production through NST results in metabolism of BAT and is regulated by uncoupling protein-1 (UCP1) and thyroid-stimulating hormone (TSH) activity (Knobel, 2014a).
            (1) The hypothalamus increases sympathetic activity, releasing TSH.
            (2) TSH releases thyroxine (T_4) and stimulates norepinephrine production.
            (3) Norepinephrine activates 5′ monodeiodinase in BAT to convert thyroxine (T_4) to triiodothyronine (T_3).
            (4) UCP1 is stimulated, resulting in the transport of protons in the mitochondria to oxidize BAT and produce heat.
         c) A heavy concentration of blood vessels gives BAT its characteristic brown color and serves to conduct heat into the circulation (Aherne and Hull, 1966).
         d) Metabolism of BAT involves the breakdown of triglycerides into glycerol and fatty acids and is dependent on the availability of oxygen, glucose, and adenosine triphosphate (ATP).
            (1) If these elements are not available, as is the case during hypoxia, acidosis, and hypoglycemia, heat production will suffer (Aherne and Hull, 1966).
         e) BAT is found in the intrascapular area; the axilla; around the kidneys and adrenal glands; in the mediastinum; and around the trachea, heart, lungs, liver, and abdominal aorta (Aherne and Hull, 1966).
         f) The amount of available BAT is dependent on gestational age, first appearing around 25 to 26 weeks, increases significantly during the third trimester, and reduces when used during exposure to cold (Aherne and Hull, 1966).
         g) Infants less than 32 weeks of gestation do not have enough BAT to produce significant amounts of heat by NST (Aherne and Hull, 1966).
   f. Metabolic processes generate energy by metabolism of fat, including BAT, glucose, and protein (Blackburn, 2018).
      1) All metabolically active tissues can generate heat. The organs that generate the greatest amount of energy are the brain, heart, and liver.

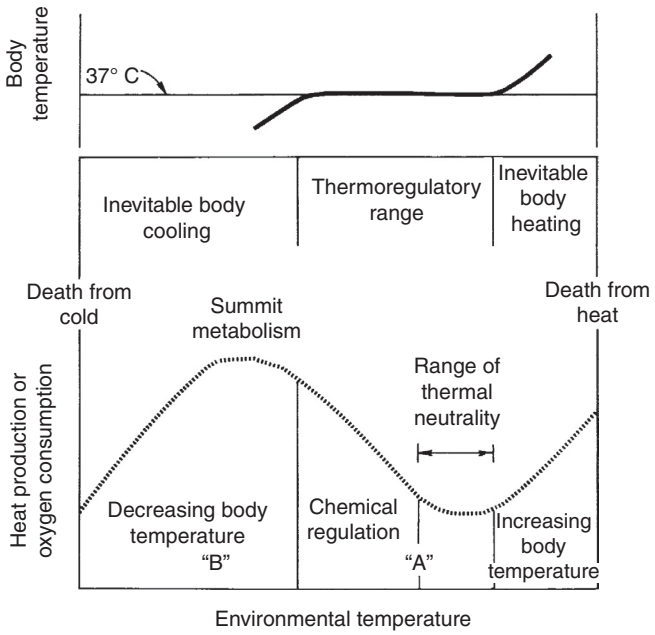

Fig. 6.2 Temperature versus oxygen consumption. *(From Fanaroff A. A. and Fanaroff J. M. [2013].* Klaus and Fanaroff's care of the high-risk neonate *[6th ed.]. Philadelphia, PA: Elsevier Saunders.)*

2) An increase in metabolic rate can produce heat but also leads to an increase in oxygen consumption (Fig. 6.2). This may be a problem in critically ill neonates with borderline oxygenation.
3) Term neonates can increase their metabolic rate by 200% to 300% through a combination of metabolic and physical responses (Blackburn, 2018).
4) VLBW infants may only be able to increase their metabolic rate by 25%, whereas ELBW infants may not be able to respond at all (Blackburn, 2018).
5) Critically ill neonates may not have the reserves of oxygen, glucose, or energy to mount an increase in metabolic rate and adapt to an unstable thermal environment.
6) Hypothermia may lead to respiratory distress, hypoglycemia, and the production of lactic acid.

g. Physical activity can generate heat, but only late preterm and term infants have enough muscle tone to produce heat by this method, and this may only be effective for a short time.
1) Increased physical activity, such as feeding, crying, restlessness, or hyperactivity, increases the metabolic rate (Blackburn, 2018).
2) Neonates receiving sedation, paralytics, or other medications leading to decreased activity or decreased muscle tone may have a blunted response to environmental temperatures.

h. Shivering is an involuntary method of heat production that is rare in the neonate. The neonate only shivers after prolonged cold stress that leads to decreased spinal cord temperature (Blackburn, 2018).

Management of the Thermal Environment

This aspect of neonatal care falls under the purview of the nurse. All infants have thermal management challenges in the delivery room and during transition. If an infant is ill or has congenital anomalies, they may continue to have problems with thermoregulation. Premature infants have ongoing needs that must be addressed until they are able to maintain their own core temperature without metabolic consequences, such as poor weight gain. It is crucial for the nurse to understand the importance of this role and to be versed in the use of equipment available to manage the thermal environment of newborn infants whether in the delivery room, the nursery, or during transport.

A. Delivery room management.
1. The primary challenge is the prevention of hypothermia, especially in those newborns who are premature, late preterm, and low birth weight.
2. The goal is to maintain the axillary temperature of nonasphyxiated newborns between 36.5° and 37.5° C (Wyllie et al., 2015).
3. Room temperature.
a. The newborn's temperature may drop 0.2° C to 1° C per minute in the delivery room. This is due to evaporative losses from amniotic fluid, convective losses to cooler room air, and radiation to cooler structures such as walls (Blackburn, 2018).
1) The gradient between the ambient room temperature in the delivery room and the neonate's skin temperature promotes heat loss.
2) The delivery room temperature should be maintained above 77° to 78.8° F (25° to 26° C) for term infants and at least 78° to 80° F (26° to 27° C) for infants less than 29 weeks of gestation (*Guidelines for Perinatal Care*, Kilpatric et al., 2017; *Textbook of Neonatal Resuscitation (NRP)*, Weiner and Zaichkin, 2016).
4. Dry the infant immediately and remove wet linen (unless using a polyethylene bag) to minimize evaporative heat.
a. Use prewarmed absorbent towels to dry the infant gently, taking care not to damage the skin.
b. Use warm blankets and prewarm any surfaces that come in contact with the infant's skin during stabilization, routine delivery care, and weighing of the infant to minimize conductive heat loss.

5. Avoid drafts to minimize convective heat loss.
6. If condition of the infant allows, drying and placing the infant against the mother's bare skin (skin-to-skin holding), then covering with a warm blanket, allows heat from the mother to maintain the infant's temperature (Wyllie et al., 2015). (Skin-to skin holding is discussed later in this chapter.)
7. Delayed cord clamping or cord milking is being practiced in some centers. Although NICU admission temperatures have not differed, the effects of this practice on the delivery room temperature should be monitored (Fogarty et al., 2018, Katheria et al., 2015).
8. Heat loss barriers.
   a. Polyethylene bags/wrap.
      1) Should be used in neonates less than 32 weeks' gestation to prevent evaporative heat loss and allow visualization and heat gain from the radiant warmer during resuscitation and stabilization (*Guidelines for Perinatal Care*, Kilpatric et al., 2017; Wyllie et al., 2015).
      2) Immediately place the infant in the wrap from the neck to the feet.
      3) Only dry the head and cover with an insulated cap to prevent evaporative losses (the infant's head represents a large surface area for heat loss to occur).
      4) Maintain the wrap until the neonate's temperature is stable in a humidified environment for 1 hour.
      5) If polyethylene is not available, food-grade plastic may be used (*Guidelines for Perinatal Care*, Kilpatric et al., 2017).
   b. Open skin defects (gastroschisis, myelomeningocele) present a major challenge to thermoregulation, as the open defect presents a permeable surface for rapid fluid losses and increased evaporative heat loss.
      1) Cover the defect with warm, sterile saline–soaked gauze and a sterile, waterproof barrier to reduce evaporative losses (see Chapter 29).
9. External heat sources.
   a. Radiant warmer or prewarmed incubator.
      1) Use in the delivery room to maintain the infant's temperature during routine care and stabilization.
      2) Radiant warmers should always be used with a servo-control to prevent overheating (*Guidelines for Perinatal Care*, Kilpatric et al., 2017).
   b. Chemical mattress.
      1) Improves thermal control in VLBW newborns in the delivery room and during transport.
      2) Place a blanket between the neonate and the chemical mattress to prevent burns.
      3) Remove the chemical mattress once the infant is warm and in a stable thermal environment.
   c. Transport incubator.
      1) The incubator usually has equipment built in or attached for monitoring, suctioning, and providing respiratory support and intravenous infusions.
   d. Passive cooling.
      1) Avoid overheating if perinatal asphyxia is suspected.
      2) Passive cooling strategies to preserve brain function may be appropriate (see Chapter 34).

B. Nursery.
1. Room temperature should be maintained at 72° to 78° F (22° to 26° C) (*Guidelines for Perinatal Care*, Kilpatric et al., 2017).
2. Humidity in the nursery should be maintained at 30% to 60% (Blackfan and Yaglou, 1933; *Guidelines for Perinatal Care*, Kilpatric et al., 2017).
3. Equipment.
   a. Use equipment according to the manufacturer's directions and unit policies and procedures.
   b. Incubators.
      1) Convective heat source.
      2) The goal of incubator care is to provide a neutral thermal environment (NTE). NTE is the temperature that is required to maintain the core temperature while minimizing metabolic needs and oxygen consumption (Fig. 6.3).
      3) Servo-control.
         a) Uses the neonate's skin temperature to control the temperature inside the incubator.
         b) It is essential that the skin probe be securely attached to the infant's skin to function correctly.
         c) Safety features to prevent overheating include the setting of upper limits of air temperature and alarms to alert the nurse to a detached probe.
         d) In this mode, the nurse must document the neonate's axillary temperature, the

Fig. 6.3 Incubator with cover. *(Courtesy Allen S. Kramer, Texas Children's Hospital, Houston, TX.)*

incubator set point, the skin temperature, and the air temperature.

4) Manual or air control.
   a) The set air temperature controls heater output.
   b) There is less variability in air temperatures compared with when servo-control is used.
   c) In this mode, the nurse must document the neonate's axillary temperature, the set point, and the air temperature.
5) An NTE chart may be used to select the initial incubator temperature, which is then adjusted as needed (Table 6.2).
   a) The NTE chart was established in the mid-1960s and had neonates on a flat mattress wearing only a diaper.
   b) Some incubators now have a built-in feature that uses age and birth weight to recommend a starting temperature.
   c) A number of factors affect the temperature needed to maintain thermal stability, including gestational age; birth weight; chronologic age; humidity; proximity to outside walls and windows; and the use of positioning devices, clothing, or swaddling.
6) Incubator covers.
   a) Decrease radiant heat loss from incubator walls (see Fig. 6.3).
   b) Incubator covers can be used with transport incubators to decrease radiant loss in cold climates and to decrease radiant gain in hot climates and on sunny days (Fig. 6.4).

Table 6.2

Neutral Thermal Environmental Temperatures

Age and Weight	Range of Temperature (° C)	Age and Weight	Range of Temperature (° C)
0 to 6 hours		72 to 96 hours	
<1200 g	34 to 35.4	<1200 g	34 to 35
1200 to 1500 g	33.9 to 34.4	1200 to 1500 g	33 to 34
1501 to 2500 g	32.8 to 33.8	1501 to 2500 g	31.1 to 33.2
>2500 g	32 to 33.8	>2500 g	29.8 to 32.8
6 to 12 hours		4 to 12 days	
<1200 g	34 to 35.4	<1500 g	33 to 34
1200 to 1500 g	33.5 to 34.4	1501 to 2500 g	31 to 33.2
1501 to 2500 g	32.2 to 33.8	>2500 g	
>2500 g	31.4 to 33.8	4 to 5 days	29.5 to 32.6
12 to 24 hours		5 to 6 days	29.4 to 32.3
<1200 g	34 to 35.4	6 to 8 days	29 to 32.2
1200 to 1500 g	33.3 to 34.3	8 to 10 days	29 to 31.8
1501 to 2500 g	31.8 to 33.8	10 to 12 days	29 to 31.4
>2500 g	31 to 33.7	12 to 14 days	
24 to 36 hours		< 500 g	32.6 to 34
<1200 g	34 to 35	1501 to 2500 g	31 to 33.2
1200 to 1500 g	33.1 to 34.2	>2500 g	29 to 30.8
1501 to 2500 g	31.6 to 33.6	2 to 3 weeks	
>2500 g	30.7 to 33.5	<1500 g	32.2 to 34
36 to 48 hours		1501 to 2500 g	30.5 to 33
<1200 g	34 to 35	3 to 4 weeks	
1200 to 1500 g	33 to 34.1	<1500 g	31.6 to 33.6
1501 to 2500 g	31.4 to 33.5	1501 to 2500 g	30 to 32.7
>2500 g	30.5 to 33.3	4 to 5 weeks	
48 to 72 hours		<1500 g	31.2 to 33
<1200 g	34 to 35	1501 to 2500 g	29.5 to 32.2
1200 to 1500 g	33 to 34	5 to 6 weeks	
1501 to 2500 g	31.2 to 33.4	<1500 g	30.6 to 32.3
>2500 g	30.1 to 33.2	1501 to 2500 g	29 to 31.8

For their table, Scopes and Ahmed had the walls of the incubator 1° to 2° C warmer than the ambient air temperatures.

Adapted from Scopes, J. W. and Ahmed, I. (1966). Range of critical temperatures in sick and premature babies. *Archives of Disease in Childhood*, 41:417. In Fanaroff A. A. and Fanaroff J. M. (2013). *Klaus & Fanaroff's care of the high-risk neonate* (6th ed.). Philadelphia, PA: Elsevier Saunders.

Fig. 6.4 Transport incubator with cover. *(Courtesy Allen S. Kramer, Texas Children's Hospital, Houston, TX.)*

7) Double-walled incubators direct warm air between the inner and outer incubator walls to reduce radiant heat loss (Bell and Rios, 1983; Laroia et al., 2007).
   a) In some double-wall incubators, an upper panel may be removed to facilitate phototherapy and results in increased nonradiant losses (Delanaud et al., 2016).
   b) Increasing the incubator air temperature by 0.15° to 0.2° C reduces nonradiant heat loss (Delanaud et al., 2016).
8) Humidity.
   a) Is recommended for thermal management of VLBW infants (Agren et al., 1998; Blackfan and Yaglou, 1933; Hammarlund et al., 1977; Kim et al., 2009).
   b) Reduces TEWL, the major source of thermal instability in the first few weeks of life due to increased body surface area, increased skin permeability, and increased extracellular fluid (Agren et al., 2006; Lund et al., 2013).
   c) Humidification can reduce the infant's fluid needs.
      (1) Start at 70% or greater for the first 7 days of life.
      (2) Gradually decrease humidity to 50% until the infant is 28 days old or 30 to 32 weeks' postmenstrual age (Lund et al., 2013).
      (3) There is less need for humidity after the first week of life due to maturation of the infant's skin and decreased TEWL (Lund et al., 2013).
      (4) Skin barrier maturation develops in 2 to 4 weeks, longer in extremely premature infants (Agren et al., 2006).
      (5) Continuing high humidity beyond the first week may slow skin maturation (Agren et al., 2006).
   d) Humidity can be provided while the infant is under a radiant warmer using a polyethylene tent coupled with a device that provides constant humidity heated to body temperature.
   e) High-absorbency cellulose/polyacrylate diapers absorb moisture in high-humidity environments and may interfere with assessment of accurate urine output (Amey et al., 2008).
   f) Current incubator humidification heats water to a temperature that kills most organisms, then introduces moisture into the environment as a vapor to avoid droplet formation, as droplets can serve as vectors for bacteria.
      (1) Avoid condensation inside the incubator (Lund et al., 2013).
      (2) Cleaning and water changes should be done according to the manufacturer's recommendations.
   g) Respiratory gases should be humidified to prevent evaporative heat loss.

c. Radiant warmers.
   1) Provides radiant heat to maintain temperature while providing improved access to the infant for assessment and procedures when compared with an incubator.
   2) Manual control is used for prewarming only.
   3) Servo-control is used when caring for an infant on a warmer and provides a feedback loop using the infant's skin temperature to regulate heater output. This is important due to the risk of underheating or overheating when on manual control.
   4) An increase in insensible water loss occurs when infants are cared for in radiant warmers.
      a) This increased fluid loss poses a risk for fluid and electrolyte imbalance.
      b) Careful documentation of intake, output, and weight are essential in managing fluid needs of infants cared for in radiant warmers.
   5) Convective losses are also increased in a radiant warmer. Care should be taken to minimize drafts.
d. Hybrid incubators.
   1) Hybrid incubators function as either incubators or radiant warmers (Fig. 6.5).
      a) Rapid conversion from one mode of thermal support to the other avoids having to move patients during emergent events and procedures, reducing the risk for

Fig. 6.5 Hybrid incubators can be used closed with porthole access to the infant or can be used as an overhead warmer with full access for procedures and emergencies without moving the infant. *(Courtesy Allen S. Kramer, Texas Children's Hospital, Houston, TX.)*

heat loss during transfer or dislodging indwelling lines or tubes (Greenspan et al., 2001).

2) It is important to keep the device closed as much as possible when using humidity. Opening the door or opening the portholes lets the humidity dissipate and may take some time to recover the desired percentage (Boyd et al., 2017).

4. Special considerations.
   a. Fluid administration temperatures
      1) Avoid administering large volumes of cold fluids to infants (Knobel, 2014b).
      2) Breast milk should be thawed and warmed before feeding (Bransburg-Zabary et al., 2015).
   b. Rewarming a cold infant (nontherapeutic cold stress).
      1) There is little research and no consensus on the speed of rewarming an infant with iatrogenic cold stress of short duration (Wyllie et al., 2015). The WHO (1997) recommends rewarming as quickly as possible.
      2) Use caution when rewarming; side effects include:
         a) Apnea.
         b) Hypotension secondary to vasodilation.
         c) Increased oxygen consumption.
   c. Weaning from an incubator.
      1) Weaning from an incubator to an open crib can be considered once the infant is medically stable and weighs 1600 g or greater (New et al., 2011, 2012; Turnbull and Petty, 2013; Zecca et al., 2010).
      2) The incubator is slowly weaned to 28° to 29° C as a thermal challenge before transferring the infant to a crib or bassinet.
      3) Swaddling, caps, and avoiding drafts are important in maintaining thermal stability.
      4) Monitor temperature and weight gain in infants who have been weaned from the incubator.
      5) Infants who are not able to maintain an axillary temperature greater than or equal to 97.7° F (36.5° C) should be returned to the incubator.
      6) Benefits of incubator weaning include positive maternal perception, potential impact on breastfeeding and infant development, and increased discharge teaching and planning by nursing staff (Schneiderman et al., 2009).
   d. Bathing.
      1) A bath typically occurs in the first few hours of life to remove blood and body fluids.
      2) The WHO (1997) recommends delay of bathing until 6 hours after birth and preferably 24 hours of life.
      3) Recent studies indicate that late preterm and term neonates given tub baths experience less variability in temperature, improved oxygen saturation, and improved heart rate (Gözen and Ar, 2018; Loring et al., 2012).
   e. Skin-to-skin (kangaroo care).
      1) Skin-to-skin holding promotes thermoregulation of neonates and is an important thermoregulation consideration in the delivery room, nursery, and low-resource areas (Boundy et al., 2016; Conde-Agudelo and Díaz-Rossello, 2016).
      2) Skin-to-skin holding is recommended for stable infants in the NICU as well, even in VLBW infants (Lorenz et al., 2017).
      3) The conduction of heat from the mother (or father) to the infant compensates for heat loss through evaporation and convection while the infant is out of the humidified incubator (Karlsson et al., 2012).
      4) Benefits of skin-to-skin contact include increased weight gain and head circumference, fewer infections, increased breastfeeding at discharge, decreased risk of mortality, and fewer hospital readmissions (Boundy et al., 2016; Conde-Agudelo and Diaz-Rossello, 2016).

Summary

Managing the thermoregulation needs of the newborn is an essential role of the neonatal nurse. The most vulnerable infants present a complex challenge, requiring a nurse with knowledge and clinical expertise to provide an appropriate environment in which they can heal and grow.

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CHAPTER 7
Physical Assessment

Ellen Tappero

OBJECTIVES

1. Review key aspects of the perinatal history as it relates to physical assessment of the newborn.
2. Describe methods of determining gestational age (GA).
3. Relate growth pattern and maturity to classification of newborns by GA and weight.
4. Describe a systematic approach in the examination of the newborn infant.

A comprehensive newborn physical examination requires a synthesis of perinatal and neonatal risk factors with a systematic approach to the examination. An understanding of growth, maturity, and gestational age (GA) risk factors provides a framework for defining wellness or subsequent problems. The nurse is in a unique position of providing a detailed observation and description within the context of these factors.

Perinatal History
(See Chapters 1, 2, 3, and 4)

Elements of a perinatal history focus on the relationship of maternal medical conditions and the overall growth and maturity of the infant. Communication from obstetric staff to neonatal staff of fetal anomalies and risk factors for abnormal growth or fetal well-being is essential to developing a thorough history.

A. Family history.
   1. Known inherited diseases/conditions: http://www.nlm.nih.gov/medlineplus/geneticdisorders.html.
      a. Cystic fibrosis, Down syndrome (translocation only), fragile X syndrome, cleft lip/palate, neural tube defects, dwarfism and osteogenesis imperfecta, muscular dystrophy.
      b. Hereditary anemia/coagulation disorders: sickle cell anemia, thalassemia, von Willebrand's disease, hemophilia.
      c. Genetic brain disorders: leukodystrophy, Tay–Sachs disease, Wilson's disease.
      d. Amino acid disorders: phenylketonuria, maple syrup urine, homocystinuria, tyrosinemia.
      e. Endocrine disorders: congenital adrenal hypoplasia, congenital hypothyroidism (15% to 20%).
   2. Chronic disorders or disabilities: diabetes, hypertension, mental retardation, cardiac lesions, renal disease, and seizures.

B. Maternal medical history.
   1. General health: age, body mass index, physical activity, diet, and exposure to potential teratogens.
   2. Chronic illness: diabetes, cardiac disease, hypertension, asthma, thyroid disorder, systemic lupus erythematosus, herpes simplex virus, addiction, and anxiety/depression disorder.
   3. Medical complications and treatments.
   4. Surgical procedures and hospitalizations.
   5. Substances/medications used before and during pregnancy inclusive of over-the-counter, prescribed, medical marijuana/illicit substances, tobacco, and alcohol.

C. Obstetric history.
   1. History of infertility: abnormal uterine structure, hormonal imbalance, infertility tests, and assisted reproductive technology.
   2. Previous pregnancies (gravida): number of live born, spontaneous or elective abortions, term versus preterm, single or multiple gestation, types of delivery.
   3. Birth weight(s) of live born, gestational age, neonatal problems, or subsequent major medical problems identified with prior children.
   4. Previous fetal demise or neonatal death(s): age of infant and cause for death.

D. **Social history:** early identification of family stressors or support and barriers to teaching.
   1. Marital status and consanguinity.
   2. Financial support, socioeconomic status, and education level.
   3. Family unit defined—number of people, family and nonfamily, living in household and health status of household members.

4. Tobacco, alcohol, and illicit drug use.
5. History of depression.
6. Domestic violence.
7. Religious and cultural considerations.
8. Factors affecting teaching.
   a. Primary language.
   b. Sensory deficits.
9. Current support agencies (if any) used by family.
10. If and when the mother returns to work, arrangements for infant care.

E. Pregnancy history.
1. Prenatal care: timing of first visit, number of visits, who provided the care, compliance with follow-up.
2. Estimated date of delivery or estimated due date (EDD).
   a. Last menstrual period.
   b. Ultrasound dating.
   c. Birth date calculator (wheel).
3. Single versus multiple gestation.
4. Weight gain and nutritional status.
5. Blood group incompatibility and risk for isoimmunization: maternal blood type and Rh status.
   a. Antepartum administration of Rh_o(D) immunoglobulin prophylaxis for D-negative blood group.
   b. Positive antibody screen (examples: Cc, Ee, Kell, and Duffy).
   c. Serial fetal surveillance for positive isoimmunization status: antibody titers, ultrasounds, amniocentesis, fetal transfusion.
6. Maternal serum screening: triple or quad screen, noninvasive prenatal screening (NIPS) (Gregg et al., 2016).
7. Group B streptococcus (GBS) culture at 35 to 37 weeks of gestation.
8. Congenital infection: rubella, syphilis, cytomegalovirus, hepatitis, human immunodeficiency virus, herpes simplex virus, human papilloma virus, *Chlamydia*, gonorrhea, and parvovirus. Congenital West Nile and Zika viruses have also been reported (Rasmussen et al., 2017; Wiley and Chimelli, 2017).
9. Maternal diabetes.
   a. Pregestational: type I or type II.
   b. Gestational.
   c. Classification.
   d. Glucose control.
10. Hypertensive disorders.
   a. Gestational hypertension (formerly called *pregnancy-induced hypertension*).
   b. Preeclampsia/eclampsia.
   c. Chronic hypertension.
   d. *H*emolysis, *e*levated *l*iver enzymes, and *l*ow *p*latelet count (HELLP syndrome).
11. Abnormal fetal growth: fundal height, serial ultrasounds.
   a. Intrauterine growth restriction (IUGR) factors: multiple maternal, placental, uterine, and fetal factors limit intrauterine growth potential (Table 7.1) (Pettker and Campbell, 2018; Simmons, 2018).
      1) Previous small-for-gestational-age (SGA) or IUGR baby.
      2) Age greater than 35 or less than 16 years, single marital status, low socioeconomic status.
      3) Unexplained history of miscarriage or stillbirth (fetal loss at >20 weeks of gestation).
      4) Multiple gestation.
      5) Infections: TORCH (toxoplasmosis, rubella, cytomegalovirus, syphilis); cytomegalovirus most common association.

Table 7.1

Causes of Intrauterine Growth Restriction

Genetic	Inheritance, Chromosomal Abnormalities, Fetal Gender
Maternal constitutional effects	Low maternal prepregnancy weight, low pregnancy weight gain, ethnicity, socioeconomic status, history of IUGR
Nutrition	Low prepregnancy weight (body mass index), low pregnancy weight gain, malnutrition (macronutrients, micronutrients), maternal anemia
Infections	TORCH infections
Decreased O_2 carrying capacity	High altitude, maternal congenital heart disease, hemoglobinopathies, chronic anemia, maternal asthma
Uterine/placental anatomy	Abnormal uterine anatomy, uterine fibroid, vascular abnormalities (single umbilical artery, velamentous umbilical cord insertion, twin-to-twin transfusion), placenta previa, placental abruption
Uterine/placental function	Maternal vasculitis (systemic lupus erythematosus), decreased uteroplacental perfusion, maternal illness (preeclampsia, chronic hypertension, diabetes, renal disease)
Toxins	Tobacco, ethanol, lead, arsenic

IUGR, Intrauterine growth restriction; *TORCH*, toxoplasmosis, rubella, cytomegalovirus, syphilis.

From Simmons, R. (2018). Abnormalities of fetal growth. In C. A. Gleason and S. E. Juul (Eds.), *Avery's diseases of the newborn* (10th ed., p. 63). Philadelphia, PA: Elsevier.

6) Tobacco exposure: dose-dependent effect; smoking in third trimester leads to increase in IUGR.

b. Large-for-gestational-age (LGA) infant (Kamana et al., 2015; Simmons, 2018).
1) Maternal factors.
a) Higher maternal age.
b) Increasing parity.
c) Maternal diabetes.
d) Large pregnancy weight gain.
e) Obesity.
2) Previous LGA infant.
3) Prolonged pregnancy.

12. Fetal anomaly: ultrasound, fetal echocardiography, amniocentesis, chorionic villa sampling, NIPS.
13. Placental or vascular abnormality.
a. Abnormal cord insertion: velamentous.
b. Abnormal umbilical artery Doppler studies: reverse end-diastolic flow, increased middle cerebral flow velocity.
c. Twin-to-twin transfusion.
14. Amniotic fluid volume: polyhydramnios, oligohydramnios.
15. Recurrent urinary tract infections; bacterial vaginosis.

F. Labor and delivery.
1. History of presenting problem.
a. Labor: preterm labor, postdates.
b. Bleeding.
c. Acute abdominal pain.
d. Hypertension.
e. Medically indicated elective delivery conditions: maternal conditions and/or poor fetal growth/status.
f. Trauma.
2. Infection risks.
a. Symptoms of chorioamnionitis: maternal or fetal tachycardia, maternal fever ≥100.4° F, uterine tenderness, elevated maternal white blood cell count.
b. GBS: revised Centers for Disease Control and Prevention (CDC) guidelines (Verani et al., 2010).
3. Risk factors that increase neonatal early-onset GBS infection: preterm premature rupture of membranes, prolonged rupture of membranes greater than 18 hours (Baker et al., 2011).
4. Intrapartum chemoprophylaxis for GBS colonization.
a. Preterm labor with intact membranes is associated with occult intra-amniotic infection (AAP and ACOG, 2017).
5. Fetal lung maturity.
a. Less than 5% risk of respiratory distress syndrome if mature fetal lung maturity test after 34 weeks of gestation.
b. Antenatal corticosteroids administered for anticipated preterm delivery at less than 34 weeks of gestation are effective in decreasing neonatal morbidity and mortality (ACOG, 2017; AAP and ACOG, 2017).
c. Optimal benefit of corticosteroids: 2 to 7 days after initial dose; may be beneficial at less than 24 hours of treatment (ACOG, 2017).
6. Spontaneous versus induced labor, indication for induction of labor.
7. Cord prolapse.
8. Fetal distress and nonreassuring fetal heart tracing.
9. Analgesic and anesthetic before and at delivery.
10. Mode of delivery: vaginal, cesarean, assisted (forceps and vacuum); indication for cesarean.
11. Presentation: vertex, breech, brow, chin, and arm.
12. Amniotic fluid.
a. Appearance.
1) Clear: normal.
2) Green: meconium stained.
3) Yellow: old meconium, old blood, and sepsis.
4) Cloudy: sepsis.
b. Foul smelling: chorioamnionitis, sepsis.
13. Shoulder dystocia (Hoppe and Benedetti, 2018; Lerner, 2018).
a. Multifactorial.
1) Maternal risk factors: uterine abnormalities, obesity, diabetes, maternal body proportions, history of prior shoulder dystocia.
2) Infant risk factors: macrosomia, transverse lie, poor tone, multiple gestation.
b. Intrapartum events.
1) Mechanical forces of labor alone.
2) Vaginal breech delivery/operative vaginal delivery.
3) Prolonged duration of labor.
4) Precipitous delivery.
5) Prolonged head-to-body interval at delivery.

G. Newborn resuscitation (see Chapter 5).

Gestational Age Instruments

The principal basis for use of GA instruments is that fetal maturity follows a predictable, organized course and that physical and neurologic characteristics are common to a given GA. An accurate GA is critical for counseling families and making treatment decisions based on known GA morbidity and mortality risks for a specific GA and birth weight.

A. General considerations (Trotter, 2019).
1. Use neonatal assessment tools from birth to 5 days, before physical characteristics change.
2. Perform within 24 to 48 hours of birth for highest accuracy.
3. Consider problems with accuracy of GA assessments when using GA-based treatment guidelines

for extremely preterm treatment or withdrawal-of-care decisions (AAP, 2016).

4. Neurologic findings may be influenced by prematurity and disease processes.

B. Most common GA tools.
   1. Dubowitz: clinical assessment of GA (Dubowitz et al., 1970).
      a. Scores criteria: 10 neurologic and 11 external (physical).
      b. Combined total score correlated to weeks of gestation; has higher correlation (±2 weeks, 95% confidence) than either component separately.
      c. SGA infants: external signs underscored and neurologic signs overscored; combined score reliable.
      d. Overestimates GA in preterm infants.
      e. Widely used before development of Ballard score.
   2. Ballard: newborn maturity rating.
      a. Simplified system based on Dubowitz's method, less time to use.
      b. Eliminates active tone scoring, passive tone more useful than active tone.
      c. Six neurologic and six physical criteria, scores totaled.
      d. GA maturity rating assigned using form chart.
   3. New Ballard Score (Ballard et al., 1991).
      a. Modified to assess GA of 20 to 44 weeks.
      b. Accurate within 2 weeks of gestation; sick or well infants.
      c. For 20 to 26 weeks of gestation: most accurate when scored within first 12 hours of life.
      d. Limitations.
         1) Examination should be done twice by two different examiners for objectivity.
         2) Infant must be in a quiet, alert state.
         3) Scoring affected by:
            a) Breech and positional deformities.
            b) Neurologic disorders and asphyxia.
            c) Infants affected by maternal medications.
   4. Eye examination: anterior vascular lens capsule evaluation (Fig. 7.1).
      a. Based on timing of embryonic lens vessels' development and atrophy.
      b. Limitations: cannot be used at less than 27 weeks of gestation and atrophies progressively until it is gone after week 34.
      c. Must be performed in first 24 to 48 hours of life. Not used routinely.

C. **GA examination technique:** Use New Ballard chart for scoring each criterion (Fig. 7.2).
   1. Neurologic criteria features.
      a. Posture.
         1) Evaluates degree of arm and leg flexion and extension and leg abduction.
         2) Flexion and hip adduction increase with increasing GA.
         3) Early in gestation, the infant's resting posture is hypotonic.
         4) Observe infant's posture, resting muscle tone, while supine and quiet.
      b. Square window.
         1) Evaluates flexion when the wrist is at a right angle to the forearm.
         2) Angle decreases with increasing GA due to influence of maternal hormones at the end of pregnancy.
         3) Findings do not change after birth.
         4) With fingers extended, flex infant's hand to the forearm by applying gentle pressure on the dorsum of the hand. Use enough pressure to get full flexion without rotating the wrist. Visually measure angle between palm and forearm.
      c. Arm recoil.
         1) Focuses on passive flexor tone of the bicep muscles.
         2) Evaluates degree of arm flexion and the strength of recoil.
         3) Place infant supine, flex arms for 5 seconds, then fully extend arms by pulling the hands downward, then release quickly.

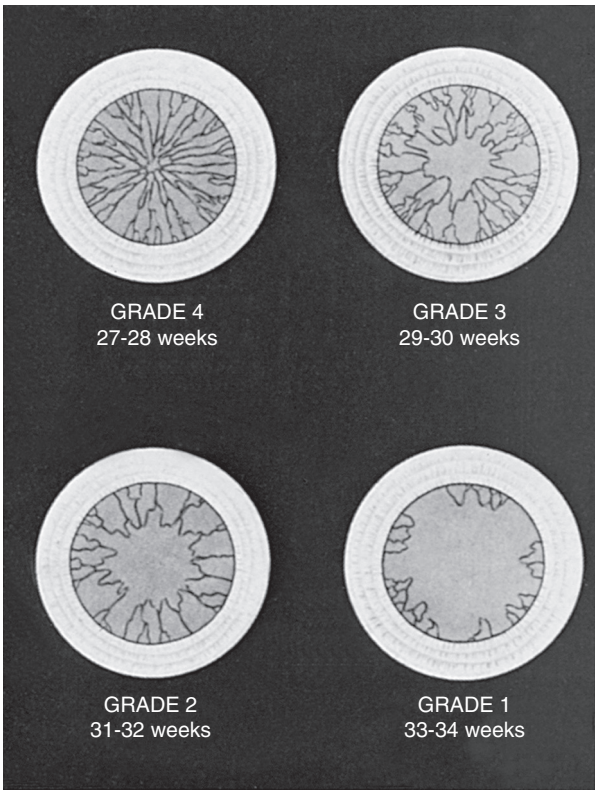

Fig. 7.1 Grading system for assessment of gestational age by examination of anterior vascular capsule of lens. *(From Hittner, H. M., Hirsch, N. J., and Rudolph, A. J. [1977]. Assessment of gestational age by examination of the anterior vascular capsule of the lens.* Journal of Pediatrics, *91[3]:455–458.)*

NEUROMUSCULAR MATURITY

	–1	0	1	2	3	4	5
Posture							
Square Window (wrist)	>90°	90°	60°	45°	30°	0°	
Arm Recoil		180°	140°-180°	110°-140°	90-110°	<90°	
Popliteal Angle	180°	160°	140°	120°	100°	90°	<90°
Scarf Sign							
Heel to Ear							

PHYSICAL MATURITY

Skin	Sticky friable transparent	Gelatinous red, translucent	Smooth pink, visible veins	Superficial peeling &/or rash, few veins	Cracking pale areas rare veins	Parchment deep cracking no vessels	Leathery cracked wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	
Plantar Surface	Heel–toe 40-50 mm: −1 <40 mm: −2	>50 mm no crease	Faint red marks	Anterior transverse crease only	Creases ant. 2/3	Creases over entire sole	
Breast	Imperceptible	Barely perceptible	Flat areola no bud	Stippled areola 1-2 mm bud	Raised areola 3-4 mm bud	Full areola 5-10 mm bud	
Eye/Ear	Lids fused loosely: −1 tightly: −2	Lids open pinna flat stays folded	Sl. curved pinna; soft; slow recoil	Well-curved pinna; soft but ready recoil	Formed & firm instant recoil	Thick cartilage ear stiff	
Genitals, male	Scrotum flat, smooth	Scrotum empty faint rugae	Testes in upper canal rare rugae	Testes descending few rugae	Testes down good rugae	Testes pendulous deep rugae	
Genitals, female	Clitoris prominent labia flat	Prominent clitoris small labia minora	Prominent clitoris enlarging minora	Majora & minora equally prominent	Majora large minora small	Majora cover clitoris & minora	

SCORE

Neuro-muscular _____

Physical _____

Total _____

MATURITY RATING

Score	Weeks
−10	20
−5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Fig. 7.2 New Ballard Score expanded to include extremely premature infants. *(From Ballard, J. L., Khoury, J. C., Wedig, K., et al. [1991]. New Ballard Score, expanded to include extremely premature infants.* Journal of Pediatrics, *119[3]:417–423.)*

d. Popliteal angle.
   1) Evaluates passive flexor tone of the knee.
   2) The angle decreases with increasing GA.
   3) Position infant supine, pelvis flat on surface; hold thigh in knee–chest position with index finger and thumb of one hand. Place the other index finger behind infant's ankle and extend leg with gentle pressure.
   4) Measure the angle between the lower leg and thigh, posterior to the knee.

e. Scarf sign.
   1) Position infant supine; take hand and pull across chest and around neck as far posterior as possible toward the opposite shoulder. Assist maneuver by lifting elbow across body.
   2) Observe the position of the elbow relative to the midline of the infant's body.

f. Heel to ear.
   1) Evaluates passive flexor tone surrounding the pelvis.

2) Position infant supine, pelvis flat on the bed. Draw foot to head as near as it will extend without force.
3) Observe distance between the foot and head and the degree of knee extension. Knee is left free and may draw down alongside abdomen.
4) Increasing resistance to this maneuver with advancing GA.

2. Physical examination criteria: observe and grade according to Fig. 7.2.
   a. Skin.
      1) With increasing GA, transparency decreases, more texture develops, vessels become obscured.
      2) As gestation progresses beyond 38 weeks, subcutaneous tissue decreases, causing wrinkling and desquamation.
   b. Lanugo.
      1) Fine, downy hair that covers the body of the fetus from 20 to 28 weeks.
      2) At 28 weeks, it begins to disappear around the face and anterior aspect of the trunk.
      3) At term, a few patches may be present over the shoulders and back.
   c. Plantar creases.
      1) Creases first appear on the anterior portion of the foot, between 28 and 30 weeks of gestation, and extend toward the heel as gestation progresses.
      2) An infant with IUGR and early loss of vernix caseosa may have more plantar creases than expected for size.
      3) After 12 hours, the skin begins to dry and plantar creases are no longer a valid indicator of GA.
   d. Breast development.
      1) Areola (nipple) size and amount of breast tissue are examined.
      2) Breast tissue increases and areola development progresses with increasing gestational age.
      3) Nutritional status may affect the amount of breast tissue present.
   e. Eyes and ears.
      1) Evaluate for fused eyelids.
      2) At 26 to 28 weeks of gestation, fused eyelids open.
      3) Assess ear formation and amount of pinna cartilage.
      4) Inward curving of the upper pinna usually begins by 34 weeks of gestation and by 40 weeks extends to the lobe.
      5) Before 34 weeks, the pinna has little cartilage and will stay folded on itself.
      6) By 36 weeks there is some cartilage, and the pinna will spring back from being folded.
   f. Genitalia.
      1) Female infant: evaluate development of the labia minora and majora and prominence of the clitoris.
         a) Early in gestation the clitoris is prominent, with small, widely separated labia.
         b) By 40 weeks, fat deposits have increased in size in the labia majora and minora so that the clitoris is completely covered.
      2) Male infant: evaluate presence of testes, degree of descent into scrotum, and development of rugae on the scrotum.
         a) The testes begin to descend from the abdomen at 30 weeks.
         b) At 34 weeks, the testes can be palpated in the inguinal canal.
         c) At 40 weeks, the testes are completely descended and scrotum is covered with rugae.
         d) As gestation progresses, the scrotum becomes more pendulous.

D. **Clinical estimate of GA** (AAP and ACOG, 2017).
   1. Document GA on all newborns.
   2. Use standard terminology.
      a. GA is the time between the last menstrual period and the day of delivery.
      b. Use obstetric estimated GA when the physical examination approximates the GA by EDD within 2 weeks (Trotter, 2019).
      c. Express in completed weeks of gestation.
   3. Document marked discrepancy between obstetric and physical data.
   4. Assign GA using assessment of all obstetric, pediatric, and nursing data (AAP and ACOG, 2017).
   5. Classify maturity (ACOG 2013; AAP and ACOG, 2017).
      a. Preterm: infant born on or before the end of the 36th week of gestation.
         1) Subcategory: "late preterm" defined as between $34^{0/7}$ and $36^{6/7}$ weeks of gestation.
         2) Replaces the phrase *near term*, emphasizes the higher morbidity and mortality of premature infants.
      b. Term: infant born from the first day of the 37th week to the last day of the 42nd week.
         1) Early term: infant born between $37^{0/7}$ weeks and $38^{6/7}$ weeks.
         2) Full term: infant born at $39^{0/7}$ weeks through $40^{6/7}$ weeks.
         3) Late term: infant born at $41^{0/7}$ weeks through $41^{6/7}$ weeks.
      c. Post-term: infant delivered from the first day of the 42nd week and beyond.

Classification of Growth and Maturity

The intrauterine growth pattern reflects fetal well-being. This pattern is influenced by race, maternal health or disease, placental function, medications, socioeconomic factors, nutrition, altitude, substance abuse, and smoking. There are multiple reasons to classify growth and maturity of the newborn infant:

- Assist in identification of the most commonly occurring problems in the newborn period.
- Estimate dating if there is no prenatal care.
- Examine discrepancy between weight and GA.
- Standardize reports of health statistics.

A. Measurement.
   1. Comparison of newborn's measurements should be of population-based growth data, representing the patient in gender, race, geographic region for altitude, and other environmental variances.
   2. Growth curves should be GA- and gender-specific for weight, length, and head circumference.

B. Obtain measurements.
   1. Type.
      a. Normal-appearing infants: weight, length, and head circumference.
      b. Dysmorphic appearance: may require more extensive measurements.
   2. Birth weight.
      a. Obtain as soon as possible after delivery.
      b. Express in grams.
      c. Weigh unclothed infant when quiet (weight inaccurate with significant motion).
      d. Classifications (regardless of GA) (AAP and ACOG, 2017).
         1) High birth weight: greater than 4000 g.
         2) Low birth weight: less than 2500 g birth weight.
         3) Very low birth weight: less than 1500 g birth weight.
         4) Extremely low birth weight: less than 1000 g birth weight.
   3. Length: crown-to-heel measurement.
      a. Most variable measurement: requires full extension of normally flexed infant.
      b. Measure length with infant supine and leg extended, head to heel.
      c. Use crown-to-rump measurement to establish proportionality when length falls below norms (referenced data in *Smith's Recognizable Patterns of Human Malformation* [Jones et al., 2013]).
         1) Congenital bone disorders.
         2) Lower extremity anomalies make crown-to-heel measurement unreliable.
         3) Head circumference.
   4. Head circumference.
      a. Occipitofrontal circumference (OFC).
      b. Measurement of largest OFC.
      c. Apply measurement tape firmly around head above the eyebrow ridges, from most prominent frontal to occipital areas.
      d. OFC as measured may be erroneous: significant cranial molding, craniosynostosis, caput succedaneum, and cephalohematoma need to be noted along with the measurement.
      e. Consider parent head size versus intracranial pathology when head size is of concern.

C. Plot newborn's weight, length, and head circumference by GA on standardized growth charts.
   1. Growth charts.
      a. Provide a means to measure the dynamic process of growth.
      b. Represent the norm: the mean of cross-sectional data ±2 standard deviations (SDs) or 5th to 95th percentile rank.
      c. Identify growth acceleration and deceleration postnatally.
      d. Predict preventable morbidity (SGA, LGA), future growth, and nutritional needs.
   2. Variety of intrauterine growth charts published.
      a. CDC national reference for term infants.
         1) Recommend use of World Health Organization (WHO) growth charts for ages 0 to 24 months; considered the standard for monitoring growth in this age group. (Grummer-Strawn et al., 2010).
         2) Available at www.cdc.gov/growthcharts.
      b. Colorado Intrauterine Growth Chart (Fig. 7.3).
         1) Colorado growth charts developed by Lubchenco in the 1960s.
         2) Limitations: developed at mile-high elevation (Denver).
         3) Tenth percentile is lower than data from centers at sea level.
         4) Overestimates number of infants greater than 90th percentile and less than 10th percentile; leads to inaccurate classification of SGA and LGA.
         5) Not gender specific.
      c. Babson and Benda fetal–infant growth graph (Fenton, 2003).
         1) Developed in the 1970s.
         2) Allows evaluation of catch-up growth by extending from 22 weeks to 10 weeks post-term.
         3) CDC growth charts could be used after 50 weeks (10 weeks post-term age).
         4) Original 1976 chart updated in 2003 (by Fenton) with growth data from the National Institute of Child Health and Human Development Neonatal Research Network.
         5) Useful in neonatal intensive care units, reflects preterm infants' postnatal weight and length delay in comparison to head growth.

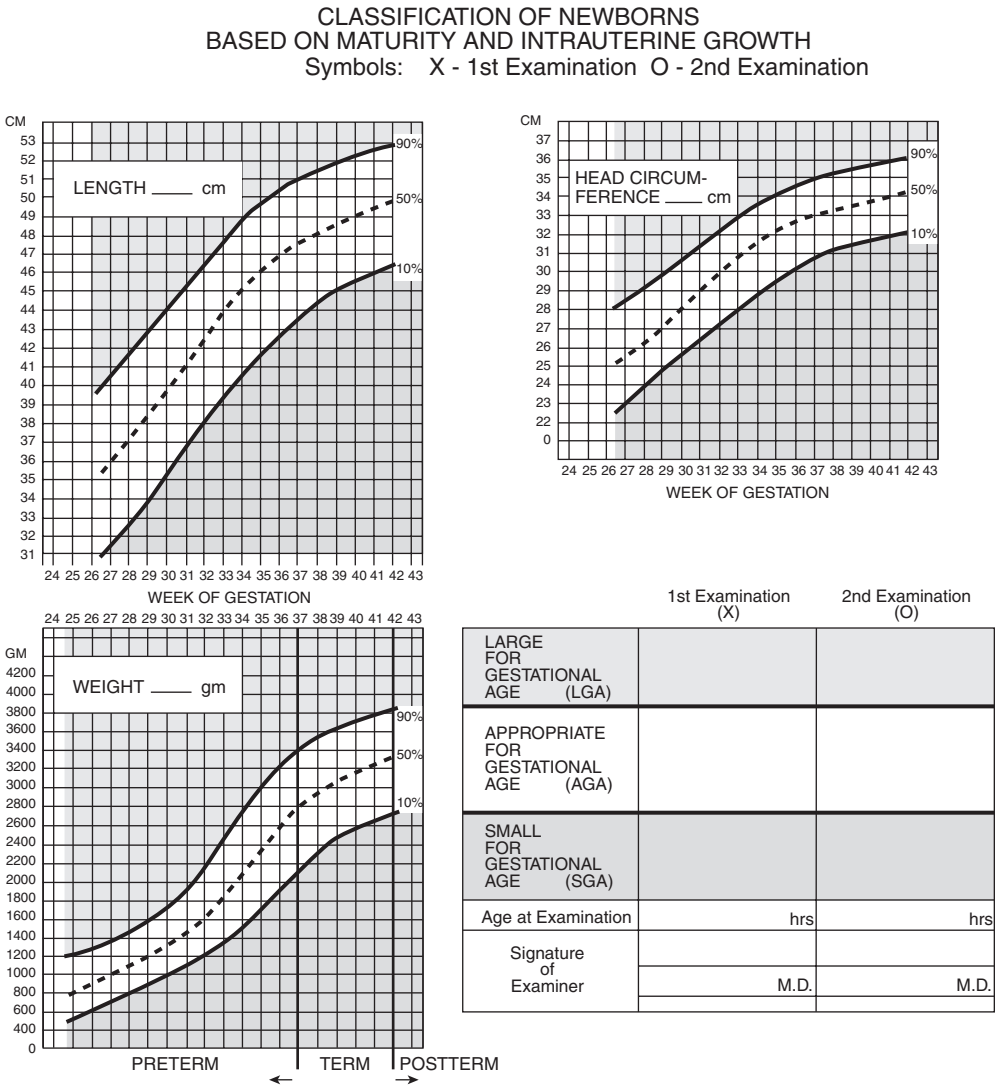

Fig. 7.3 Estimating gestational age: Newborn classification based on maturity and intrauterine growth. *(From Lowdermilk, D. L. and Perry, S. E. [2016].* Maternity & women's health care *[11th ed.]. St. Louis, MO: Elsevier Mosby; modified from Lubchenco, L., Hansman, C., Boyd, E. [1966]. Intrauterine growth in length and head circumference as estimated from live births at gestational ages from 26 to 42 weeks.* Journal of Pediatrics, *37:403; Battaglia, F. and Lubchenco, L. [1967]. A practical classification of newborn infants by weight and gestational age.* Journal of Pediatrics, *71[2]:159–163.)*

6) Open access with credit given, available online at http://www.biomedcentral.com/1471-2431/3/13.

d. Olsen Growth Curve (Olsen et al., 2010).
   1) Goals: develop a new set of growth curves for the assessment of weight, length, and head circumference of preterm infants.
   2) Results based on neonatal intensive care unit (NICU) setting with large, racially diverse U.S. sample.
   3) Results compared with the Lubchenco curves.
   4) Findings: Olsen curves had lower average weights, lengths, and OFC at younger GAs than the Lubchenco curves until 30 to 36 weeks; the new curves had higher average growth measurements at older GAs.
   5) Results supported the need for updated and gender-specific growth curves.
   6) Olsen and WHO charts are not connected; "smoothing process" of the two charts distorts the estimates of percentile lines for both.
   7) Available online at http://www.pediatrix.com/workfiles/NICUgrowthCurves7.30.pdf.

e. Fenton Preterm Growth Chart (Clark et al., 2014; Fenton and Kim, 2013) (Fig. 7.4).
   1) Correlates the Fenton Preterm Growth Chart with the new WHO growth standard.

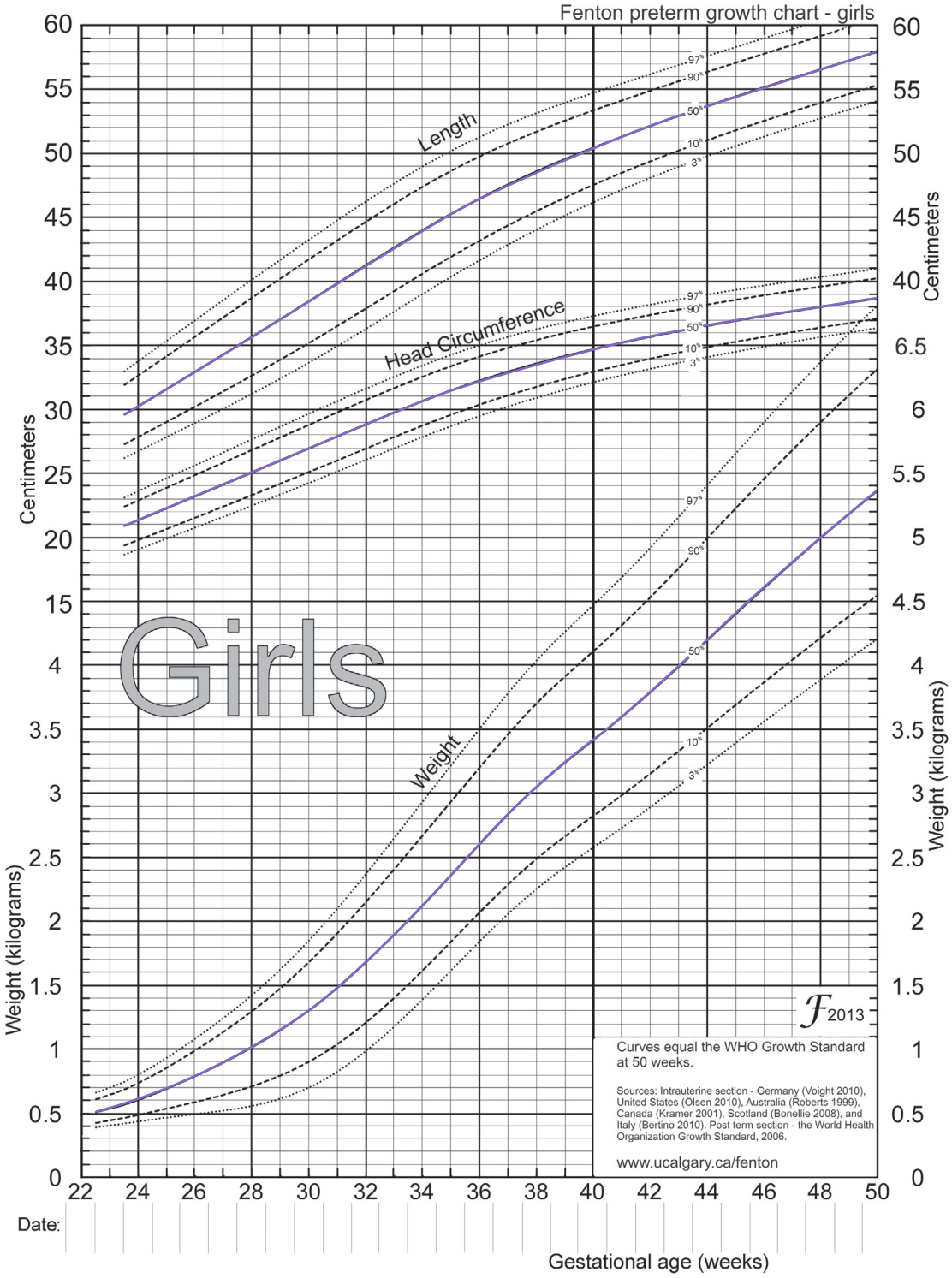

Fig. 7.4 Fenton Preterm Growth Charts for girls (A) and boys (B). http://www.ucalgary.ca/fenton/files/fenton/fenton2013growthchartcolor-girls.pdf and http://www.ucalgary.ca/fenton/files/fenton/fenton2013growthchartcolor-boys.pdf.

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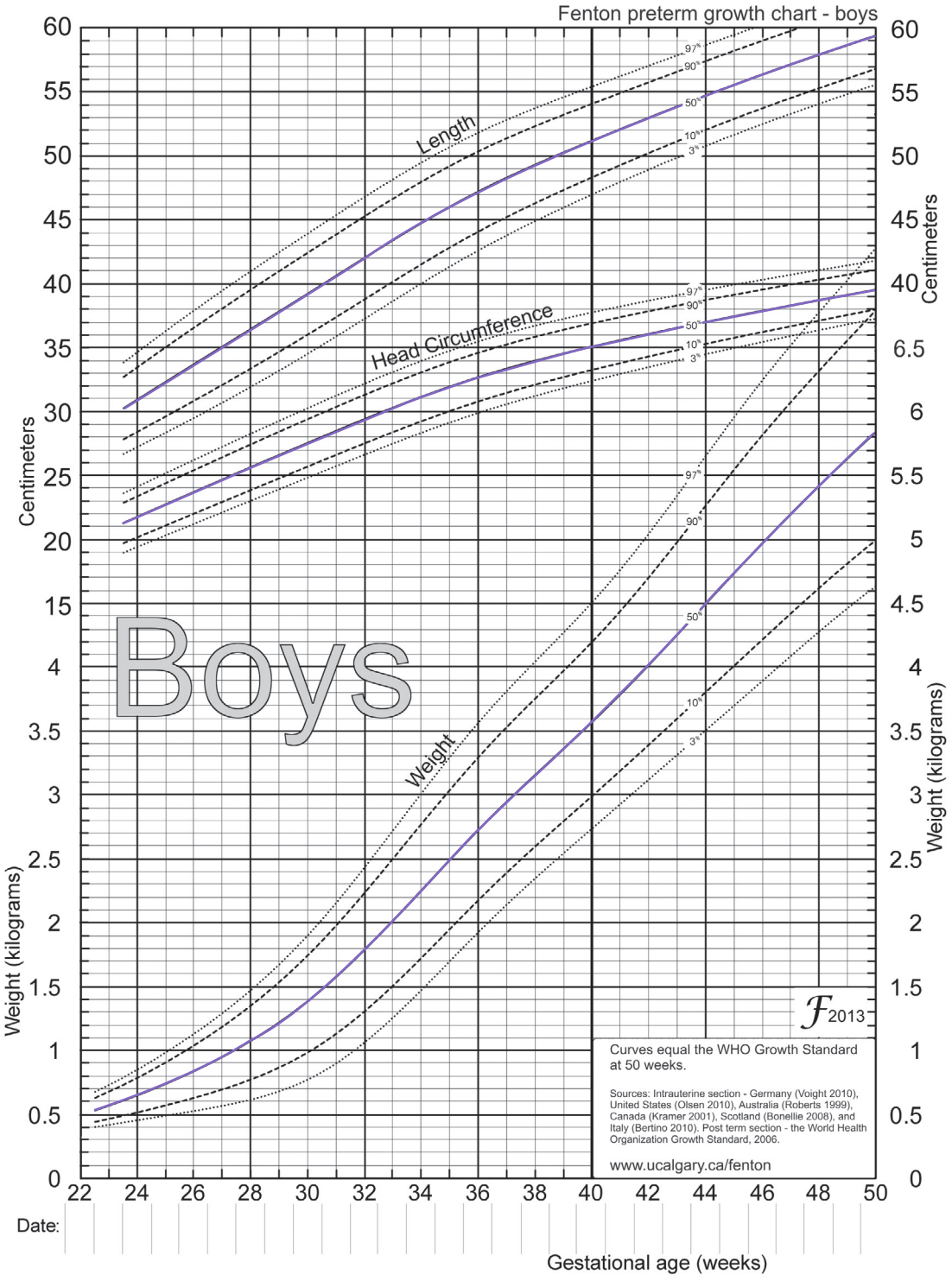

Fig. 7.4, cont'd

2) Based on recommended growth goal for preterm infants. Smoothed the data between preterm growth monitoring from 22 to 36 weeks to the WHO growth charts; equivalent to WHO charts at 50 weeks gestational age.
3) Gender-specific growth curves.
4) Commonly used in NICUs today.
5) Open access with credit given, available online at: http://www.ucalgary.ca/fenton/2013chart.

D. Compare weight with GA to determine size classification (weight compared with established norm).
   1. SGA: birth weight less than 10th percentile.
   2. Appropriate for gestational age (AGA): birth weight within 10th and 90th percentiles.
   3. LGA: birth weight greater than 90th percentile.

E. Compare all growth parameters (head circumference, birth weight, and length) with GA.
   1. IUGR/SGA.
      a. Process of slowing of intrauterine growth rate.
      b. IUGR infants may or may not be SGA.
      c. Below expected norms for weight and length at birth based on GA, race, and gender.
   2. Classifications.
      a. Symmetrical.
         1) Proportional decreased growth.
         2) Measurements for weight, length, and OFC all within the same growth curve, all less than 10th percentile. May set cutoff of the third percentile, which is mean ±2 SD.
         3) Etiology: significant impact on cell replication (reduced cell number) and overall growth potential (see "Pregnancy History").
            a) Intrauterine congenital infection.
            b) Congenital malformation.
            c) Chromosomal disorder.
      b. Asymmetrical (head-sparing).
         1) Disproportionate reduction in weight and length at birth compared with head circumference.
         2) Weight below expected norms for GA, race, and gender.
         3) Etiology: normal number of cells, reduced cell size, possibility of subsequent catch-up growth.
            a) Associated with poor placental perfusion or nutritional deficits late in pregnancy.
            b) Predisposing conditions include maternal malnutrition, maternal preeclampsia, and chronic fetal distress.

F. Determine neonatal mortality risk based on classification of newborns by standardized birth weight norms and GA.
   1. Morbidity and mortality statistics: standardized reporting of reproductive health statistics.
   2. Establishment of level of risk for short- and long-term complications.
   3. Mortality risk (Fig. 7.5).
   4. Morbidity risk by birth weight and GA (Fig. 7.6).

G. Identify infants at risk for respiratory disease, hypoglycemia, and thermal instability based on classification(s).
   1. Preterm: problems with immaturity of body systems: respiratory distress syndrome, necrotizing enterocolitis, and patent ductus arteriosus.
   2. Late preterm (Kardatzke et al., 2017).
      a. Subgroup of later-gestation preterm infants with increased morbidity and mortality compared with term infants.
      b. GA $34^{0/7}$ weeks through $36^{6/7}$ weeks.
      c. Potential problems: temperature instability, hypoglycemia, respiratory distress, apnea, bradycardia, feeding difficulty, and hyperbilirubinemia.
   3. Post-term: problems associated with placental insufficiency—asphyxia and meconium aspiration.
   4. IUGR (Subhani, 2005; Trotter, 2019).
      a. Infant who has not grown at the expected in utero rate for weight, length, or OFC.
      b. Generally, demonstrates restricted fetal growth subsequent to a pathophysiologic process occurring during the perinatal period.
      c. Caused by factors that diminish the overall growth rate and exert effects early in gestation.
      d. Focus initial examination on identification of congenital anomalies and dysmorphic features.
      e. Associated with chromosomal syndromes, single-gene defects, intrauterine drug exposure, and viral infections.
      f. Typical appearance of asymmetrically growth-restricted infant.
         1) Head disproportionately large for trunk.
         2) Appear wasted, skin appears to be hanging.
         3) Facial appearance is shrunken or "wizened."
         4) Large anterior fontanelles with cranial sutures wide or overlapping.
         5) Thin umbilical cord, diminished Wharton's jelly, may be meconium stained.
         6) Scaphoid abdomen.
         7) Skin: petechiae, loose, decreased subcutaneous fat, dry, flaky, little or no vernix caseosa.

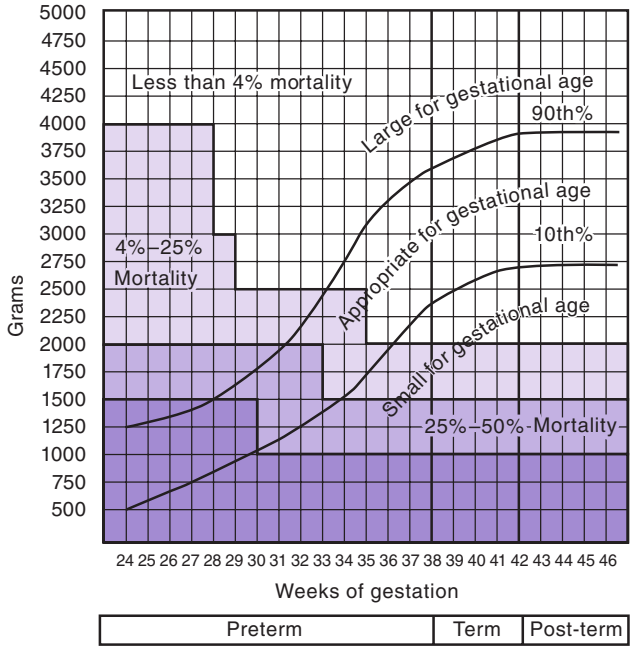

Fig. 7.5 University of Colorado Medical Center classification of newborns by birth weight and gestational age and by neonatal mortality risk. *(From Battaglia, F. and Lubchenco, L. [1967]. A practical classification of newborn infants by weight and gestational age.* Journal of Pediatrics, *71(2):159–163.)*

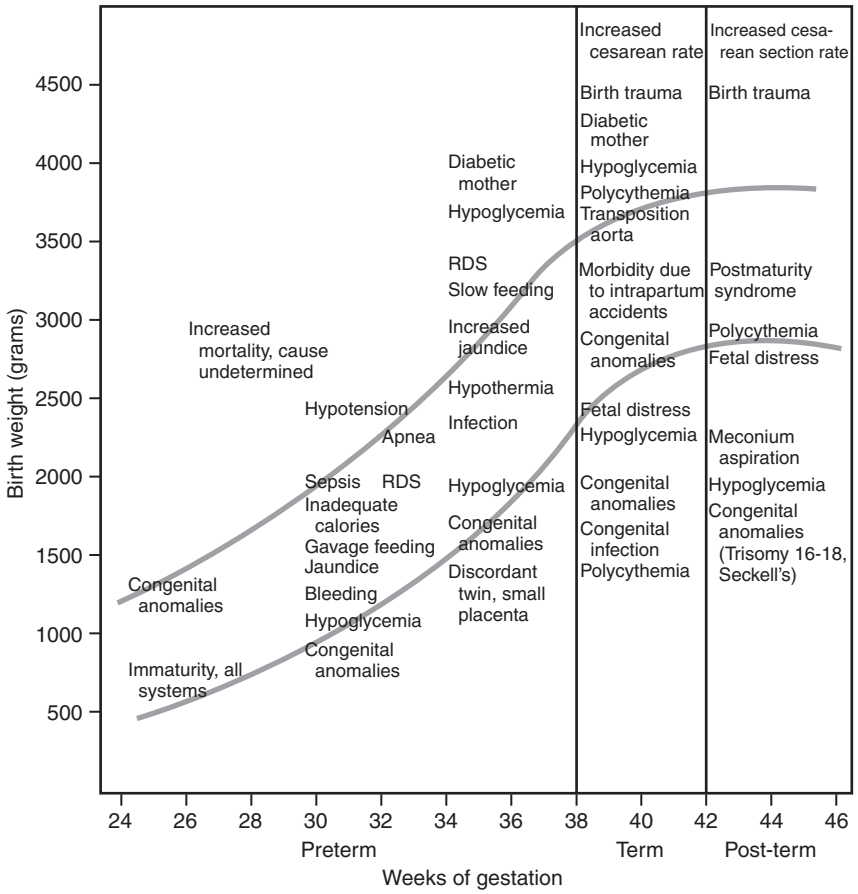

Fig. 7.6 Specific neonatal morbidity by birth weight and gestational age. *RDS*, Respiratory distress syndrome. *(From Lubchenco, L. O. [1976]*. The high-risk infant. *Philadelphia, PA: W.B. Saunders.)*

8) Tone and alertness dependent on degree of IUGR.
   a) Mild/moderate IUGR: hyperalert, jittery, hypertonic.
   b) Severe: hypotonic, "apathetic."

g. Potential problem list; increased risk at all GAs with IUGR.
   1) Hypoglycemia due to limited fat stores, increased tissue glucose utilization, and ineffective free fatty acid and triglyceride oxidation.
   2) Hypothermia: high demand plus inadequate adipose tissue to maintain temperature.
   3) Polycythemia/hyperviscosity: increased red blood cell production in utero caused by chronic hypoxia or endocrine/metabolic or chromosomal disorder.
   4) Hypoxia: birth asphyxia, persistent pulmonary hypertension, and meconium aspiration.
   5) Infection.
   6) Problems related to etiology of growth restriction.
   7) Long-term morbidity and mortality dependent on etiology: 10 to 20 times perimortality of AGA infants.

5. LGA infant.
   a. Typical appearance.
      1) Macrosomia: greater than 4000 g at birth; greater than 90th percentile.
      2) Infant of diabetic mother.
         a) Characteristic large body with head circumference within normal limits for GA (insulin does not cross the blood–brain barrier).
   b. Potential problem list (Kamana et al., 2015; Riskin and Garcia-Prats, 2018).
      1) Abnormal glucose metabolism after birth, hyperinsulinemia, and hypoglycemia.
      2) Birth trauma from difficult extraction (fractured clavicle, brachial plexus injury) or asphyxia.
      3) Complications from operative or assisted delivery: respiratory distress, adverse effects of anesthesia.
      4) Iatrogenic prematurity: overestimation of fetal GA.

5) Association with other problems related to infant of diabetic mother: respiratory distress syndrome, transient tachypnea of the newborn, hypoglycemia, hypocalcemia, hypomagnesemia, polycythemia, and hyperbilirubinemia.
6) Congenital anomalies.
   a) Cardiovascular anomalies: transposition of the great arteries (TGA), ventricular septal defect (VSD), truncus arteriosus, tricuspid atresia, double outlet right ventricle, and coarctation of the aorta.
   b) Caudal regression syndrome.
   c) Small left colon syndrome.
   d) Beckwith–Wiedemann syndrome: LGA, macroglossia, hypoglycemia, umbilical hernia, undescended testes.
7) Thermal instability as a result of central nervous system (CNS) trauma or infection.

Physical Examination

Timing of the physical examination of the newborn often depends on circumstance. An overall quick assessment can be completed in the delivery room unless the infant is clinically stable and has been placed skin-to-skin with the mother. A systematic approach to physical examination should be performed in the first 12 to 24 hours of life after successfully transitioning. This prevents pertinent omissions and provides a detailed description that can be utilized in communication of alterations in anatomic structure or changes in physiology or function. These observations ultimately must be made within the context of the patient's history and GA. Communication to the primary care provider is essential for further evaluation and prompt treatment.

A. Assessment techniques.
   1. Examine in well-lit room; direct light should not be in infant's face.
   2. Warm hands and equipment.
   3. Keep infant warm by using overhead heat source or uncovering small areas at a time to prevent hypothermia.
   4. Complete detailed observations before physical contact.
   5. Auscultate only in a quiet environment.
   6. Handle the infant gently.
   7. Order of examination:
      a. Depends on the purpose of the examination and the current state of the infant (Fletcher, 1998).
      b. Generally: least invasive observations to most disturbing techniques.
      c. Observe skin throughout the examination.
      d. Evaluate neurobehavior within the context of the infant's behavioral state.
   8. Document physical examination in patient care record inclusive of description of abnormalities and vital signs.

B. Timing of examinations (AAP and ACOG, 2017).
   1. Recognize life-threatening symptoms and address those before performing a comprehensive examination.
   2. Modify elements of examination based on infant's state or illness.
      a. Initial examination in delivery room.
      b. Apgar scoring.
      c. Inspection for birth injury or major congenital malformation.
      d. Evaluation of pulmonary and cardiovascular adjustment to extrauterine life.
      e. Notification of primary care provider.
         1) Apgar score less than 5.
         2) Maternal fever.
         3) Abnormal examination findings.
         4) Evidence of and/or suspected substance abuse.
   3. Comprehensive newborn examination.
      a. Within 12 to 24 hours of life: evaluation of size, growth, and GA; transition to extrauterine life; and congenital anomalies.
      b. Discharge examination: focus on problem(s) during hospitalization, problems with feeding and weight gain, and ability of parent(s) to meet infant's needs.

C. General appearance: initial impression.
   1. State: indicator of well-being.
      a. Sleep states: deep sleep and light sleep.
      b. Awake states: quiet alert, actively alert, and crying.
   2. Color.
      a. Most reliable indicator of color: mucous membranes. Other areas include conjunctiva, nail beds, lips, buccal mucosa, earlobes, and soles of feet.
      b. Lighting and color of blankets can affect perception of color.
      c. Central cyanosis; always abnormal.
         1) Recognition influenced by hematocrit, temperature, facial bruising, and environmental factors.
         2) Central cyanosis: superficial capillaries exceed 5 g/dL unsaturated hemoglobin (Park, 2014).
         3) Variety of etiologies: cardiac, pulmonary, infection, metabolic, neurologic, and hematologic.
      d. Acrocyanosis.
         1) Suggests instability of peripheral circulation.
         2) Cyanosis limited to hands, feet, and circumoral area (lips).
         3) May be a result of cold, stress, shock, and polycythemia.
         4) Normal finding for 24 to 48 hours after birth.

e. Pallor: pale, white appearance.
   1) Reflects poor perfusion and circulatory failure or acidosis.
   2) With bradycardia, indicates anoxia or vasoconstriction found in shock, sepsis, or severe respiratory distress.
   3) With tachycardia, can indicate anemia.
f. Plethora: ruddy or red appearance.
   1) May indicate polycythemia.
g. Jaundice: yellow pigmentation in skin or conjunctivae due to deposition of bilirubin.
   1) Abnormal in the first 24 hours of life. Needs immediate investigation.
   2) Cephalocaudal progression.
h. Mottling: checkerboard red-and-white pattern.
   1) May be normal in neonatal period, especially in preterm infants. Reflects vasomotor instability and unequal capillary blood to cutaneous tissue.
   2) May be seen in cold stress, hypovolemia, and sepsis.
   3) Cutis marmorata: exaggerated marbling greatest on extremities but also present on trunk (Fletcher, 1998).
i. Harlequin sign: distinct midline demarcation.
   1) Pale on one side and red on the opposite side.
   2) Due to immature autoregulation of blood flow.

3. Respiratory effort.
   a. Rate.
      1) Normal: 40 to 60 respirations per minute.
      2) Rate can vary with activity of infant.
   b. Quality: absence of "work of breathing."
      1) Retractions: occur more often in premature infant as a result of highly compliant chest wall.
      2) Nasal flaring: diameter of nares increased as mechanism to decrease airway resistance.
      3) Expiratory grunting: increase in intrathoracic pressure to prevent volume loss during expiration as a result of alveolar collapse.
4. Wheezing: due to increased airway resistance. High-pitched rhonchi heard more loudly on expiration.
5. Stridor: partially obstructed airway.
6. Nutritional status.
   a. Well nourished: increased subcutaneous fat, without loose skin.
   b. Growth restricted: thin and wasted appearance, no subcutaneous fat, loose skin.
7. Tone.
   a. Based on GA expectations.
   b. Initial position reflects intrauterine position and may reflect limitation of movement or increased pressure on head, trunk, or extremities.
   c. Degree of flexion and amount of resistance demonstrated with examiner's extension of extremities.
   d. Decreased flexion (hypotonia) or increased flexion (hypertonia) should be evaluated further.
8. Congenital defects.
   a. Malformation: structural defect of organ or tissue resulting from abnormal developmental process due to genetic or teratogenic reasons (e.g., congenital heart defect, neural tube defect).
   b. Deformation: altered form or position of a body part. Fully formed but influenced by in utero environment (e.g., altered head shape, clubfoot).
   c. Disruption: defect of a body part due to a breakdown of normally developed tissue (e.g., amniotic banding).
   d. Dysplasia: Tissue anomaly due to abnormal organization of cells in that tissue; may be localized (e.g., hemangioma) or generalized (e.g., achondroplasia).
   e. Describe anatomic structures fully: size, number, shape, position, color, texture, continuity, and alignment.
9. Temperature (see Chapter 6).

D. Skin (see Chapter 36).
1. General considerations.
   a. Findings differ with GA, especially with extremely low birth weight.
   b. Indicators of underlying illness: petechiae, pigmentation, rashes, and pustules.
   c. Congenital lesions may not be apparent at birth; influenced by maternal hormones.
   d. Differentiate between findings at birth versus injury after birth (medical interventions).
   e. Use basic descriptors: color, quantity, size, shape, pattern of distribution, and texture.
2. Skin is soft, smooth, and opaque and should be warm to the touch; cold, clammy skin may indicate shock.
3. Inspect lesions, rashes, bruises, and birthmarks. Differentiate between benign findings and those suspicious of infection or hematologic or neurologic disturbance.
4. Palpate for texture (raised, flat) unless lesion is open.
5. Vernix caseosa.
   a. White or yellow material on the skin; discolored with postmaturity, hemolytic disease, and meconium staining.
   b. Sebaceous gland secretions and exfoliated skin cells.
   c. Presents during third trimester and decreases with increasing GA.
6. Lanugo: fine, soft hair covering face and trunk.
   a. Amount and distribution are GA dependent.
   b. Covers entire body in preterm, disappears at 32 to 37 weeks from face and lower back.
   c. At term, present on upper back and limbs.

7. Erythema toxicum (newborn rash).
   a. Erythematous macules, each containing a central papule (yellow or white).
   b. Papules contain eosinophils in a fluid that is sterile.
   c. Persist for several days and then resolve spontaneously.
   d. Most often located on trunk, arms, and perineal areas.
   e. Never located on soles of feet or palms of hands.
8. Pustular melanosis.
   a. Benign, transient, nonerythematous pustules and vesicles.
   b. Single or clusters, rupture leaves a discolored flat spot surrounded by very fine white scales.
9. Ecchymosis: nonblanching blue or black area.
   a. Extravasation of blood into tissue.
   b. Related to trauma of blood vessels.
10. Petechiae.
   a. Tiny red or purple, nonblanching pinpoint macules.
   b. Benign when found on presenting part; result from areas of compression during delivery.
   c. More diffuse distribution suggests general thrombocytopenia.
   d. Require further evaluation when progressive.
11. Vascular nevi.
   a. Common cutaneous malformation(s) that can occur anywhere on the body.
   b. May present at birth or may develop in early infancy.
   c. Types.
      1) Nevus simplex or capillary hemangiomas (stork bite).
         a) Macular patches with diffuse borders.
         b) Found on forehead, nape of neck, glabella, and eyelids.
         c) Blanch when pressure is applied.
         d) Resolve spontaneously.
      2) Nevus flammeus (port wine stain).
         a) Flat, sharply defined lesion.
         b) Most common on back of neck.
         c) If present over the face following branches of trigeminal nerve (forehead and upper eyelid), may be associated with Sturge–Weber syndrome.
         d) Will not blanch with pressure.
         e) May fade with time but will not resolve.
12. Café-au-lait spots.
   a. Light tan or brown macules with well-defined borders.
   b. Deeper pigmentation than surrounding skin.
   c. Six or more may be pathologic.
13. Strawberry hemangioma(s).
   a. Red, raised, circumscribed, and compressible.
   b. Can occur anywhere on the body.
   c. Proliferate: increase in size and number.
   d. Most involute spontaneously.
   e. No treatment is required unless they affect vital function.
   f. Occur with increasing frequency with decreased GA.
14. Epidermolysis bullosa.
   a. Blistering internally and externally.
   b. May be either autosomal dominant or recessive.
15. Staphylococcal scalded skin syndrome.
   a. Skin response to *Staphylococcus aureus*.
   b. Scalded skin appearance.
16. Sucking blisters: skin erosion on thumbs, index fingers, hand, wrist, or forearm from intrauterine sucking.

E. Head.
1. General considerations.
   a. Up to 90% of the congenital malformations present at birth are apparent on the head and neck (Jones et al., 2013).
   b. Review perinatal history, abnormal ultrasound findings, and mode of delivery.
   c. Many variations are transient or racial, gender, or familial traits.
   d. Generally, the head circumference in centimeters is equal to one fourth of the body length in centimeters.
2. Obtain head circumference (OFC measurements).
   a. Measurement reflects brain growth.
   b. Predictable measurement: follows norms for GA and weight.
   c. Usually OFC falls on same percentile curve as length. Determine etiology of abnormal growth if length and OFC differ by more than one quartile.
   d. Normal OFC 33 to 35 cm for full-term AGA (normal variation 32.5 to 37.5 cm).
      1) Microcephalic: poor brain growth, atrophy, or premature cranial synostosis.
      2) Macrocephalic: familial (follows persistently higher but consistent growth curve) and pathologic (hydrocephalus: increase in cerebrospinal fluid results in increasing OFC).
3. Observe shape and symmetry; may reflect effect of birth process or in utero position or significant anatomic defect.
   a. Molding.
      1) Occurs with vaginal delivery from a vertex position; adaptive mechanism to facilitate passage through birth canal.
      2) Elongation of head with prominence of occiput and overriding sagittal suture line.
      3) Resolution in first week of life.
      4) Not uncommon for overriding sutures to persist longer than 1 week in the extremely low birth weight infant.
   b. Rounded head occurs with delivery by cesarean section without labor; flat head with increased

occipitofrontal diameter occurs with breech delivery.
c. Abnormal prominence, depressions, or flattening.
d. Abnormal shape of skull.
1) Craniosynostosis: premature closing of one or more cranial sutures.
a) Scaphocephaly or dolichocephaly: fusion of sagittal suture; narrow skull elongated anteroposterior (AP) length.
b) Brachycephaly: fusion of coronal suture; widened skull with shortened AP dimension.
c) Plagiocephaly: closure of a coronal or lambdoidal suture on one side; asymmetrical appearance of head, flattened.
2) Anencephaly: failed closure of neural tube without skull formation.

4. Palpate sutures and fontanelles (Fig. 7.7).
a. Sutures: check for mobility by placing thumb on opposite sides of suture and alternately pushing (gently).
1) Well approximated.
2) Overriding.
a) Molding.
b) Fused suture: premature synostosis.
3) Wide sutures.
a) May be wide in the absence of increased intracranial pressure.
b) Widened lambdoid suture: indicates increased pressure.
c) Sagittal and metopic sutures normally wider in black infants (Fletcher, 1998).
4) Craniotabes: soft demineralized area typically found in parietal bone near the sagittal or lambdoidal suture lines.
a) Under gentle pressure, the area will collapse and then recoil.
b) Infant engaged in the vertex position for a prolonged period.
c) Pressure of skull against maternal pelvis results in delayed ossification or reabsorption of bone.

b. Anterior fontanelle.
1) Location: junction of metopic, coronal, and sagittal sutures.
2) Shape: diamond.
3) Size: measures 0.6 to 4.7 cm at the largest diameter (bone to bone) (Johnson, 2019).
4) Normally closes by 18 to 24 months.

c. Posterior fontanelle.
1) Location: junction of lambdoidal and sagittal sutures.
2) Shape: triangular.
3) Size: usually fingertip.
4) Normally closes by 2 to 3 months of age.

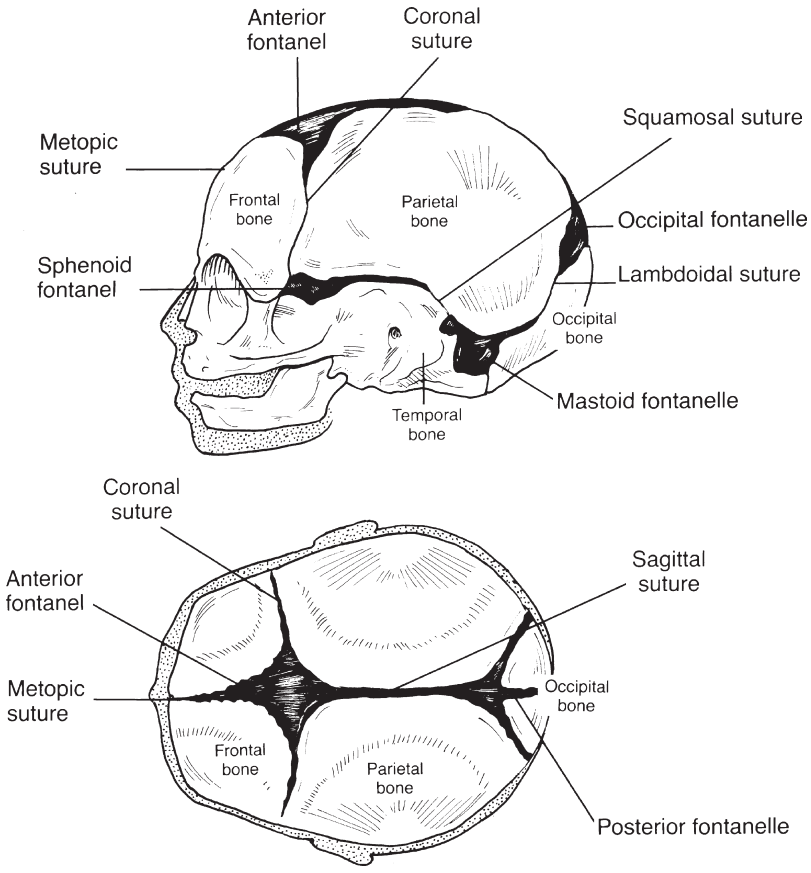

Fig. 7.7 Two views of the skull, showing fontanelles and sutures.

d. Abnormal findings.
   1) Third fontanelle: between anterior and posterior fontanelles along the sagittal suture (may be associated with congenital anomalies).
   2) Size: large fontanelle, considerable racial variations; not pathognomonic for any condition (Fletcher, 1998).
   3) Closed fontanelles with immobile, rigid sutures suggest premature synostosis.
   4) Bruit over temporal, frontal, or occipital area associated with high-output cardiac failure and arteriovenous malformation.
   5) Abnormal tension.
      a) Bulging, tense, full fontanelle: associated with increased intracranial pressure secondary to hydrocephalus, birth injury, bleeding, or infection.
      b) Depressed fontanelle: associated with dehydration.

5. Palpate soft tissue findings on scalp, face, and neck (Johnson, 2019).
   a. Caput succedaneum: common finding in infants born in the vertex position as a result of restriction of venous return and lymph flow during labor and delivery.
      1) Maximal swelling present at birth.
      2) Edema extends across suture lines and has poorly defined borders.
      3) Edema can shift to dependent position.
      4) Ecchymosis, petechiae, or purpura.
      5) Disappears within 24 to 48 hours.
   b. Cephalohematoma: subperiosteal hemorrhage due to delivery trauma.
      1) Typically not present at birth, increases in size over the first day of life.
      2) Unilateral; fixed, firm, and palpable mass.
      3) Swelling does not cross suture lines.
      4) Often no ecchymosis.
      5) Poor tone, feeding, and decreased activity may be indication of underlying skull fracture.
      6) Resolution may not occur for several months, often leaving a calcified rim.
   c. Subgaleal hemorrhage: due to forces that compress and drag the head through the pubic outlet.
      1) Is a clinical emergency.
      2) Ballotable scalp mass present at birth that is mobile, not fixed.
      3) Swelling crosses suture lines and fontanelles, poorly defined margins.
      4) Rapidly can increase in size and shape with significant acute blood loss, resulting in shock as the presenting symptom.
      5) Bleeding, seen as swelling, can expand to orbital ridges, around the ears, and dissect along tissue planes into the neck.
      6) Least common of the birth injuries; however, has the greatest potential for complications.

6. Inspect the scalp.
   a. Intact skin.
   b. Normal hair pattern (direction of growth) and distribution (Johnson, 2019).
      1) Color concordant racially with parents; genetic disorders can present with hypopigmentation of scalp hair.
      2) Localized patches of hypopigmentation (e.g., white forelock: Waardenburg's syndrome).
      3) Hair consistency and growth patterns reflect, racial, familial, and developmental variations.
      4) Areas of diffuse or localized absence or abundance of hair.
      5) Hair texture: brittle, fragile, twisted, woolly, excessively kinky.
      6) Anterior and posterior hair margins.
   c. Abnormal findings.
      1) Lacerations or abrasions as the result of instruments at delivery or scalp electrode.
      2) Vesicles: electrode site and behind the ears.
      3) Cutis aplasia: localized absence of skin associated with trisomy 13.
      4) Hair whorls: spiral hair growth pattern; multiple hair whorls or abnormal placement may represent abnormal brain growth or development.
      5) Anterior hairline well onto the forehead and low hairline on neck.

7. Note position in which infant holds head at rest.
   a. Reflects fetal position.
   b. Usual position: anterior neck flexion.
   c. Observe for full range of motion.

F. Face.
   1. Observe for symmetry and location of eyes, nose, and mouth.
      a. Divide the face into thirds for inspection: one third, forehead; one third, eyes and nose; and one third, mouth and chin.
      b. At rest and with crying or sucking.
         1) Asymmetry when infant crying.
            a) Facial nerve compression from in utero positioning or forceps pressure; most resolve spontaneously.
            b) Congenital hypoplasia of depressor anguli oris muscles; most evident with crying; localized paralysis of one corner of mouth with rest of facial movement intact.
         2) Symmetrical: Möbius sequence; mask-like facies due to sixth and seventh cranial nerve palsy (Jones et al., 2013).
   2. Observe relationship and location of eyes, nose, and mouth.
      a. Eyes.
         1) Open spontaneously with upright position and gentle forward and backward motion.

2) Space between inner and outer canthus of one eye approximates the width between the two inner canthi.
   a) Hypertelorism (widened distance between orbits); hypotelorism (decreased distance between orbits) associated with various syndromes.
3) Number: anophthalmos (absent); cyclopia (one).
4) Conjunctiva and sclera.
   a) Subconjunctival hemorrhage: results from pressure on fetal head during delivery.
   b) Sclera color usually white.
   c) Blue sclera: extreme prematurity, osteogenesis imperfecta, other chromosomal associations.
   d) Yellow sclera: jaundiced.
5) Cornea, iris, and pupils.
   a) Cornea relatively cloudy at birth.
      (1) Term infant: cloudiness resolves within a few days.
      (2) Asymmetrical or dense cloudiness abnormal.
      (3) Infantile cataracts: rubella, cytomegalovirus, familial association, and chromosomal defect.
      (4) Congenital glaucoma: cornea size greater than 12 mm diameter with tearing and light sensitivity. Need immediate ophthalmology consult (Örge and Grigorian, 2015).
   b) Iris: dark blue until 3 to 6 months of age, then eye color may change.
      (1) Brushfield spots: speckled appearance around the circumference; associated with trisomy 21; also, normal variant.
      (2) Coloboma: most common congenital anomaly of eye. Cleft-shaped fissure (keyhole-shaped pupil); can be sporadic or in association with trisomy 13, trisomy 18, or CHARGE sequence (posterior *c*oloboma, *h*eart defect, choanal *a*tresia, *r*etardation, *g*enital and *e*ar abnormalities).
   c) Pupils.
      (1) PERRL (*p*upils *e*qual, *r*ound, and *re*active to *l*ight).
      (2) Pupillary reflexes present after 28 to 30 weeks.
   d) Red reflex: reflection of ophthalmoscope's light on the retina.
      (1) Color range: normal red (light-skinned infant) to yellow (dark-skinned infant).
      (2) White (leukocoria): congenital cataracts, tumor, chorioretinitis.
      (3) Absence: retinoblastoma, glaucoma, or hemorrhage.
6) Symmetry of eye movements.
   a) Eyelids.
      (1) Should open to above midpoint of pupil when the eye is in a neutral position.
      (2) Edema: related to birth process or chemical irritation with eye prophylaxis.
      (3) Fused eyelids: extreme prematurity; generally not fused by 28 weeks of gestation; should not be used as an indicator of viability or nonviability.
      (4) Ptosis: abnormal drooping of one or both eyelids.
   b) Palpebral fissures.
      (1) Slant is primarily racially determined.
      (2) Variations typical of several syndromes.
   c) Epicanthal folds.
      (1) Vertical fold of skin at inner canthus of eye on either side of the nose.
      (2) Common in trisomy 21 and infants of Asian descent.
      (3) Manifestation of in utero compression (Potter facies).
   d) Eyelashes, eyebrows.
      (1) Appear at 20 to 23 weeks.
      (2) Abnormalities.
         (a) Absent lashes or long lashes.
         (b) High-arched eyebrows or synophrys (meeting of eyebrows in middle).

b. Nose.
   1) Shape and size.
      a) Positional deformities often due to birth process; resolve without treatment.
      b) Abnormal shape: may be associated with a congenital syndrome.
      c) Abnormal: flat, broad nasal bridge.
   2) Patency of nostrils.
      a) The neonate is an obligate nose breather. If blockage is suspected, alternately occlude each nares and observe for distress.
      b) Causes of nasal obstruction.
         (1) Choanal atresia or stenosis: membranous or bony obstruction; unilateral or bilateral.
         (2) Iatrogenic: swollen mucosa from suction catheters.
         (3) Inflammation and secretions.
         (4) Nares deformity: Differentiate nasal compression from true septal deviation. Gently compress naris on side of asymmetrical naris.

(5) Nasal compression will correct; dislocated septum remains angled at base. Consult ear, nose, and throat physician for septal dislocation: relocation of dislocated septum should be done within a few days of birth for best outcome (MacDonald, 2013).

c. Mouth, tongue, and perioral region.
1) Mouth should be symmetrical and positioned in the midline.
a) Microstomia: very small mouth; may be associated with trisomy 18.
b) Macrostomia: large mouth; often associated with mucopolysaccharidosis, Beckwith–Wiedemann syndrome, or hypothyroidism.
c) Suck-and-swallow reflex develops at 32 to 34 weeks, and root and gag response at 36 weeks. They should be elicited during the examination.
2) Cleft upper lip: can vary from a niche in the lip to a complete separation extending up onto the floor of the nose.
3) Thin upper lip in association with flat philtrum: fetal alcohol syndrome.
4) Soft and hard palate should be visually inspected, then palpated.
a) Presence of submucous or membranous clefts.
b) Narrow or high-arched palate may indicate a decrease in neuromotor activity or sucking in utero.
5) Mucosal cysts.
a) Epithelial or Epstein's pearls: small, white epidermal cysts commonly found on the hard and soft palates and on gum margins; disappear after a few weeks.
b) Bohn's nodule: found on the gums and equivalent to milia on the skin.
c) Gingival or alveolar cysts.
6) Dental eruptions and neonatal teeth.
a) If mobile or poor root formation: generally removed.
b) Consult with pediatric dentist; may be primary teeth.
7) Frenulum.
a) Small lingual frenulum normal.
b) Ankyloglossia (tongue-tied): short frenulum that limits tongue movement. Abnormal; tip of tongue will form an inverted V shape. Rarely problematic. If persistent feeding problems, frenotomy may be indicated (Johnson, 2019).
8) Tongue.
a) Large tongue (macroglossia): generally part of syndrome (Beckwith–Wiedemann).
b) Large tongue can obstruct the airway.
c) Protruding tongue: trisomy 21 and Beckwith–Wiedemann syndrome.
9) Thrush: oral moniliasis: usually contracted from mothers with vaginal moniliasis at time of delivery.
a) Lacy white material present on surface of oral mucous membranes.
b) Does not wipe away with a cotton-tipped swab.

3. Observe other facial features.
a. Nasolacrimal ducts (Örge and Grigorian, 2015).
1) Tears are rare until 2 to 4 months of age.
2) Excessive tearing (epiphora) does not occur until after the first 3 weeks when lacrimal gland becomes functional.
3) Obstruction: visible mass.
a) Dacrostenosis: stagnant pool of tears in lacrimal sac.
b) Dacryocystocele: bluish mass adjacent to but lower than inner canthus.
4. Inspect facial skin.
a. Milia: 1-mm white or yellow papules without erythema; resolve spontaneously within first weeks of life.
b. Miliaria: clear, thin vesicles (1 to 2 mm) that develop in sweat glands; primarily seen on forehead, scalp, and creases.
c. Lacerations, ecchymosis, abrasions from forceps.
d. Petechiae over head and neck: typically from nuchal cord, rapid second stage of labor.
e. Pits or sinus: facial cleft syndromes.
5. Observe for size of jaw and relationship to maxilla.
a. Micrognathia: abnormally small jaw with normal-sized tongue.
1) May present serious airway problem.
2) Seen in Pierre Robin, Treacher Collins, and de Lange's syndromes.

G. **Ears** (Isaacson, 2018; Johnson, 2019).
1. Note presence or absence of external ear.
2. Determine position and rotation.
a. Helix attaches to scalp at a point horizontal to the inner canthus of the eye.
b. Normal: 30% of pinna above imaginary line drawn from the inner canthi of the eyes toward the occiput and tragus (cartilaginous projection in front of the external meatus of the ear).
c. Cranial molding may distort landmarks; ears may appear low-set.
d. Low-set ears may be associated with various syndromes and chromosomal abnormalities.
3. Check for presence of ear canals; visualization of eardrums not typically necessary.
4. Examine for abnormal findings.
a. Microtia: dysplastic malformed ear.
1) Associated with atresia of auditory meatus and conductive hearing loss.

2) Variations.
a) Lop ear: helix folded downward because of inadequate development of the antihelix.
b) Cup ear: small cup-shaped ear.
b. Preauricular pits and sinus.
1) Pinpoint openings at base of helix or front of tragus.
2) Increased risk of congenital deafness and renal abnormalities.
c. Preauricular ear appendages (tags).
1) Single or multiple; vary in size.
2) Differentiate from accessory auricle or tragus.
3) Consistently seen in Goldenhar's syndrome: syndrome with wide range of facial, ear, and vertebral defects (Jones et al., 2013).
4) Associated with other brachial arch abnormalities: cleft lip, cleft palate, and hypoplasia of mandible.
5) Isolated skin tags are usually benign. Those associated with other dysmorphic features such as CHARGE, a family history of deafness, maternal history of gestational diabetes, or increased risk for renal anomalies are recommended to have a renal ultrasound (Isaacson, 2018).

H. Neck and clavicles.
1. Inspect and palpate neck.
a. Mass: note location.
1) Most common: cystic hygroma.
a) Multiloculated cyst arising from lymphatic channels typically located posterior to the sternocleidomastoid muscle and extending into the scapula and axillary and thoracic compartments.
b) Can distort the anatomy of the airway.
2) Thyroglossal duct cyst or branchial cleft cyst.
b. Webbing.
1) Excessive skinfold extending from the mastoid process to the shoulders.
2) Associated with Turner's and Noonan's syndromes and trisomy 21.
c. Torticollis: rotation limited due to unilateral contraction of the sternocleidomastoid muscle.
2. Gently palpate neck and clavicles.
a. Crepitus: due to clavicular fracture with bone ends rubbing together.
1) Swelling, discoloration, or tenderness associated with fractured clavicle.
2) Observe for asymmetrical arm movement with the Moro reflex or signs of pain with manipulation.
b. Cleidocranial dysostosis: partial or complete absence of clavicles.

I. Chest and lungs.
1. Review influencing factors: GA, timing of examination, intrapartum and delivery history, maternal drugs, and cool environment.
2. Inspect the shape and size of the chest (Fig. 7.8).
a. Compare size relationship of the thorax and abdomen.
b. Normal: round symmetrical shape with the AP diameter approximately the same as the transverse diameter.
c. Large or barrel-shaped chest: associated with air trapping and hyperinflation.
d. Pigeon chest or protrusion of sternum: associated with Marfan syndrome.
e. Chest wall itself depressed or funnel shaped: pectus excavatum; no clinical significance.
f. Short sternum: associated with trisomy 18.
g. Rib margins apparent in premature infants: thinner layers of muscle and fat.
3. Observe.
a. Color: refer to "C. General appearance: initial impression."
b. Respiratory rate and pattern.
1) Should be evaluated at rest and before any manipulation.
2) Rate: normal—30 to 60 breaths per minute, easy, unlabored, and typically abdominal or diaphragmatic.

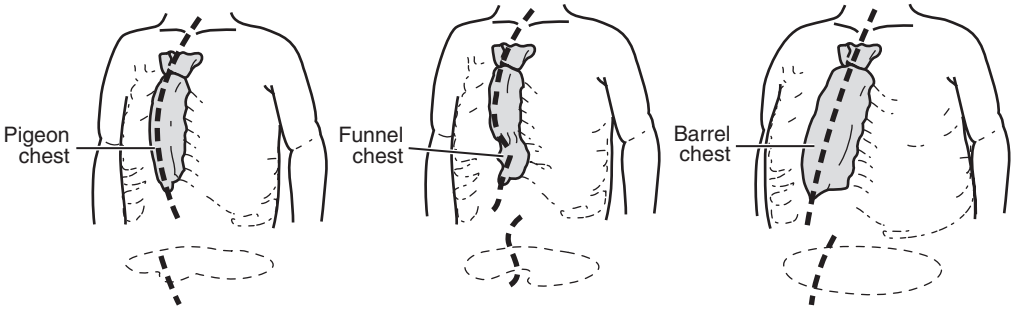

Fig. 7.8 Different chest shapes. *(Adapted from Alexander, M. M. and Brown, M. S. [1979].* Pediatric history taking and physical diagnosis for nurses *[2nd ed.]. St. Louis, MO: Mosby.)*

3) Tachypnea: rate greater than 60 breaths per minute—lung pathology, cardiac disease, infection, overheating, fever, and pain.
4) Bradypnea or shallow respirations: CNS depression.
5) Periodic breathing: 5- to 20-second pauses without changes in color, tone, or heart rate.
6) Apnea: cessation of breathing for more than 20 seconds. May be accompanied by bradycardia, change in muscle tone, or color change; apnea of prematurity, infection, respiratory insufficiency, gastroesophageal reflux.
7) Slow, gasping respirations: respiratory failure and acidosis.

c. Depth and ease of respirations.
1) Normal: irregular and varying depth.
2) Chest pulled inward as abdomen rises with inspiration as a result of normal diaphragmatic excursion.
3) Retractions: accessory muscles used.
a) Note depth (minimal, marked).
b) Subcostal, substernal: common after birth. Persistence may indicate respiratory problems.
c) Intercostal.
4) Nasal flaring, retractions, tachypnea, and grunting—symptomatic of respiratory distress.

4. Auscultate breath sounds.
a. Compare and contrast each side of chest.
b. Presence of air entry: normal, fair, or poor.
c. Asymmetrical breath sounds: pneumothorax, cystic adenomatoid malformation, or congenital diaphragmatic hernia (CDH).
d. Normal breath sounds: clear and equal, little differentiation between inspiration and expiration.
e. Adventitious breath sounds.
1) Crackles: fine or coarse, lower pitched, fine crackles heard on inspiration, often present after birth due to clearing lung fluid.
2) Wheeze: high pitched, usually heard on exhalation, reactive airway.
3) Rhonchi: low pitched, arise from partial obstruction by mucus or secretions.
4) Stridor: rough, harsh sound worse during inspiration, caused by reduced airway diameter (edema, mass, vascular ring).
5) Diminished breath sounds: atelectasis, effusion, decreased air entry, poor respiratory effort.
6) Peristaltic sounds: bowel sounds indicate CDH.
7) Friction rub: pleural effusion.

5. Inspect breasts and nipples.
a. Size.
1) Based on GA.
2) Enlarged breasts: effects of maternal estrogen, transient.
3) Unilateral redness or firmness indicates infection; mastitis.
b. Location and symmetry: widespread nipples—distance between nipples more than 25% of full chest circumference; may indicate variety of conditions (e.g., Turner's syndrome).
c. Number: supernumerary nipples; small, raised, pigmented areas 5 to 6 cm below normal nipple but may be located anywhere on a vertical line drawn through the true nipple; familial.
d. Discharge.
1) Witch's milk.
a) Milky discharge produced in response to maternal hormones.
b) Secretion lasts for 1 to 2 weeks with enlargement lasting several months.
2) Purulent: mastitis due to staphylococcal infection.

J. Heart and cardiovascular system (Vargo, 2019; Walker, 2018).

1. General considerations: congenital heart defects are associated with other congenital malformations, chromosomal defects, maternal medication or substance use (phenytoin [Dilantin], alcohol), maternal health or illness (diabetes), viral illness, and familial association.
2. Observe color.
3. Heart rate: normal range 120 to 160 beats per minute (bpm), varies with infant's behavioral state.
a. Bradycardia: rate less than 80 bpm in term newborn.
1) May be associated with apnea, cerebral defects, vagal response, congenital heart block.
2) Healthy term infant in deep sleep can have a heart rate of 80 to 90 bpm; should increase as infant awakens.
b. Tachycardia: more than 160 bpm sustained.
1) May increase to ≥180 bpm with stimulus: activity, crying, feeding, fever.
2) May be associated with respiratory distress, anemia, congestive heart failure, hyperthermia, shock, and supraventricular tachycardia.
c. Brief irregularities are common; identification of abnormality cannot be made by auscultation alone.
4. Location of point of maximal intensity.
a. Normal: left side, fourth intercostal space, either at or to the left of the midclavicular line.
b. Shift in location can indicate tension pneumothorax.
c. Right-side location: dextrocardia, CDH.
d. Observe precordial activity.
1) Within first hours of birth, may be visible along left sternal border due to normal right ventricle dominance at birth.
2) Visible for longer periods in premature infants.

3) Associated with congestive heart failure, heart disease, and fluid overload when seen after postnatal transition.

5. Auscultate heart sounds.
   a. First heart sound (S_1).
      1) Sound produced by closure of mitral and tricuspid valves; accentuated at birth.
      2) Increase in intensity: patent ductus arteriosus, VSD, tetralogy of Fallot, anemia, hyperthermia, and arteriovenous fistula.
   b. Second heart sound (S_2).
      1) Sound produced by closure of aortic and pulmonary valves.
      2) S_2 single sound at birth; splitting of S_2 normal at 1 to 2 days with respirations.
      3) Wide splitting of S_2 abnormal—associated with atrial septal defect (ASD), pulmonary stenosis, mitral regurgitation or partial anomalous pulmonary venous return, and right bundle branch block.
      4) S_3 and S_4 abnormal in the newborn.
   c. Muffled heart sounds: may indicate pneumopericardium, pneumomediastinum, or CDH.
6. Auscultate murmur: turbulence in blood flow (Fig. 7.9).
   a. Can be innocent or pathologic (underlying cardiovascular disease).
   b. Timing of appearance.
      1) First 48 hours of life: can be related to cardiovascular transition; should be followed up.
      2) Audible after transition complete: VSD, turbulence in pulmonary arteries secondary to obstruction; severe outflow tract obstruction.
   c. Location and radiation.
      1) Describe as interspace, midclavicular, midsternal, or axillary.
      2) Transmission: auscultate back or axilla.
   d. Timing within cycle.
      1) Holosystolic or pansystolic: occurs throughout systole.
      2) Continuous: heard through both systole and diastole.
      3) Systolic ejection murmur: most common murmur; heard at mid to upper sternal border, just after S_1; described as vibratory; flow across pulmonary valve.
   e. Loudness or quality.
      1) Grade I: barely audible.
      2) Grade II: soft but easily audible.
      3) Grade III: moderately loud but no thrill.
      4) Grade IV: loud (may be associated with thrill).
      5) Grade V: very loud; audible with stethoscope placed lightly on chest.
      6) Grade VI: extremely loud; audible with stethoscope placed near chest.
7. Palpate pulses: strength and equality (upper to lower and side to side).
   a. Brachial, radial, and palmar.
   b. Femoral, popliteal, posterior tibial, and dorsalis pedis.

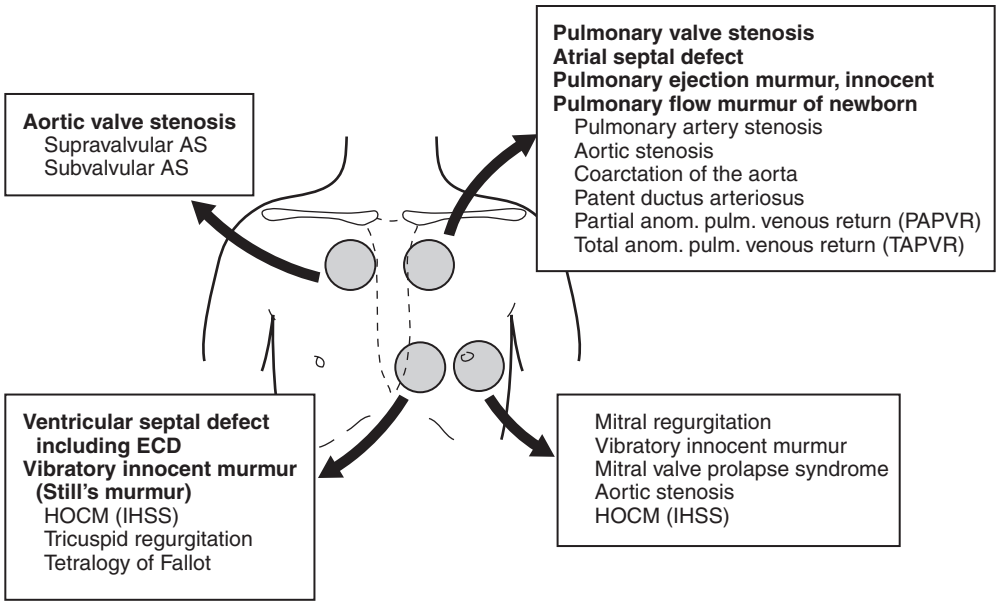

Fig. 7.9 Diagram showing systolic murmurs audible at various locations. Less common conditions are shown in lighter type. *AS*, Aortic stenosis; *ECD*, endocardial cushion defect; *HOCM*, hypertrophic obstructive cardiomyopathy; *IHSS*, idiopathic hypertrophic subaortic stenosis. *(From Park, M. K. [2008]. Pediatric cardiology for practitioners [5th ed.]. St. Louis, MO: Elsevier Mosby.)*

c. Grading scale.
   1) 0: Not palpable.
   2) +1: Very difficult to palpate; weak, thready, easily obliterated with pressure.
   3) +2: Difficult to palpate; may be obliterated with pressure; normal in newborn.
   4) +3: Easy to palpate; not easy to obliterate with pressure.
   5) +4: Strong and bounding; not obliterated with pressure; associated with patent ductus arteriosus.

d. Absent femoral: associated with coarctation of aorta.

8. Assess capillary refill or perfusion.
   a. Press and release skin over abdomen until area blanches.
   b. Count number of seconds until color returns to area.
   c. Normal: ≤3 seconds.
9. Blood pressure (BP) (Fig. 7.10).
   a. Depends on GA, birth weight, and postnatal age.
   b. Differential greater than 20 mm Hg between upper and lower extremity BP indicates obstruction (coarctation of aorta).
   c. BP in lower extremities should be slightly higher than in the upper extremities.

K. Abdomen.
1. General considerations: review history for feeding intake, emesis, stooling, maternal medications affecting bowel function, maternal blood type, and intrauterine infection.
2. Observe abdomen: slightly rounded, soft, and symmetrical.
   a. Scaphoid abdomen: abdominal contents in chest (diaphragmatic hernia). May appear slightly concave at birth but will become distended as bowel fills with air.
   b. Complete or partial absence of abdominal muscles; large, flaccid, wrinkled abdominal wall (Eagle Barrett syndrome—formerly called *prune belly syndrome*).
   c. Distention: obstruction, infection, masses, or enlargement of an abdominal organ.
3. Observe for abdominal wall defect.
   a. Etiology: disruption in migration of abdominal contents from the umbilical cord and defect in the development of abdominal wall musculature.
   b. Omphalocele: abdominal contents usually covered with a membrane; umbilical cord inserts into sac; commonly associated with cardiac lesions, trisomy 13, trisomy 18, Beckwith–Wiedemann syndrome.
   c. Gastroschisis: abdominal wall defect resulting in protrusion of abdominal contents not covered with a membrane.
      1) Typically located to the right of midline.
      2) Abdominal contents often thickened, edematous, and matted as a result of exposure to amniotic fluid.
   d. Umbilical hernia: bulge at umbilicus related to weakness in abdominal muscle.

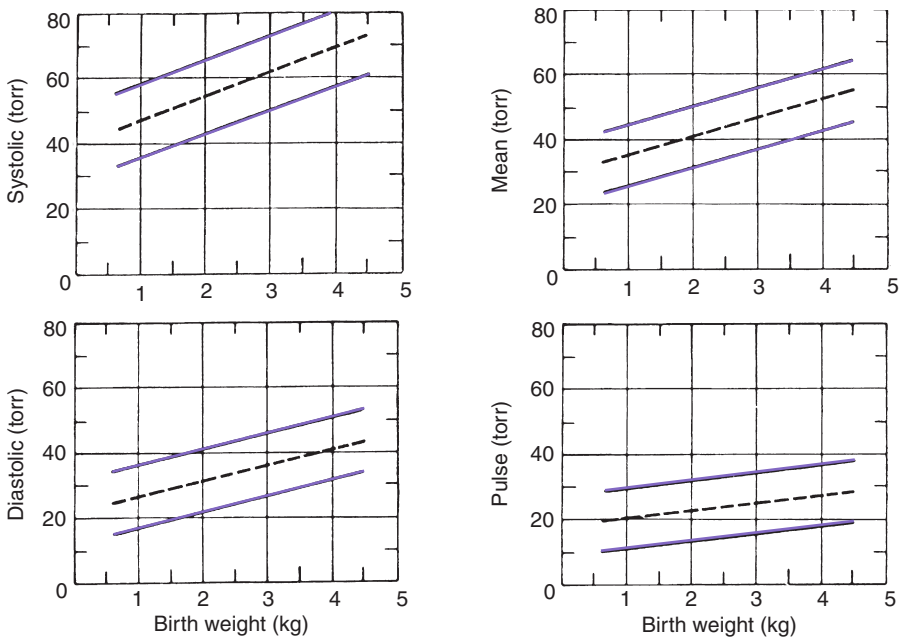

Fig. 7.10 Blood pressure by birth weight. *(From Versmold, H. T., Kitterman, J. A., Phibbs, R. H., et al. [1981]. Aortic blood pressure during the first 12 hours of life in infants with birth weight 610 to 4200 grams.* Pediatrics, *67[5]:607–613.)*

4. Palpate gently for enlargement in liver or presence of masses.
   a. Normal: liver edge 1 to 2 cm below right costal margin in midclavicular line.
   b. Begin palpation in right lower quadrant and progress upward so liver edge will not be missed.
   c. Enlarged liver: congenital heart disease, infection, hemolytic disease, and arteriovenous malformation.
   d. A normal spleen is rarely palpable; palpable spleen more than 1 cm below left costal margin is abnormal.
   e. Abdominal mass: most often of urinary tract origin.
5. Palpate kidneys and bladder.
   a. Place one hand under the flank and palpate gently from above with the fingertips of the other hand.
   b. Normal kidney in term infant is 4.5 to 5 cm from pole to pole.
   c. Further evaluation needed: absence of palpable kidney or enlarged kidneys.
   d. Bladder can be palpated 1 to 4 cm above pubic symphysis when urine present.
6. Auscultate for bowel sounds.
   a. Absent or hyperactive bowel sounds may indicate obstruction.
7. Inspect the umbilical cord (Palazzi and Brandt, 2018; Voskamp et al., 2013).
   a. Important clues to fetal growth, development, and well-being.
   b. Normal: bluish white, moist, and gelatinous.
   c. Diameter of cord varies and is related to Wharton's jelly.
      1) Supportive covering protecting the cord vessels from compression or occlusion.
      2) Increases with GA.
      3) Thin cord may reflect placental insufficiency and IUGR.
   d. Total length of cord: normal 35 to 80 cm.
      1) Lengthens through gestation from a mean of 32 cm at 20 weeks to 60 cm at term; length highly variable.
      2) Length determined by intrauterine space and fetal activity.
      3) Short umbilical cord (<35 cm): associated with placental abruption and developmental abnormalities. Infants with limited fetal activity (Down syndrome, congenital neuromuscular disorders) have short cords.
      4) Longer umbilical cords: increased risk of cord knots, nuchal cords, cord prolapse, thrombi, and fetal demise.
   e. Color: green or yellow (meconium); red (blood); depth of staining correlates with duration of exposure.
   f. Number of vessels.
      1) Normally contains two arteries and one vein.
      2) Single umbilical artery (SUA).
         a) Seen more frequently in SGA, premature infants, and twins.
         b) Twenty percent to 30% with SUA have structural anomalies mostly of the heart, gastrointestinal (GI) tract, and CNS; no increased chromosomal anomalies if an isolated finding.
         c) SUA is an isolated finding in 70% to 80% of infants; may be associated with renal anomalies such as hydronephrosis.
         d) Controversial whether further imaging is needed for healthy term infant with isolated SUA because is associated with renal anomalies in only 7% of cases.
   g. Urine draining from umbilicus: patent urachus (embryologic communication between bladder and umbilicus).

L. Genitalia and anus.
   1. General considerations.
      a. Review pertinent history.
         1) GA; appearance changes with GA.
         2) Oligohydramnios or polyhydramnios: possible renal/urinary or GI/pulmonary anomaly.
         3) Family history: associated genetic predisposition.
      b. Congenital defects are relatively rare but highly stressful to parents.
      c. Normal variations are more common than pathologic conditions.
      d. Genitourinary anomalies are highly associated with other system disorders (see Chapter 33).
      e. Breech deliveries can cause significant bruising and edema of genitalia and perineum.
      f. No circumcision should be done in infants with epispadias, hypospadias, or chordee.
   2. General inspection and palpation: position infant supine for examination.
      a. Gender identification: if not clearly distinguishable, do not assign sex until further evaluation. Inform parents of ambiguity and need for further testing.
      b. Anus: locate position in relation to genitalia and determine patency.
         1) Anal opening: approximately midline.
         2) Slightly more anterior to genitalia in females.
         3) Check for anal wink in any infant suspected of neural tube defect; stroke anal opening lightly; observe positive constriction.
      c. Passage of meconium; ensures open communication only.
         1) Fistulas: anteriorly or posteriorly placed; may be accompanied by bowel distention.
            a) Rectovaginal fistula (female) or rectoperineal fistula (male).

2) Constant dribbling of loose stool: suspect neural tube defect.

d. Inguinal area.
1) Assess for hernia(s) when inguinal mass observed.
2) Groin bulge: may be unilateral or bilateral; increases in size with crying or straining, or spontaneously reduces.
3) Palpate from lower abdomen along the inguinal canal to the labia or scrotum.
4) Attempt to gently compress bowel back toward abdomen. Irreducible hernias are at high risk for incarceration and subsequent necrosis.

3. Male.
a. Penis: inspect size, appearance, and foreskin.
1) Normal.
a) Straight, may be erect.
b) Size proportionate to body, average term length 2.5 to 3.5 cm from pubic bone to glans tip (Fletcher, 1998).
c) Glans covered by prepuce (foreskin) in uncircumcised infant.
d) Physiologic phimosis: tight, nonretractable foreskin; does not retract until 2 to 3 years of age.
e) Prepuce: foreskin or fold of skin over the glans.
(1) Amount and distribution: hooded (appearance of distal foreskin).
(2) Small, white epithelial cysts on distal prepuce.
2) Abnormal.
a) Chordee: curving or bowing of penis; sometimes occurs in conjunction with hypospadias.
b) Micropenis: less than 2.5 cm in the term neonate.

b. Determine position of urinary meatus.
1) Normal: midline at the glans tip.
2) Abnormal (Cavaliere, 2019).
a) Hypospadias.
(1) Urethral opening located at the ventral surface of the penis; associated with chordee, meatal stenosis, inguinal hernia, and undescended testes.
(2) May be blind dimple or pit in the glans at expected location of meatus.
b) Epispadias: urethral opening located on the dorsal surface of the penis.

c. Urine: observe strength, direction of stream, and color.
1) Normal.
a) Straight, forceful, and continuous stream.
b) Most newborns void within first 24 hours of birth.
c) Uric acid crystals (flaky, rust-colored) are a normal variant.
2) Abnormal.
a) Altered stream direction may indicate urinary obstruction; urine from perineum or abdomen indicates urinary fistula.
b) Abnormal color: red (hemoglobin or myoglobin), brown (bilirubin), brown-yellow (concentrated).

d. Scrotum and testes: inspect for size, symmetry, color, presence of rugae, and location of testes.
1) Normal.
a) Firm, smooth testes of equal size palpable in scrotal sac; undescended testes in inguinal canal normal for preterm infants.
b) Darker skin pigmentation.
2) Abnormal: scrotal swelling or discoloration, nonpalpable testes (Kolon et al., 2014; Shnorhavorian and Fechner, 2018).
a) Cryptorchidism (undescended testes, extrascrotal testes position): needs further investigation with possible karyotyping. Ultrasound of undescended testes unnecessary before referral, as they rarely assist in decision making.
b) Nonpalpable testes: if not detected bilaterally in phenotypic male, evaluate for disorder of sexual differentiation (DSD)—virilizing adrenal hyperplasia.
(1) Unilateral nonpalpable testicle and hypospadias: evaluate for DSD—mixed gonadal dysgenesis or ovotesticular DSD.
(2) Imaging not recommended before referral, which should occur by 6 months of age.
c) Bifid scrotum: deep midline cleft in the scrotum.
d) Hydrocele: unilateral or bilateral fluid collection in scrotal sac, positive transillumination.
e) Testicular torsion: blue discoloration, palpable firm mass, tender or nontender, negative transillumination. May be surgical emergency.

4. Female.
a. Labia and clitoris: separate labia and exert gentle downward traction to evaluate structures.
1) Normal: smooth, wrinkling with weight loss, hyperpigmented from hormonal influence.
2) Edematous at birth due to maternal hormones.
3) Perineum is smooth, no dimpling; fingertip width.
4) Abnormal.
a) Labial bulge may indicate inguinal hernia or ectopic ovary.

b) Labioscrotal fusion, female virilization.
c) Clitoromegaly, pseudohermaphroditism.
d) Genitourinary anomalies: abnormal spacing between orifices.
e) Rugae: ambiguous genitalia.

b. Vagina.
1) Normal: pink, patent.
a) White or blood-tinged discharge due to hormonal influence (pseudomenstruation); can persist 2 to 4 weeks.
b) Redundant hymen tissue and vaginal skin tags are common.
2) Abnormal.
a) Rectovaginal fistula: feces from vagina, indicates rectovaginal fistula.
b) Imperforate hymen: secretions pool in vagina; can be confused with enlarged Bartholin cysts.
c) Hydrometrocolpos: membrane covering vaginal opening causes uterine enlargement and pooling of vaginal secretions; seen as perineal or suprapubic mass.

c. Urethral meatus.
1) Normal position: below clitoris; often obscured by hymen.
2) Abnormal: anterior displacement.

5. Intersex conditions.

M. Back, spine, and extremities.
1. General considerations.
a. Influencing factors: GA, maternal hormones, in utero position, delivery mode/history, and timing of examination.
b. Many abnormalities are deformations from compression and contracture in utero rather than congenital defects.
c. Review for relevant history.
1) Elevated maternal α-fetoprotein (neural tube defects).
2) Maternal diabetes mellitus (sacral agenesis).
3) Maternal deficiency of folic acid or zinc; use of anticonvulsant medication.
4) Decreased fetal movement (congenital neuromuscular disorders).
5) Postnatal *S. aureus* sepsis (risk for osteomyelitis).
6) Family history (hip dysplasia).

2. Observe infant at rest: appropriate number of limbs and digits; size and symmetry of upper and lower extremities; movement, position of comfort, range of motion, and trauma.
3. Palpate for joint or bone swelling, tenderness, or crepitus.
4. Back: position infant prone.
a. Inspect for symmetry of sides, scapula position and symmetry, spine alignment and integrity, and presence of dermal lesions over spine or masses.
b. Inspect skin.
1) Hyperpigmented macule (Mongolian spot).
a) Normal variant; macular gray or blue-green lesions from melanocyte concentration in dermis.
b) Most commonly in lumbosacral region but can be found on legs, back, and shoulders.
c) Occurs more often in African American, Hispanic, Asian, and Native American infants.
d) Benign; fades during childhood.
2) Subtle cutaneous findings can indicate hidden spinal defects; observe for sacral pits or dimples, sacral tracts (pilonidal cysts), skin tags, abnormal hair distribution or hair tufts, soft or cystic masses, unusual pigmentation, hemangiomas, or lipomas (Johal et al., 2017; Walker, 2018).

c. Congenital spine defects (Johal et al., 2017).
1) Closed spinal dysraphism: umbrella term that describes several closed spinal defects that present at birth; involve the distal part of the spinal cord and have an intact dermal covering.
a) Spinal lipoma.
b) Dermoid tumor.
c) Tethered cord.
d) Split cord malformation.
e) Skin tags and appendages, human tail.
f) Dermal sinus tract.
2) Neural tube defect.
a) Failure of posterior neural tube closure (see Chapters 34 and 35).
b) Defect can be open, with spine and nerves exposed, or covered with skin or tissue.
3) Sacrococcygeal teratoma: tumor (mainly benign).
4) Scoliosis: lateral spine curvature; evaluate for associated genitourinary tract anomalies.

5. Extremities (Tappero, 2019).
a. Upper extremities.
1) Absent humerus, radius, or ulna: associated with syndromes.
2) Clavicle or humerus fractures: associated with birth injury or osteogenesis imperfecta.
3) Blisters on hands or forearms: in utero sucking.
4) Brachial plexus injury: stretching or tearing of nerve roots by lateral traction on shoulder during birth, or pressure from the maternal sacral promontory during fetal descent.
a) Erb's palsy ("waiter's tip"): paralysis of arm with intact grasp; asymmetrical Moro reflex.

b) Klumpke's paralysis: forearm paralysis with absent grasp.
c) Total brachial plexus injury; because the neonate cannot move the shoulder, the arms remain extended and turned inward, with the flaccid hand suggesting a "waiter's tip" hand.

5) Observe the shape of hands and digits.
a) Syndactyly: webbing between adjacent digits of hands.
b) Polydactyly: supernumerary digits.
c) Clinodactyly: congenital deviation (curvature) of digits; may be an isolated anomaly or a sign of a genetic syndrome—trisomy 21, Turner's, Cornelia de Lange syndrome.
d) Brachydactyly: shortened digit from shortened finger joint; normal variant; associated with achondroplasia and trisomy 21.

6) Simian crease: single palmar crease; normal variant, positive finding in less than 50% of trisomy 21 infants (Jones et al., 2013).

7) Nails: yellowing from meconium or postmaturity; dysplasia with chromosomal defects.

b. Buttocks.
1) Observe for blanching or cyanosis of extremities or buttocks while umbilical catheter in use; indicates circulation compromise and potential necrosis.
2) Dimple on buttocks can indicate congenital anomaly of femur (Fletcher, 1998).

c. Hips.
1) Positional hip abduction: persistent joint flexion or contraction with knee extension resulting from prolonged breech position in utero.
2) Developmental dysplasia of the hip (AAP, 2000; Tappero, 2019).
a) Asymmetrical creases of buttocks and thighs due to shortened adductor muscles.
b) Uneven knee level (positive Galeazzi sign) when positioned supine with feet flat and knees flexed.
c) Ortolani maneuver: detects dislocated hips.
d) Barlow maneuver: determines dislocatable hips (Fig. 7.11).

d. Lower extremities.
1) Legs normally slightly bowed, internal tibial torsion with everted feet.
2) Genu recurvatum: knee hyperextension; related to in utero position.
a) Usually found in breech position, females more often than males.
b) Mild cases are benign; severe cases may require splinting/casting.
3) Limb or digit amputation (amniotic band syndrome).
a) Strands of amnion can wrap around any digit or, more frequently, a limb.
b) Causes constriction and amputation.
4) Metatarsus adductus.
a) May be positional or structural.
b) Most common foot deformity.
c) Medial deviation of the forefoot with hindfoot in normal position; convex shape to lateral border of foot (C-shaped).
5) Talipes equinovarus; clubfoot; may be positional, teratologic, or congenital.
a) Congenital: isolated anomaly.
b) Teratologic: neuromuscular disorder such as arthrogryposis.
c) Positional: normal foot held in equinovarus position in utero.
d) Three primary components:
(1) Adduction of the forefoot (points medially).
(2) Varus of heel (turned inward).
(3) Pointing of toes and foot downward.
6) Talipes calcaneovalgus: related to intrauterine position; sole of foot is flattened against uterine wall. Hyperdorsiflexion of foot results in forefoot resting on anterior surface of lower leg.
7) Rocker-bottom foot: arch looks like rocker bottom.

N. Neurologic examination.
1. General considerations.
a. Repeat examination of abnormal findings; assess changes over time.
b. Review history: familial, genetic, or neurologic diagnosis; birth trauma; difficult delivery; perinatal depression; maternal medication, alcohol, and/or drugs.
c. GA is an important consideration; responses of preterm infant are immature.
d. Timing and sequence of examination may alter the neurologic examination (Volpe, 2018).
1) Optimal timing for older newborns is about two thirds of time between feedings.
2) Clinical condition may necessitate exclusion of parts of examination.

2. Observe for skin lesions related to neurologic disorders (Jones et al., 2013).
a. Neurofibromatosis: café-au-lait spots, longer than 1.5 cm in length or in numbers of six or more.
b. Sturge–Weber syndrome: nevus flammeus noted unilaterally, following the trigeminal nerve tract on the face and possibly involving the upper trunk.

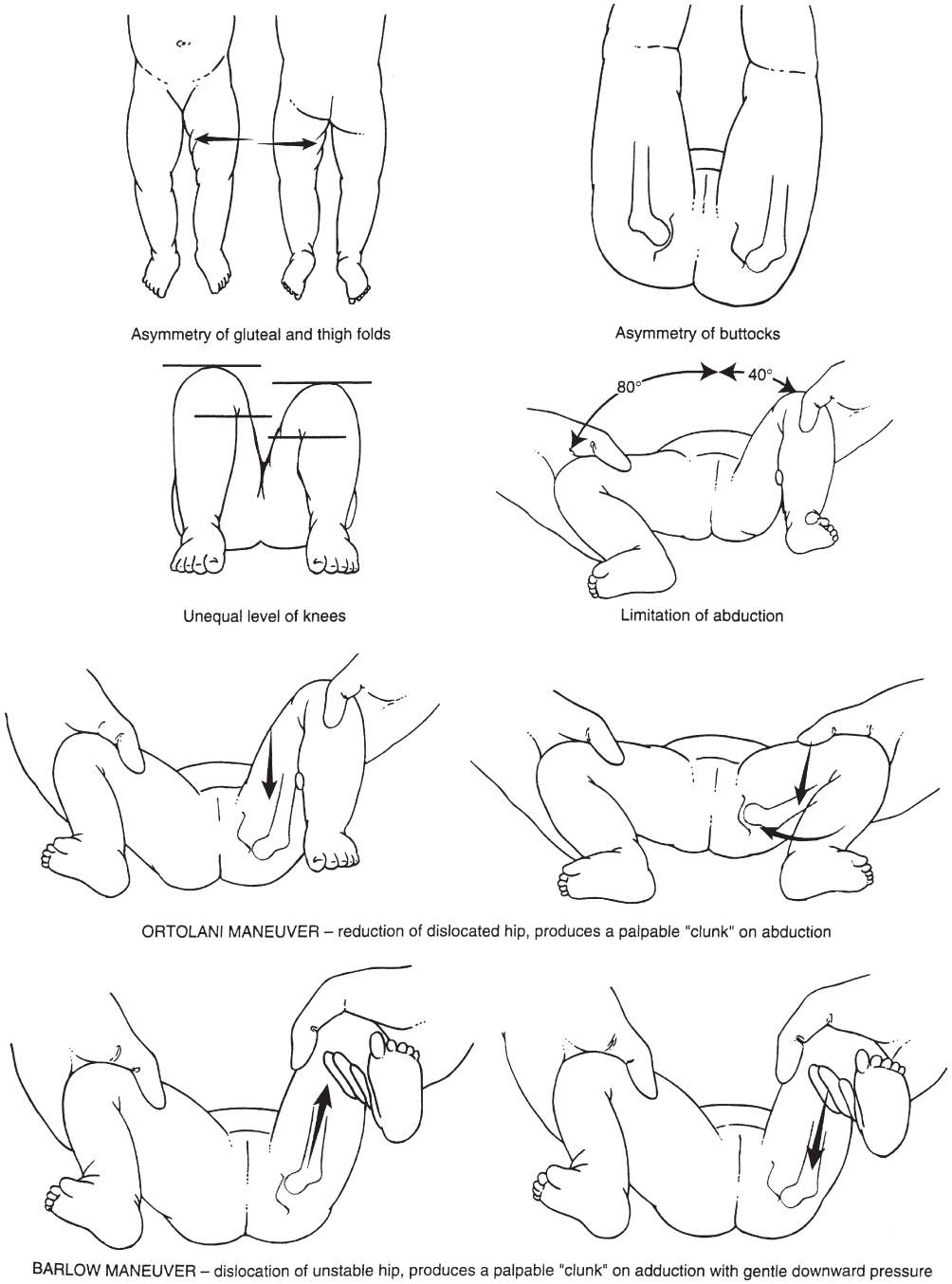

Fig. 7.11 Assessment of newborn infant for dislocated or unstable hip includes gluteal and thigh folds, buttocks, knees, abduction, Ortolani maneuver, and Barlow maneuver. *(From Nichols, F. H. and Zwelling, E. [1997].* Maternal-newborn nursing: Theory and practice. *Philadelphia, PA: W.B. Saunders.)*

   c. Tuberous sclerosis: areas of hypopigmented (white) macules on the skin.
3. Assess posture: assess infant in quiet awake, quiet active, or light sleep state(s); unswaddled; position supine with head midline.
   a. Term infant lies with arms adducted, hips abducted and partially flexed, moderate flexion of all extremities, and with loosely clenched fists.
   b. Preterm infant becomes more hypotonic with decreasing GA.
   c. Abnormal.
      1) Persistent neck extension (opisthotonus).
      2) Obligate thumb flexion (cortical thumb).
      3) Elbow flexion with dorsum of hands on bed.
      4) Frog-leg position at greater than 36 weeks of gestation.
4. Observe spontaneous movement.
   a. Term infant moves limbs smoothly.
   b. Preterm infant's movements may be jittery and jerky, with tremors.

c. Environmental stimuli or discomfort produces mass movements.
d. Coarse tremors and brief chin trembling are normal.
e. Jittery: rhythmic movements of equal intensity.
1) Occurs more after startle or crying.
2) Distinguish between tonic and clonic seizures using gentle restraint: tremors will stop; seizures will continue.

5. Cry.
a. Lusty, with normal pitch: normal-term infant.
b. Weak or monotonous cry: depressed, ill, or preterm infant.
c. High-pitched cry: neurologic or metabolic abnormalities, drug withdrawal.

6. Tone.
a. With decreasing GA, it may be more difficult to distinguish between random movement and true recoil.
b. Note weak, absent, or unequal responses.
c. Assess resistance to movement (passive tone).
1) Limb recoil, heel-to-ear, scarf sign.
2) Tendon reflex: only patellar reflex is reliable at birth; note sustained clonus.
d. Assess resistance to gravity (active tone).
1) Traction response: pull-to-sit, ventral suspension; note degree of resistance.
2) Ventral and horizontal suspension.

7. Reflexes.
a. Developmental reflexes (primitive reflexes): should be elicited in the normal-term infant. Note any exaggerated or absent responses.
1) Sucking reflex: gently stimulate lips; infant opens mouth and begins to suck.
a) Evaluate the coordination and strength of the suck with a gloved finger.
b) Present at birth even in the premature infant, although it is not as strong as at term.
2) Rooting reflex: stroke cheek; infant turns head and opens mouth toward the stimulated side.
3) Palmar grasp: stroke the infant's palm with finger; infant will grasp the finger.
a) Attempts to remove the finger will elicit a tighter grasp.
b) Grasp should be equal bilaterally.
4) Tonic neck reflex (fencing position).
a) Position the infant supine. Turn the infant's head to one side.
b) The infant will extend the upper extremity on the side where the head is turned and flex the opposite upper extremity.
5) Moro reflex (startle reflex): "head drop" method preferred depending on the infant's condition. The high-risk neonate can be startled by making a loud noise close to the ear and noting the response.
a) Hold infant supine in a neutral position several inches off the bed.
b) Hold one hand behind the upper back and the other supporting the head. Infant's arms should cover the chest.
c) Head is held midline and dropped back 1 cm with supportive hand.
d) Infant will partially abduct shoulder, extend, and then smoothly adduct arms.
(1) Evaluate arm responses only.
(2) Repeat two or three times as needed for detailed observation.
(3) Asymmetrical response may indicate brachial plexus injury.
6) Stepping reflex: hold the infant upright, allowing the soles of the feet to touch a flat surface; infant will alternate stepping movements.
7) Babinski's reflex.
a) Stimulate sole of foot; infant will either flex or extend toes.
b) Persistent absence of reflex can indicate CNS depression or spinal nerve dysfunction.
b. Spinal reflexes.
1) Truncal incurvation reflex (Galant reflex).
a) Hold infant in ventral suspension.
b) Apply firm pressure along the side parallel to spine.
c) Infant should flex pelvis toward the stimulated side.
d) Indicates T2–S1 innervation.
2) Anocutaneous reflex (anal wink).
a) Stimulate perianal skin.
b) External sphincter constricts.
c) Indicates S4–S5 innervation.

8. Cranial nerves (CNS).
a. Observation and maneuvers during the routine examination provide partial assessment of function of 12 cranial nerves (Table 7.2).
b. Olfactory (CN I).
1) Not usually assessed in newborns.
2) Can attempt in infants with strong scents such as clove or peppermint placed under nose; evaluate for sniffing, grimace, or startle reflex.
c. Optic (CN II).
1) Evaluate visual acuity and fields by using tracking methods.
2) Watch for wandering or persistent nystagmus.
3) Check pupils for size and constriction in response to light.
d. Oculomotor (CN III), trochlear (CN IV), and abducens (CN VI) nerves: supply pupils and extraocular muscles.
1) Observe pupil response to light.
2) Doll's eye reflex (vestibular response): move infant's head from side to side, eyes should move away from the direction of rotation.
3) Fixed position or movement in same direction may indicate brainstem or oculomotor dysfunction.

Table 7.2

Cranial Nerve Examination

Nerve	Name	Function	Evaluation Method
I	Olfactory (and track)	Smell	Not tested
II	Optic (and retina)	Visual acuity and fields	Facies or object with black and white concentric circles
III	Oculomotor response, lid elevation	Extraocular movements; pupillary reflex	Observation of tracking; doll's eye reflex
IV	Trochlear	Extraocular movements	Observation of tracking; doll's eye reflex
V	Trigeminal	Mastication; facial sensation	Corneal and suck reflexes; nasal stimulation
VI	Abducens	Extraocular movements	Observation of tracking; doll's eye reflexes
VII	Facial	Facial expression; taste	Nasal stimulation; corneal and sucking reflexes
VIII	Auditory	Hearing; spatial orientation	Sounds and behavioral response; doll's eye reflex
IX	Glossopharyngeal	Swallowing; vocalization	Sucking and swallowing reflex; gag reflex; quality of cry
X	Vagus	Swallowing; vocalization	Sucking and swallowing reflex; gag reflex; quality of cry
XI	Spinal accessory	Head and shoulder movement	Observation
XII	Hypoglossal	Tongue movement	Observation; atrophy; fasciculations

From Lissauer, T. (2015). Physical examination of the newborn. In R. J. Martin, A. A. Fanaroff and M. C. Walsh (Eds.). *Neonatal-perinatal medicine: Diseases of the fetus and infant* (10th ed., pp. 402–403). Philadelphia, PA: Elsevier.

e. Trigeminal nerve (CN V): supplies sensory nerves of jaw and face.
   1) Touch the cheek; infant will demonstrate rooting reflex.
   2) Place a gloved finger in the infant's mouth to evaluate sucking and biting reflex.
f. Facial nerve (CN VII): controls facial expression.
   1) Observe for symmetrical movement of the face.
   2) Inability to wrinkle brow or close eyes with crying indicates injury.
g. Auditory nerve (CN VIII): tested only grossly without proper auditory equipment (see "9. Sensory function responses").
h. Glossopharyngeal nerve (CN IX): evaluate and inspect tongue movements and elicit gag reflex; quality of cry.
i. Vagus nerve (CN X): supplies the soft plate, pharynx, and larynx.
   1) Listen to cry: determine the presence or absence of stridor, hoarseness, or aphonia.
   2) Evaluate infant's ability to swallow.
j. Accessory nerve (CN XI): supplies neck muscles (sternocleidomastoid and trapezius).
   1) Turn infant's head from midline to one side.
   2) Infant should attempt to bring head back to midline.
k. Hypoglossal nerve (CN XII): supplies tongue muscles. Evaluate suck, swallow, and gag reflexes.

9. Sensory function responses.
   a. Touch.
      1) Painful stimulus to a foot elicits a withdrawal reflex.
      2) Touch sole of the foot with a pin to provoke flexion of the limb and extension of the contralateral limb.
      3) Absence of flexion in the stimulated leg is abnormal.
   b. Light: shining a penlight into the infant's eye results in eyelid closure.
   c. Sound.
      1) Ring a bell sharply within a few inches of the infant's ear while the infant is lying supine.
      2) Response is based on observable attentiveness to the sound.
      3) A brainstem auditory evoked response is recommended in the newborn period for all infants.

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CHAPTER 8
Fluid and Electrolyte Management

Susan Givens Bell

OBJECTIVES

1. Identify the influences on fluid and electrolyte homeostasis in the newborn infant.
2. Describe fluid and electrolyte management in the neonate.
3. Compare fluid and electrolyte management of the full-term infant and the prematurely born newborn.
4. Discuss acid–base balance in the neonatal period.

An essential part of the successful transition to extrauterine life is the achievement of fluid, electrolyte, and acid–base homeostasis and control. Because mature control of these processes may not occur for days to weeks after birth, premature and other stressed neonates can have transient disturbances of fluid, electrolyte, and acid–base balance.

Fluid Balance

PHYSIOLOGIC AND ASSESSMENT CONSIDERATIONS

A. Fluid homeostasis in the fetus and neonate.
   1. Body water distribution. Water, the most abundant component of the body, is distributed in two main compartments: intracellular fluid (ICF) and extracellular fluid (ECF); the latter is composed of intravascular and interstitial spaces. As gestation progresses, the fetus undergoes changes in total body water (TBW) content and its distribution (Fig. 8.1).
      a. Early in gestation, water makes up 95% of total body weight, with the majority in ECF compartments.
      b. By term, water makes up 75% of body weight and a greater proportion has shifted from ECF to ICF compartments. These changes are largely due to increases in body fat content.
   2. Fluid adjustments after birth.
      a. An acute increase in intravascular volume occurs after birth. Timing of cord clamping can influence the volume increase.
      b. A physiologic contraction of ECF volume occurs with diuresis in the first week of life, resulting in postnatal weight loss. This is reflected in a weight loss of 5% to 10% in term infants and up to 20% in preterm infants. This may be related to levels of circulating atrial natriuretic peptide (Blackburn, 2018).

B. Regulation of fluid balance.
   1. Renal mechanisms.
      a. Because water and electrolyte balance is regulated by the placenta, the role of the fetal kidneys is primarily to maintain amniotic fluid volume. Fetal nephrons are functional but immature until 34 weeks. Renal blood flow, renal tubular function, and glomerular filtration rate (GFR) are all immature in the fetus and in the extremely premature infant (Kenagy and Vogt, 2013).
      b. After birth, renal blood flow increases as renal vascular resistance falls. Improved renal function in the days after birth from increased GFR is more pronounced in the term than in the preterm infant.
      c. Both term and preterm infants can dilute urine; however, when faced with a rapid fluid load, the preterm infant may have a delayed response, resulting in fluid retention.
      d. Reabsorption of sodium, bicarbonate, and glucose is limited in the newborn infant.
   2. Hormonal mechanisms.
      a. Antidiuretic hormone (ADH) is released by the posterior pituitary in response to a variety of stimuli, including hypotension and hyperosmolality. ADH influences water balance by stimulating the kidneys to conserve water. In the absence of ADH, the distal tubules remain impermeable to water, which is excreted as urine.
      b. Because of decreased responsiveness to ADH, neonates cannot efficiently concentrate urine in response to fluid deprivation.

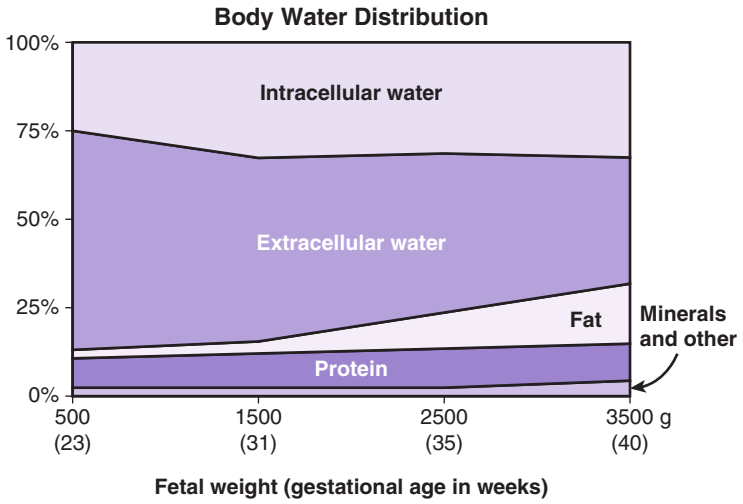

Fig. 8.1 Body composition in relation to fetal weight and gestation age. *(From Dweck, H. S. [1975]. Feeding the prematurely born infant: Fluids, calories, and methods of feeding during the period of extrauterine growth retardation.* Clinics in Perinatology, *2:183–202. Data from Widdowson, E. M. [1968]. Growth and composition of the fetus and newborn. In N. S. Assali [Ed.]:* Biology of gestation *[Vol. 2]. New York, NY: Academic Press.)*

C. Fluid losses in the neonatal period.
   1. Renal losses: Urine output ranges from 1 to 4 mL/kg/hr. The highest flow rates occur during the physiologic reduction in ECF.
   2. Insensible water losses (IWLs): These are the nonmeasurable losses that occur through the skin and respiratory system. Factors influencing IWLs are summarized in Box 8.1.
      a. Transepidermal water loss (TEWL): TEWL occurs as body water diffuses through the immature epidermis and is lost to the atmosphere. Skin features such as poor keratinization, high water content, low subcutaneous fat, large surface area, and high degree of skin vascularity all predispose the premature infant to high evaporative losses.
         1) TEWL increases with decreasing gestational age (Oranges et al., 2015; Ringer et al., 2019)
         2) TEWL is the major source of IWL in very premature infants.
         3) TEWL is highest on the first day after birth, decreasing on subsequent days as the barrier function of the skin improves. This improvement slows with decreasing gestational age, taking several weeks for the development of a fully functional stratum corneum in the extremely premature infant (Oranges et al., 2015; Ringer et al., 2019).

Box 8.1

Environmental Influences on Insensible Water Loss (IWL)

Factors That May Increase IWL
Extreme prematurity
Postnatal age less than 1 week
Low relative ambient humidity
Radiant warmer use
High ambient temperature
Hyperthermia
Convection, drafts
Ventilation with dry gases
Tachypnea
High minute ventilation
Phototherapy
Activity

Factors That May Decrease IWL
Increasing gestation
Increasing postnatal age
High relative ambient humidity
Double-walled incubator use
Neutral thermal environment
Heat shields/plastic blankets
Humidification of inspired gases
Ointments or transparent dressings on skin
Clothing

4) TEWL is closely related to ambient relative humidity. It increases with decreasing ambient humidity.
5) TEWL does not appear to be influenced by antenatal steroids or gender (Jain et al., 2000).
6) Failure to account for TEWL increases the possibility of inaccurate estimates of fluid needs, with resultant fluid and electrolyte imbalances.
7) Caring for very premature infants in an incubator capable of providing measured humidity has been shown to decrease TEWL.

b. Respiratory losses: Roughly 0 to 10 mL/kg/day; related to the temperature and humidity of inspired gases and to minute ventilation.

3. Stool losses: Estimated to be 5 mL/kg/day in the first week of life, increasing to 10 mL/kg/day thereafter.
4. Other losses are possible. These include but may not be limited to gastric drainage, enterostomies, surgical wounds, and pleural fluid drainage.

D. Fluid therapy.
1. Goal of fluid therapy: The goal is to permit physiologic, adaptive fluid, and electrolyte changes to occur appropriately (Nyp et al., 2016).
2. General principles guiding fluid volume decisions. No fixed fluid administration schedules are appropriate for all infants. Lower fluid administration rates are associated with a lower incidence of morbidity, such as patent ductus arteriosus (PDA) and necrotizing enterocolitis (Bell and Acarregui, 2014).
a. During the first 3 to 5 days after birth, fluid intake should be at a level that allows a reasonable weight loss yet avoids intracellular dehydration. Provision of 60 to 100 mL/kg/day, depending on the degree of control over IWL, is a typical starting point. Extremely premature infants require more fluid relative to body weight because of a larger IWL. Fluids given to correct shock, hypoglycemia, or acidosis must be considered.
b. Fluid intake is gradually increased on subsequent days to 150 to 175 mL/kg/day, although fluids may be restricted longer for infants with severe cardiorespiratory disorders, renal failure, and postasphyxial syndrome.
c. Infants with ongoing fluid losses (chest tube drainage, gastric drainage, enterostomy drainage, diarrhea) may need replacement of these volumes with appropriate fluids.
d. It is generally recommended to use birth weight, rather than current body weight, to calculate fluids on a per-kilogram basis until birth weight is regained.

3. Fluid constituents.
a. Dextrose 10% in water is most commonly used for initial fluid therapy. Decreasing dextrose concentrations may be prescribed initially for infants who weighed less than 1 kg at birth because of the incidence of hyperglycemia in this population.
b. Electrolytes are not usually added to maintenance intravenous (IV) fluids for the first 24 to 48 hours after birth. Serum electrolyte levels and urine output are used to determine when to add these electrolytes to IV fluids.

E. **Assessment of fluid balance:** Quantifying fluid requirements in extremely preterm infants is difficult. Fluid restriction places the infant at risk for dehydration, whereas fluid excess places the infant at risk for intravascular fluid overload (Nyp et al., 2016). Close monitoring of hydration status is imperative, with some infants requiring assessment of their fluid balance as often as every 6 to 8 hours.
1. Body weight: Weight changes with alterations in fluid balance only if there is a net change in TBW; internal shifts of body fluid may not be detected by weight alone. Because the procedure for weighing the extremely low birth weight (ELBW) infant is prone to errors and is a significant source of stress for the infant, some neonatal intensive care units (NICUs) have abandoned weighing these infants in the first few days after birth. In-bed electronic scales may be used; however, weights obtained in this manner can be affected by the amount of equipment attached to the infant and how the neonate is handled during weighing.
2. Urine volume: For greatest possible accuracy, urine output must be measured right after it occurs; urine collected onto diapers lying under radiant warmers may evaporate before the diapers are weighed for determination of output.
3. Specific gravity of urine: an indirect measure of urine osmolality. Normal values (1.002 to 1.012) reflect a normal urine osmolality (100 to 300 mOsm/L). Specific gravity is an unreliable predictor of urine osmolality if glucose, blood, or protein is present.
4. Assessment parameters.
a. Physical assessment: Quality of skin turgor, mucous membranes, presence of edema, appearance of eyes, and level of anterior fontanelle.
b. Hemodynamic assessment: Pulse quality, blood pressure, and perfusion (capillary refill time, temperature, and acid–base balance).
5. Laboratory evaluation of hydration status: Serum sodium level, osmolality, blood urea nitrogen (BUN), creatinine, and/or hematocrit.

Disorders of Fluid Balance

Disorders of fluid balance in the newborn infant do not always fit neatly into categories such as "fluid depletion" or

"fluid excess"—some involve elements of both. One such disorder is septic shock, in which low intravascular volume (a fluid deficit) can coexist with interstitial and cellular edema (a fluid surplus). For simplicity, an attempt is made here to group clinical conditions according to the primary effect on TBW (e.g., decreased, as in dehydration, or increased, as in congestive heart failure), even though there may be an overlap.

FLUID DEPLETION

A. **Pathophysiology:** Fluid can be lost from the body acutely or gradually. Sudden loss of body fluid can result in signs and symptoms of shock. If lost fluid is not restored, the body will attempt to compensate by retaining sodium and water. Gradual or chronic fluid loss, even though central blood pressure may be maintained, can result in serious metabolic disturbances.

B. **Causes and precipitating factors.**
   1. Extreme prematurity (<28 weeks of gestation, <800 g). The large TEWL and rapid contraction of the ECF result in a sodium excess that cannot be excreted efficiently by the kidneys. If fluid intake is inadequate, hyperosmolar hypernatremic dehydration ensues.
   2. Acute blood loss/hypovolemia: Hemorrhagic losses at birth, postnatal internal hemorrhage, surgical blood loss, or the removal of large volumes for laboratory tests.
   3. Diarrhea.
   4. Diabetes insipidus (pure renal water loss from failure to secrete or respond to ADH). This condition is treated with intranasal arginine vasopressin (DDAVP) or an oral solution compounded from the intranasal formulation (Mavinkurve et al., 2017).
   5. Abdominal or pleural cavity exposure during surgery.
   6. Unreplaced losses from gastric suction.
   7. Medications that may cause diuresis: Caffeine and theophylline.
   8. Breastfeeding malnutrition: Inadequate intake in a breastfed infant with a cycle of reduced milk production and decreasing demand, resulting in severe malnutrition, dehydration, and hypernatremia.

C. Clinical presentation and assessment.
   1. Weight loss if net reduction in TBW.
   2. Low urine output (<0.5 mL/kg/hr); possibly high specific gravity. Urine output may be normal or even high in the ELBW infant during postnatal diuresis.
   3. Poor skin turgor (gently pinched skin is slow to retract) and dry skin and mucous membranes.
   4. Hemodynamic changes: Tachycardia or decreased pulses with peripheral vasoconstriction (pale, cool, mottled skin with prolonged capillary filling time), increased core–peripheral temperature differential, central blood pressure either normal or low.
   5. In breastfeeding malnutrition, possible excessive sleepiness, disinterest in feeding, or irritability.

D. Diagnostic studies.
   1. Serum sodium can be low, normal, or high, depending on the cause of dehydration/fluid loss.
   2. With dehydration, BUN and creatinine levels may be elevated.
   3. Hematocrit levels may be increased or decreased with blood loss.
   4. Blood gas values may reveal metabolic acidosis in the infant with hypovolemia.

E. Patient care management.
   1. Hypovolemic states (shock, hemorrhage) are managed acutely with volume replacement and vasoactive inotropic agents (see Chapter 28).
   2. The type of fluid given to replace other fluid deficits depends on the constituents of lost fluid (e.g., free water loss, electrolyte loss) and the infant's electrolyte levels. Determination of the fluid constitution can be guided by evaluating the electrolyte composition of the fluid being lost.
   3. Management of severe dehydration involves replacing the free water deficit slowly over several days to avoid a rapid fall in serum osmolality.

F. Fluid management of hypernatremic hyperosmolar dehydration in the preterm infant.
   1. Prevention of TEWL is more effective than replacing these losses. This is because the fluid lost is mostly solute free, whereas replacement fluids contain solutes that can aggravate hyperosmolality.
   2. The single method or combination of methods most effective in reducing TEWL has yet to be proved. Each of the following strategies will decrease TEWL to some degree.
      a. Use of incubators rather than radiant warmers. TEWL is higher under radiant warmers because of the lower ambient relative humidity and increased air currents the neonate is exposed to when on a radiant warmer.
      b. Supplemental humidity. Devices to saturate the air immediately surrounding the infant can be used with both incubators and radiant warmers. Humidifier temperature, airflow setting, and seasonal ambient relative humidity variations can significantly affect the achievable humidity level.
      c. Heat shields or plastic film "blankets" increase ambient humidity by using the infant's own trapped evaporative losses.
      d. Semipermeable dressings (adhesive or nonadhesive) may help reduce TEWL.
   3. Reduce respiratory water losses by using humidified gas mixtures.
   4. Even with maximal reductions in IWL, fluid intake must occasionally be increased, especially in ELBW

infants. Giving too much fluid in response to hypernatremic dehydration can aggravate hyperglycemia and increase the risk of heart failure, pulmonary edema, and central nervous system (CNS) injury. It is usually recommended to give just enough fluid to maintain the serum sodium in the high-normal range (145 to 150 mEq/L) during the first 24 to 72 hours of life (Nyp et al., 2016).

5. Restrict sodium (unless the infant is hyponatremic), adding gradually when serum sodium level decreases and diuresis begins.
6. Monitor hydration closely. Weight loss may be accepted if other parameters indicate adequate hydration.

G. Complications.
1. Excessive weight loss.
2. Hypotension, tissue damage, or metabolic acidosis from hypoperfusion.
3. Impaired excretion of drugs when urine output is minimal.
4. Electrolyte imbalances from slow excretion of daily solute load.
5. Renal failure and vascular thrombosis: Possible result of severe dehydration.

FLUID EXCESS

A. **Pathophysiology:** The spectrum of disease that can cause body fluid excess in the neonate is broad. Many of the disorders are characterized by edema, which is the abnormal accumulation of ECF within the interstitial spaces. Edema can be caused by the following:
1. Low colloid osmotic pressure (decreased plasma protein concentration).
2. Increased capillary permeability to water and protein (may be secondary to tissue hypoxia).
3. Increased hydrostatic pressure within the capillaries.
4. Impaired lymphatic drainage of interstitial fluids and proteins.

With some of the disorders associated with these pathologic processes, a combination of venous congestion, renal failure, and edema suggests a state of fluid overload even when circulating blood volume is low.

B. Etiologies and precipitating factors.
1. Cardiac dysfunction: Congenital heart disease, congestive heart failure, PDA.
2. Respiratory distress syndrome and bronchopulmonary dysplasia (BPD). Therapeutic use of oxygen and positive pressure ventilation causes endothelial injury with subsequent fluid leakage. In the first few days after birth, increased lung fluid complicates the picture of respiratory distress, and failure to clear the fluid adds to the possibility of developing BPD (Blackburn, 2018; Martin and Crowley, 2013).
3. Perinatal asphyxia.
4. Sepsis, necrotizing enterocolitis.
5. Hydrops fetalis.
6. Renal failure.
7. Miscalculation of fluid needs or provision of too much fluid (possibly from failure to account for all sources of fluid, such as flush solutions, medications, and colloids).
8. Use of neuromuscular blocking agents.
9. Syndrome of inappropriate antidiuretic hormone (SIADH): Usually associated with CNS infection or injury. ADH secretion is inappropriate to usual osmotic and volume stimuli. The result is fluid retention with hyponatremia, low serum osmolality, and high urinary sodium loss.

C. Clinical presentation and assessment.
1. Weight gain if there is a net increase in TBW.
2. Urine output: Possible decrease.
3. Edema: Peripheral, generalized, pulmonary.
4. Hemodynamic changes: Dependent on intravascular volume status. When increased, there may be symptomatic PDA, tachycardia, and increased pulses or blood pressure. With congestive heart failure, venous filling pressure is high.

D. Diagnostic studies.
1. Serum osmolality is low (<280 mOsm/L); urine osmolality is normal.
2. In SIADH, osmolalities and sodium levels of urine and serum are diagnostic (urine output is low with high specific gravity and high sodium levels; serum has low sodium level and low osmolality).

E. **Patient care management:** In addition to therapy aimed at the underlying disease process:
1. Precise fluid management with fluid restriction is necessary. Daily fluid calculations must consider renal function and the extra fluids given to administer medications and flush intravascular catheters.
2. Diuretics may be useful.
3. Infants with severe edema and low intravascular volume (shock) present a challenge. Maintenance of an adequate circulating blood volume may require volume expansion and vasoactive agents while minimizing maintenance fluid administration.
4. Edema may predispose the infant to necrotic injury of the skin. The skin must be protected from pressure with careful repositioning, support, and the use of a nonrigid sleeping surface, such as a gel- or water-filled mattress.

F. Complications.
1. Fluid sequestration in static body fluid compartments ("third spacing") can result in a loss of effective blood volume, compromising the delivery of oxygen and nutrients to tissues throughout the body. This can lead not only to serious metabolic imbalances but also to permanent tissue damage.
2. Excessive fluid administration early in life has been associated with worsening of respiratory distress

syndrome and development of BPD, symptomatic PDA, and necrotizing enterocolitis.

Electrolyte Balance and Disorders

SODIUM

A. **Sodium homeostasis:** Reference ranges vary slightly between laboratories. In general, a range of 135 to 145 mEq/L is acceptable.
   1. Functions of sodium (Na). Na, the major extracellular cation, is closely involved in water balance. Na and other electrolytes are found in varying concentrations in all body fluid compartments. Electrolytes determine the tonicity of the fluid compartment and influence the passage of water through the vascular and cell membranes, thereby controlling the osmotic equilibrium between compartments. With a surplus of Na, blood becomes hypertonic, causing a shift of fluid from intracellular to extracellular spaces, which results in cellular dehydration. A deficit of Na causes hypotonicity, and fluid shifts into the cells (cellular edema).
   2. Regulation of Na. Cellular transport of Na is achieved by the sodium–potassium pump, which maintains the electrochemical Na and potassium gradients across the cell membrane. Renal (GFR, tubular function) and hormonal (aldosterone, ADH) mechanisms influence the body content of Na. Although preterm infants can excrete Na, a low GFR early in life may hamper this ability. In addition, minimal responsiveness to aldosterone and ADH contributes to a baseline salt-wasting tendency.
   3. Positive Na balance. Na intake greater than Na losses. This is a prerequisite for the growth of new tissue.

B. Hyponatremia.
   1. Pathophysiology: A serum Na below 130 mEq/dL. Reflects either an excess of body water relative to normal body Na content or a primary Na depletion. When urinary Na wasting occurs, a proportionate loss of water (isotonic dehydration) can reduce ECF volume and lead to oliguria.
   2. Causes and precipitating factors.
      a. Prematurity (renal and hormonal immaturity, with tendency to excrete Na). Preterm infants are most vulnerable to hyponatremia just after the period of postnatal extracellular volume contraction due to higher Na excretion/decreased Na reabsorption (Nyp et al., 2016; Wright et al., 2018).
      b. Conditions associated with low intravascular volume (e.g., shock). Baroreceptor stimulation of ADH results in reduced renal water excretion and a dilutional hyponatremia.
      c. Dilutional hyponatremia from excessive free water intake.
      d. Renal losses related to prematurity or medications (furosemide, methylxanthines). Urine Na excretion rate should be measured to rule out excessive Na losses.
      e. Inadequate Na intake during period of rapid growth, especially in preterm infants fed exclusively human milk. Called *late hyponatremia* because it occurs after the first week of life.
      f. Serum Na can be factitiously low in the presence of hyperlipidemia.
   3. Clinical presentation and assessment.
      a. Usually asymptomatic, but apnea, irritability, twitching, or seizures can occur if Na drops acutely or falls to less than 115 mEq/L.
      b. Infants with late hyponatremia may fail to gain weight.
   4. Patient care management.
      a. Provide Na supplementation after postnatal diuresis begins (usually on day 2). Maintenance Na requirement is 1 to 4 mEq/kg/day and is usually given as sodium chloride (NaCl), though sodium acetate may be used if the infant has metabolic acidosis. In very small infants, early Na supplementation has been associated with increased risk of BPD (Wright et al., 2018).
      b. A chronic hyponatremic state is corrected gradually over 48 to 72 hours to prevent injury to brain cells (Wright et al., 2018).
      c. Monitor weight, urine output, parameters of hydration, and adequacy of intravascular volume (monitoring of central venous pressure, capillary refill time, and core–peripheral temperature differential).
      d. When hyponatremia is associated with an excess of body water, fluids are restricted. True SIADH is managed with fluid restriction and monitoring of Na, osmolality, and urine output.
      e. Commercial preparations designed to fortify human milk supply additional dietary Na for this population.
   5. Complications.
      a. Acute drops in the serum Na can lead to a shift of fluid into brain cells and cellular edema. This may result in apnea and seizures.
      b. The degree to which the infant's brain may be able to adapt to chronic hyponatremia is not known; however, chronic hyponatremia does impair skeletal and tissue growth.

C. Hypernatremia.
   1. Pathophysiology: A serum Na level greater than 150 mEq/L. Usually reflects a deficiency of water relative to total body Na content and thus is actually a disorder of water balance rather than one of Na balance.

2. Causes and precipitating factors.
   a. Excessive IWL with insufficient fluid intake (even without added Na).
   b. High inadvertent Na intake (saline infusions in arterial catheters, $NaHCO_3$, medications) or early addition of maintenance NaCl.
   c. Breastfeeding malnutrition in term infants. Elevated human milk Na content accompanying insufficient lactation and decreased amount of free water contribute to the hyperosmolar state.
   d. Diabetes insipidus: Deficiency of pituitary-secreted ADH, causing loss of water in excess of loss of Na.
3. Clinical presentation and assessment.
   a. Signs of dehydration may be present.
   b. In severe hypernatremia, high-pitched cry, lethargy, irritability, and apnea can progress to seizures and coma.
4. Patient care management.
   a. Gradually restrict Na to avoid sudden fall in plasma osmolality. If maintenance Na administration has not been started, it is usually delayed.
   b. Recalculate fluid intake. Fluids may have been restricted too much in light of insensible losses.
   c. Prevent hypernatremia in ELBW infants. Na supplementation may be withheld longer than usual after birth if serum Na level remains normal. In addition, measures to reduce TEWL will aid in the prevention of hypernatremia (Nyp et al., 2016; Wright et al., 2018).
   d. The need for saline solutions to maintain catheter patency presents a dilemma. Attempts to lower the infused Na concentration too far result in administration of hypotonic solutions, with risk of hemolysis.
5. Complications: As hypernatremia develops, intracellular water can be drawn out, causing cells to shrink. If this process is rapid, this can affect the brain. Sudden increases in plasma osmolality can also contribute to intraventricular hemorrhage.

POTASSIUM

A. **Potassium homeostasis:** A generally accepted reference range is 3.5 to 5.5 mEq/L.
   1. Functions of potassium (K): The major cation in ICF, K contributes to intracellular osmotic activity and in part determines ICF volume. K plays a fundamental role along with Na in regulating cell membrane potential.
   2. Regulation: K is distributed both intracellularly and extracellularly. The distribution of K between ICF and ECF is regulated by the sodium–potassium pump and is influenced by acid–base balance, insulin, and glucagon. The excretion of K from the body depends on kidney function, GFR, urine flow rate, and aldosterone sensitivity.

B. **Hypokalemia:** Serum K less than 3.5 mEq/L.
   1. Pathophysiology: Because K is 90% intracellular, it is assessed indirectly by measuring the quantity in the serum. A subnormal serum K implies insufficient K within the cells, which may impede their function. Muscle cells of the gastrointestinal system and the heart can be affected.
   2. Causes and precipitating factors.
      a. Loss of K in the urine (kaliuresis) during postnatal diuresis, before K supplementation is begun.
      b. Inadequate K intake.
      c. Increased gastrointestinal losses from an enterostomy or nasogastric tube output or vomiting.
      d. Metabolic alkalosis. A high serum pH drives K into cells, resulting in a low serum K.
      e. Medications, including bicarbonate, diuretics, and insulin. Insulin increases cellular uptake of K through stimulation of activity of the sodium–potassium pump.
   3. Clinical presentation and assessment: cardiac effects (flattened T waves, prominent U waves, ST segment depression), hypotonia, abdominal distention, and ileus.
   4. Patient care management.
      a. Begin K supplementation when urine output is well established, usually on the second or third day of life. The maintenance K requirement is 2 to 3 mEq/kg/day.
      b. Correction of hypokalemic states must be done cautiously, with continuous cardiac monitoring.
   5. Complications.
      a. Rapid administration of K to correct hypokalemia can lead to fatal arrhythmias.
      b. Hypokalemia potentiates digitalis toxicity.

C. **Hyperkalemia:** Serum K greater than 6.5 mEq/L.
   1. Pathophysiology: Heel-stick samples are often hemolyzed, rendering results unreliable. Venipuncture or arterial line sample must be obtained to determine level. In the ELBW infant, the normal postnatal shift of K from the intracellular to the extracellular compartment is intensified. During the prediuretic phase, this excess K is not efficiently excreted secondary to a low GFR and a low Na excretion rate (Wright et al., 2018).
   2. Causes and precipitating factors.
      a. Extreme prematurity. Nonoliguric hyperkalemia (hyperkalemia in the absence of renal failure), most likely secondary to a shift in K from intracellular space to extracellular space.
      b. Endogenous release of K from tissue destruction, hypoperfusion, hemorrhage, and bruising.
      c. Metabolic acidosis. A low serum pH shifts K out of cells.
      d. Renal failure, with decreased K clearance. Tests of renal function: BUN, creatinine should be measured concomitantly.

e. Adrenal insufficiency.
f. Transfusion with blood stored longer than 3 days.

3. Clinical presentation and assessment: Cardiac effects may be seen—ventricular tachycardia, peaked T wave, or a widened QRS complex. An electrocardiogram should be obtained to detect cardiac arrhythmias. Serum ionized calcium should also be assessed, as hypocalcemia may potentiate cardiac toxicity from hyperkalemia.
4. Patient care management.
   a. For prevention of hyperkalemia, K is withheld from early IV fluids. Serum K is monitored as diuresis (and K excretion) begins; K is added when serum K stabilizes in the 4- to 4.5-mEq/L range.
   b. Acidosis is corrected.
   c. Diuretics and low-dose dopamine therapy may improve renal excretion of K. Dopamine also enhances K uptake by stimulation of activity of the sodium–potassium pump.
   d. Temporary measures may be needed to reduce the effects of circulating K until the total body K level can be reduced.
      1) Administration of calcium gluconate will lower the cell membrane threshold transiently, antagonizing the effects on the heart muscle.
      2) Glucose/insulin infusion to enhance cellular uptake of K. Close monitoring of serum glucose is imperative with this strategy, and the clinician should anticipate the need for increasing the glucose infusion rate. The insulin infusion tubing must be primed to ensure delivery of the drug once the infusion is begun.
      3) $NaHCO_3$ (metabolic alkalosis shifts K into cells).
   e. When other measures fail to normalize K:
      1) Cation exchange resins, used in the past, are considered contraindicated in neonates, particularly premature neonates (National Institutes of Health, U.S. Library of Medicine, 2016).
      2) Exchange transfusion.
      3) Peritoneal dialysis or continuous arteriovenous hemofiltration for severe, intractable hyperkalemia.
5. Complications.
   a. Hyperkalemia is life threatening because of the risk of cardiac arrest.

CALCIUM

A. **Calcium homeostasis:** A reference range of 8.5 to 10.2 mg/dL is generally used for serum calcium (Ca). Some care providers prefer to follow the ionized calcium (iCa). An acceptable reference range for iCa is 4.4 to 5.3 mg/dL (1.1 to 1.45 mmol/dL).
   1. Functions of Ca: Ca plays a central role in many physiologic processes, maintaining cell membrane permeability and activating enzyme reactions for muscle contraction, nerve transmission, and blood clotting. Ca is vital for normal cardiac function and development of the skeleton, where 99% of the body's Ca is stored.
   2. Regulation.
      a. Parathyroid hormone (PTH) increases serum Ca by mobilizing Ca from the bone and intestines and reducing renal excretion of Ca. PTH is stimulated by low serum Ca and magnesium (Mg) levels and is suppressed by high Ca and Mg levels.
      b. Vitamin D acts with PTH to restore Ca to normal levels by increasing absorption of Ca and phosphorus from the intestines and bone.
      c. Calcitonin, a Ca counterregulatory hormone secreted from thyroid C cells, lowers Ca levels primarily by inhibiting bone resorption.
      d. Phosphorus (P) also inhibits the absorption of Ca (the higher the P, the lower the absorption of Ca).
   3. Serum Ca is transported in three forms:
      a. Protein-bound Ca, accounting for 40% of total serum Ca.
      b. Inactivated Ca (complexed with anions such as bicarbonate, lactate, and citrate), accounting for 10% of total serum Ca.
      c. Free iCa, the physiologically active form that can cross the cell membrane, accounting for 50% of the total serum Ca. Blood pH influences the amount of iCa: acidosis increases iCa, and alkalosis decreases iCa.

B. **Fetal Ca metabolism:** Fetal Ca needs are met by active transport of Ca across the placenta. Ca accretion increases during the last trimester as Ca is incorporated into newly forming bones. Because maternal PTH and calcitonin do not cross the placenta, the fetus is relatively hypercalcemic, which suppresses fetal PTH and stimulates fetal calcitonin.

C. **Neonatal Ca metabolism:** When the supply of Ca ceases at birth, the neonate depends on stored and dietary Ca to avoid hypocalcemia. After birth, the Ca level declines to its nadir by 24 hours of age, but PTH activity remains low. By 48 to 72 hours, PTH and vitamin D levels rise and the calcitonin level declines, allowing Ca to be mobilized. The serum Ca level returns to normal despite a low Ca intake. Renal medullary calcification (nephrocalcinosis) is seen most commonly in premature infants treated with loop diuretics such as furosemide. Nephrocalcinosis is multifactorial and has been reported in infants who have not received loop diuretics. Aminoglycoside, xanthines, and corticosteroids may also contribute

to the development of nephrocalcinosis. Nephrocalcinosis develops in approximately 27% to 65% of preterm neonates in the NICU (Kenagy and Vogt, 2013; Mohamed et al., 2014).

D. **Hypocalcemia:** Serum Ca less than 7 mg/dL or iCa less than 4.4 mg/dL (1.1 mmol/L).
   1. Pathophysiology: Failure to achieve Ca homeostasis after birth can result from inadequate Ca stores, immature hormonal control, inability to mobilize Ca, or interference with Ca use. Hypocalcemia increases cellular permeability to Na ions and increases cell membrane excitability.
   2. Causes and precipitating factors.
      a. "Early" hypocalcemia.
         1) Prematurity: Reduced Ca stores and relative hypoparathyroidism (blunted PTH response to hypocalcemia).
         2) Infant of a diabetic mother (IDM): Prolonged delay in PTH production by infant after birth.
         3) Placental insufficiency: Reduced Ca stores.
         4) Perinatal asphyxia and stress, which precipitate a surge in calcitonin that suppresses Ca. In addition, tissue damage and glycogen breakdown release phosphorus into the circulation, which decreases Ca uptake.
         5) Maternal anticonvulsant therapy, which affects hepatic enzymes involved in vitamin D metabolism.
         6) Low intake of Ca.
         7) Factors that may decrease iCa even when the total serum Ca is normal: Exchange transfusion, IV administration of lipid emulsion, alkalosis, or alkali therapy for acidosis.
      b. "Late" hypocalcemia.
         1) Hypomagnesemia.
         2) Transient congenital hypoparathyroidism or secondary hypoparathyroidism from maternal hyperparathyroidism. An increased PTH level in the mother raises the fetal Ca level and suppresses the fetal parathyroid gland. After birth, the suppressed gland cannot maintain a normal Ca level.
         3) DiGeorge syndrome: Absence of thymus and parathyroid glands.
         4) High-phosphate formulas or cereals. The neonate cannot excrete the excess phosphate; the hyperphosphatemia suppresses Ca.
         5) Intestinal malabsorption.
   3. Clinical presentation and assessment.
      a. Early hypocalcemia is usually asymptomatic; signs of neuromuscular excitability (jitteriness, twitching) may be present.
      b. Severe hypocalcemia (neonatal tetany) is rare and presents with jitteriness, seizures, high-pitched cry, laryngospasm, stridor, and a prolonged Q-T interval.
   4. Patient care management.
      a. Monitor serum Ca of infants at risk: Premature, IDM, asphyxiated.
      b. Early, mild hypocalcemia often resolves without treatment.
      c. Serious hypocalcemia is treated with boluses and/or continuous infusions of calcium gluconate (can also be given orally).
      d. Treatment of late hypocalcemia depends on the underlying cause.
   5. Complications.
      a. Rapid infusion of Ca can cause bradycardia or cardiac arrest. Infusions for rapid correction of hypocalcemia should be administered slowly, over 20 to 30 minutes by syringe pump, while the heart rate is monitored.
      b. Tissue necrosis and calcifications can result from extravasated Ca infusions.
      c. Intestinal necrosis and liver necrosis have been reported with Ca infusion given via incorrectly placed umbilical catheters.

E. Metabolic bone disease.
   1. Pathophysiology: Infants born prematurely can miss all or most of the period of greatest intrauterine mineral accretion, which places them at risk of having inadequate postnatal bone mineralization. The primary cause of metabolic bone disease (MBD) is inadequate Ca and P intake rather than vitamin D deficiency.
   2. Causes and precipitating factors.
      a. Prematurity: The more immature the infant, the higher the MBD rate.
      b. Parenteral nutrition: Low Ca and P intakes.
      c. Unfortified human milk feeding (inadequate Ca and P content) or use of formulas not designed for the preterm infant.
      d. BPD secondary to fluid restriction and use of diuretics, with renal Ca wasting.
   3. Clinical presentation and assessment.
      a. MBD is asymptomatic; it is often detected initially on routine x-ray examination.
      b. Skeletal fractures may be seen in the thoracic cage or extremities.
      c. Other reported presentation is late-onset respiratory distress from "softening" of the ribs.
      d. Pain may occur with handling; close monitoring of response is necessary.
   4. Diagnostic tests.
      a. Serum: Normal Ca, low P, high alkaline phosphatase, and low or often normal 25(OH)D_3 (cholecalciferol) levels. Ca and P levels alone are not good indicators of MBD.
      b. Urine: Low or absent P excretion; increased urinary Ca.
      c. Radiologic bone examinations; wrist x-ray films at age 6 to 8 weeks may be used to monitor for

MBD. Early evidence can be difficult to discern because bone mineral content must decrease by 30% to be visible. Photon absorptiometry may be done in centers where the necessary equipment is available.

d. X-ray examination; findings may include "washed out" (undermineralized) bones, known as *osteopenia,* or epiphyseal dysplasia and skeletal deformities, known as *rickets* (Koves et al., 2018).

5. Patient care management and prevention of MBD.
   a. Maintain Ca/P ratio in parenteral nutrition at 1.3:1 to 1.7:1.
   b. For enteral feeding, use preterm formulas or human milk fortification.
   c. Direct supplementation of Ca and P may be needed. Ca given without P will be inadequately used, resulting in hypercalciuria and possibly nephrocalcinosis.
   d. Gentle handling of infants at risk and avoidance of chest physiotherapy are warranted to prevent fractures.

F. **Hypercalcemia:** Serum Ca greater than 11 mg/dL or iCa greater than 5.8 mg/dL (1.45 mmol/L).
1. Pathophysiology: A rise in the serum Ca level can rapidly overwhelm the infant's compensatory mechanisms for Ca equilibrium. An excess supply of Ca has multiple effects and is potentially lethal.
2. Causes and precipitating factors.
   a. Iatrogenic: Overtreatment with Ca or vitamin D.
   b. Hyperparathyroidism: Primary neonatal disorder or secondary to maternal hypoparathyroidism, with chronic stimulation of the fetal parathyroid gland. In hyperparathyroidism, the serum Ca level is high, phosphate levels may be low, and urinary Ca and phosphate excretion are high.
   c. Phosphate depletion: caused by low dietary intake; may be associated with low phosphate content in human milk.
   d. Subcutaneous fat necrosis: Found over the back and limbs; associated with difficult delivery, hypothermia, and maternal diabetes. Pathogenic mechanism is unknown.
   e. Familial infantile hypercalcemia.
   f. Hypervitaminosis D: Excessive maternal intake of vitamin D.
3. Clinical presentation and assessment.
   a. Hypotonia, weakness, irritability, and poor feeding, all from a direct effect of Ca on the CNS.
   b. Bradycardia.
   c. Constipation.
   d. Polyuria, dehydration (associated with severe hypercalcemia).
4. Patient care management.
   a. Hydrate infant and promote excretion of Ca (furosemide has calciuretic action).
   b. Restrict Ca and vitamin D intake; increase phosphate intake.
5. Complications.
   a. Nephrocalcinosis from hypercalciuria but may be seen with normal serum Ca levels.
   b. Metastatic calcification of damaged cells or tissues throughout the body, including the brain.
   c. Cardiac effects: Bradycardia and arrhythmias.

MAGNESIUM

A. **Mg homeostasis.** A reference range of 1.5 to 2.5 mg/dL is usually accepted.
1. Functions: Mg is a catalyst for many intracellular enzyme reactions, including muscle contraction and carbohydrate metabolism, and is critical for normal parathyroid function and bone–serum Ca homeostasis. Mg is regulated primarily by the kidneys.
2. Fetal and neonatal Mg homeostasis: The fetus receives its supply of Mg by active transport across the placenta. Maternal health and diet can influence the amount of Mg accrued by the fetus. After birth, Mg level falls along with Ca level, then rises to normal within 48 hours.
3. Serum total Mg versus the ionized form: Ionized Mg (iMg) is the biologically active fraction of Mg. Total Mg concentration in the serum does not necessarily reflect iMg activity.
4. Concurrent use of Mg and gentamicin potentiates the neuroblocking effect of the Mg, which may result in apnea. Clinical status must be monitored closely. Slow infusion times for gentamicin are indicated (Micromedex, 2017).

B. **Hypomagnesemia:** Serum Mg level less than 1.5 mg/dL.
1. Pathophysiology: A low neonatal Mg level is directly related to the maternal level before birth. Although an acute decline in Mg stimulates PTH release, chronic Mg deficiency suppresses PTH and blocks the hormone's actions on the bone and kidneys. Hypocalcemia ensues.
2. Causes and precipitating factors.
   a. Decreased Mg supply: Prematurity, placental insufficiency and intrauterine growth restriction, low dietary intake.
   b. Increased Mg losses: Renal and intestinal disorders, including renal tubular acidosis, diarrhea, and short bowel syndrome.
   c. Endocrine causes: Neonatal hypoparathyroidism, maternal hyperparathyroidism.
3. Clinical presentation and assessment.
   a. Tremors, irritability, and hyperreflexia, progressing to seizures.
   b. Failure to respond to therapy for hypocalcemia: hypomagnesemia a possibility.
4. Patient care management.
   a. If hypomagnesemia is severe, administration of magnesium sulfate may be necessary to relieve symptoms until Ca balance is restored.

b. Seizures are usually unresponsive to anticonvulsant agents.

5. Complications: Overtreatment with magnesium sulfate can result in hypotonia and respiratory depression, hypotension, and cardiac arrhythmias.

C. **Hypermagnesemia:** Serum Mg greater than 2.5 mg/dL.

1. Pathophysiology: Excess Mg is slow to be excreted by the neonatal kidneys. Very high Mg levels can cause CNS and neuromuscular depression.
2. Causes and precipitating factors.
   a. Excessive Mg load: Magnesium sulfate treatment in labor, excess administration of Mg to neonate.
   b. Reduced excretion of Mg: Renal failure, oliguria.
3. Clinical presentation and assessment (may be asymptomatic).
   a. Respiratory depression, apnea.
   b. Neuromuscular depression: Lethargy, poor suck, loss of reflexes, flaccidity, hypotonia.
   c. Gastrointestinal hypomotility, abdominal distention.
4. Patient care management.
   a. Prepare to resuscitate infants born to mothers receiving large doses of magnesium sulfate.
   b. Hypermagnesemia usually resolves with adequate hydration and urine output. Mg excretion can be increased with furosemide.
   c. If infant is unresponsive to treatment, exchange transfusion may be necessary.
5. Complications: Cardiac arrest and respiratory failure are possible.

Acid–Base Balance and Disorders

ACID–BASE PHYSIOLOGY

A. **pH:** Acid–base balance is normal when the pH of the blood is between 7.35 and 7.45. The pH is determined by the hydrogen ion (H^+) concentration in the ECF. An acid is an H^+ donor; a base is an H^+ receptor. A complex system of buffers, compensation, and excretion regulates the H^+ concentration, thus keeping the pH in the normal range. Note that normal fetal pH is between 7.25 and 7.35, and the clinician should expect values obtained during the early transition period to reflect this lower pH.

B. **Buffering system:** This is the first line of defense against excess H^+ concentration. Buffers, including bicarbonate (HCO_3^-), plasma proteins, and hemoglobin, act rapidly to pick up excess H^+. The major buffer, HCO_3^-, teams with H^+ to form carbonic acid, which dissociates into water and CO_2 to be eliminated. The normal HCO_3^- level in the neonate is 22 to 26 mEq/L, which is lower than in the adult.

C. **Lung regulation:** The lungs act to lower the H^+ level in the blood by removing CO_2, which is produced as a waste product of cellular metabolism. It is then transported to the lungs, where it is removed from the body by ventilation. The rate of CO_2 removal can be increased or decreased by altering minute ventilation.

D. **Kidney regulation:** The kidney acts to maintain equilibrium between acids and bases in the body by reabsorbing HCO_3^- and other buffers and by excreting H^+ and other acids. In this way, the body eliminates the daily load of nonvolatile acids produced by normal metabolism.

E. **Compensation:** When one or more of the body's regulatory systems fail, other systems have a limited ability to maintain the acid–base equilibrium. When the pH is outside the normal range (<7.35 or >7.45), compensation has failed.

1. An acid–base deviation is respiratory if it is due to an abnormal P_{CO_2} and metabolic if it is due to an abnormal level of plasma HCO_3^-.
2. The lungs attempt to compensate for a metabolic aberration, and the kidneys for a respiratory aberration. The result is a change in pH toward normal, despite an abnormal blood P_{CO_2} or HCO_3^-. The lungs compensate much more quickly than the kidneys; however, neither can totally normalize the pH unless the underlying disorder is corrected.

DISORDERS OF ACID–BASE BALANCE

Only those disorders classified as primary metabolic problems are discussed here.

A. Metabolic acidosis.

1. Pathophysiology: A pH of less than 7.35 or serum HCO_3^- of less than 22 mEq/L can result from the loss of HCO_3^- (buffering capacity) or from excess acid production. The immature kidneys contribute to acidosis by failing both to reabsorb HCO_3^- and to excrete H^+ when faced with an acid load. When cells do not receive enough oxygen (because of low blood oxygen levels or diminished perfusion), they must use anaerobic metabolism to meet energy needs. This results in the accumulation in the body of lactic acid (lactate), the level of which reflects the severity of tissue oxygen deficiency. Blood lactate may be a more sensitive indicator of tissue hypoxia than pH and base-excess values (Inder and Volpe, 2018). Calculation of the anion gap (difference between positive and negative ions) can be a useful tool to differentiate between excess acid and insufficient HCO_3^- as cause of acidosis. Anion gap = (serum $Na^+ + K^+$) − (serum $Cl^- + HCO_3^-$ [*or serum* CO_2]). Usual range is 8 to 16 mEq/L. If high (>20 mEq/L), acidosis is due to excess acid. If normal with elevated chloride level, acidosis is due to loss of HCO_3^-.
2. Causes and precipitating factors.
   a. Loss of HCO_3^-: Normal anion gap.
      1) Prematurity: Poor renal conservation of HCO_3^-.

Part 2

2) Renal tubular acidosis: Decreased proximal reabsorption.
3) Severe diarrhea or ileal drainage.

b. Excess acid load: Ingestion or endogenous production of acid greater than the ability to excrete it; increased anion gap.
1) Lactic acidosis from conditions resulting in hypoxia or hypoperfusion: Respiratory distress, congenital heart disease, PDA, sepsis, asphyxia, or shock/hypovolemia. Plasma lactate level greater than 2.5 mmol/L; may be elevated in some conditions, such as early sepsis, even when the pH is normal.
2) Inborn errors of metabolism: Disorders of organic acid and carbohydrate metabolism.
3) Caloric deprivation: Catabolism of protein or fat for energy.
4) Parenteral amino acid solutions.
5) "Late metabolic acidosis" of prematurity caused by intolerance of cow's milk protein.

3. Clinical presentation and assessment.
a. Metabolic acidosis occurring early in life is primarily related to systemic illness (e.g., respiratory, cardiac); thus, the signs and symptoms are those of the underlying condition(s).
b. Late metabolic acidosis may present at 1 to 3 weeks of age with poor growth, hyponatremia, and persistent renal acid excretion (urinary pH <5). Urinary pH greater than 7 with systemic acidosis suggests renal tubular acidosis.
c. Infants with profound acidosis (metabolic defects such as congenital lactic acidosis) may have respiratory compensation (tachypnea, hyperpnea) or neurologic depression (seizures, coma) reflecting CNS acidosis.

4. Patient care management.
a. Treat the underlying cause of acidosis.
b. Use of $NaHCO_3$, even in the presence of severe acidosis (pH <7.20), is increasingly controversial (Collins and Sahni, 2017). Normal saline bolus (10 mL/kg) to correct volume depletion and improve end-organ perfusion is the preferred treatment strategy. If $NaHCO_3$ (0.5 mEq/mL) is used, the dose is a 1- to 2-mL/kg dose, administered slowly (over 1 to 2 hours) by syringe pump or continuous drip; a rapid increase in osmolality and pH may be dangerous. Sodium acetate solutions in place of sodium chloride solutions can be infused through umbilical artery catheters and peripheral arterial lines, and sodium and potassium acetate can be added to IV fluids/total parenteral nutrition (TPN), when supplementation is appropriate, to effect a slower change in less severe metabolic acidosis.
c. Late metabolic acidosis, if not self-correcting, is sometimes treated with oral $NaHCO_3$.

5. Complications.
a. Severe acidosis: May depress myocardial contractility and cause arteriolar vasodilation, hypotension, and pulmonary edema.
b. Impaired surfactant production.
c. Electrolyte imbalance: Decreased iCa, hyperkalemia.
d. Adverse effects of HCO_3^-: Cerebral hemorrhage or edema related to wide swings in plasma osmolality. Increased cerebral blood flow, more pronounced when infused rapidly (Katheria et al., 2017). $NaHCO_3$ can also worsen acidosis by rapidly increasing CO_2 if lung disease is present and ventilation is inadequate. $NaHCO_3$ can aggravate hypernatremia and cause tissue injury in extravasation.

6. Outcome: In follow-up studies, metabolic acidosis was correlated with poor developmental outcome in very low birth weight (VLBW) infants (Seth et al., 2014).

B. Metabolic alkalosis.
1. Pathophysiology: Metabolic alkalosis (pH >7.45 or HCO_3^- >26 mEq/L) results from an excess of HCO_3^- or from a loss of acid.
2. Causes and precipitating factors.
a. Gain of HCO_3^- from overcorrection of acidosis with $NaHCO_3$.
b. Loss of H^+ during vomiting or nasogastric suction.
c. Increased renal acid loss from diuretic therapy.
d. Rapid ECF reduction (contraction alkalosis).
3. Patient care management.
a. Decrease $NaHCO_3$ intake if alkali therapy is the cause of alkalosis.
b. Restoring fluid and electrolyte balance is critical.
4. Complications: Severe alkalosis causes tissue hypoxia, neurologic damage, and electrolyte disturbances (increased iCa, hypokalemia).
5. Please refer to Chapter 26 for discussion of respiratory acidosis and respiratory alkalosis.

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CHAPTER 9
Glucose Management

Debra Armentrout

OBJECTIVES

1. Describe the mechanisms of glucose homeostasis in the fetus and newborn.
2. Discuss hypoglycemia and hyperglycemia in the neonate.
3. Discuss infants of diabetic mothers.
4. Differentiate neonatal diabetes from hyperglycemia.

Organ systems, especially the human brain, are primarily dependent on glucose as their major energy source. Compared with adults, infants have a higher brain–to–body weight ratio, resulting in a higher glucose demand in relation to glucose production capacity. Cerebral glucose utilization accounts for 90% of the neonate's total glucose consumption. Continuous glucose and energy delivery to the fetus is provided from the maternal circulation via the placenta, so there is no need for fetal glucose production in utero. An essential part of the neonate's successful transition to extrauterine life therefore is the maintenance of euglycemia. Whereas most infants are indeed able to readily adapt to the metabolic demands of extrauterine life, newborns in general remain extremely susceptible to any condition that may impair their ability to establish normal glucose homeostasis during this transition process (Devaskar and Garg, 2015; Hume et al., 2005; Jain et al., 2012).

Glucose Homeostasis

Glucose is vital for cellular metabolism throughout the body. Blood glucose concentration is determined by the balance between intake/production of glucose and glucose use by the body.

A. Glucose production.
   1. Glucose taken in but not used for immediate energy needs is converted to glycogen via glycogenesis and stored in the liver, heart, and skeletal muscles. During fasting, glycogen is broken down to re-form glucose that is then released from the liver in a process known as *glycogenolysis*. The infant's ability for glycogenolysis varies according to fetal growth and maturity.
   2. The other main source of glucose is gluconeogenesis: production of glucose and glycogen in the liver by means of nonglucose precursors such as lactate, pyruvate, glycerol (fat), and amino acids (Devaskar and Garg, 2015; Hume et al., 2005).

B. Glucose metabolism (Blackburn, 2018; Hawdon, 2016).
   1. Glucose can be metabolized in the body in several ways: production of energy, storage as glycogen, and conversion to gluconeogenic precursors.
   2. In the brain, oxidized glucose provides 99% of the cerebral energy production, a process dependent on a number of important enzymes and reactions.
      a. Glucose molecules are transported across the blood–brain barrier and into the brain cells by glucose transporter proteins.
      b. Within the cytoplasm, glucose is metabolized by glycolysis to pyruvate. Pyruvate is then oxidized to acetyl-coenzyme A (acetyl-CoA), which is transported to the mitochondrion for entry into the citric acid cycle. The end products are carbon dioxide, water, and energy released in the generation of adenosine triphosphate (ATP).
      c. Of importance to the neonate is that during hypoglycemia other substrates (ketone bodies, lactate, glycerol, and amino acids) can also be converted to pyruvate, enter the citric acid cycle, and produce ATP, thus serving as a source of energy for the brain.

C. Hormonal regulation of glucose homeostasis (Blackburn, 2018; Hawdon, 2016).
   1. Insulin: Secreted by the pancreatic beta cells in response to an increase in plasma glucose, insulin decreases the blood glucose level by promoting glycogen formation, suppressing hepatic glucose release, and driving the peripheral uptake of glucose. Insulin does not control the entry of glucose into the brain or liver.
   2. Glucagon: Secreted by the pancreatic beta cells when blood glucose levels decrease, glucagon

promotes glycogenolysis and gluconeogenesis. Glucagon is called a counterregulatory hormone because it opposes the effect of insulin by raising the blood glucose level. Other counterregulatory hormones include catecholamines, cortisol, and growth hormone. Although these hormones may not be important regulators in the fast-feed cycle of healthy neonates, minimum basal levels may be needed to maintain euglycemia.

D. Fetal glucose homeostasis.
   1. Glucose reaches the fetus by carrier-facilitated diffusion across the placenta at a concentration of about 70% to 80% of the maternal glucose concentration (Devaskar and Garg, 2015).
   2. Glycogen storage for postnatal energy needs begins early in gestation, with most glycogen accumulating during the third trimester.
   3. Fetal insulin is detectable by 8 to 11 weeks of gestation, but the response to a glucose load is not fully developed even at term (Blackburn, 2018; Stokowski, 2014).
   4. The fetus is capable of gluconeogenic activity, using substrates such as lactate, if needed, to meet metabolic demands in utero.

E. Neonatal glucose homeostasis.
   1. After cord clamping, the neonate's blood glucose concentration falls, reaching a nadir at 1 to 2 hours of age.
   2. In the first postnatal hours, the neonatal brain metabolizes lactate, which is abundant, so that even though the glucose concentration is low, the brain is not fuel deficient.
   3. The neonate gradually mobilizes glucose to meet energy needs by secreting glucagon and catecholamines and suppressing insulin release. Thus, even if a healthy term newborn infant is not fed soon after birth, blood glucose levels rise at 3 to 4 hours of age.
   4. Hepatic glycogen, however, is rapidly depleted if feeding is not established early and the infant is dependent on gluconeogenesis and lipolysis as the primary modes of maintaining euglycemia (Devaskar and Garg, 2015; Hume et al., 2005).

Hypoglycemia

A. Definition of hypoglycemia (Adamkin and Committee on Fetus and Newborn, 2011; Blackburn, 2018; Rozance and Hay, 2006).
   1. Most clinicians believe that, rather than a specific value, neonatal hypoglycemia lies on a continuum of low blood glucose values of varied duration and severity that is influenced by a number of different factors.
      a. Conceptual and postmenstrual age.
      b. Adequacy of gluconeogenic pathways.
      c. General health status.
      d. Presence or absence of symptoms.
   2. A widely used cutoff point for plasma glucose concentration is 40 mg/dL as the typical threshold for intervention in both premature and term neonates, with some authors advocating 55 to 70 mg/dL (Rozance and Hay, 2006; Steinkrauss et al., 2005).
   3. The optimal range for plasma glucose is 70 to 100 mg/dL, and there is no evidence that neonates have a lower requirement for glucose concentrations or that the neonatal brain can better tolerate hypoglycemia when compared with older infants and adults (Jain et al., 2012).

B. Incidence.
   1. Overall incidence is 1 to 5 per 1000 live births.
   2. The incidence in at-risk infants may be as high as 30%, occurring in 8% of large-for-gestational-age (LGA) infants and in 15% of premature and small-for-gestational-age (SGA) infants (Burris, 2017).

C. Pathophysiology (Blackburn, 2018; Jain et al., 2012).
   1. The immediate postnatal drop in blood glucose concentration is physiologic. Failure to increase glucose concentrations after 4 hours is pathologic. Subsequently, hypoglycemia is usually a result of inadequate hepatic glucose production that cannot meet peripheral demand or excessive insulin production.
   2. Glucose delivery is dependent on blood glucose concentration and blood flow rate. During hypoglycemia, the brain increases blood flow to improve glucose delivery that may predispose the neonatal brain to hemorrhagic and hyperoxic injury if there is diminished cerebral autoregulatory ability.
   3. When glucose consumption exceeds delivery, the brain uses alternative fuels such as ketone bodies, lactic acid, free fatty acids, and glycerol, if they are available. The production of energy from these sources involves the use of brain structural components such as proteins and phospholipids that may play a contributory role in neuronal damage.
   4. Lactic acid becomes elevated in late fetal and early postnatal life, and healthy term infants produce ketones effectively on days 2 and 3 of life, thus protecting their brains from fuel deficiency if the blood glucose level falls while feeding becomes established. However, the ability of preterm infants and of infants who are SGA to mount a counterregulatory ketogenic response at any time is severely limited, so these infants are heavily dependent on an adequate glucose supply (Rozance and Hay, 2006).
   5. Prolonged hypoglycemia, when not compensated for by a supply of alternative fuels, induces biochemical changes at the cellular level that may damage the neuronal and glial cells of the brain.

It is thought that an accumulation of excitatory amino acids, especially glutamate, during hypoglycemia leads to prolonged cellular depolarization with entry of water and calcium into the cell, first impairing neuronal growth and eventually causing cell death. In addition, the hypoglycemic brain may be more vulnerable to the damaging effects of ischemia. Degrees of ischemia and hypoglycemia that alone would not result in brain injury might do so in combination (Perlman and Volpe, 2018).

D. Etiologies and precipitating factors.
   1. Inadequate production or supply of glucose accounts for the more common causes of neonatal hypoglycemia. These conditions involve decreased substrate (glycogen, lactate, glycerol, amino acids) availability, immature or altered enzyme pathways, or altered responses to neural or hormonal factors (Blackburn, 2018; Hawdon, 2016).
      a. Prematurity: Possible diminished oral and parenteral intake, immature counterregulatory response to low glucose concentration, and insufficient glycogen stores and release.
      b. Intrauterine growth restriction: Low glycogen and fat stores, increased substrate utilization.
      c. Delayed feedings, insufficient breastfeeding, or fluid restriction.
      d. Inborn errors of metabolism: Defective gluconeogenesis and/or glycogenolysis (e.g., galactosemia, amino acid disorders, organic acid deficiencies, fatty acid oxidation disorders).
      e. Glycogen storage disease: Autosomal-recessive defects characterized by a deficient or abnormally functioning enzyme involved with formation or degradation of glycogen in the liver.
      f. Perinatal stress/hypoxia, respiratory distress, hypothermia, polycythemia/hyperviscosity, infection, adrenal hemorrhage, congestive heart failure.
   2. Increased uptake of glucose related to hyperinsulinism (Steinkrauss et al., 2005).
      a. Infant of diabetic mother (IDM).
      b. Persistent neonatal hyperinsulinism and nesidioblastosis: Autosomal-recessive disorders thought to be caused by regulatory defects in beta cell function. Surgical exploration may be necessary for definitive diagnosis, with subtotal pancreatectomy the required therapeutic measure.
      c. Beckwith–Wiedemann syndrome: Possibly genetic, as a majority of cases, but not all, involve a defect in the short arm of chromosome 11; characterized by omphalocele, macroglossia, visceromegaly, and hypoglycemia. Pancreatic islet cell hyperplasia is noted. The resultant hypoglycemia may be quite profound and difficult to treat (Blackburn, 2018; Devaskar and Garg, 2015).
      d. Rh incompatibility: Severe cases can have associated beta cell hypertrophy and hyperinsulinemia.
      e. High glucose infusion and tocolytics used before delivery. β-Adrenergic agonists such as terbutaline can stimulate fetal pancreatic beta cells.
      f. Iatrogenic: Position of tip of umbilical artery catheter near the pancreas can cause glucose to be directly delivered to the pancreas via the celiac artery, resulting in excessive insulin secretion.

E. Clinical presentation and assessment (Blackburn, 2018; Hawdon, 2016; Jain et al., 2012; Perlman and Volpe, 2018).
   1. Clinical signs of hypoglycemia are nonspecific and may be present at varying blood glucose concentrations in different infants, or symptoms may not be evident at all even though the infant is experiencing severe hypoglycemia. In addition, signs often linked with hypoglycemia may occur in conjunction with other clinical conditions.
      a. Tremors, jitteriness, irritability, exaggerated Moro reflex.
      b. Abnormal cry: High-pitched or weak.
      c. Respiratory distress: Apnea, irregular respirations, tachypnea, cyanosis.
      d. Stupor, hypotonia, lethargy, refusal to feed.
      e. Hypothermia, temperature instability.
      f. Seizures.

F. Diagnostic studies.
   1. Point-of-care blood glucose screening.
      a. Enzymatic reagent strips. Their reliability is questioned because they:
         1) May underestimate the true glucose level, as whole blood gives a reading 10% to 15% lower than the plasma value.
         2) May fail to detect clinically important hypoglycemia because of unpredictable measurement errors.
         3) Are sensitive to error from technical and operator variables such as timing, blotting, and distribution of blood droplets (Adamkin and Committee on Fetus and Newborn, 2011).
      b. Absorption photometry and electrochemical glucose meters.
      c. Subcutaneous microdialysis (Devaskar and Garg, 2015; Jain et al., 2012).
         1) Decreases the need for frequent blood sampling.
         2) Enables long-term glucose monitoring.
         3) Cannot measure glucose levels below 45 mg/dL with accuracy; large variance seen with high glucose values.
   2. All current techniques require laboratory confirmation for establishing a diagnosis of neonatal

hypoglycemia; however, appropriate interventions should be initiated promptly and not wait on laboratory confirmation (Adamkin and Committee on Fetus and Newborn, 2011).

3. In suspected hyperinsulinism, additional testing may include concurrent insulin and glucose levels, ketone and free fatty acid levels, and cortisol and growth hormone levels.

G. Patient care management (Adamkin and Committee on Fetus and Newborn, 2011; Rozance et al., 2016).
   1. Identify infants at risk.
   2. Prevent hypoglycemia by providing glucose substrate.
      a. Early enteral feedings.
      b. Intravenous (IV) glucose at 4 to 6 mg/kg/min.
   3. Assess glucose status with blood glucose screening.
      a. Perform blood glucose screening test on infants at risk on admission, frequently during the first 4 hours of life, and then at 4-hour intervals until the risk period has passed.
      b. Clinically unstable infants and any infant with signs of a possible low blood glucose concentration require regular monitoring.
      c. Early and exclusive breastfeeding will meet the nutritional and energy needs of healthy full-term infants, and routine blood glucose screening of these infants is not presently recommended.
      d. Utilization of a 40% dextrose buccal gel along with feeding may lessen hypoglycemia in at-risk term and late preterm infants in the first 48 hours after birth (Harris et al., 2013; Newman and Bunch, 2017).
   4. If hypoglycemia persists despite feeding, correction is with IV glucose infusion. A minibolus (dextrose 10% in water, 2 mL/kg), followed by continuous infusion at a rate of 6 to 8 mg/kg/min, rapidly raises the blood glucose level but does not treat the underlying hormonal and metabolic causes of the hypoglycemia.
   5. Monitoring of blood glucose levels must then continue, with documentation of the resolution of hypoglycemia with IV therapy and subsequently during the transition to full enteral feedings. Oral feedings should be initiated once clinical symptoms have resolved (Rozance and Hay, 2006).
   6. Persistent hypoglycemia raises the possibility of hyperinsulinism, although some infants without biochemical hyperinsulinism also have transiently high glucose requirements. Those with true hyperinsulinism may require the following:
      a. High IV glucose infusion rates (12 to 16 mg/kg/min). Delivery of concentrated glucose (>12.5%) requires a central line for safe administration.
      b. Hormonal therapy, which may include the following (Devaskar and Garg, 2015):
         1) Glucagon: Stimulates glycogen release from the liver. However, glucagon may also stimulate insulin release, so its use requires the presence of an IV glucose infusion. Mainly used to diagnose hepatic glycogen storage disease.
         2) Diazoxide: Suppresses pancreatic insulin secretion. Its use is reserved for situations of profound hyperinsulinism that have failed other therapies. It has been used for prolonged periods (years) without significant side effects noted. The usual dose is 5 to 20 mg/kg/day administered orally 2 to 3 times per day.
         3) Somatostatin: Suppresses insulin and glucagon secretion; however, its use is limited by its extremely short half-life and short duration of action.
      c. Corticosteroids, which stimulate gluconeogenesis from noncarbohydrate (protein) sources (Rozance et al., 2016).
         1) Hydrocortisone or prednisone may be used when parenteral glucose therapy is greater than 15 mg/kg/min.
         2) Gradual decreases in corticosteroid dosage and decreases in parenteral glucose concentrations are required as oral intake is increased.
      d. Subtotal or total pancreatectomy if severe, persistent hyperinsulinism is unresponsive to medical therapy (Burris, 2017).

H. Complications.
   1. Hypoglycemia will often recur when a bolus of glucose is not followed by a continuous infusion.
   2. Extravasations of peripheral glucose infusions may cause necrosis of skin and other tissue (Lund and Kuller, 2014).
      a. Hyaluronidase can be injected subcutaneously around the periphery of any extravasation site to prevent or limit tissue injury.
      b. Skin injury can be prevented by making multiple puncture holes using an aseptic technique over the involved area and allowing the fluid to be infiltrated.
      c. Elevation of the affected area, if an extremity may limit the leakage of the exudate.
      d. Use of an occlusive dressing (hydrocolloid dressing; hydrogel sheets, and amorphous gel) will provide for exudate management, adherence without damaging the surrounding tissue, and a microbial barrier; débridement and compression should be used.
   3. Reactive hypoglycemia with return of symptomatology may occur if the IV glucose infusion infiltrates or is stopped abruptly.

I. Outcome.
   1. Potential long-term sequelae remain unclear because there often are coexisting medical conditions that also predispose to brain injury (Hawdon, 2016).
   2. In general, outcome studies show that transient hypoglycemia in an otherwise healthy neonate has a good prognosis, whereas neonates with seizure-associated and/or persistent hyperinsulinemic hypoglycemia have the worst neurologic prognosis (Devaskar and Garg, 2015; Perlman and Volpe, 2018).

Infant of Diabetic Mother

A. **Incidence:** 20% of infants of women with gestational diabetes mellitus and 35% of infants of mothers with other forms of diabetes (Blackburn, 2018).
B. **Pathophysiology:** The hormonal and metabolic changes that complicate diabetic pregnancy can adversely affect the developing fetus and neonate in a number of ways (Blackburn, 2018; Stokowski, 2014).
   1. Early in gestation during organogenesis, the abnormal metabolic milieu is teratogenic, resulting in a higher incidence of congenital malformations.
   2. Throughout pregnancy and particularly in the third trimester, the pregnant diabetic woman is increasingly insulin resistant and often has hyperglycemia and hyperaminoacidemia. Excess glucose and amino acids are freely delivered to the fetus, but maternal insulin is not. These nutrients stimulate the fetal pancreas to produce insulin to use the excess fuels, resulting in beta cell hyperplasia and hyperinsulinemia. This fetal hyperinsulinemia, in turn, stimulates protein, lipid, and glycogen synthesis, causing a high rate of fetal growth, increased deposition of fat and visceral enlargement (especially the heart and liver), and subsequent macrosomia. This fetal macrosomia does not involve the brain or kidneys.
   3. After birth, the neonate's pancreas continues to produce insulin, and available glucose is rapidly used. The infant's ability to mobilize glycogen stores is decreased. The IDM may exhibit an exaggerated and persistent hypoglycemia. Maternal glucose homeostasis during pregnancy, as well as maternal glycemia during delivery, influences the degree of neonatal hypoglycemia.
   4. The IDM is at risk of having neural impairment because, even with plentiful adipose tissue, ketogenesis and lipolysis are suppressed by hyperinsulinemia, leaving the brain without a supply of alternative fuels for metabolism during hypoglycemia.
C. Clinical presentation and assessment (Rozance et al., 2016).
   1. Hypoglycemia: It may occur immediately after birth without symptoms. In one large retrospective series, hypoglycemia (defined as serum glucose <40 mg/dL) occurred in about one third of IDMs. The majority of those responded rapidly to treatment, but 10% had persistent hypoglycemia despite treatment.
   2. Macrosomia/LGA (approximately 35% of IDMs): Some infants are SGA because of placental insufficiency in advanced stages of the maternal diabetes.
   3. Increase in preterm births in association with diabetic pregnancy: Hyperbilirubinemia in IDMs may be secondary to prematurity.
   4. Respiratory distress syndrome and other conditions such as transient tachypnea of the newborn infant: Fetal hyperinsulinemia may delay the maturation of various aspects of the pulmonary surfactant system and not just inhibit surfactant production, delaying lung maturation.
   5. Polycythemia (venous hematocrit >65%): The insulin-induced high glucose uptake and high metabolic rate cause a cellular hypoxia, leading to an elevated erythropoietin level (Hawdon, 2016). Newborns with polycythemia do not always look plethoric, so the hematocrit level must be measured.
   6. Hypocalcemia and hypomagnesemia thought to result from a functional hypoparathyroidism due to maternal magnesium loss (Jain et al., 2012).
   7. Cardiomyopathy and visceromegaly possibly related to maternal diabetes control and to fetal/neonatal hyperinsulinemia.
   8. Congenital malformations: Cardiac defects (especially transposition), neural tube defects, sacral agenesis, and caudal regression are 2 to 4 times more frequent than in the general population. The anomalies are thought to be due to the diabetic intrauterine environment during organogenesis, frequently before the pregnancy is recognized and prenatal diabetic treatment initiated.
   9. Oral motor difficulties may be seen in severe cases.
D. Diagnostic studies.
   1. Blood glucose screening with laboratory confirmation of plasma glucose.
   2. Other laboratory analyses, including calcium and magnesium levels and venous hematocrit.
   3. X-ray examination if fractures from traumatic delivery are suspected.
   4. Echocardiography.
E. Patient care management (Rozance et al., 2016; Stokowski, 2014).
   1. The main goal of the treatment of gestational diabetes is to achieve and maintain euglycemia. Tight control of intrapartum glucose levels may reduce the incidence of neonatal complications.

2. Anticipate problems of IDM before delivery; prompt recognition and treatment of neonatal morbidities postdelivery.
3. Provide early feeding of human milk, donor human milk, or formula orally or via gavage tube if the infant does not feed well. IV administration of glucose is necessary for infants too small or sick to tolerate enteral feeding.

F. Complications.
1. Seizures resulting from cerebral fuel deficiency.
2. Shoulder dystocia: Macrosomic infants delivered with forceps or vacuum extraction may have brachial plexus injury (Erb's palsy) or fractures.
3. Renal vein thrombosis (secondary to polycythemia/hyperviscosity).
4. Development of juvenile insulin-dependent diabetes with a 2% transmission risk for female IDM and 6% for male IDM (Jain et al., 2012).

G. Outcome (Rozance et al., 2016; Stokowski, 2014).
1. Increased perinatal mortality rate results from relatively high rates of congenital malformations, stillbirths, and premature delivery.
2. Morbidities associated with IDM include neurologic sequelae, developmental delay, behavioral differences, obesity, and diabetes.
3. Maternal complications, including poor glycemic control, vascular disease, infection, and pregnancy-induced hypertension, are associated with poorer perinatal outcome. Improved outcomes are seen in IDMs when maternal diabetes is metabolically controlled.
4. The outcomes for SGA infants born to women receiving intensive therapy for gestational diabetes may be worse than those of appropriate-for-gestational-age or LGA infants.

Hyperglycemia

A. **Definition:** Uncertain, but concerns raised when whole blood glucose concentration greater than 120 to 125 mg/dL or a plasma glucose concentration greater than 150 mg/dL.

B. **Incidence:** Prevalence of 29% to 86% in low birth weight infants overall; 2% of infants weighing more than 2000 g, 45% of infants less than 1000 g, and up to 80% of infants weighing less than 750 g (Burris, 2017; Jain et al., 2012; Le Compte et al., 2012; Rozance et al., 2016).

C. **Pathophysiology.**
1. Normally, an infant responds to an exogenous glucose supply with a rise in insulin, suppressing endogenous glucose production and enhancing peripheral uptake of glucose. Though clinically stable, extremely low birth weight (ELBW) infants may be able to regulate glucose in this manner; however, many of them become hyperglycemic.
2. Hepatic glucose production in this latter group continues in the presence of hyperglycemia and circulating insulin. This represents a failure of glucose autoregulation involving both the pancreas and liver of infants with hyperglycemia.
3. Corticosteroid therapy stimulates glycogenolysis and gluconeogenesis and may block insulin secretion as well as inhibit its peripheral action.

D. Etiologies and precipitating factors.
1. Low birth weight, extreme prematurity, and intrauterine growth restriction (IUGR).
2. Excessive glucose load (>6 to 8 mg/kg/min), with 50% of infants receiving a glucose infusion rate (GIR) of 11 mg/kg/min and all infants receiving a GIR of 14 mg/kg/min developing hyperglycemia.
3. Stress related to clinical problems such as sepsis or infection.
4. Transient or permanent neonatal diabetes mellitus (see "Transient or Permanent Neonatal Diabetes").
5. Side effects of medications such as corticosteroids.
6. Lipid infusion, which may contribute to hyperglycemia.
7. Release of catecholamines secondary to surgery/anesthesia.

E. Clinical presentation and assessment.
1. Onset can be as early as 24 hours of age; usually before 3 days of life.
2. No characteristic clinical presentation.
3. Symptoms may include glycosuria, dehydration, weight loss, fever, ketosis, metabolic acidosis, and failure to thrive.

F. Diagnostic studies.
1. Serum or plasma blood glucose levels greater than 125 mg/dL or 150 mg/dL, respectively.
2. Urinary glucose. Very low birth weight (VLBW) infants have a low renal threshold for glucose and may spill sugar at blood glucose levels as low as 80 to 100 mg/dL.
3. Investigation for possible underlying cause (sepsis workup to rule out infection or insulin level to rule out neonatal diabetes mellitus).

G. Patient care management.
1. Monitor blood glucose of infants at risk for developing hyperglycemia, particularly when fluid intake is increased on day 2 or 3 of life.
2. Decrease glucose load as much as possible to allow the blood glucose level to stabilize in a normal range (<125 mg/dL, or plasma glucose <150 mg/dL).
3. Monitor weight, urine output, fluid intake, GIR, electrolytes, and acid–base balance.
4. Insulin is sometimes administered to ELBW infants along with parenteral nutrition in an attempt to normalize blood glucose levels without reducing the caloric intake. Insulin is also used to treat transient neonatal diabetes. Insulin normalizes blood glucose by suppressing hepatic glucose production

and by increasing peripheral glucose utilization. However, premature infants have a very small mass of insulin-dependent tissue, with only 10% of their glucose utilization being insulin dependent. Severe hyperglycemia may occur in the VLBW infant despite decreased GIRs. Continuous insulin infusion may be used, although routine use is not advised because of adverse effects (Alsweiler et al., 2012).

5. Begin enteral feedings when feasible because the subsequent release of gut hormones may promote insulin secretion, allowing for improved blood glucose control.

H. Complications.
1. Neonatal hyperglycemia may be accompanied by urinary loss of glucose and an osmotic diuresis with its risk of dehydration. In addition, possible resultant hyperosmolarity of extracellular fluid in the brain may increase the premature infant's chance for intraventricular hemorrhage (IVH) (Jain et al., 2012).
2. Insulin management may be difficult in the ELBW infant; blood glucose levels can fluctuate widely. A precisely controlled continuous-infusion pump is essential. Priming of the tubing is required because insulin tends to adhere to the catheters. Whether insulin therapy promotes linear growth or just converts glucose into fat is not yet fully understood (Alsweiler et al., 2012).
3. Electrolyte abnormalities, elevated CO_2 retention, and an elevated triglyceride level.

I. Outcome.
1. Controversy exists concerning the outcome of neonatal hyperglycemia.
   a. Hypothesized that hyperglycemia in the premature neonate may increase the risk of IVH because rapid fluctuations in osmolarity negatively affect the germinal matrix.
   b. There is a strong association between neonatal hyperglycemia and increased mortality rates or poor neurodevelopmental outcomes among survivors (Hays et al., 2006; Kao et al., 2006).
   c. Neonatal hyperglycemia is usually self-limiting and not associated with adverse outcomes.
   d. Possible association between hyperglycemia and severe retinopathy of prematurity in ELBW infants (Chavez-Valdez et al., 2011).

Transient or Permanent Neonatal Diabetes

A. **Definition:** Hyperglycemia requiring insulin therapy occurring within the first month of life and lasting at least 2 weeks to several months; can be lifelong (Ozlu et al., 2006).

B. **Incidence:** 1:500,000. Predominantly occurring in SGA infants, with 46% developing permanent diabetes in the neonatal period, 23% in childhood or adolescence; 31% are resolved in the neonatal period (Hawdon, 2016).
1. Appears in the first week of life and persists for longer than 2 weeks (Stokowski, 2014).
2. Etiology is variable, including dysfunctional insulin molecule or receptor deficiencies and activating mutations of the K_{ATP} channel (Stokowski, 2014).
3. Instances of transient neonatal diabetes are associated with abnormalities of an imprinted region on chromosome 6q24. Mutations in encoder genes have been attributed to instances of permanent and transient neonatal diabetes (Babenko et al., 2006; Burris, 2017).

C. Pathophysiology.
1. Both transient and permanent neonatal diabetes mellitus are due to a failure of pancreatic beta cells causing an endogenous insulin deficiency, with the exact pathogenesis involved not yet fully understood (Ozlu et al., 2006; Stokowski, 2014).
2. The IUGR commonly seen with affected infants is due to insufficient insulin secretion (Stokowski, 2014).

D. Clinical presentation.
1. The transient form appears within the first week of life, resolves within weeks or months, and reappears in late childhood. The permanent form appears within days or months of birth and persists throughout life (Stokowski, 2014).
2. Hyperglycemia (frequently >600 mg/dL), polyuria, glycosuria, weight loss, dehydration, fever, failure to thrive, ketosis, metabolic acidosis (may or may not be evident), and low levels of C-peptide and plasma insulin (Ozlu et al., 2006; Stokowski, 2014).

E. Patient care management.
1. Restore intravascular volume.
2. Replace fluid and electrolyte losses as indicated and provide for ongoing needs.
3. Correct the hyperglycemia; monitor glucose levels.
4. Provide adequate nutrition for growth and development.
5. Usually, a daily dose of 0.2 to 3 units/kg/day of insulin is necessary to achieve plasma glucose levels of 100 to 180 mg/dL; however, individualization of insulin requirement is needed.
6. Average length of insulin therapy varies from 2 weeks to 18 months. Tapering of insulin dose as requirement decreases lessens the risk of recurrent hyperglycemia (Ozlu et al., 2006; Stokowski, 2014).

F. **Complications:** See "Hyperglycemia" section earlier.

G. **Outcome.**
1. Course of disease is highly variable.
2. Close follow-up is recommended after remission because of a high rate of recurrence later in childhood.

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CHAPTER 10
Nutritional Management

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OBJECTIVES

1. Describe the effects of prematurity on the gastrointestinal (GI) physiology of digestion and absorption.
2. Identify nutritional store deficiencies most common in premature and term infants.
3. Describe basic nutritional requirements for premature and high-risk term infants and factors that influence these requirements.
4. Identify nutritional components, uses, methods of delivery, complications, and nursing care issues for parenteral nutrition (PN).
5. Review the use of commercial preterm and full-term infant formulas for enteral nutrition management.
6. Review human milk feedings for premature and high-risk term infants and related nursing care issues.
7. Review the use of human milk supplements in enteral nutrition management for premature infants.
8. Describe the various methods of providing enteral feedings and the advantages and disadvantages of each.
9. Describe minimal enteral feedings and application in initiating enteral nutrition for premature infants.
10. Describe risks and interventions for feeding intolerances and nutritional deficiency states in premature infants.
11. Describe assessment of an infant's readiness for enteral nutrition.
12. Describe assessments used to determine premature and high-risk infant nutritional status.
13. Describe the standards used to assess growth in term and premature infants.

Neonatal nurses face challenges in helping to meet the basic nutritional requirements and support the growth needs of premature and high-risk infants. Tremendous advances in technology and pharmacology permit the survival of very premature infants who require intensive and specialized care and support for immature body systems. Nutritional care is of vital importance for premature infants, who are deprived of transplacentally acquired nutrient stores and have rapid extrauterine growth rates. Other high-risk infants have special needs related to illness-associated metabolic demands and physiologic instability.

Neonatal nurses with knowledge of the effects of prematurity on gastrointestinal (GI) functioning, the special nutritional needs of premature and high-risk infants, and methods of delivering nutritional support can better assess infant status and contribute to nutritional management. This chapter reviews the nutritional requirements of premature and high-risk infants, methods for providing parenteral and enteral nutrition, and nursing interventions for optimal nutritional support.

Anatomy and Physiology of the Premature Infant's GI Tract

A. Anatomic and functional development of the GI tract.
   1. Anatomic development (Blackburn, 2013; Dimmitt et al., 2018; Moore et al., 2016).
      a. Pylorus and fundus of stomach present and gastric glands formed by 14 weeks of gestation.
      b. Esophageal sphincter present by 28 weeks of gestation.
      c. GI tract resembles that of a term infant by 20 weeks of gestation.
      d. GI tract lengthens to 250 to 300 cm by term, and gastric capacity is about 30 mL.
   2. Functional development (Blackburn, 2013; Dimmitt et al., 2018).
      a. Premature infants have limited production of GI digestive enzymes and growth factors.
      b. By 28 weeks, biochemical and physiologic capacities for limited digestion and absorption are present.

c. Major GI-regulating polypeptides—gastrin, motilin, cholecystokinin, pancreatic polypeptide, and somatostatin—are present in limited amounts by the end of the first trimester; they act locally to regulate growth and development of the GI system and reach adult levels by term gestation.
d. Intestinal transport of amino acids occurs by 14 weeks, glucose by 18 weeks, and fatty acids by 24 weeks of gestation.
e. Lactose is the predominate source of carbohydrate in human milk and formula. Lactase reduces lactose to glucose.
f. Lactase activity is first seen at 9 weeks of gestation; at 24 weeks of gestation, activity is less than one fourth that of a term infant; dramatically increases between 32 and 34 weeks of gestation to the activity level of a term infant.
g. Disaccharidases, such as salivary amylase and mucosal glucoamylase, are functionally active after 27 to 28 weeks of gestation.
h. Fat (lipid) emulsification and hydroxylation to free fatty acids and monoglycerides result from lipase and bile acid activity.
i. Lingual and gastric lipases present by 26 weeks of gestation but are limited in volume and function. Additional lipases are also in human milk; they function well in conditions with low bile acid synthesis and stores, such as in premature infants.
j. Bile acid secretion occurs by 22 weeks of gestation.
k. Bile acid synthesis and stores in premature infant are decreased compared with term infants, which is 50% of adult levels.
l. Gastric gland secretion activity is seen by 20 weeks of gestation; gastric acid secretion is lower than adult levels even at term gestation; activated with enteral feedings.
m. Ingested proteins are denatured by gastrin, cleaved by pepsin, and further reduced by pancreatic proteolytic enzymes into oligopeptides and amino acids. Pepsin activity is induced by increased gastric acid resulting from enteral feedings.
n. GI motility is the movement of food from ingestion to elimination; includes suck–swallow and esophageal, stomach, and intestinal peristalsis. Immature GI motility is a major limitation to digestion; presence of disorganized, random contractions between 25 and 30 weeks of gestation; motility improves after 30 to 32 weeks of gestation, gradually becoming more organized closer to term gestation (Blackburn, 2013; Dimmitt et al., 2018).

B. Postnatal development of the GI tract.
1. GI motility is a major barrier to providing enteral nutrition to premature infants (Dimmitt et al., 2018).
a. Nonnutritive suck coordination present around 28 weeks of gestation; suck–swallow coordination for adequate consumption of milk from breast or nipple develops closer to 34 to 36 weeks of gestation; appears to be dependent on neuromaturation related to postmenstrual age rather than chronologic age (age in days since birth) (Blackburn, 2013).
b. Well-developed tone and swallow-related relaxation in the lower esophageal sphincter (LES) allows food passage into the stomach from the esophagus; transient LES relaxation related to immaturity allows gastric contents to reenter the esophagus (gastroesophageal reflux [GER]); diminishes closer to term gestation (Ferguson, 2018; Kwok et al., 2017).
c. Delayed gastric emptying related to disorganized and random peristalsis contractions with immature duodenal response to feedings; duodenal contractions in premature infants cease rather than increase in response to feedings, thus delaying gastric emptying. Peristalsis becomes more organized; duodenal responses and gastric emptying time improve with increasing gestational age. Regular enteral feeding may have positive maturational effect on duodenal response for premature infants (Blackburn, 2013; Dimmitt et al., 2018; Ferguson, 2018).
2. Influences on postnatal development of GI function include genetic endowment, GI trophic factors, and hormonal regulatory mechanisms, as well as enteral feeding initiation and feeding type (Blackburn, 2013).
a. GI trophic factors include nutrients, hormones, and peptides. Principal nutrients: iron, zinc, vitamin B_{12}, vitamin A, and folate; principal hormones: insulin and growth factor; principal peptides: epidermal growth factor, transforming growth factor, insulin-like growth factors, and somatostatin.
b. Hormonal regulatory mechanisms have a critical role in mediating GI development after birth. GI development is stimulated by increases in specific GI hormones and enteric neuropeptides, such as enteroglucagon, which promotes intestinal mucosal growth; gastrin, which stimulates gastric mucosa and exocrine pancreas growth; motilin and neurotensin, which stimulate development of GI motility; and gastric inhibitory peptide, which promotes glucose tolerance.
c. Initiation of enteral feeding is a major stimulus for hormonal regulatory mechanisms in both premature and term infants; response is delayed in premature and high-risk infants receiving only parenteral nutrition (PN) without enteral feedings.
d. Type of enteral feeding influences GI maturation; human milk contains high levels of trophic factors, which enhance postnatal GI maturation.

e. Minimal enteral feeding, also known as trophic feeding or gut or GI priming, may stimulate hormonal regulatory mechanisms, with subsequent GI development; as little as 0.5 to 1 mL/kg/hr seems beneficial; initiation recommended within the first 24 hours of life (Blackburn, 2013; AAP Committee on Nutrition, 2014; Salas et al., 2017; Schneider et al., 2018; Ziegler, 2011).

C. **Nutrient deficiencies of premature infants:** Cessation of transplacental transfer of nutrients during the third trimester, a critical period for somatic and brain growth (Schneider et al., 2018).

1. Carbohydrate, lipid, and protein.
   a. Glucose is the primary source of carbohydrate. During the third trimester, glucose is stored as glycogen in the liver and cardiac and skeletal muscle, and to a lesser extent in the kidneys, intestines, and brain; glycogen stores of term infants are significantly greater than those of adults (Blackburn, 2013).
      1) Glucose is the primary fetal energy source; accounts for 80% of fetal energy.
      2) Carbohydrate in the form of lactose and glucose provides 40% of the postnatal caloric intake (Blackburn, 2013; AAP Committee on Nutrition, 2014; McNelis et al., 2017; Tudehope, 2013).
   b. Lipid stores; significant lipid accretion and increased adipose tissue deposition occur in the fetus between 24 and 40 weeks. At 26 to 28 weeks, fat stores account for approximately 3.5% of body composition, 30 to 34 weeks 8%, and by 35 to 38 weeks 16%; weight gain due to fat deposition is about 14 g/day (Moore et al., 2016).
      1) Adipose tissue: White and brown (Blackburn, 2013; Moore et al., 2016; Nedergaard and Cannon, 2017).
         a) White adipose tissue: Subcutaneous tissue; acts as a heat insulator, shock absorber, and calorie storage unit.
         b) Brown adipose tissue: Accumulates in the neck, scapulae, axillae, mediastinum, and perirenal tissues; critical for nonshivering thermogenesis, a major method of neonatal heat production.
      2) Lipids contribute minimally to fetal energy needs; critical component of brain development (neuronal and glial membranes and myelin sheath), retinal development, cell membrane formation, synthesis of surfactant and other phospholipids bile, serum lipoprotein, and adipose tissue deposition (Blackburn, 2013; Herrera and Ortega-Senovilla, 2017).
      3) Lipids provide approximately 50% of the postnatal caloric intake; major postnatal energy source (Blackburn, 2013; Herrera and Ortega-Senovilla, 2017; Tudehope, 2013).
   c. Protein stores; major structural and functional components of all cells of the body; during the third trimester, fetal accretion rate is 3.6 to 4.8 g/kg/day (Blackburn, 2013; Brown et al., 2017; van Goudoever and Matthews, 2017).
      1) Amino acids and lactate as a secondary fetal energy source; critical in all organ development, growth, and function.
      2) Protein catabolism contributes approximately 10% of postnatal caloric intake.
   d. Premature infants have minimal adipose tissue and glycogen stores at birth; stores decrease with decreasing gestational age; at birth, sources are quickly depleted if sufficient exogenous sources to meet energy needs are not provided (Blackburn, 2013).
   e. Healthy term infants have sufficient glycogen and fat stores to provide for energy demands during the relative state of low nutrient intake that normally occurs during the first few days of life (Blackburn, 2013).
      1) Estimated 90% of liver and 50% to 80% of cardiac and skeletal muscle glycogen stores are used within the first 24 hours after birth.
      2) Fat is a major source of stored calories for the term infant and is the preferred energy source for the high energy demands of the heart and the adrenal cortex.
2. Vitamins and minerals.
   a. Fat-soluble vitamins A and E are stored in body fat and organs (Greer, 2012; Ross et al., 2017; Segar et al., 2017).
      1) Vitamin A is transferred to the fetus throughout pregnancy, increases in the third trimester; adequate fetal level maintained despite variations in maternal diet; essential for epithelial cell growth and differentiation, vision, healing, reproduction, and immune competency; stored primarily in the liver.
      2) Vitamin E gradually increases throughout pregnancy with a direct correlation between vitamin E level and body weight and adipose tissue; stored primarily in the liver, adipose tissue, and skeletal muscle; low levels after birth and throughout infancy, depending on diet (human milk, formula) for adequate supply; provides protection from oxidant free-radical damage.
   b. Calcium, phosphorus, and magnesium (Blackburn, 2013; Namgung and Tsang, 2017).
      1) Two thirds of the calcium accumulated in a term infant is transplacentally transferred to the fetus during the third trimester; allows for rapid fetal bone mineralization.

2) Fetal phosphorus levels are higher than maternal levels during the third trimester; play an important role in fetal intermediary metabolism and bone mineralization.
3) Eighty percent of magnesium in term infants is accrued in the third trimester; important for plasma membrane excitability; plays a regulatory role in numerous biological processes; involved in energy storage, transfer, and production; significant in calcium and bone homeostasis.

c. Trace elements: Copper, selenium, chromium, manganese, molybdenum, cobalt, fluoride, iodine, iron, and zinc are transferred to the fetus during pregnancy; essential for various metabolic processes, cell and organ function and development (Blackburn, 2013; Hambidge and Krebs, 2017).
1) Iron plays a prominent role in oxygen transport, principally in hemoglobin; a 28-week fetus has 64 mcg iron per gram of fat-free tissue, and a term infant has 94 mcg; in term infants, almost 80% of the iron is stored in hemoglobin; required by virtually all cells for normal growth and metabolism; rapidly growing and differentiating cells have particularly high iron requirements; necessary for the development and functional integrity of the immune system (Greer, 2012; AAP Committee on Nutrition, 2014; McArdle and Georgieff, 2017).
2) Fetal zinc levels markedly increase midpregnancy, then gradually decrease over the third trimester; plays an important biological role in protein structure and function, enzymes, transcription factors, hormonal receptor sites, cell membranes, and DNA and RNA metabolism.

Nutritional Requirements

A. Term infants (Table 10.1).
1. Fluid requirements (Blackburn, 2013; Dell, 2015).
a. Parenteral: 100 to 120 mL/kg/day.
b. Enteral: 120 to 150 mL/kg/day.
2. Energy (caloric) intake requirements.
a. Parenteral: 80 to 90 kcal/kg/day.
b. Enteral: 100 to 120 kcal/kg/day.
3. Carbohydrate, fat, and protein (Blackburn, 2013).
a. Total caloric intake should be represented by the following:
1) Carbohydrate: approximately 40%; 8 to 12 g/kg/day.
2) Fat.
a) Parenteral: 2 to 4 g/kg/day; 20% intravenous (IV) lipid emulsion preferred over 10%, and has a lower phospholipid-to-triglyceride ratio and thus is better tolerated; newer formulations of lipids including fish-oil lipid emulsions and Smoflipid, may reduce PN-associated liver disease (Guthrie et al., 2017; Sorrell et al., 2017). The usual dose for Smoflipid therapy for neonates is 3 g/kg/day.
b) Enteral: 3 to 4 g/kg/day.

Table 10.1

Daily Nutritional Requirements for Term Infants

Nutrient	Parenteral	Enteral
Fluid (mL/kg/day)*	100 to 120	120 to 150
Energy (kcal/kg/day)†	80 to 90	100 to 120
Protein (g/kg/day)‡	2 to 2.5	2 to 2.5
Carbohydrate (g/kg/day)	10 to 15	8 to 12
Fat (g/kg/day)	2 to 4	3 to 4
Sodium (mEq/kg/day)	2 to 3	2 to 3
Potassium (mEq/kg/day)	2 to 3	2 to 3
Chloride (mEq/kg/day)	2 to 3	2 to 3
Calcium (mg/kg/day)§	60 to 80	130
Phosphorus (mg/kg/day)§	40 to 45	45
Magnesium (mg/kg/day)	5 to 7	7
Iron (mg/kg/day)‖	0.1 to 0.2	1 to 2
Vitamin A (IU/day)¶	2300	1250
Vitamin D (IU/day)	400	300
Vitamin E (IU/day)**	7	5 to 10
Vitamin K (mg/day)	0.05	0.2
Vitamin C (mg/day)	80	30 to 50
Vitamin B_1 (mg/day)	1.2	0.3
Vitamin B_2 (mg/day)	1.4	0.4
Vitamin B_6 (mg/day)	1	0.3
Vitamin B_{12} (mcg/day)	1	0.3
Niacin (mg/day)	17	5
Folate (mcg/day)††	140	25 to 50
Biotin (mcg/day)	20	10
Zinc (mcg/kg/day)‡‡	250	830
Copper (mcg/kg/day)‡‡,§§	20	75
Manganese (mcg/kg/day)§§	1	85
Selenium (mcg/kg/day)¶¶	2	1.6
Chromium (mcg/kg/day)	0.2	2
Molybdenum (mcg/kg/day)	0.25	2
Iodine (mcg/kg/day)	1	7

*After immediate postnatal initiation of fluid therapy.

†Adjust according to weight gain and stress factors.

‡Requirements increase with increasing degree of prematurity.

§Inadequate amount in total parenteral nutrition solutions because of risk of precipitation.

‖Initiate between 2 weeks and 2 months of age. Delay initiation in preterm infants with progressive retinopathy.

¶Supplementation might reduce the incidence of bronchopulmonary dysplasia.

**Supplementation might reduce the severity of retinopathy of prematurity.

††Not present in oral multivitamin supplements.

‡‡Increased requirement in patients with excessive ileostomy drainage or chronic diarrhea.

§§Removed from total parenteral nutrition solutions in patients with cholestatic liver disease.

¶¶Not present in standard trace element solution for neonates.

Adapted from Blackburn, S. T. (2013). *Maternal, fetal, & neonatal physiology: A clinical perspective* (4th ed.). St. Louis, MO: Saunders.

3) Protein: both parenteral and enteral: 2 to 2.5 g/kg/day.

b. Human milk and commercial infant formulas supply these nutrients within acceptable ratios (American Academy of Pediatrics [AAP] Section on Breastfeeding, 2014; Blackburn, 2013; AAP Committee on Nutrition, 2014).

4. Vitamins, minerals, and trace elements.
   a. Dietary reference intakes for enteral nutrition and PN are summarized in Table 10.1.
   b. Pediatric PN, human milk, and commercial infant formulas provide adequate amounts of most vitamins to meet the needs of infants (Greer, 2012; AAP Committee on Nutrition, 2014).
   c. Newborn deficiencies in fat-soluble vitamins A, D, E, and K well described; prevented with human milk and formulas; significant vitamin deficiency rare (Greer, 2012; AAP Committee on Nutrition, 2014).
      1) Vitamin K is the only vitamin routinely given at the time of birth; sufficient levels are sustained for the first 3 months of life in exclusively breastfed infants even though human milk does not meet dietary reference intakes; formulas have sufficient vitamin K to meet dietary reference intakes. Oral forms of vitamin K are not recommended because they may not provide adequate vitamin K necessary to prevent hemorrhage later in infancy unless repeated doses given during the first 4 months of life.
      2) Beginning in the first 2 months of life, the AAP recommends vitamin D supplementation for breastfed or formula-fed infants unless taking at least 500 mL/day of vitamin D–fortified formula or human milk (AAP Section on Breastfeeding, 2014).
      3) Fluoride supplements should not be provided for the first 6 months of life for any infant; after 6 months, fluoride supplementation is recommended only if the fluoride level in drinking water supply is less than 0.3 parts per million (ppm); consideration should include other fluoride sources: food, toothpaste, other fluid sources (AAP Section on Breastfeeding, 2014).
      4) Iron supplements may be needed for healthy term infants before 6 months to support iron stores; recommended in the first 6 months of life for infants with hematologic disorders or infants with inadequate iron stores at birth (AAP Section on Breastfeeding, 2014).
      5) Vitamin B_{12} supplementation recommended for infants of vegan mothers with inadequate B_{12} intake.

B. Premature infants (Blackburn, 2013; Goldberg et al., 2018; AAP Committee on Nutrition, 2014; Tudehope, 2013).
   1. General considerations.
      a. Recommendations for nutritional requirements and advisable intakes are used as guidelines.
      b. Individual premature infant nutritional needs vary with gestational age and health status.
      c. Recommendations for parenteral and enteral nutritional needs are summarized in Table 10.2.
   2. Fluid requirements.
      a. Parenteral: 120 to 150 mL/kg/day.
      b. Enteral: 150 to 200 mL/kg/day.
      c. Varies with hydration state (e.g., dehydration to overhydration/edematous states), estimated insensible water losses, gestational age, postmenstrual age, generalized health status, and underlying disease state of the infant (e.g., presence of patent ductus arteriosus, bronchopulmonary disease, postrecovery phase of necrotizing enterocolitis [NEC], and short bowel syndrome).
   3. Energy (caloric) intake requirements.
      a. Based on an estimation of the caloric need of 90 to 120 kcal/kg/day for premature infants as summarized in Table 10.3.
      b. Parenteral: 80 to 100 kcal/kg/day.
      c. Enteral: 110 to 130 kcal/kg/day.
      d. Varies depending on day of life, fluid intake, thermal environment, activity, maturation, health status, underlying disease state, and growth rate.
   4. Carbohydrate, fat, and protein (Bhatia et al., 2013; Blackburn, 2013; Brown et al., 2017; Herrera and Ortega-Senovilla, 2017; AAP Committee on Nutrition, 2014).
      a. Carbohydrate.
         1) Parenteral: 10 to 15 g/kg/day; glucose IV infusion.
         2) Enteral: 8 to 12 g/kg/day; primarily lactose.
         3) Glucose intake must be adequate to maintain serum levels greater than 45 mg/dL.
         4) Premature infants rapidly become hypoglycemic with inadequate glucose intake. Hyperglycemia can also be a problem in extremely premature infants. Hyperglycemia contributes to hyperosmolality and may be a risk factor for intracranial hemorrhage.
      b. Fat.
         1) Parenteral: 2 to 3.5 g/kg/day.
         2) Enteral: 3 to 4 g/kg/day.
         3) Medium-chain triglycerides (MCTs) are easier to absorb than long-chain triglycerides; MCTs are absorbed by passive diffusion and do not require bile salts.
            a) Premature infant formulas use a combination of MCTs and shorter-chain vegetable fatty acids.

Table 10.2

Daily Nutritional Requirements for Premature Infants

Nutrient	Parenteral	Enteral
Fluid (mL/kg/day)*	120 to 150	150 to 200
Energy (kcal/kg/day)†	80 to 100	110 to 130
Protein (g/kg/day)‡	3 to 4	3 to 4.3
Carbohydrate (g/kg/day)	10 to 15	8 to 12
Fat (g/kg/day)	2 to 3.5	3 to 4
Sodium (mEq/kg/day)	2 to 3.5	2 to 4
Potassium (mEq/kg/day)	2 to 3	2 to 3
Chloride (mEq/kg/day)	2 to 3	2 to 3
Calcium (mg/kg/day)§	60 to 90	210 to 250
Phosphorus (mg/kg/day)§	40 to 70	112 to 125
Magnesium (mg/kg/day)	4 to 7	8 to 15
Iron (mg/kg/day)‖	0.0 to 0.2	1 to 2
Vitamin A (IU/day)¶	700 to 1500	700 to 1500
Vitamin D (IU/day)	120 to 260	400
Vitamin E (IU/day)**	2 to 4	6 to 12
Vitamin K (mg/day)	0.06 to 0.1	0.05
Vitamin C (mg/day)	35 to 50	20 to 60
Vitamin B_1 (mg/day)	0.3 to 0.8	0.2 to 0.7
Vitamin B_2 (mg/day)	0.4 to 0.9	0.3 to 0.8
Vitamin B_6 (mg/day)	0.3 to 0.7	0.3 to 0.7
Vitamin B_{12} (mcg/day)	0.3 to 0.7	0.3 to 0.7
Niacin (mg/day)	5 to 12	5 to 12
Folate (mcg/day)††	40 to 90	50
Biotin (mcg/day)	6 to 13	6 to 20
Zinc (mcg/kg/day)‡‡	400	800 to 1000
Copper (mcg/kg/day)‡‡,§§	20	100 to 150
Manganese (mcg/kg/day)§§	1	10 to 20
Selenium (mcg/kg/day)¶¶	1.5 to 2	1.3 to 3
Chromium (mcg/kg/day)	0.2	2 to 4
Molybdenum (mcg/kg/day)	0.25	2 to 3
Iodine (mcg/kg/day)	1	4

*After immediate postnatal initiation of fluid therapy.

†Adjust according to weight gain and stress factors.

‡Requirements increase with increasing degree of prematurity.

§Inadequate amount in total parenteral nutrition solutions because of risk of precipitation.

‖Initiate between 2 weeks and 2 months of age. Delay initiation in preterm infants with progressive retinopathy.

¶Supplementation might reduce incidence of bronchopulmonary dysplasia.

**Supplementation might reduce severity of retinopathy of prematurity.

††Not present in oral multivitamin supplement.

‡‡Increased requirement in patients with excessive ileostomy drainage or chronic diarrhea.

§§Removed from total parenteral nutrition solutions in patients with cholestatic liver disease.

¶¶Not present in standard trace element solution for neonates.

Adapted from Blackburn, S. T. (2013). *Maternal, fetal, & neonatal physiology: A clinical perspective* (4th ed.). St. Louis, MO: Elsevier Saunders.

Table 10.3

Estimation of Caloric Requirements for the Low Birth Weight Infant

Physiologic Activity	kcal/kg/day
Energy expended	40 to 60
Resting metabolic rate	40 to 50
Activity	0 to 5
Thermoregulation	0 to 5
Synthesis	15
Energy stored	20 to 30
Energy excreted	15
Total energy intake	90 to 120

Adapted from American Academy of Pediatrics Committee on Nutrition. (2014). *Pediatric nutrition handbook* (7th ed.). Elk Grove Village, IL: American Academy of Pediatrics.

b) Linoleic acid is an essential fatty acid and should account for at least 3% of total calories; achieved with adequate intake of human milk and commercial premature infant formulas.
c) Very-long-chain fatty acids—arachidonic acid and docosahexaenoic acid—are derivatives of linoleic and linolenic acids and are found in human milk but not infant formulas; associated functionally with cognition and vision.

c. Protein (Brown et al., 2017; Tudehope, 2013; van Goudoever and Matthews, 2017).
1) Parenteral: 3 to 4 g/kg/day.
a) Extremely low birth weight (ELBW) infants (less than 1000 g birth weight): 3.5 to 4.0 g/kg/day.
b) Very low birth weight (VLBW) infants (less than 1500 g birth weight: 3.0 to 3.5 g/kg/day).
2) Enteral: 3.0 to 4.3 g/kg/day; higher protein amounts for low birth weight (LBW) infants.
3) Protein requirements for VLBW infants controversial due to uncertainty related to ability to tolerate protein and what is actually needed to provide for growth and development.
a) Protein losses can be significant for VLBW infants when not receiving amino acids; ELBW infants lose 1.5 g/kg/day body protein, equaling approximately 1.5% body protein, when they should be accumulating at a rate of 2% per day; 3 days of no protein intake results in a 10% body protein deficit.
b) Early administration of amino acids compensates for potential protein losses; providing 1.5 to 2 g/kg/day as soon as possible after birth preserves body protein stores in ELBW infants even at

low caloric intake; increasing caloric intake will improve protein accretion.

c) Ultimate goal of parenteral amino acid administration is to achieve a rate of fetal protein accretion; evidence shows that 3.5 to 4.0 g/kg/day is tolerated in ELBW infants.

d) Protein and energy intakes should be determined concurrently to optimize nitrogen retention and promote proportionate body composition (lean-to-fat mass ratio) growth; protein-to-energy intake ratio recommendations for VLBW infants range from 2.25 to 3.6 g/100 kcal.

e) In addition to the eight essential amino acids necessary for cell growth, premature infants require four conditionally essential amino acids: histidine, taurine, cysteine, and tyrosine.

5. Vitamins, minerals, and trace elements (Brown et al., 2017; Greer, 2012; Hambidge and Krebs, 2017; McArdle and Georgieff, 2017).
   a. Dietary reference intakes for enteral nutrition and PN are summarized in Table 10.2.
   b. Pediatric PN and commercial premature infant formulas provide adequate amounts of most vitamins; premature infants receiving primarily human milk will require an oral multivitamin supplement (AAP Committee on Nutrition, 2014).
   c. Newborn deficiencies in fat-soluble vitamins A, D, E, and K are well described but are prevented with human milk and formulas; significant vitamin deficiency is rare even for premature infants.
      1) Vitamin K per intramuscular injection at birth; oral forms are not recommended (AAP Section on Breastfeeding, 2014).
      2) Vitamin D supplementation for breastfed or formula-fed infants until intake of vitamin D–fortified formula exceeds 500 mL/day (AAP Section on Breastfeeding, 2014).
   d. Iron supplements recommended for premature infants due to inadequate iron stores at birth and iatrogenic blood losses, unless they have received multiple blood transfusions; required with erythropoietin treatment for anemia (AAP Section on Breastfeeding, 2014; Blackburn, 2013; AAP Committee on Nutrition, 2014).
6. Electrolytes (Blackburn, 2013; Dell, 2015).
   a. Sodium, potassium, and chloride: Necessary for growth; significant role in water and acid–base balance.
   b. Premature infants, especially VLBW infants, have increased urine sodium and obligatory water loss during the transitional neonatal period.
   c. After reduction of the extracellular fluid, loss of body weight slows and urinary excretion of sodium chloride decreases. VLBW infants may require sodium supplements until renal tubular function matures.
   d. Premature infant formulas provide higher amounts of sodium, potassium, and chloride than term infant formulas; human milk from mothers of premature infants has higher sodium and chloride levels than that from mothers of term infants (after 4 weeks); may still need supplementation until renal tubular function matures.

Parenteral Nutrition (Denne, 2018; AAP Committee on Nutrition, 2014)

PN is indicated for initiation of nutritional support for premature and high-risk neonates; provides nutritional support when enteral intake is not possible or does not provide sufficient caloric requirements. The initial goal of PN is to minimize losses and preserve existing body stores and progresses to provide nutrition to promote growth and development.

A. Indications for PN in the neonatal period.
   1. Congenital and/or surgical GI disorders: Gastroschisis, tracheoesophageal fistula, malrotation, and intestinal obstruction.
   2. Short bowel syndrome.
   3. Acute GI conditions, such as NEC or intestinal perforation.
   4. Renal failure.
   5. Insufficient caloric or nitrogen (protein) content of enteral feeds.
   6. Severe respiratory or cardiac disease.

B. PN administration.
   1. Peripheral route.
      a. IV access may become problematic for prolonged PN use; however, use of peripherally inserted central catheter (PICC) lines has significantly reduced the problem. Limit dextrose concentrations to 12.5% or less to prevent irritation of small peripheral veins.
      b. Provides up to 90 kcal/kg/day with dextrose and lipid emulsions and adequate fluid intake.
   2. Central route.
      a. Prolonged dwell time for central catheters, decreases IV access problems; dextrose concentrations not restricted except by desired glucose infusion rate (GIR).
      b. Complications of central catheters: sepsis; thrombosis of large vessels; pleural or pericardial effusions due to malposition outside the vessel; hemorrhage associated with erosion of central vessels; thrombophlebitis.

c. PICCs provide prolonged venous access; inserted at the bedside with a strictly aseptic technique by qualified personnel.
d. Surgically placed central venous catheters (i.e., Broviac or Hickman) provide long-term venous access; require anesthesia; recommended for home PN use.
e. All central venous catheters require radiographic confirmation for placement before initiation of PN.

C. Guidelines for determining appropriate intake, compositions of available preparations, and guidelines for IV administration (Denne, 2018).
1. Fluid.
a. Minimum requirement approximately 100 to 150 mL/kg/day.
b. Varies with gestational age, postnatal age, and environmental conditions, such as incubator versus radiant heat source and phototherapy. Incubators decrease insensible water losses, whereas radiant warmers and phototherapy increase these losses.
2. Calories.
a. Parenteral requirements are about 20% less than enteral intake: 80 to 100 kcal/kg/day.
1) Caloric values must be adjusted to meet activity levels, body temperature, and degree of stress.
2) Activity and catabolic states can cause a 25% to 75% increase in metabolic demands.
3. Nutrients (Blackburn, 2013; Denne, 2018; Heald et al., 2012; AAP Committee on Nutrition, 2014; Morgan, 2015; Patel and Bhatia, 2017; Sinclair et al., 2011; van Goudoever and Matthews, 2017).
a. Carbohydrates: Glucose monohydrate (dextrose): 3.4 kcal/g.
1) Dextrose preparations are made according to the infant's tolerance; standard dextrose concentrations are available in 5% or 10% solutions (percentage: grams of dextrose per deciliter of solution). Other concentrations may be tailored to the individual needs of the infant.
2) Guidelines for carbohydrate administration.
a) A GIR of 8.6 to 11.5 g/kg/day (6 to 8 mg/kg/min) is the starting point; equal to endogenous production; provides for minimal caloric intake, protein metabolism, and growth; serves to preserve limited neonatal carbohydrate stores.
b) Gradual increase in GIR to 13 to 17 g/kg/day (9 to 12 mg/kg/min) over 2 to 7 days usually tolerated in the presence of amino acid administration; maintain serum glucose 45 to 120 mg/dL; maximum GIR recommended: 18 g/kg/day (12.5 mg/kg/min); higher rates exceed glucose oxidative capacity, causing extensive lipogenesis.
c) In some VLBW infants (especially those weighing <1000 g), severe hyperglycemia may present and continue despite reduced GIR; continuous insulin infusion may be used; routine use not advised because of side effects. The usual infusion of insulin is 0.01 to 0.1 unit/kg/hr to maintain blood glucose levels between 150 and 200 mg/dL.
b. Fat: 20% lipid preparations, 2 kcal/mL (Beken et al., 2014; Pawlik et al., 2014; Salama et al., 2015).
1) Two types of IV lipid preparations are currently available in the United States; intralipids composed of 100% soybean oil; Smoflipid composed of 30% soybean oil, 30% MCT oil, 25% olive oil, and 15% fish oil; Smoflipid may decrease inflammation, resulting in decreased parenteral-associated liver disease and retinopathy of prematurity.
2) Lipid emulsions of 0.5 to 1 g/kg/day prevent deficiency of essential fatty acids; should be introduced as a component of PN by 24 to 48 hours of age. Controversy exists regarding initiation dose and how quickly to advance; early intake important for cognitive development.
3) Premature infants less than 28 weeks of gestational age have limited lipoprotein lipase activity and triglyceride clearance; may require slower advances in IV lipid infusion rate to improve tolerance.
4) Although heparin releases lipoprotein lipase from the endothelium into circulation, there is no evidence that this increases lipid utilization in premature infants; therefore, routine addition of heparin into lipid infusion is not recommended.
c. Protein: Amino acids, 4 kcal/g. Recommended intake: 2.25 to 4 g/kg/day; should be started as early as possible after delivery (Osborn et al., 2018; Patel and Bhatia, 2017).
1) The smaller and less mature the infant, the higher the recommended protein intake; for example, infants weighing less than 1000 g may require 4 g/kg/day protein intake (refer to the "Nutritional Requirements, B. Premature Infants" section).
2) Pediatric amino acid solutions designed to mimic plasma amino acid concentrations in healthy 20-day-old breastfed infant (TrophAmine) or fetal or neonatal cord blood amino acid concentrations (Primine);

no evidence to support superiority of one solution over the other.

a) Glutamine, an amino acid abundant in human milk, not included in available amino acid solutions due to issues of stability.

b) Tyrosine has limited solubility, and so a small amount is included; TrophAmine contains a soluble derivative of tyrosine but appears to have poor bioavailability; current research suggests that tyrosine supply in amino acids is suboptimal for VLBW infants.

c) Cysteine is unstable for long periods; cysteine hydrochloride supplement can be added to PN just before administration; there is conflicting evidence as to whether cysteine improves protein accretion.

d. Calcium and phosphorus.

1) PN preparations for infants receiving 100 to 150 mL/kg/day should contain 50 to 60 mg/dL (12.5 to 15 mmol/L) elemental calcium and 40 to 47 mg/dL (12.5 to 15 mmol/L) phosphorus; provides 50 to 90 mg/kg/day calcium and 40 to 70 mg/kg/day phosphorus; a calcium-to-phosphorus ratio of 1.7:1 by weight (1.3:1 by molar ratio) maintains optimal bone mineralization.

2) Precipitation of calcium and phosphorus remains an issue in the United States due to commercially available solutions; not possible to supply VLBW infants with adequate amounts of parenteral calcium and phosphorus to support optimal bone mineralization.

e. Vitamins and trace elements are summarized in Tables 10.1 and 10.2.

f. Suggestions for monitoring growth and biochemical laboratory tests during PN administration are summarized in Table 10.4.

D. Complications associated with PN administration (Blackburn, 2013; Denne, 2018; Lane and Murray, 2017).

1. Increased risk of metabolic derangements (e.g., hyperglycemia, hypoglycemia, azotemia, acidosis, alkalosis) and electrolyte imbalances: Require close blood chemistry monitoring; alleviated with manipulation of PN components.

2. Cholestasis and cholestatic jaundice as a result of hepatic dysfunction: Initial intracellular and intracanalicular cholestasis is followed by portal inflammation; progressing to bile duct proliferation after several weeks of PN administration; may progress to portal fibrosis and cirrhosis. Most often resolves gradually with cessation of PN when on full enteral nutrition; rare instances of irreversible liver failure after several months of continuous PN.

a. Precise cause unknown; probably multifactorial, including lack of enteral nutrition, soy-based intralipid formulations, prematurity, prolonged use of PN, and sepsis (Lane and Murray, 2017; Patel and Bhatia, 2017; Yan et al., 2017).

b. Clinical features: Hyperbilirubinemia and jaundice.

1) Direct bilirubin (DB) level greater than 2 mg/dL (34.2 μmol/L).

2) Sensitive, nonspecific early indicator: Increase in γ-glutamyltransferase.

3) Later: Increase in aspartate transaminase (serum glutamic-oxaloacetic transaminase) and alanine transaminase (serum glutamate-pyruvate transaminase).

c. Limiting soy-based intralipid formulations and use of Smoflipid may help treat and prevent (Guthrie et al., 2017; Sorrell et al., 2017).

3. PN-induced osteopenia: Long-term PN associated with osteopenia and bone demineralization (Greer, 2012; Rehman and Narchi, 2015; Ukarapong et al., 2017).

a. Inadequate administration of calcium and phosphorous, hypercalciuria due to diuretics and glucocorticoids, prolonged PN, and prematurity.

b. Aluminum-containing PN solutions; metabolic bone disease characterized by reduced bone

Table 10.4

Suggested Monitoring Schedule for Infants Receiving Parenteral Nutrition

Parameter	SUGGESTED FREQUENCY PER WEEK	
	Initial Period*	Later Period*
Anthropometric		
Weight	7	7
Length	1	1
Head circumference	1	1
Metabolic (Blood or Plasma)		
Electrolytes	2 to 4	1
Calcium, magnesium, and phosphorus	2	1
Acid–base status	2	1
Blood urea nitrogen/creatinine	2	1
Albumin	2	1
Liver function tests	1	1
Hemoglobin/hematocrit	2	1
Prevention and Detection of Infection		
Clinical observations (e.g., activity, temperature)	Daily	Daily
White blood cell count, differential	As indicated	As indicated
Cultures	As indicated	As indicated

*Initial period refers to the time before full intake is achieved, as well as any period during which metabolic instability is present or suspected (postoperative, symptoms of sepsis). Later period refers to any time there is metabolic stability.

Adapted from Heird, W. C. (2006). Intravenous feeding. In P. J. Thureen and W. W. Hay (Eds.), *Neonatal nutrition and metabolism* (2nd ed.). New York, NY: Cambridge University Press.

formation and aluminum accumulation in bone correlating with decreased bone formation.
   c. Decreased mineral retention; inappropriate mineral ratio; suboptimal minerals in PN during periods of rapid growth rate.
   d. Vitamin D deficiency rare in infants receiving PN containing pediatric IV vitamins; does not contribute to PN-related metabolic bone disease.
4. Sepsis: Infection is a complication of PN; incidence higher in VLBW infants; increases with longer PN duration; related to both PN administration and central venous access.
   a. Two most common bacterial pathogens: *Staphylococcus epidermidis* and *S. aureus*.
   b. Two most common fungal pathogens: *Candida albicans* and *Malassezia furfur*.
5. Measures to prevent or minimize complications associated with PN.
   a. Standardized procedures/policies to facilitate consistent methods to prevent and/or minimize complications.
   b. Record intake and assess IV insertion site hourly.
   c. Readjust fluid volume, dextrose concentration, protein and/or fat intake, electrolytes, and minerals as needed in response to blood chemistry results.
   d. Initiate enteral feedings as soon as possible.
   e. Pharmacy preparation of PN under laminar airflow hood; nothing should be added to PN solution once it leaves the pharmacy; filter central PN with an inline filter.
   f. Wash hands scrupulously before handling any PN tubing or IV sites; use sterile techniques for dressing changes.

Enteral Feedings: Human Milk and Commercial Formulas for Term, Special-Needs, and Premature Infants

A. Comparison of human milk, donor milk, and commercial infant formulas (AAP Section on Breastfeeding, 2014; AAP Section on Breastfeeding, 2017; Bhatia and Greer, 2008; Blackburn, 2013; Cortez et al., 2018; AAP Committee on Nutrition, 2014; Le Doare et al., 2018; Moro et al., 2015; Radmacher and Adamkin, 2017; Tudehope, 2013).
   1. Human milk: Contains host resistance factors and antimicrobial properties (e.g., lactoferrin, lysozyme, and secretory immunoglobulin A [IgA]), hormones (e.g., cortisol, somatomedin-C, insulin-like growth factors, insulin, thyroid hormone), growth factors (e.g., epidermal and nerve growth factors), and protective bacteria; increased bioavailability of fat, amino acid, and carbohydrate with enhanced absorption, digestion, gastric motility, and gastric emptying; very-long-chain fatty acids (may be important for cognition, growth, and vision); increased absorption of zinc and iron; low renal solute load; optimal distribution of calories (7% protein, 55% fat, 38% carbohydrate); provides variability in nutrient content between feeds and/or time of day, which may enhance sensory development and acceptance of new flavors and foods later. A comparison of term and premature human milk is summarized in Table 10.5.
      a. Contraindications to human milk consumption: Relatively few true contraindications exist.
         1) Galactosemia; cannot ingest lactose-containing milk (e.g., human milk and commercial bovine milk–based formulas).
         2) Human immunodeficiency virus (HIV): In the United States, counseled regarding risks to infant of breastfeeding, recommend not breastfeeding. Globally, health risks of the infant need to be balanced against the risk of acquiring HIV.
         3) Human T-cell lymphotropic virus: No breastfeeding.
         4) Miliary tuberculosis: No breastfeeding while contagious (needs documentation, generally approximately 2 weeks).

Table 10.5

Composition of Premature and Mature Human Milk

Component	Premature Human Milk (1 Week)	Mature Human Milk (1 Month)
Volume (mL)	100	100
Energy (kcal)	67	70
Protein (g)	2.4	1.8
% Whey/casein	70/30	70/30
Fat (g)	3.8	4
% MCTs/LCTs	2/98	2/98
Carbohydrate (g)	6.1	7
% Lactose	100	100
Calcium (mg)	25	22
Phosphorus (mg)	14	14
Magnesium (mg)	3.1	2.5
Sodium (mg)	50	30
Potassium (mg)	70	60
Chloride (mg)	90	60
Zinc (mcg)	500	320
Copper (mcg)	80	60
Vitamin A (IU)	560	400
Vitamin D (IU)	4	4
Vitamin E (mg)	1	0.3
Vitamin C (mg)	5.4	5.6

LCTs, Long-chain triglycerides; *MCTs*, medium-chain triglycerides.

Adapted from Blackburn, S. T. (2013). *Maternal, fetal, & neonatal physiology: A clinical perspective* (4th ed.). St. Louis, MO: Saunders.

5) Herpetic lesions: No breastfeeding if localized to breast; vaginal herpetic lesions not a barrier to breastfeeding.
6) Varicella lesions on breast: Provide expressed human milk until completely crusted over; infant should receive varicella immune globulin.
7) Breast cancer; treatment should not be delayed; no breastfeeding with antimetabolite chemotherapy.
8) Maternal use of prescription and/or over-the-counter medications; direct contraindications for breastfeeding include cytotoxic drugs; some drugs have strong associations with adverse effects in infants; extra caution is needed with premature infants; LactMed (published by the National Institutes of Health) provides information on the safety of certain drugs during breastfeeding: https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm.
9) Illicit drug abuse: Recommend counseling; no breastfeeding until free of abused drug(s); stable mothers in opioid treatment programs may breastfeed (Reece-Stremtan and Marinelli, 2015).

2. Commercial infant formulas for term infants are bovine milk or soy based; available in powder, concentrate, and ready-to-feed forms; all should be iron fortified. Both types support adequate weight gain for term infants.
   a. Bovine milk–based formulas recommended except for infants with galactosemia, primary lactase deficiency, IgE-mediated reaction to bovine milk–based formulas, or parents seeking a vegan-based diet for term infant.
   b. Extensively hydrolyzed protein formula should be considered for infants with documented bovine milk protein allergy; 10% to 14% of these infants also have a soy protein allergy.
   c. Soy-based formulas are not recommended for premature infants.

B. Term infants (AAP Section on Breastfeeding, 2014; Bhatia and Greer, 2008).
1. Human milk is the ideal food for term infants. Exclusive breastfeeding should be encouraged for the first 6 months of life, at which time complementary foods are introduced; breastfeeding should be encouraged for at least the first year of the infant's life and beyond for as long as mutually desired by mother and child.
2. Commercial term infant formulas used primarily when breastfeeding is contraindicated, as a supplement to breastfeeding during inadequate human milk supply or poor infant growth, or maternal preference not to breastfeed.

C. Infants with special nutritional requirements.
1. Infants with inborn errors of metabolism (IEM); also referred to as *inherited metabolic disorders*; disorders resulting from genetically inherited disruption of enzymatic activities that occur in normal metabolic processes (Saudubray and Garcia-Cazorla, 2018).
   a. Nutrition plays an important role in the management of treatable IEM disorders; modification of diet can alter biochemical imbalances to improve mental and physical development.
   b. Goals for nutritional support: Provide all essential nutrients and supply the optimal amount of any nutrient that is restricted as a result of IEM to promote growth and correct metabolic imbalances.
   c. Management depends on the specific biochemistry and pathophysiology of the diagnosed IEM; includes restriction of any compound or precursor of metabolites that could accumulate as a result of the missing or defective enzyme(s) and/or supplement deficient end products and cofactors not produced as a result of the missing or defective enzyme(s).
   d. Premature infants have the same risk for IEM as term infants; may not be suspected because symptoms resemble more common problems expected in premature infants; diagnostic tests may be altered by common treatments (e.g., early blood transfusions producing false-negative newborn screen testing for galactosemia).
   e. Examples of IEM with dietary restrictions and/or supplements requiring special formula compositions.
      1) Phenylketonuria: Restriction of the amino acid phenylalanine; supplement with tyrosine.
      2) Maple syrup urine disease: Restriction of branched-chain amino acids; supplement with valine and isoleucine.
      3) Galactosemia: Restriction of galactose/lactose; supplement with calcium.
      4) Glycogen storage disease, type I (glucose-6-phosphatase deficiency): Restriction of galactose/fructose; modified fat and moderate protein; frequent feedings, nocturnal continuous feedings; cornstarch in feedings.
      5) Urea cycle disorders: Low-protein diet with nonessential amino acid restriction; supplement with carnitine, biotin, folate, and pyridoxine.
2. Infants with altered fluid and/or caloric intake requirements.
   a. Bronchopulmonary disease (BPD): May have increased metabolic demands, respiratory workload, oxygen consumption; energy needs may increase by 20% to 40% above that of healthy

infants. Postnatal growth failure is common, extends beyond early neonatal life for several years. Multifactorial causes of feeding difficulties related to fluid restriction, long-term PN, oral feeding intolerance, and GER; recover more quickly if given adequate caloric intake (Blackburn, 2013; Dani and Poggi, 2012; Lista et al., 2017; McCain et al., 2012; Park et al., 2015).

1) Relative fluid restriction may be necessary to reduce pulmonary edema, which may complicate the pathology of BPD.
2) Infants with BPD may have higher caloric requirements to meet the demands of healing tissue and growth requirements.
3) May benefit from specially developed nutritional products to allow for fluid restriction and support optimal growth, including increased calorie-dense formula and/or fortified human milk mixtures.
4) May require special approaches to transition from gavage feeds to bottle or breast feeds in accordance with feeding readiness cues, ability to regulate frequency, duration of feed, and volume tolerated per feed based on respiratory and energy status.

b. Cardiac problems: Poor growth may result from increased metabolic demands, higher metabolic rate and oxygen consumption secondary to increased cardiac and respiratory workload; tissue hypoxia, protein loss, increased associated frequency of infections, and decreased nutrient absorption due to diminished GI blood flow; may be fluid and sodium restricted to reduce overcirculation; infant may easily fatigue and become tachypneic and stressed with oral feeding (Blackburn, 2013; Ehrmann et al., 2018; Karpen, 2016).

1) Caloric requirements to improve growth may be met with increased caloric density and/or increased protein content of formula and/or human milk.
2) Often described as having poor oral skills, give fewer feeding readiness cues, and are less responsive to caregivers during feeds.
3) Formula and/or human milk may be fortified to meet higher caloric needs while not exceeding possible fluid restriction.
4) Osmolarity of formulas and human milk mixtures increases by approximately the same percentage as the caloric increase; strict attention must be paid to the renal solute load and osmolarity when concentrating formulas and adding calories to human milk beyond 24 cal/oz.

3. Infants with short bowel syndrome: Intestinal length (normal small bowel length not clearly established; estimated 250 to 270 cm at term) reduced because of surgical resection resulting from congenital anomaly (e.g., gastroschisis, midgut volvulus, intestinal atresias) or NEC; results in reduction of the intestinal absorptive surface area; remaining sections of bowel may have been ischemic, resulting in villous atrophy; full enteral feedings might be achieved if at least 15 cm of the small bowel with ileocecal valve or 40 cm without ileocecal valve remains after surgical resection (Blackburn, 2013; Mayer and Kerner, 2017).

a. Depending on the length of the intestine, may need PN for prolonged period until enteral feeds are tolerated and linear growth occurs.
b. Slow initiation of enteral feedings, similar to minimal feeding regimen of premature infants, may be beneficial.

D. Premature infants.

1. Human milk from mothers of premature infants contains slightly higher concentrations of protein, sodium, and chloride; more lipid, energy, vitamins, and trace elements; lower concentrations of phosphorus and calcium; and has lower osmolality than human milk from mothers of term infants; differences decline as lactation progresses, becoming similar in composition between 2 and 4 weeks. A comparison of premature and mature human milk is summarized in Table 10.5 (Blackburn, 2013; Radmacher and Adamkin, 2017).

a. The significant benefits of mother's milk for premature infants warrant encouraging and actively supporting mothers to pump and provide milk for their infants (Meier et al., 2017).

1) Importance of mother's milk for premature infants should be discussed during the first visit with parents; counseling as early as possible (best accomplished before delivery) increases the likelihood that mothers will initiate lactation without increasing maternal stress and/or anxiety.
2) Important to begin expressing mother's milk as early as possible after delivery; initiation before 1 hour or, at the latest, 6 hours after delivery improves lactation success (Parker et al., 2012).
3) Initial volume may be few drops of colostrum for the first 24 to 48 hours postpartum; may have considerable delay before substantial production begins; delays are often seen in mothers delivering premature infants.
4) Encourage expressing milk at least 8 times in 24 hours; break in frequency while establishing milk supply may seriously compromise potential of maximum production.
5) Goal of 500 to 750 mL/day by day 10 to 14; milk production typically plateaus by 14 days postpartum.

6) Once milk production is established, it can be maintained with at least 6 pumps per day; needs to be monitored for ongoing success.
7) Optimal milk expression technique includes the following:
   a) Supportive environment for mother.
   b) Regular breast massage with good technique.
   c) Simultaneous pumping of both breasts with high-quality breast pump and properly fitting milk expression shield.
   d) The use of hand expression (massage and compression of the breasts) may increase milk production in the first few days after delivery.
8) Donor human milk: Recommended for use in VLBW infants when mother's own milk is not available; procurement recommended from human milk banks for safe use; differs from individual mother's mature human milk in nutrient content and energy value; pasteurizing recommended to decrease transmission of HIV, cytomegalovirus, hepatitis B and C; pasteurizing reduces secretory IgA, lactoferrin, lysozyme, insulin-like growth factors, hepatocyte growth factor, water-soluble vitamins, bile salt–stimulated lipase, lipoprotein lipase, and antioxidant activity and good bacteria; does not decrease oligosaccharides, long-chain polyunsaturated fatty acids, gangliosides, lactose, fat-soluble vitamins, or epidermal growth factor; may negatively affect growth (Ng et al., 2017; Radmacher and Adamkin, 2017).

b. Storage, handling of human milk: needs to be collected, processed, and stored to ensure microbiological safety and nutrition quality (AAP Section on Breastfeeding, 2014; Eglash and Simon, 2017).
   1) Wash hands with soap and warm water.
   2) Collection kits should be rinsed, cleaned with hot soapy water, and air-dried.
   3) Freeze milk that is not to be used within 48 hours; single milk expressions in each container, labeled with name, date, and time of pumping; keeps from 3 to 6 months in the rear of freezer compartment.
      a) Freezing preserves many of the nutritional and immunologic benefits of human milk.
      b) Thaw completely with tepid running (not hot) water or commercial human milk thawing machine; never thaw or warm in microwave oven; once thawed, do not refreeze; use completely within 24 hours refrigerated at 4° C; recent evidence suggests human milk may be stored at 4° C in refrigerator for up to 96 hours with minimal change in macronutrients, IgA, lactoferrin, total fat and protein, and no increase in bacterial count.
   2. Human milk fortifiers are needed for growth and nutrient retention; provide additional protein, fat, carbohydrate, sodium, potassium, phosphorus, and calcium; 4 packets added to 100 mL human milk averages 24 cal/oz, 2.7 g protein, 4.5 g fat, and 7.5 g carbohydrate; powdered forms not recommended for use due to risk of contamination (AAP Section on Breastfeeding, 2014; Blackburn, 2013; Radmacher and Adamkin, 2017; Schanler, 2015).
   3. Human milk–based formulas are derived from pooled donated human milk; available in a variety of products, which increase calories and provide additional electrolytes and minerals; may decrease risk of NEC (Hair et al., 2016).
   4. Commercial premature infant formulas, 24 cal/oz, have increased amounts of protein, carbohydrate, fat, sodium, potassium, calcium, and phosphorus; supply these nutrients within acceptable ratios similar to human milk with added human milk fortifier; formulas with increased calories (27 and 30 cal/oz) and increased protein content are also available (Blackburn, 2013; AAP Committee on Nutrition, 2014).
   5. Transitional premature infant formulas provide 22 cal/oz and more calcium, phosphorus, and magnesium than term infant formulas but less than premature infant formulas, and are designed for use after hospital discharge; studies vary as to how long to continue using the transitional formulas (Blackburn, 2013; AAP Committee on Nutrition, 2014; Lapillonne and Griffin, 2013; Natarajan et al., 2014; Young et al., 2016).

Enteral Feeding Methods

Enteral feedings are achieved via several routes, including nasogastric, orogastric, transpyloric, and gastrostomy tubes, as well as orally by bottle or breast. Decisions regarding enteral feeding are dependent on gestational age, birth weight, and clinical condition of the infant. When to initiate feeding, type of feeding, method of delivery, feeding frequency, concentration of feeding, and rate of advancement may vary according to unit practices (Blackburn, 2013; AAP Committee on Nutrition, 2014).

A. Minimal enteral nutrition or trophic feeding (Blackburn, 2013; AAP Committee on Nutrition, 2014; Salas et al., 2017; Ziegler, 2011).
   1. Have benefit without adverse consequences for most VLBW infants.
   2. Defined as ≤24 mL/kg/day of human milk or premature infant formula.

3. Not intended for primary source of nutrition.
4. Given concurrently with PN as primary nutrition.
5. Intended to provide physiologic effects, including stimulating and maintaining digestive–absorptive, immunologic, and neuroendocrine functions of the GI tract.
   a. Promotion of gut mucosal development.
   b. Stimulation of intestinal motor activity.
   c. Increased secretion of GI hormones and peptides.
   d. Colonization of the gut with normal flora, limiting colonization by other pathogenic organisms, helps development of the innate immune system of the GI tract.
6. Does not increase the incidence of NEC.
7. Dilute formula or human milk or sterile water does not stimulate GI motor activity as well as full-strength formula or human milk.
8. Recommended initiation within 48 hours after birth; length of minimal enteral nutrition: 1 to 5 days; more than 3 days provides no additional benefit and increases times to reach full feedings (Salas et al., 2017; Ziegler, 2011).

B. Initiation of feedings, advancing feeds, and feeding tolerance/intolerance in VLBW infants (Blackburn, 2013; Gomella, 2013; AAP Committee on Nutrition, 2014; Louis et al., 2016; Malhotra et al., 2016; Naberhuis et al., 2016; Oddie et al., 2017).
   1. Perceived contraindications for initiating and/or continuing feeds: Hypoxic–ischemic insults at birth, apnea and/or bradycardia, sepsis, umbilical arterial catheters, indomethacin administration, patent ductus arteriosus (PDA), and inotropic agents (dopamine); but little evidence exists regarding benefits to delaying or not advancing feedings.
   2. No evidence that advancing enteral feedings 30 to 40 mL/kg/day versus 15 to 20 mL/kg/day is associated with increased incidence of NEC (Oddie et al., 2017).
   3. Assessing for feeding tolerance/intolerance: Feeding intolerance has no uniform definition; in premature infants it refers to not digesting formula or human milk rather than intolerance to the carbohydrate source of formulas (e.g., lactose intolerance). Manifestations of intolerance vary, based on pre-feed gastric residual volume, color, and associated clinical manifestations such as abdominal distention, emesis, and/or presence of frank/occult blood in stools, apnea, and bradycardia.
      a. Gastric aspirates; pre-feed gastric residuals.
         1) Fasting basal gastric residuals average 3 mL every 4 hours in infants of 28 to 36 weeks of gestational age; more than 2 mL in less than 760-g infants and 3 mL in greater than 750-g infants; volume of greater than 50% of the milk given during previous feedings may be abnormal and requires more extensive evaluation.
         2) Routine evaluation of pre-feed gastric residuals may not be indicated unless other symptoms of feeding intolerance are present (Torrazza et al., 2014).
         3) Bile-stained aspirate may not be sufficient reason to withhold feeds; may be due to immature gut motility, leading to periodic antiperistalsis.
         4) Determination of significance of gastric aspirate may need to rely on what volume is reasonably expected at the infant's gestational age, or what is "normal" for an individual infant, and the presence of clinical manifestations.
         5) Clinical manifestations: Abdominal distention, emesis, blood in stools, apnea, and bradycardia.
            a) Abdominal distention: Visual examination for visible bowel loops, erythema, auscultate for bowel tones, palpate to assess whether soft, firm, and for tenderness; ascertain when last stool occurred.
            b) Emesis: May result from decreased LES tone or increased abdominal pressure resulting from NEC, obstruction, or undigested formula or human milk.
            c) Blood in stools: Can be due to trauma from nasogastric tube; swallowed maternal blood (if soon after delivery); bleeding disorder (such as vitamin K deficiency, disseminated intravascular coagulation, congenital coagulopathy); stress ulcer; severe fetal asphyxia; NEC; medications (such as indomethacin, corticosteroids).
            d) Apnea and bradycardia: Generalized response to change in condition, sepsis, NEC.

C. Nasogastric and orogastric tube feeding (Blackburn, 2013; Gomella, 2013; AAP Committee on Nutrition, 2014).
   1. Most commonly used method in the neonatal intensive care unit (NICU); used for very premature or critically ill infants who are unable to coordinate a suck–swallow–breath feeding pattern to reduce risk of aspiration and to conserve energy.
   2. Procedure for gastric (nasal or oral) insertion.
      a. Gather equipment: Infant feeding tube, sterile water (lubricant), syringe (5 to 10 mL), transparent dressing, gloves, suctioning equipment.
      b. Monitor heart rate and respiratory function throughout the procedure.
      c. Place infant supine; head of bed may be elevated.
      d. Choose size of gastric tube: General guideline—for infants less than 1000 g, No. 5 French gastric tube; ≥1000 g, No. 6 to 8 French gastric tube.
      e. Determine the length of tubing required to reach the stomach: Measure the distance from

the nose to the earlobe to the mid-umbilicus; mark the tube at the appropriate length (Cirgin-Ellett et al., 2011).

f. Moisten the tip of the tube with sterile water and insert via mouth or nare.
   1) Oral insertion: Push the tongue down and insert the tube into the oropharynx; advance as tolerated to desired length. The oral route is preferable because neonates are obligate nose breathers, and use of the nasal route may increase airway resistance.
   2) Nasal insertion: Flex neck, push nose up, insert the tube straight back into the nares, and advance as tolerated to desired length.

g. Verify correct positioning in the stomach.
   1) Aspirate contents from the tube with a syringe; assess color and consistency of aspirate to determine whether the aspirate is consistent with gastric contents; repositioning and reaspiration may be necessary if no aspirate is obtained.
   2) Auscultation for a whoosh after injecting a small amount of air into the tube is not recommended for verification of gastric feeding tube placement.
   3) Definitive verification of tube placement is with chest/abdominal radiographic imaging.

h. Complications.
   1) Apnea and bradycardia: Due to vagal response; usually resolves without specific treatment beyond stimulation.
   2) Hypoxia: Resolves with correction of apnea and bradycardia response; may require oxygen to resolve; if severe, may need positive pressure ventilation with bag and mask. If this continues, suspect misplacement of tube into the trachea and remove the tube immediately.
   3) Perforation of the esophagus, posterior pharynx, stomach, or duodenum is a rare complication; the tube should never be forced during the insertion procedure.
   4) Aspiration: Complication of misplacement into the trachea, esophagus, or hypopharynx; results from stomach distention or failure of feeding to continue through the GI tract. Verify position of tube and the presence of residuals before every bolus feeding or periodically with continuous feeding infusion.

3. Feeding may be accomplished by bolus or continuous infusion of human milk or formula (Blackburn, 2013; Gomella, 2013; AAP Committee on Nutrition, 2014; Premji and Chessell, 2011; Rovekamp-Abels et al., 2015).
   a. Bolus feeds every 2 to 3 hours is similar to feeding pattern when bottle- or breast-feeding; may be associated with improved nutrient absorption.
   b. Continuous infusions do not increase feeding intolerance or growth in premature infants; may be considered necessary with early feeding initiation; should transition to bolus feeds as tolerated. Human milk fat and MCT additives adhere to feeding tube surfaces, and nutrient loss from human milk fortifiers further reduces nutrient intake and energy density provided by continuous enteral tube feeding.

D. Transpyloric and gastrostomy tube feeding (Blackburn, 2013; Gomella, 2013; AAP Committee on Nutrition, 2014; Premji and Chessell, 2011).
   1. Transpyloric tube feeding bypasses the stomach and reduces the digestive capability of the GI tract.
      a. Feeds can only be by continuous infusion; placement is confirmed with radiographic imaging.
      b. Associated with significant risks: Abdominal distention, gastric bleeding, bilious vomiting, and mortality.
      c. Does not improve energy intake or growth.
      d. Should be used only in rare instances of prolonged gastroparesis or dysmotility.
      e. Gastric feedings should be resumed as soon as possible.
   2. Gastrostomy tube feeding is via a tube surgically placed through the abdominal wall directly into the stomach; can be bolus or continuous infusion; used primarily for infants unable to sustain full oral feeds or maintain sufficient caloric intake to promote growth, such as abnormal neurologic status, congenital anomalies of the GI tract (e.g., esophageal atresia), or other conditions requiring long-term gavage feedings.

E. **Oral feeding, breast or bottle:** Often a criteria for discharge; determined by the infant's ability to coordinate a suck–swallow–breathe pattern, sustain an alert–awake behavior, and maintain cardiorespiratory stability; premature infants are limited by weak flexor control and immature musculature (AAP, 2008; Blackburn, 2013; McCain et al., 2012).
   1. Oral feeding readiness.
      a. Infant should be free of signs and/or symptoms of respiratory distress (e.g., respiratory rate <60 breaths per minute; blood gas values within normal limits); criteria may be modified for infants with BPD or congenital heart disease.
      b. Infant demonstrates suck–swallow–breathe coordination with an intact gag reflex.
         1) Swallow reflex is well developed by 28 to 30 weeks, easily exhausted; matures by 34 weeks.
         2) Gag reflex matures by 34 weeks.
         3) Suck maturation related to gestational, not postnatal, age; nonnutritive suck present at less than 32 to 33 weeks of gestation; nutritive suck appears by 32 to 33 weeks; matures by 37 weeks of gestation.

4) Suck–swallow reflexes are present by 28 weeks; synchrony of suck–swallow appears by 32 to 34 weeks; complete coordination develops by 36 to 37 weeks of gestation.

2. Oral feeding initiation: Major goal of nurses and families: Assist premature infants to develop safe and effective early oral feeding skills, improve breastfeeding outcomes.
   a. Healthy infants ≥34 weeks of gestation may have oral feedings initiated as soon after birth as indicated. Factors to be considered include infant behavior and stability and maternal preference for breastfeeding or bottle-feeding (Blackburn, 2013).
   b. Transition from gastric tube feeding to oral feeding (breast or bottle) may be dependent on infant behavior and stability, unit-specific feeding policy, and/or gestational age criteria (Lucas and Smith, 2015).
      1) Cue-based feeding associated with an earlier transition to full oral infant feedings, improved feeding performance, increased infant stress, and decreased length of stay (Dalgleish et al., 2016; Ludwig and Waitzman, 2007; Wellington and Perlman, 2015).
      2) Careful monitoring is essential during feedings to ensure safe intake without complications of aspiration, desaturation (or increased requirement for fractional inspired oxygen), apnea, and bradycardia; may occur less frequently during breastfeeding than bottle-feeding.
   c. Infants at risk for oral feeding problems include infants with moderate to severe BPD, neurologic disorders including hypoxic ischemic encephalopathy, seizure, congenital heart defect (CHD), and an abnormal airway; may benefit from early occupational or speech therapy; may require outpatient therapy; gastric tube placement may be necessary (Jadcherla, 2016; Steltzer et al., 2016; Tregay et al., 2017).
   d. VLBW infants are often referred for treatment of significant, persistent feeding problems after discharge; during hospitalization, provide positive feeding experiences and identify feeding problems at an early stage when most amenable to change.

Nursing Interventions to Facilitate Tolerance of Enteral Feedings

A. Sensory–motor–oral stimulation and nonnutritive sucking provided during gavage feedings (Foster et al., 2016; Kaya and Aytekin, 2017; Lucas and Smith, 2015).
   1. Promotes earlier oral feeding and earlier attainment of full oral feeds and decreases length of stay.
   2. Promotes earlier transition to full breastfeeding.
   3. May enhance sucking patterns and coordination.
   4. Associated with no negative outcomes.

B. Colostrum oral care (Rodriguez et al., 2010; Rodriguez et al., 2015; Sohn et al., 2016).
   1. Administration of small amounts of mother's own milk or colostrum into the buccal cavity of infants.
   2. May improve growth, decrease length of stay, and decreased infections.

C. Assessment of infant readiness.
   1. Defined in terms of readiness for both initiation of oral feedings and for identification of specific feeding times.
   2. May enhance oral feeding initiation and success.
   3. May promote feeding performance and decreased stress.
   4. May promote successful breastfeeding of premature infants.
      a. Premature infants may be able to breast-feed successfully as early as 32 weeks of gestation and may establish a mature suck–swallow–breathe coordination earlier with breastfeeding than with bottle-feeding.
      b. Test-weighing of infants (before and after breastfeeding) with an electronic scale is a reliable method of determining infant intake of human milk from the breast (Rankin et al., 2016).

D. Position of infant during and after feedings (Corvaglia et al., 2007; Elser, 2012).
   1. Kangaroo care (skin-to-skin positioning of infant on mother's chest) during gavage feeding may increase breast milk production and improve lactation success.
   2. Prone or left lateral positions are associated with fewer GER-like episodes and improved gastric emptying.

Nutritional Assessment and Standards for Adequate Growth

Nutritional management is meant to improve growth and minimize harm; requires nutritional assessment tools to provide for growth in an efficacious and safe manner (Bhatia, 2013; Blackburn, 2013; Fenton and Kim, 2013; Goldberg et al., 2018; Gomella, 2013; AAP Committee on Nutrition, 2014; Olsen et al., 2010; Rehman and Narchi, 2015; Weintraub et al., 2015).

A. Nutritional intake: Ascertain whether the prescribed nutritional intake is provided.
   1. Monitor volume and caloric intakes daily: Follow current recommended intakes for gestational age and condition of infant; adjust intake accordingly to maintain nutritional goals.
   2. Periodically review all dietary intakes from birth; early and sufficient nutrition has a profound impact on long-term growth and development.

B. Laboratory assessment: Serves a key role in the assessment of nutritional adequacy and toxicity.
   1. Electrolytes, sodium (Na^+), potassium (K^+), chloride (Cl^-), bicarbonate ($NaCO_3^-$).
      a. Provide information on renal function and fluid status.
      b. Results need to be assessed in relation to an infant's fluid status (intake and output), condition, and previous trends in electrolyte results.
   2. Blood urea nitrogen (BUN) and creatinine (Cr).
      a. BUN may not be a good indicator of protein intake and/or tolerance in the first weeks of life for VLBW infants; should not be considered a biochemical marker during this period; reflects more the fluid status.
      b. BUN level has improved validity for protein intake and tolerance with serial levels in stable, older VLBW infants who are receiving enteral nutrition, if taken into consideration with glomerular filtration rate (GFR) and renal function indicators (Cr level) and anthropometric growth parameters.
      c. Cr and Cr clearance are valid biochemical markers for renal function assessment for VLBW infants.
   3. Calcium (Ca^+), magnesium (Mg^+), phosphorus (PO_4^-), and alkaline phosphatase (alk phos).
      a. Followed for management and surveillance of metabolic bone disease and assessment of bone mineralization status. Decreased calcium and phosphorus levels or increased alkaline phosphatase levels may indicate bone demineralization; alkaline phosphatase levels greater than 500 to 700 mg/dL or radiologic evidence of rickets indicates need for increased calcium and phosphorus intake. Hypophosphatemia (serum concentration <4 mg/dL) considered an early indicator of decreased bone mineralization.
      b. Calcium levels may remain within the normal range, preserved at the expense of bone calcium stores; serum alkaline phosphatase level is a more direct method to assess increased bone turnover.
      c. Medications that have a negative effect on calcium and phosphorus stores: furosemide, caffeine citrate, and glucocorticosteroids.

C. Anthropometric measurements.
   1. Daily approximate weight gains with recommended caloric intake.
      a. 24 to 32 weeks: 15 to 20 g/kg/day.
      b. 33 to 36 weeks: 14 to 15 g/kg/day.
      c. 37 to 40 weeks: 7 to 9 g/kg/day.
      d. 40 weeks to 3 months: 30 g/day.
   2. Weekly length and head circumference measurements. Although it is common to discuss growth expectations of VLBW infants in terms of weight gain, gains in head circumference and lengths are just as important to determine optimal growth. Head circumference has a close relationship with the growth of brain volume. Length in comparison with weight gives good indication of body composition if accurately measured (Goldberg et al., 2018; Schneider et al., 2018).
      a. Length measurement.
         1) Typically crown to heel of naked infant.
         2) For accurate measurement, two people perform the procedure with a length board specific for premature infants (e.g., Premie Length Board [O'Leary, Ellard Instrumentation, Seattle, WA]); one person holds the head in place against the board top, and another provides gentle straightening of the body and lower extremities with one hand while pushing the moveable footrest into place with the other hand; average of two to three measurements.
         3) Average gain in length from 24 to 40 weeks of gestation: 0.69 to 0.75 cm/wk.
      b. Head circumference, also known as *occipital–frontal circumference*.
         1) Determined by applying a paper or plasticized paper measurement tape firmly around the head above the supraorbital ridges, over the most prominent part of the frontal bulge anteriorly, and the part of the occiput that gives the maximum circumference; average of two to three measurements.
         2) Average gain in head circumference from 24 to 40 weeks of gestation: 0.1 to 0.6 cm/wk.
   3. Plot weight, head circumference, and length on growth chart weekly.

D. Growth charts (AAP Committee on Nutrition, 2014).
   1. Term infant growth charts include incremental growth curves and percentiles of weight, length, and head circumference; developed by the National Center for Health Statistics and the National Center for Chronic Disease Prevention and Health Promotion; available at http://www.cdc.gov/growthcharts.
   2. Premature infant growth charts include incremental growth curves and percentiles of weight, length, and head circumference (Blackburn, 2013; Fenton and Kim, 2013; Olsen et al., 2010).
      a. Adequate growth to genetic potential for premature infants implies lean mass accumulation, brain volume development, and somatic growth to maintain body composition comparable to that of a fetus of similar gestational age.
      b. Typical growth curve charts with weight, length, and head circumference used in the NICU to establish growth patterns and are based upon fetal and newborn growth and, less frequently, on the growth of former VLBW infants.

3. Postnatal growth curves for premature infants based on actual growth of premature infants.
   a. Postnatal growth curves reflect a slower growth velocity than is seen with growth curves based on intrauterine and newborn growth curves.
   b. Postnatal growth restriction is associated with a poorer neurologic outcome (Schneider et al., 2018; Stoll et al., 2010).

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CHAPTER 11
Developmental Support

Carol Turnage Spruill

OBJECTIVES

1. Assess physiologic and behavioral organization of preterm and ill newborn infants using the neurobehavioral subsystems from Als's Synactive Framework.
2. Design a developmental care plan that respects and supports each infant's unique needs as related to the environment, direct caregiving, parent support, and consistency of care.
3. Engage parents in active participation in their infant's plan of care.

Individualized developmentally supportive care (IDSC) is based on a philosophy of respect for the unique needs of preterm and high-risk infants susceptible to neurodevelopmental disadvantage in part due to the complex, atypical environment of the neonatal intensive care unit (NICU) and separation from the nurturing of parents (Fig. 11.1). Family-centered IDSC promotes a culture that supports family adaptation and involvement so that parents can be parents to their recovering infant.

Preterm infants are especially vulnerable to cognitive, neuromotor, and neurosensory problems after discharge from the NICU. Fluctuations in cerebral circulation have been demonstrated in routine care procedures, and smaller-than-expected brain volumes at 36 to 40 weeks may play a significant role in increased morbidity in these infants. Altered cerebral oxygenation and blood volume measured with near-infrared spectroscopy have been exhibited during diaper changes, endotracheal tube suctioning, repositioning, physical examination, and nasogastric tube insertion (Limperopoulos et al., 2008). These brain changes are associated with early parenchymal abnormalities.

Threats to Development

A. The perinatal period is a critical time for central nervous system development. Internal and external signals are important in forming and joining neural connections that are sensitive to fetal and neonatal compromise. Some threats to neurodevelopment are:
   1. Neuroinflammation: infections, both maternal and neonatal and hypoxia–ischemia, are believed to affect synaptic organization and function (Mottahedin et al., 2017).
   2. Prenatal stress: significantly fewer connections between the amygdala and the thalamus, hypothalamus, and brainstem in very preterm and extremely preterm infants place them at high risk for autism spectrum disorder and socioemotional problems (Scheinost et al., 2016).
   3. Prematurity: degree of prematurity is related to intraventricular hemorrhage (IVH) and key brain connectivity of the thalamus, cerebellum, superior frontal lobe, and other areas altering the structure of the brain network; affect executive function, memory, attention, information processing, reaction inhibition, and emotional regulation (Batalle et al., 2017).
   4. Microbiome: intestinal microbiota indirectly harms the brain by transmitting stress signals triggered by immune–microbial disruption in the gut to alter neurodevelopment (Sherman et al., 2015).
   5. Postnatal stress: environmental factors, like living in the NICU, are thought to affect genetic expression and influence the preterm infant's phenotype or their observable attributes such as behaviors.
      a. Early adversity in the life of the preterm infant includes unpleasant experiences, pain from procedures, maternal separation, early exposure to light/noise, medications, and modified nutrition that, through epigenetic mechanisms, changes an individual's developmental path (Fig. 11.2).
      b. Early life adversity and the epigenetic impact result in alterations to hypothalamic–pituitary–adrenal (HPA) axis function, thereby modifying the regulation of stress and subsequent behavioral responses (Fig. 11.3). The interaction

Fig. 11.1 High-risk infant in NICU environment. *(Courtesy Texas Children's Hospital, Houston, TX; photographer Carol Turnage Spruill.)*

between genes and the environment is bidirectional so that positive, nurturing experiences may reverse the effects of adverse early experiences when provided during sensitive and critical periods of development. Staff in caregiving environments like NICUs protect against epigenetic factors by creating opportunities for parental nurturing (e.g., skin-to-skin holding). The knowledge that early life experiences influence the genetic expression of infants in NICUs supports the advancement of evidence-based, age-appropriate care for optimal outcomes now and in the future (Coughlin, 2017; Provenzi et al., 2018b; Tammen et al., 2013).

B. Adverse neurodevelopmental outcomes in extremely premature infants ≤25 weeks include cognitive disability (5% to 36%), cerebral palsy (9% to 18%), blindness (0.7% to 9%), and deafness (2% to 4%). Older premature infants tend to exhibit milder degrees of neurodevelopmental disability (Jarjour, 2015). The absence of three major morbidities in preterm infants, including bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), and severe neurologic damage, is linked to a positive outcome on all domains of the Bayley-III Scales of Infant Development (e.g., cognition, language, and motor scores). Furthermore, very preterm infants who spend less time on positive pressure assistance and total parenteral nutrition demonstrate better outcomes in the same domains (Asztalos et al., 2017).

C. Rapid plasticity of the brain suggests the potential for early neonatal experiences and environmental modifications to support better neurodevelopmental outcomes. The earlier the intervention during critical periods of brain development, the better synaptic plasticity will be elicited to improve brain connections that improve outcomes (Spittle and Treyvaud, 2016).

Early Experience

A. The influence of early environmental, medical, and other perinatal atypical exposures is not clear even

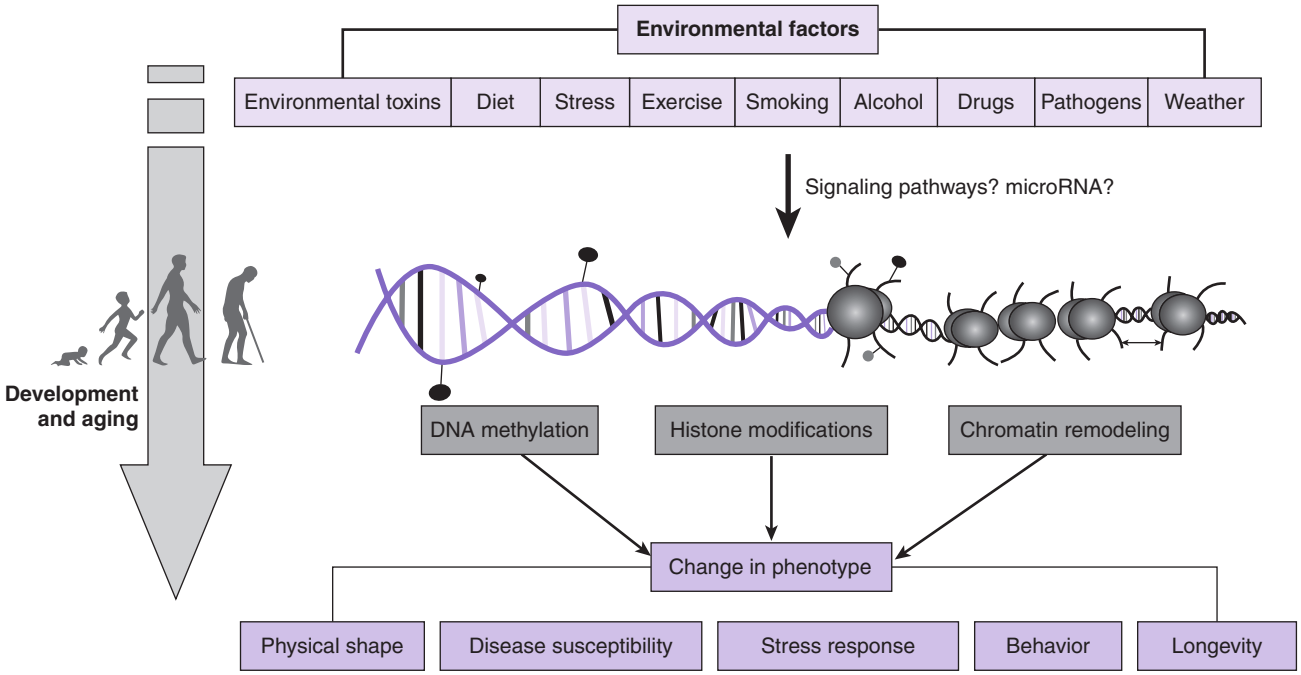

Fig. 11.2 Epigenetic mechanisms provide the link between environmental factors and phenotypical changes during the whole lifetime. *(Copyright 2013, Elsevier. Tammen, S.A., Friso, S., Choi, SW. Used with permission).*

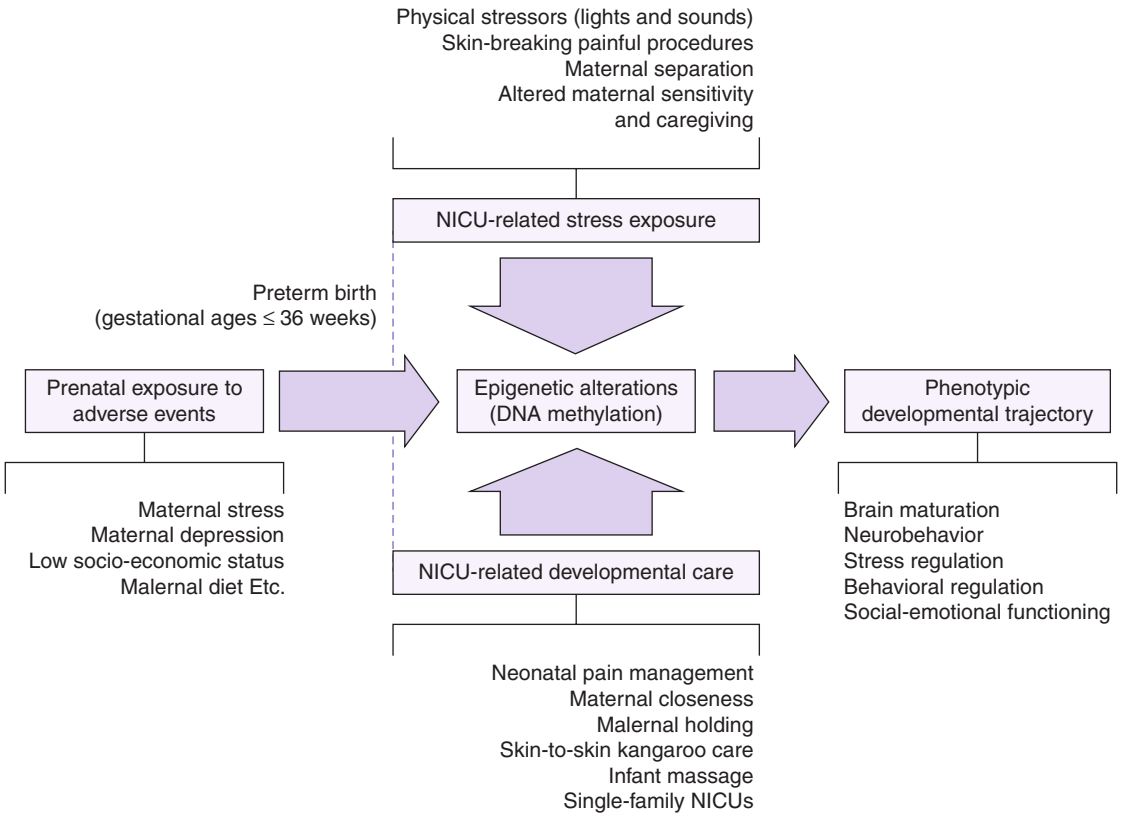

Fig. 11.3 Theoretical model for Preterm Behavioral Epigenetics research. *NICU*, Neonatal intensive care unit. *(Copyright 2018, Elsevier. Provenzi, L., Guida, E., Montirosso, R. Used with permission. Note: Adapted from Montirosso and Provenzi 2015).*

though developmental problems are more frequent in preterm infants after their NICU stay. Preterm infants display a different pattern of behavior on the NICU Network Behavioral Scale at term equivalent compared with full-term infants (Pineda et al., 2013).

1. Weaker orientation ($P < 0.001$).
2. Less ability to tolerate handling ($P < 0.001$).
3. Poorer self-regulation ($P < 0.001$).
4. Weaker reflexes ($P < 0.001$).
5. Higher stress response ($P < 0.001$).
6. More hypertonicity or hypotonia ($P < 0.001$).
7. Increased tendency toward excitability ($P < 0.007$).

B. Important changes are observed in behaviors of preterm infants at 34 weeks postconceptional age compared with term equivalent.
   1. Increasing arousal and excitability ($P < 0.001$).
   2. Decreasing quality of movement ($P = 0.006$).
   3. Increasing levels of hypertonia ($P < 0.001$) and decreasing hypotonia ($P = 0.001$).
   4. Less lethargy ($P < 0.001$).

C. **Infants with brain injury demonstrate more excitability ($P = 0.002$).** These neurobehavioral changes highlight the importance of interventions beginning immediately in the delivery room and throughout the NICU stay.
   1. Developmental support during care is a strategy to reduce the influence of environment, care practices, handling, and other disruptions stressful to the NICU infant to optimize outcomes.

What is Developmental Care?

A. Developmental care is more about the caregiver who (Robison, 2003):
   1. Acknowledges the environmental risks of the NICU on the developing brain and body of the high-risk newborn.
   2. Recognizes that health and neurodevelopmental problems occur at much higher frequency in preterm infants.
   3. Realizes infants need early developmental support to reach optimal cognitive, physical, and social/emotional potential.
   4. Commits to providing developmental support during all care and procedures; adapts the environment to better suit individual infants.
   5. Supports parents as essential to their infant's physical and developmental progress from the moment of birth.

B. The Universe of Developmental Care (UDC) (Coughlin, 2017; Gibbins et al., 2008; Gibbins et al., 2010; Milette et al., 2017a and Milette et al., 2017b) expands

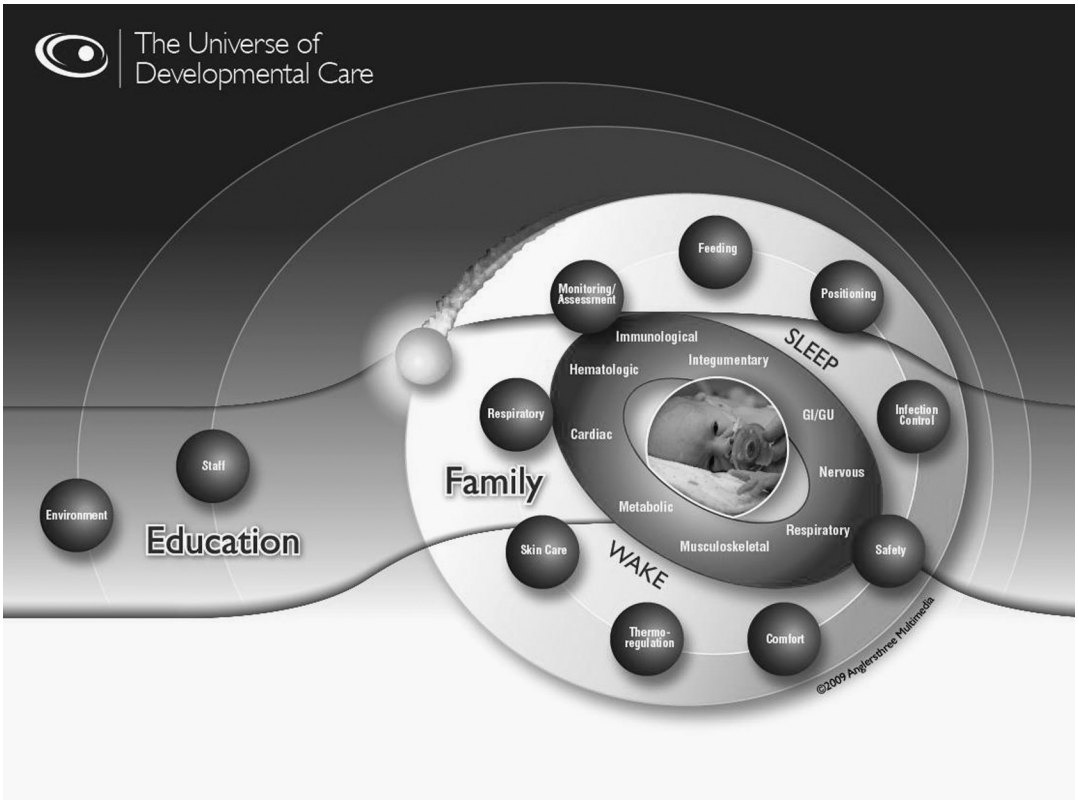

Fig. 11.4 The universe of developmental care. *(Copyright 2009, Koninklijke Philips N.V. Used with Permission.)*

Als's Synactive Theory (Lawhon and Als, 2010) to accentuate the neurodevelopmental interface of the infant's skin that links the baby to the environment of care and caregivers (Fig. 11.4). Aside from tactile opportunities, this shared surface is integrated with the entire sensory system (visual, auditory, vestibular, etc.) and affords the caregiver a practical approach to care through an interactive link to the actual body surface within the NICU context.

1. The model is based on a solar system concept, where the inner circle, or sun, is the core that explains the planetary movement and purpose while also keeping the entire system together. In the UDC, the infant's position is equivalent to the sun so the model is focused on the patient. The family is closest to the infant so they can be involved in care and parenting. The ring closest around the infant is composed of physiologic systems needed for optimal functioning and is where medical and nursing care is necessary should there be a disruption in one or more systems. These physiologic systems are also influenced by the infant's sleep–wake behavioral states surrounding the physiologic ring.
2. The planets represent aspects of care practices based on systematic reviews and meta-analyses of literature on developmental care and infant outcomes. Staff orbit protectively around the infant and family, accessing the shared care surface during nursing care customized to the infant's individual requirements from knowledge of the available evidence-based practice symbolized by the planets that circumnavigate around the core (sun–infant).
3. The context for all interaction is the physical, human, and operations of the health care setting or NICU. The Milky Way exemplifies education as a persistent theme encompassing all orbital planes. Learning needs extend across staff, physicians, leaders, and families committed to safe, quality care and optimal outcomes.
4. The skin as the shared surface for interaction makes sense, especially because it originates from the ectodermal layer during embryology, as does the brain. As the neurodevelopmental interface for care, the outer layer of the skin may be viewed as the brain's surface. Obviously, the brain cannot be observed directly in the NICU; therefore, caregivers use the skin or shared surface to operationalize or translate this model into bedside application of developmental care practices (Table 11.1).

Table 11.1

Expanded Developmental Care Practices Within the Universe of Developmental Care Model

Monitoring/Assessment	Feeding	Positioning
Vital sign assessment	Early feeds	Supine
Behavioral assessment	Trophic	Prone
Electrodes	Donor milk	Side-lying
Invasive catheters	Cue-based feeds	Flexion
Invasive/noninvasive monitoring	Nonnutritive sucking	Containment
CO_2 monitor	Breast-milk mouth care	Midline orientation (proper body alignment)
Saturation monitor	Enteral feedings	Boundaries
Cerebral monitor	Breast shields	Hand-to-mouth opportunity
	Bottle feed	Safety
	Breastfeed	
	NGT feeds	
Infection Control	**Safety**	**Comfort**
Occlusive dressings	Patient ID bands	Pain assessment practices
Handwashing	Enteral only/Parenteral only tubings	Pharmacologic practices
Antibiotic use		Sucrose use
Prep solutions		
Antimicrobial ointments	Gentle touch	Skin-to-skin
Jewelry policies	Infant security systems	Massage therapy
Postoperative practices	Gel mattresses	Sleep regulation
Environmental issues (ventilation, garbage disposal)	Environmental issues (flooring, equipment)	Environmental factors
Thermoregulation	**Skin Care**	**Respiratory Care**
Humidity control	Touch	Intubation practices
Temperature control	Soaps and emollients	CPAP interface
Swaddling	Bathing practices	Oxygen delivery systems
Plastic wrap	Cleansers and solutions	Instillations (surfactant, saline, nebulizers)
Room temperature	Adhesive removal	Suctioning practices
Solution temperature	Transdermal drug interface	
Clothing	Topical anesthetics	
Bedding	Wound care	
Family	**Staff**	**Environment**
Satisfaction	Satisfaction	Light levels
Level of involvement	Knowledge	Noise levels
Knowledge	Autonomy	Cultural, racial, religious sensitivity
Autonomy		Leadership quality

CPAP, Continuous positive airway pressure; *ID*, identification; *NGT*, nasogastric tube.

From Gibbins, S., Hoath, S., & Coughlin, M. (2008). The Universe of Developmental Care: A new conceptual model for application in the neonatal intensive care unit. *Advances in Neonatal Care*, *8*(3),145. Reprinted with permission of Wolters Kluwer Health.

Operationalizing Developmental Care

A. Physical and behavioral assessment.
   1. Assessment of stable or self-regulating behavior, as well as stress responses (Fig. 11.5), is ongoing during care and periods of rest and provides the information necessary for developmentally supportive care individual to each infant (Table 11.2). The framework for understanding preterm infant behavior is based on the work of Dr. Heidelise Als (1998). An infant's observable channels of communication are used in a systematic assessment by caregivers to provide individualized, developmentally appropriate care. Als's Synactive Theory proposes the hierarchical integration of subsystem development and integration with the other developing subsystems to eventual competent functioning without physiologic or autonomic stress and destabilization.
      a. Autonomic/visceral cues—changes in infant color, heart rate, respiratory patterns.

Fig. 11.5 NICU infant demonstrating stress cues. *(Courtesy Texas Children's Hospital, Houston, TX; photography by Carol Turnage Spruill.)*

b. Motor system—quality of tone and movement, posture.
c. State system—quality and range of states, transitions between states.
   1) Attention and interaction.
   2) Self-regulation. For example, competent functioning is demonstrated when Misha, now 35 weeks, is able to focus on suck, swallow, and breathing during an oral feeding examination while maintaining physiologic and motor stability in a quiet, alert state.

B. Individualized developmental care relies on both the moment-to-moment caregiver adaptations while in interaction with an infant and the formal plans based on infant assessment that provide overall guidance for

Table 11.2

Neurobehavioral Organization and Facilitation

Subsystem	Signs of Stress	Signs of Stability	Interventions
Autonomic			
Respiratory	Tachypnea, pauses, irregular breathing pattern, slow respirations, sighing, or gasping	Smooth, unlabored breathing; regular rate and pattern	Reduce light, noise, and activity at bedside (place pagers/phone on vibrate, lower conversation levels at bedside)
Color	Pale, mottled, red, dusky, or cyanotic	Stable, overall pink color	Use hand containment and pacifier during examinations, procedures, care Slowly awaken with soft voice before touch, including all procedures, examinations, and care unless hearing impaired; use slow movement transitions
Visceral	Several coughs, sneezes, yawns; hiccups, gagging, grunting, and straining associated with defecation, spitting up	Visceral stability, smooth digestion, tolerates feeding	Pace feedings by infant's ability and cues
Autonomic-related motor patterns	Tremors, startles, twitches of face and/or body, extremities	Tremors, startles, twitching not observed	Gently reposition while containing extremities close to body if premature Minimize sleep disruption Position appropriately for neuromotor development and comfort; use nesting/boundaries or swaddling as needed to reduce tremors, startles Manage pain appropriately
Motor			
Tone	Either hypertonia or hypotonia; limp/flaccid body, extremities and/or face; hyperflexion	Consistent, reliable tone for postmenstrual age (PMA); controlled or more control of movement, activity, and posture	Support rest periods/reduce sleep disruption; minimize stress; contain or swaddle
Posture	Unable to maintain flexed, aligned, comfortable posture	Improved or well-maintained posture; with maturation posture sustainable without supportive aids	Provide boundaries, positioning aids, or swaddling for flexion, containment, alignment, and comfort as appropriate
Movement	Stiff extension of arms and/or legs, fingers stiffly outstretched (salute), arching, neck hyperextension; jerky, flailing movements	Less self-stimulating motor arousals; control of movement improving; smoother, less awkward; may get hands together or to face/mouth	Use swaddling, boundaries, nesting, or hand containment to minimize motor arousal and support overall calming, assist hands to face/mouth
Level of activity	Frequent squirming, frantic flailing activity or little to no movement	Activity consistent with environment, situation and PMA	Intervene as needed for pain management, environmental modification, less stimulation; encourage skin-to-skin holding

Continued

Table 11.2

Neurobehavioral Organization and Facilitation—cont'd

Subsystem	Signs of Stress	Signs of Stability	Interventions
State			
Sleep	Restless, facial twitching, movement, irregular respirations, fussing, grimacing, whimpers or makes sounds; responsive to environment	Quiet, restful sleep periods, less body/facial movement, little response to environment	Comfortable and age-appropriate positioning for sleep with a quiet, dim environment and no interruptions except medical necessity Position with hands to face or mouth or so they can learn to achieve this on their own
Awake attention/interaction	Low-level arousal with unfocused eyes; hyperalert expression of worry/panic; cry face or crying; actively avoids eye contact by averting gaze or closing eyes; irritability, prolonged awake periods; difficult to console or inconsolable	Alert, bright, shiny eyes with focused attention on an object or person; robust crying; calms quickly with intervention, consolable in 2 to 5 minutes	Encourage parent holding as desired, either traditional or skin-to-skin May be ready for brief eye contact around 30 to 32 weeks without displaying stress cues Support awake moments with PMA-appropriate activity based on stress and stability data for individual infant
Self-regulation	Little attempt to flex or tuck body, few attempts to push feet against boundaries, unable to maintain hands to face or mouth, sucking a pacifier may be more stressful than soothing	Strategies for self-regulation include foot bracing against boundaries or own feet/leg; hands grasped together; hand to mouth or face, grasping blanket or tubes, tucking body/trunk; sucking; position changes	Examine using blanket swaddle or nest to support infant regulation by removing only a small part of the body at a time while keeping most of body contained Ask a parent or nurse to provide support during examinations, tests, procedures Swaddle or contain as needed to keep limbs close to body during care or exams and to provide boundaries for grasping or foot bracing Position for sleep with hands to face or mouth Provide pacifier intermittently when awake and at times other than examinations, care, or procedures
State transitions	Rapid state transitions, unable to move to drowsy or sleep state when stressed, states are not clear to observers	Transitions smoothly from high-arousal states to quiet-alert or sleep state; focused attention on an object, person; maintains quiet-alert state without stress or with some facilitation	Give older infants something to hold (maybe a finger or blanket) Encourage parenting to support parenting skill; teach parents communication cues and behaviors; model appropriate responses to cues Consistently avoid rapid disruption of state behavior (e.g., starting an examination without preparing the baby for the intrusion) by awakening slowly with soft speech or touch, use indirect lighting or shield eyes depending on PMA during examinations, care Assist return to sleep or quiet-alert state after handling Provide auditory and facial visual stimulation for quietly alert infants based on cues; premature infants may need to start with only one mode of stimulation initially, adding others based on cues Swaddling or containment to facilitate state control or maintenance

From Spruill-Turnage, C., & Papile, L. A. (2012). Developmentally supportive care. In J. P. Cloherty, E. C. Eichenwald, A. R. Hansen, & A. R. Stark (Eds.), *Manual of neonatal care* (7th ed.). Philadelphia, PA: Lippincott, Williams & Wilkins; reprinted with permission. Modified from Als, H. (1982). Toward a synactive theory of development: Promise for the assessment and support of infant individuality. *Infant Mental Health Journal*, *3*, 229–243; Als, H. (1986). A synactive model of neonatal behavior organization: Framework for the assessment of neurobehavioral development in the premature infant and for support of infants and parents in the neonatal intensive care environment. *Physical and Occupational Therapy in Pediatrics*, *6*, 3–55; Hunter, J. G. (2001). The neonatal intensive care unit. In J. Case-Smith, A. S. Allen, and P. N. Pratt (Eds.), *Occupational therapy for children* (p. 593). St. Louis, MO: C. V. Mosby; and Carrier, C. T., Walden, M., & Wilson, D. (2003). The high-risk newborn and family. In M. J. Hockenberry (Ed.), *Wong's nursing care of infants and children* (7th ed.). St. Louis, MO: C. V. Mosby.

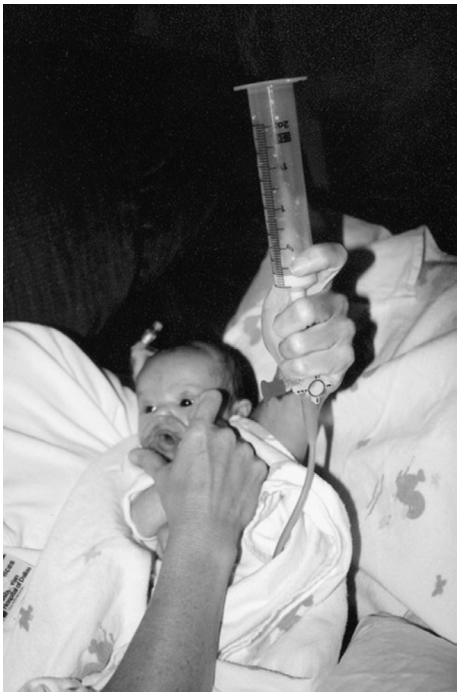

Fig. 11.6 Caregiver interacts with infant to promote enjoyment during a tube feeding. *(Courtesy Texas Children's Hospital, Houston, TX; photography by Carol Turnage Spruill.)*

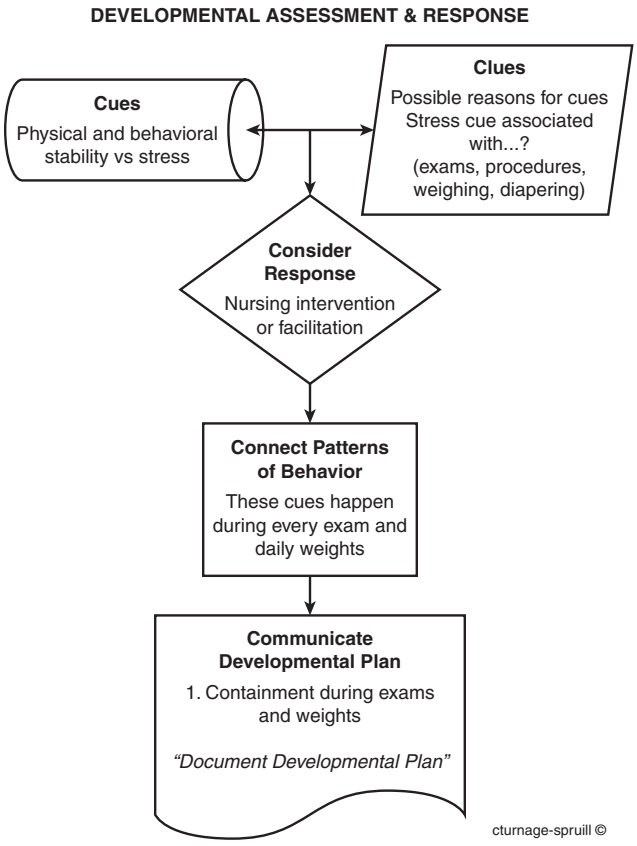

Fig. 11.7 The Developmental Care Model: Five Constructs. *(Courtesy Carol Turnage Spruill.)*

care of that particular infant. Both are flexible, in that changes may need to be made based on infant responses at any given moment. A nurse must be present and in the moment with an infant to identify cues and respond appropriately. In a fast-moving society, it is sometimes difficult to maintain focus in the present without thinking ahead to other tasks/activities even though it is an essential component of caregiving.

1. Care is dynamic and responsive, although dependent on the caregiver being completely in tune and in interaction *with* the infant rather than performing care as tasks *on* the infant (Fig. 11.6). Cues without context or an experience make it difficult for caregivers to apply appropriate interventions during care and in the overall plan of care.
2. The Five Constructs of Developmental Care (Fig. 11.7) can be used as a learning tool to guide the caregiver through the whole experience of the infant by using their assessment within the context of the environment and situation to initiate interventions in the moment or use patterns of responses for developing plans of care. Finally, continuity and consistency among caregivers require that this information is communicated to the infant's health care team and family to gather input on the developmental plan of care and link interventions to medical goals.
   a. The Five Constructs are a simple way to look at all the elements of operationalizing developmental principles into practical application (see Fig. 11.7).
      1) Cues—observe infant cues and determine whether the behaviors indicate stability or stress.
      2) Clues—check the situation and environment for clues to the observed behavior. (Is the care stressful? Is the environment noisy?)
      3) Consider—what is your best response given your knowledge of this infant and the cues/clues you identified within the best evidence available to the UDC. How is the shared interface useful in delivering care or interventions?
      4) Connect—if you see a pattern of behavior, think about events that frequently trigger the infant's stress cues (weighing on scale elicits extended arms and stiffly outstretched fingers, and oxygen saturation decreases from 4% to 6%).
      5) Communicate—document and report the developmental plan based on your observation and analysis of individual behaviors and potential triggers to ensure consistent responses among caregivers.

C. Evaluate developmental care practices in the NICU (Coughlin et al., 2009; Gibbins et al. 2010; Milette et al., 2017a; Milette et al., 2017b).
   1. Core measures for developmentally supportive care (Table 11.3) are based on five repetitive themes from the evidence base of developmental and quality care practices for NICU patients. Each measure includes attributes with corresponding criteria that set the minimum requirements for successful attainment of developmental care in a NICU. These criteria can be translated into measurable indicators to monitor, benchmark, and analyze the

Table 11.3

Core Measures of Developmental Care

Attribute	Criteria
1. Protected Sleep	
Infant sleep–wake states assessed and documented and guide all infant interactions	• All nonemergent caregiving is provided during wakeful states • Support integration of hunger cues with sleep cycles • Scheduled caregiving contingent on infant's sleep–wake states and adapted accordingly
Care strategies that support sleep are individualized for each infant and documented	• Provide caregiving activities that promote sleep (i.e., facilitative tuck, swaddled bathing, and kangaroo care) • All caregiving activities are modified according to infant's state • Maintain light and sound levels within recommended range and implement cycled lighting to support nocturnal sleep
Families are educated on importance of sleep safety in the hospital and the home; this education is documented	• Family education on caregiving activities that promote safe sleep is provided • Parenting opportunities are provided to promote infant sleep • Staff role model "Back to Sleep" practices for families once the infant has demonstrated physiologic flexion of the upper body in supine and discharge home is anticipated
2. Pain and Stress: Assessment and Management	
Assessments of pain and/or stress are performed routinely and documented	• Each infant is assessed for pain/stress every 4 hours, at a minimum, or with each infant interaction • Each infant is assessed for pain/stress during all procedures and caregiving activities • A valid pain assessment tool is utilized
Pain and/or stress is managed before, during, and after all procedures until infant reaches baseline; interventions and infant responses are documented	• Utilize nonpharmacologic and/or pharmacologic measures before anticipated stressful/painful procedures • Adapt caregiving activities to minimize pain and stress • Document infant's response to pain-relieving/stress-relieving interventions
Family is involved and informed of pain and stress management plan for their infant(s); involvement and information sharing are documented	• Family is offered choice to be present during invasive procedures • Family education regarding infant pain and stress cues is provided • Family is encouraged to provide comfort to their infant
3. Developmentally Supportive Activities of Daily Living	
Positioning: Infant positioning will provide comfort, safety, physiologic stability, and optimal neuromotor development and is documented	• Each infant is positioned and handled in flexion, containment, and alignment during all caregiving activities • Infant position is evaluated with every infant interaction and modified to support symmetric development • Positioning aides are gradually removed and Back to Sleep and Tummy to Play practices are implemented as the infant demonstrates physiologic flexion
Feeding: Feeding will be infant-driven, individualized, nurturing, functional, and developmentally appropriate to ensure safety	• Offer NNS with each nonoral feeding contingent on infant's state • Feeding readiness and quality of nippling and appropriate caregiver techniques are utilized • Education regarding benefits of breastmilk is provided, and family choice is supported
Skin care: Infant skin integrity is assessed and protected, and care is documented	• Infants are bathed no more frequently than every 3 days or as indicated on individualized assessment • Skin integrity is assessed using a reliable assessment tool once per shift and documented (Braden Q Scale or similar neonatal tool) • Skin surface interface is protected during application, utilization, and removal of adhesive products

Table 11.3

Core Measures of Developmental Care—cont'd

Attribute	Criteria
4. Family-Centered Care	
Family (defined by infant's parents and/or guardians) has 24-hour unrestricted access to their infant and is provided opportunity to parent; family definition and participation are documented	• Family is offered opportunity to be present and/or participate in medical rounds and change-of-shift report • Family is offered opportunity to be present during invasive procedures and/or resuscitative interventions to provide comfort and reassurance • Family is supported in parenting activities to include kangaroo care, holding, feeding activities, dressing, bathing, diapering, singing, and bonding interactions
Family's level of emotional well-being and parental confidence and competence are assessed and documented weekly	• Mental health professionals (social/spiritual) are accessible to family on weekly basis • Family observations and input regarding infant are sought by direct-care provider and documented in the medical record • Health care providers share unbiased infant information weekly with family
Family has access to resources and support that assist in short- and long-term parenting, decision making, and parental well-being	• Families are invited to participate in a support group • Culturally sensitive family education on infant safety and infant care is available in various formats • Resources for the social, spiritual, and financial needs of families are provided
5. The Healing Environment	
A quiet, dimly lit, private environment that promotes safety and sleep	• Continuous background sound and transient sound in the NICU shall not exceed an hourly Leq of 45 dB and an hourly L10 of 50 dB; transient sounds or Lmax shall not exceed 65 dB • Ambient light levels ranging between 10 and 600 lux or 1 to 60 ftc shall be adjustable and measured at each infant bed space • Physical and auditory privacy is offered at each patient bed space
A collaborative health care team that emanates teamwork, mindfulness, and caring	• Interdisciplinary care rounds occur at least weekly • Direct-care providers demonstrate caring behaviors, which include adherence to hand hygiene protocols, cultural sensitivity, open listening skills, and a sensitive relationship orientation • Nurse–doctor collaboration is defined, practiced, and reinforced on a daily basis
Evidence-based policies, procedures, and resources are available to sustain the healing environment over time	• Core measures of developmental care provide the standard of care for all patient care providers • Resources are available 24/7 to support implementation of developmental care • A system is present to ensure staff accountability for the practice of core measures of developmental care

NICU, Neonatal intensive care unit; *NNS*, non-nutritive sucking.

From Coughlin, M., Gibbins, S., & Hoath, S. (2009). Core measures for developmentally supportive care in neonatal intensive care units: Theory, precedence and practice. *Journal of Advanced Nursing*, *65*(10), 2243–2245, with permission of John Wiley and Sons.

current quality of developmental care practices in the NICU (Table 11.4). The ability to substantiate and quantify developmentally supportive nursing care using metrics based on the core measures may provide data on the impact of this care model on family/staff satisfaction and clinical and economic outcomes.

2. The five core measures of developmental care.
   a. Protected sleep—behavioral state guides caregiving activities, interventions to promote sleep, and parents' education about sleep protection in the NICU and at home.
   b. Assessment and management of stress and pain—defined intervals of stress/pain assessment with validated pain scoring tool and infant cues, interventions for stress/pain documented and reassessed at appropriate intervals, nonpharmacologic and/or pharmacologic interventions for stress/pain utilized and documented.
   c. Developmentally supportive daily living activities—positioning, infant-driven feeding, and skin care.
   d. Family-centered care—opportunities to participate in care, daily rounds, and change-of-shift report; receive education on their infant's cues and care; input on plan of care; culturally sensitive interactions; access to social, spiritual, and financial support. Family is satisfied with their

Table 11.4

Example of Protected Sleep Core Measure With Attribute and Criteria With Potential Quality Measurement

Core Measure	Attribute	Criteria	Quality Indicator
Protected sleep	Nursing care that is individualized to promote sleep for each infant is documented and reported	1. Care is adapted based on infant state 2. Sleep is promoted with care such as hand containment, swaddled bathing, skin-to-skin holding 3. Light and sound levels are within recommended range (White et al., 2013)	1. Sleep–wake states are assessed and documented correctly with vital signs and care activities in 95% of audited records 2. Skin-to-skin holding by parent choice is documented in 100% of records audited 3. Random light and sound levels of monthly audits do not exceed 45 dB for continuous background sound or 65 dB for transient loud sounds

hospital experience and reassured they are receiving timely communication about their infant.

e. Healing environment—human, physical, and organizational environment that includes evidence-based policies, procedures, and appropriate resources. A bloodstream infection bundle is part of a healing environment of care.

Developmentally Supportive Environment

A. Many NICUs are building single-family rooms (SFRs) to improve the environment of care for both infant and family.

B. The goal of SFRs is to improve outcomes and provide a place where parents can be present with their infant as much as possible. There have been numerous reported benefits to SFRs, such as decreased length of hospital stay and decreased cases of chronic lung disease, apnea, and infection, as well as increased breastfeeding, environmental control, parent presence, and better staff/parent satisfaction. Although the benefits are compelling, studies have also found babies cared for in SFRs showed delayed maturation on amplitude integrated electroencephalography (aEEG), abnormal near-term magnetic resonance imaging (MRI), and more language delay (Dunn et al., 2016). The same studies reported staff and families experienced feelings of isolation. They found with further examination that the infants in the SFRs were cuddled and held skin-to-skin less often than those in the open bay. Total visitation was a little over 24 hours per week. In units where maternal involvement is high, infants at 18 months show improved neurodevelopmental outcomes (Dunn et al., 2016; Lester et al., 2016). Preterm infants cared for in SFRs demonstrate higher Bayley language and cognitive scores and receive more human milk (Lester et al., 2014). Variations in outcomes were seen based on type of insurance that are not fully understood (Vohr et al., 2017). More research is needed to understand these negative effects in some infants. For now, parents should be encouraged to spend as much time as they can with their infant in SFRs. In cases where parents are unable to visit, strategies must be in place to provide appropriate stimulation to offset the long periods lacking parental presence or touch. Most of the studies show infants have an advantage to being in SFRs during a NICU hospitalization.

C. Just because a room is "private," that does not mean it is necessarily designed to reduce or minimize the effects of light and sound. Environments with toxic products containing volatile compounds or formaldehyde are still being used for building materials and furniture in some hospital facilities.

D. There are also areas where building or renovating is not an immediate option. Resources and professionals exist to help leaders and administrators improve the NICU environment (White et al., 2013). Environmental modifications are intended to reduce stress, protect sleep, and allow parent–infant interaction with less distraction.

1. Sound environment: hiring a professional acoustic engineer is money well-spent when deciding to renovate or build a NICU for sound abatement. The sound "floor," or baseline for sound levels before adding equipment, patients, and staff, has to be much lower than the 45-dB level for ambient sound, and an acoustical engineer can make that happen. Operational noise in the NICU can be ≥20 dBA above a 35- to 45-dBA background due to large groups of staff/families, hard surfaces, space between beds, and equipment.
2. The hourly Leq (average) of 45 dB and an hourly L10 (10% of the time) of 50 dB, both A-weighted and slow response, is recommended for infant rooms and adult sleeping spaces.
3. Transient sounds, or Lmax, shall not exceed 65 dB, A-weighted, slow response. Standards for the

neonatal hospital environment can be found in the American Academy of Pediatrics and American College of Obstetricians and Gynecologists *Guidelines for Perinatal Care* (2012) and Recommended Standards for Newly Designed NICUs (White et al., 2013). It is not recommended that infants wear eye goggles or earmuffs for protection against NICU noise and light due to increased stress responses of premature infants while such devices are in place (Aita et al., 2013).

a. Ototoxic medications coupled with a noisy NICU environment may contribute to hearing loss in preterm infants (Zimmerman and Lahav, 2013).
b. Most hearing loss in preterm infants has no known etiology.
c. Potential for atypical development of auditory pathways from NICU noise experience.

4. Noise abatement.
   a. Monitor noise levels either continuously or intermittently.
   b. Heighten awareness of physicians, staff, and parents regarding the effects of noise and their responsibility in decreasing it at the individual level.
   c. Communication devices such as phones and pagers can be used on the vibration setting.
   d. Locate sources of loud sounds and request the facilities or building department to assist in reducing or eliminating those sounds whenever possible.
   e. Eliminate overhead paging.
   f. Intense noise levels (>55 to 60 dBA) disrupt sleep states and interfere with brain development and organization (White et al., 2013).
   g. Ambient noise must be low enough for an infant to distinguish the maternal voice to optimize auditory development.
5. Lighting.
   a. Whereas sound must be managed overall, lighting needs to be individualized to the patient (Lasky and Williams, 2009).
   b. Quilted incubator covers that are dark on the infant's side will reduce both light and sound.
   c. Sudden increase in light poses a stressor to premature infants and can influence physiologic stability; gradual increases are better tolerated (Ozawa et al., 2010).
   d. Visual stimulation around 30 to 32 weeks frequently results in observable stress responses.
   e. Protection from light during procedures is especially important, as procedure lights are more intense than ambient light levels.
6. Healthy environment (White et al., 2013).
   a. Ceilings, wall, flooring surfaces, furnishings, countertops, and other facility structures should not contain substances that are teratogenic, mutagenic, carcinogenic, or known to cause harm to humans.
   b. Cleaning of surfaces and furniture should be simple and require no toxic chemicals; soap and water preferred.
   c. Polyvinyl chlorides (PVCs), such as in vinyl flooring, can affect air quality and should not be used.
   d. Phthalate plasticizers are chemicals used to soften plastics and are found in many foods (meat and dairy), food packaging (plastic wrap) and processing, fragrances, adhesives, and floor and wall products. Lead and phthalate are banned from use in children's toys. One phthalate well-known to health care is DEHP (di[2-ethylhexyl] phthalate), used to soften medical devices frequently used in NICUs (e.g., intravenous bags, tubing, catheters, and enteral feeding bags). They can be absorbed, ingested, or inhaled and are associated with reproductive, immune system, and developmental damage. Many NICUs are now DEHP free (Lunder, 2016).
   e. Volatile organic compounds (VOCs) and persistent bioaccumulative toxins (PBTs), such as those found in some paints and ceiling tiles, are not recommended.
   f. Rubber flooring (latex) must be certified as nonallergenic.
   g. A minimum of 2 weeks may be needed for adhesives and flooring material to be ready for infants to move into any new space.
   h. The benchmark organization for green buildings is Leadership in Energy and Environmental Design (LEED), which has standards to help hospitals choose smart designs that are environmentally responsible and healthy for humans (http://leed.usgbc.org/leed.html).

E. **Nurses and other health team members can learn more about environments that can compromise patient care and safety.** Websites such as https://www.noharm-uscanada.org and http://www.ewg.org, to name a few, are educational for staff interested in learning more about environmental safety. A pregnant woman passes chemicals to the fetus through the placenta. The Environmental Working Group (EWG) reported 287 chemicals found in neonatal cord blood were linked to cancer, neurotoxins, and birth defects (Environmental Working Group, 2009; Houlihan et al., 2005). Neurotoxins transmitted to the developing fetus may interfere with processes required for normal brain development and function. By improving knowledge about healthy environments and keeping up-to-date, nurses can be prepared to advocate for better hospital environments for mothers and babies.

Developmental Care Practices

A. **Developmental care of infants within a medical context necessitates a collaborative team with family participation.** Various models of care delivery attempt to make this happen with a primary team that stays with the baby and family, building trust and learning the infant's cues and support needs. Essential to the continuity and consistency of care is sharing the infant's cues and needs with parents, other staff, therapists, consultants, and the health care team. Documentation in the medical record, plan of care, shift huddle, and report are ways to communicate important developmental support information.
   1. Examinations, nursing care, therapy, and procedures are carried out as often as possible around infant while attentive and responsive to the infant's communication cues.
      a. Care is provided when infant is in the alert state.
      b. Care providers prepare infant for touch by speaking softly as they approach the bed.
      c. Infants are further prepared for care or touch with hand containment before moving hands for care/procedures so an infant can adjust to touch.
      d. Sleep cycles are protected with the understanding that synaptic connections around learning and memory are being wired.
      e. Behavioral cues are respected and responses prompt to avoid escalation of stress when stress cues are identified.

B. **Interventions that support positioning depend on the individual infant's needs.** For infants who are immobile or cannot maintain their own posture, supportive positioning will be essential to avoid acquired deformities. Positioning support devices should not cause restraint so infants have enough room to push against boundaries and develop their neuromuscular and skeletal systems (Fig. 11.8). Positioning interventions include (Hunter, 2010):
   1. Flexion, containment, midline alignment regardless of position (Fig. 11.9).
   2. Assessment of comfort (physiologic and behavioral) after positioning.
   3. Use of aids to support and maintain positions without restriction so an infant can move and push against boundaries without loss of motor stability (materials for "nest" or boundaries are blanket rolls, commercially available positioning aids; Fig. 11.10).
   4. Repositioning is often every 3 to 4 hours, depending on the infant age and condition; however, an infant may become uncomfortable before time to reposition. Signs of discomfort, such as squirming, irritability, frowning, or grimacing, may indicate a need to reposition before scheduled.
   5. To ensure quality, audit positioning or ask staff to self-audit with a tool (Table 11.5), such as the Infant Position Assessment Tool (IPAT) or the Neonatal Postural Assessment (neoPAW) worksheet.

C. Handling preterm infants using developmental principles minimizes the stress of movement by combining

Fig. 11.8 Positional support that allows movement against boundaries and eye shielding. *(Courtesy DandleLION, Inc.)*

Fig. 11.9 Positioning principles applied for flexion, containment, alignment, and comfort. *(Courtesy Texas Children's Hospital, Houston, TX; photographer Carol Turnage Spruill.)*

Fig. 11.10 Positioning can be accomplished using commercially available positioning supports or carefully rolled towels. Consider the external forces against the baby and select an appropriate mattress to reduce the risk of pressure ulcers. *(Photograph provided courtesy Philips Healthcare.)*

Table 11.5

Infant Position Assessment Tool (IPAT)

Patient's name:				
Clinician performing assessment:				
Date/time of assessment:				
Infant position (circle): supine side-lying prone				
Indicator	0	1	2	Total score
• Shoulders	Shoulders retracted	Shoulders flat/in neutral	Shoulders softly rounded	
• Hands	Hands away from the body	Hands touching torso	Hands touching face	
• Hips	Hips abducted/externally rotated	Hips extended	Hips aligned and softly flexed	
• Knees, ankles, feet	Knees extended, ankles and feet externally rotated	Knees, ankles, feet extended	Knees, ankles, and feet are aligned and softly flexed	
• Head	Head rotated laterally (L or R) greater than 45 degrees from midline	Head rotated laterally (L or R) 45 degrees from midline	Head positioned midline to less than 45 degrees from midline (L or R)	
• Neck	Neck hyperextended	Neck neutral but poorly aligned with spine	Neck in neutral position, slightly flexed forward and aligned with spine	
			Cumulative score	

Infant Position Assessment Tool (IPAT) (Copyright 2010 Koninklijke Philips electronics N.V. All Rights Resreved).

Fig. 11.11 Transfer small preterm infants with extremities contained, and slowly transition to parent for skin-to-skin holding or for repositioning. *(Courtesy Texas Children's Hospital, Houston, TX; photography by Carol Turnage Spruill.)*

flexion and containment with a slow transfer. Smaller infants can be transferred by gently containing the extremities and lifting in prone or side-lying position with less disruption and stress (Fig. 11.11). Diaper changes can be made with an infant in side-lying position with less handling and stress. Lifting the legs and lower body to change a diaper was measured with near-infrared spectroscopy showing alterations in cerebral oxygenation and blood volume (Comaru and Miura, 2009). The same effects were associated with other frequent care activities, including endotracheal tube suctioning, repositioning, physical examination, and gavage feeding. Early parenchymal brain injury is associated with these routine caregiving events (Papile and Spruill-Turnage, 2017).

D. Every opportunity to rethink care in a more supportive manner may affect neurodevelopment with positive information received repeatedly by the evolving brain.

E. **Feeding is frequently viewed as a routine task.** The preterm infant's transition to breast or bottle requires thoughtful planning for developmental support as he or she learns to feed. The Infant-Driven Feeding (Ludwig and Waitzman, 2007) approach is associated with a significant decrease in length of stay (LOS) and time to full feeding, an effect enhanced in infants greater than 28 weeks gestational age. More studies are needed to validate this feeding method. Developmental support during feeding requires consideration of (McGrath et al., 2010):
   1. Preparing the environment to minimize distraction and stressors (bright light, noise, swaddling).
   2. Infant feeding readiness cues to start feedings without the confines of specific time intervals and duration, measuring quality of feeding objectively, and careful facilitation only when an infant requires it are all part of the Infant-Driven Feeding model.
   3. Removing gavage tubes to enhance the experience.
   4. Trying feedings when infant displays more energy.
   5. Providing frequent opportunities for parents to feed their infant.

F. The tactile sensation is the first sensory system to begin functioning in the fetus, at about 7 weeks, and through the skin becomes the neurodevelopmental

interface between the infant and the world upon arrival at birth. Tactile stimulation using various methods can be pleasant or unpleasant to an infant, especially if high risk or premature. Touch is fundamental for newborn development; however, there continues to be reluctance in supporting parents in the early days of their newborn's critical illness or prematurity, even though stressful and/or painful procedures/tests are often performed. Touch by parents can begin on admission with sensitive nurses guiding them in techniques (Livingston et al., 2009) that are nurturing and less likely to elicit a stress response.

1. Hand containment or facilitated tuck can be taught to parents on the first day. This approach of low-stress touch has been associated with a decreased stress and pain response (Fig. 11.12).
2. Kangaroo care or skin-to-skin care (SSC) is associated with improved outcomes in both infant (i.e., fewer respiratory complications, better weight gain, temperature stability, decreased mortality in developing countries, duration of quiet sleep, modulation of pain, etc.) and mother (i.e., increased breast milk volume, increased parenting confidence, more positive and adaptive to infant cues, longer breastfeeding duration, etc.).
   a. The SSC intervention is reported to show significant differences in EEG complexity in an SSC group compared with standard care at term (Burke, 2018; Jefferies and the Canadian Paediatric Society, Fetus and Newborn Committee, 2012; Spruill-Turnage and Papile, 2012).
   b. The impact of SSC on breastfeeding is a highly significant benefit to this way of holding infants. SSC is associated with greater expressed milk volumes and longer duration of exclusive breastfeeding.
   c. During SSC, safety necessitates continuous cardiorespiratory monitoring and frequent observation that correct head position is maintained for airway patency. Infants with arteriovenous intravascular access devices, endotracheal tubes, multiple tubings from infant to devices, and other equipment require special care in transferring in/out of SSC. Two people may be necessary to maneuver SSC transfers (e.g., two nurses, nurse and respiratory therapist, or nurse and occupational or physical therapist).
   d. Sleep during SSC is improved with better organization of sleep states, less rapid eye movement (REM) sleep and arousals. During SSC, more total sleep and time spent in quiet sleep have been observed. Infants spend more time alert and observant during awake states.
   e. SSC has positive benefits for both infants and mothers even after discharge from the NICU (Fig. 11.13).
   f. No adverse effects of SSC on physiologic stability in preterm infants as young as 29 weeks' gestational age and averaging 1096 g on mechanical ventilation have been reported (Azevedo et al., 2012).
   g. Fathers enjoy opportunities for holding their infant SSC style, though they may not ask, so staff might need to encourage their participation (Fig. 11.14).
   h. When there is a question whether SCC is an appropriate intervention, the health care team and family can evaluate the situation and decide on timing (Baley and Committee on Fetus and Newborn, 2015).
3. Massage (Niemi, 2017) is another intervention for preterm and term infants who are stable and might gain from a variation in tactile stimulation. Often, infants are around 32 weeks when massage is

Fig. 11.12 Hand containment supports neurobehavioral organization and modifies pain response. *(Photograph provided courtesy Philips Healthcare.)*

Fig. 11.13 Kangaroo or skin-to-skin care in the NICU. *(Courtesy the Salinas Family, Houston, TX.)*

Fig. 11.14 Not for mothers only; fathers enjoy kangarooing their infant too. *(Courtesy the Salinas Family, Houston, TX.)*

considered, but there may be individual differences as to when it is beneficial.

a. Benefits for caregivers.
   1) Improved mood, confidence, and caregiver–infant attachment.
   2) Decrease in maternal postnatal depression symptoms after massage classes compared with mothers in a support group.
b. Benefits for infants.
   1) Enhanced growth and development when massaged with moderate pressure.
   2) Infants who receive moderate-pressure massage gain more weight, sleep better, and cry/fuss less than those getting light-pressure massage.
   3) Decreased LOS.
   4) Less late-onset sepsis in the less-than-32-week infant.
c. The technique is taught to parents, who provide the massage to their infant, with support from a certified infant massage therapist trained to perform this skill on hospitalized preterm and term infants in the NICU. Parents often attend a class on infant massage to learn and practice before attempting on their infant. Abdominal massage should be limited to trained providers because intestinal volvulus has been reported in preterm infants after massage therapy. Massage is considered a safe, effective opportunity to bring infant and parents together for a nurturing experience.
d. Adverse physiologic effects of massage are more likely when an infant cannot tolerate additional stimulation, is clinically unstable, has skin problems or wounds, is easily overstimulated, or has a reaction to massage oil after a skin test.

4. The maternal voice (Provenzi et al., 2018a) is heard in utero, although it is much different in quality/intensity than in the NICU. Studies on maternal voice effects on the preterm infant suggest:
   a. Hearing the maternal voice may be a benefit to maturation of specific areas of the brain as an experience-dependent stimuli.
   b. A possible effect on feeding behaviors resulting in improved weight gain.
   c. Better visual and auditory performance at 3 months.
   d. Consistent effects on cognitive and neurobehavioral development and may be predictive of general language development and expressive language at 18 months.

Parent Support and Involvement (Papile and Spruill-Turnage, 2017; Pineda et al., 2018)

Parents have expressed a variety of emotions about having to wait to touch or hold their baby in the NICU. They sometimes convey feelings of fear due to the NICU environment, their fragile baby, and all the medical devices on or around their infant. On the first day of admission, parents need assistance in understanding ways to touch their premature or sick infant that are nurturing and will not provoke stress responses. Helping parents recognize their own baby's specific behaviors will lead them to respond more appropriately. This time is an incredible opportunity to model nurturing, behaviorally supportive care that may be sustained after discharge. Encouraging parents to attend rounds, ask questions, and provide suggestions on supportive care directly influences their team involvement.

Becoming a parent in the NICU is a challenge because the environment is so foreign, and providing care so publicly may affect the ability to achieve one's role as a parent. The more parents understand their infant's communication, the better they can participate in everyday care. Getting to know their baby as a unique individual who can convey needs and emotions is essential for attachment.

A. **Parental support strategies.** The key to supporting mutually satisfying parent–infant interaction is to establish a family-centered approach on admission that will empower the parents to assume the natural parental role of advocating for their child's needs and desires

and become the primary nurturer to their infant. Supporting the parents' ability to understand their infant's level of communication through the infant's behavior will place the parents in a better position to respond to and interact with their infant in a developmentally supportive manner. Positive outcomes are associated with more parent visitation (Reynolds et al., 2013), such as increased holding ($P < 0.001$), while infants had better movement quality ($P < 0.02$), were less aroused ($P = 0.01$), and were less excitable ($P = 0.03$). The increased infant holding was also associated with better movement quality ($P < 0.01$), lower stress ($P < 0.01$), and fewer episodes of arousal ($P = 0.04$) and excitability ($P < 0.01$). In another study, medical and demographic factors were related to parent visitation, holding, and SSC. If a parent or family is not visiting, the nurse must explore the barriers with the parent(s)/family so the right resources can be provided, such as case management or social services. Social disparities affect parent(s)/family presence with their infant on a regular basis, including race, single-parent status, employment, siblings, traveling distance from home, and insurance type. The health team needs to discuss these barriers early in the infant's hospitalization to make a difference in these inequities.

1. Establish an atmosphere in the NICU that is welcoming to parents and does not treat them as "visitors," but as parents who deserve respect as important members of their infant's care team (invite parents to join daily team rounds).
2. Help parents identify the most effective techniques for interacting with their infant (e.g., recognizing stress and time-out signs). Place parents in situations in which they will succeed in interacting positively with their infant.
3. Help parents identify both the consoling measures unique to their infant and how their child is providing feedback concerning the consoling measures. Parents can add to the developmental plan of care after they discover the likes/dislikes and learn the supportive techniques their baby responds to in certain situations.
4. Recommend the caregiving team work with parents to plan specific activities (i.e., SSC, biologically meaningful smells and tastes, verbal interaction, eye contact, use of toys, therapeutic touch) for parental interaction when appropriate.
5. Encourage parents to assume caregiving responsibilities as soon and as much as possible.
6. Discuss parents' expectations and goals for themselves and their infant. Encourage families to write down these expectations and goals. Writing down these dreams and goals or journaling will be the beginning of a lifelong care plan.
7. Encourage the parents to use their child's medical record as a communication tool.

B. **Be aware of and involve the family's support system.** Encourage parent-to-parent support if possible, either in a formal or an informal manner. Recognize that the parents are the constant in the child's life and that health professionals will come and go. Parents and families will have the most effect on their infants' outcomes in the long term. NICU professionals must be ready to engage, interact, teach, respect, and build a relationship with them that supports the assimilation of the knowledge, skills, and attitudes they need to succeed as parents long after their infant is discharged from the NICU.

Teamwork and Continuity of Care (Spruill and Heaton, 2015)

A. **Collaboration fosters care that is consistent among caregivers.** Consistency and collaboration by caregivers who establish familiarity and predictable routine inspire trust from both infant and family. Consistency of caregivers is not only important for developmental planning and intervention but provides a measure of safety toward the recognition of clinical and behavioral changes requiring prompt intervention. The evolution of larger and larger NICUs requires critical appraisal of ways to maintain continuity, consistency, and communication to sustain safe clinical and developmental care.
   1. Consistency of care is a continuum that requires documentation of individual stress and stability cues, written plans of care based on individual assessment of each infant's response to the environment, care, procedures, and medical treatments.
   2. Communication through the medical record, easily accessible assessment and care plans, and direct communication between and among caregivers at shift report and/or daily medical/nursing rounds foster collaborative practice and enhance consistent care.
   3. A familiar group of people who care for individual infants provide reassurance that establishes trust and builds a partnership that is rewarding to the entire team, especially the family.

B. **Safe, quality care happens by design and not by accident.** Communication among caregivers who know the infant and family through repeated interactions enables them to deliver quality developmental care safely and effectively.

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CHAPTER 12
Pharmacology

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OBJECTIVES

1. Define the concepts of pharmacology, pharmacodynamics, and pharmacokinetics.
2. Describe the developmental changes that affect medication absorption, distribution, metabolism, and elimination.
3. Identify specific considerations when one is administering medications of the following types to a neonate: antimicrobial agents, cardiovascular agents, central nervous system (CNS) agents, diuretics, and immunizations.
4. Describe nursing responsibilities and interventions when administering medication to the neonate.

The study and clinical application of neonatal pharmacology can facilitate safe medication administration in the neonate. The application of pharmacologic principles involves evaluating existing knowledge related to the pharmacodynamic and pharmacokinetic responses of the neonate to specific medications. Unfortunately, this body of knowledge is extremely limited in the neonatal population due to a lack of controlled clinical trials with these patients. Confounding factors relative to gestational and chronologic age, weight, fluid status, and the health–illness state of individual organ systems make dosing medications in the neonatal population a challenging and perpetual learning process. The decision to administer a medication should be evaluated for the desired response and the potential for an undesirable reaction. The nurse is in the ideal position to observe and evaluate both response and reaction and to intervene if necessary.

This chapter provides pharmacologic information specific to the neonate. Information on medication dosages and implications for medication administration are provided in individual clinical chapters. Additional current reference materials should also be available in the neonatal intensive care unit (NICU).

Principles of Pharmacology

TERMINOLOGY

A. **Pharmacology:** the science of the properties of medications and their effects in the body.
   1. **Pharmacotherapy:** the administration of a medication to a patient with the intent of preventing, diagnosing, or treating disease.
   2. **Medication:** any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease in human beings or animals.
   3. **Pharmacodynamics:** the relationship between medication concentrations at the site of action and the pharmacologic response (intensity and time course of therapeutic and adverse effects). This is what the drug does to the body.
   4. **Pharmacokinetics:** the fate of a medication in the body from the time it enters until it and all of its metabolites are removed. This includes medication absorption, distribution, metabolism, and excretion. It is also the specialized study of the mathematical relationship between a medication dosage regimen and the resulting serum concentration. This is what the body does to the drug.
   5. **Bioavailability:** the portion of the administered dose that reaches the site of action in the body. This is usually the amount entering the circulation and may be reduced when medications are given by mouth versus when given intravenously.
   6. **Therapeutic range:** a range of medication concentrations within which the probability of the desired clinical response is relatively high and the probability of unacceptable toxicity or subtherapeutic response is relatively low.
   7. **Therapeutic drug monitoring (TDM):** determinations of plasma medication concentrations to optimize medication therapy. TDM is valuable when:
      a. A good correlation exists between the pharmacologic response and plasma concentration.
      b. Wide intersubject variation in drug plasma levels results from a given dose.

c. The medication has a narrow therapeutic range.
d. The medication's desired pharmacologic effects cannot be readily assessed by other simple means.

8. **Steady state:** a term used to refer to a situation in which the amount of medication administered is equal to the amount of medication eliminated. When steady state is reached in a patient, the blood concentrations remain "steady." Therefore, at steady state, all peak drug levels and all trough drug levels should be the same.
9. **Half-life:** the time necessary for a measured medication concentration to fall to half its original value. A medication's duration of action is often related to its half-life, and the half-life may also indicate when another dose should be given. It takes approximately five half-lives to reach steady state.
10. **Types of medication levels.**
    a. *Peak level:* a drug level that is drawn after the dose is given and after adequate time is allowed for the drug to distribute throughout the body. The time for the drug to distribute varies with each medication and the route of administration.
    b. *Trough level:* a drug level that is drawn just before the dose.
    c. *Random level:* a drug level that is drawn at any time after a dose is given. These levels are often used to follow drug levels in patients with changing renal function or changing volume status.

Pharmacodynamics

A. **Receptor concept:** The principle that medications act by forming a complex with a specific macromolecule in a way that produces a given response. This response may include inhibition or potentiation of the macromolecule's activity to create the desired medication effect. Receptor effects are as follows:
   1. The medication's affinity for binding to the receptor plays a large part in the determination of the concentration of the medication required to achieve the desired response.
   2. The individual characteristics of the receptor are responsible for the selective nature of medication response.
   3. The receptor theory of medication action allows an explanation of medication antagonists. The antagonist medication may alter the characteristics of the receptor molecule in a way that limits or inhibits the response to the original medication (e.g., naloxone and morphine) or stimulus (e.g., a β-blocker such as propranolol).
   4. Some medications do not appear to act through receptors. Their action is related to a direct response in the recipient.

B. General mechanisms of medication action.
   1. Based on the nature of the receptor–medication complex.
   2. Types of receptor–medication complexes.
      a. Receptor–medication complexes that regulate gene expression.
         1) One common class of medications acts by mediating a response that ultimately involves gene expression and new protein synthesis.
         2) These medications generally do not have a rapid effect after initial administration (e.g., epoetin alfa).
      b. Receptor–medication complexes that change cell membrane permeability.
         1) Many clinically useful medications act by changing the cell membrane permeability and therefore altering membrane characteristics.
         2) These medications may have a relatively short lag time between administration and response (e.g., penicillin).
      c. Receptor–medication complexes that increase the intracellular concentration of a second messenger molecule.
         1) These medications increase production and activity of enzyme systems within the cell.
         2) These medications may stimulate a rapid response in changing cell characteristics (e.g., dopamine).

C. Relationship between medication dose and clinical response.
   1. Individuals in a population receiving a medication may have a wide range of responses to a medication dose. An idiosyncratic medication response is an abnormal response to a medication that is not usually observed. These unpredictable responses include the following:
      a. Low sensitivity: a patient who, on receiving the usual medication dose, exhibits a clinical or biological response that is less intense than expected (e.g., inadequate pain relief with usual doses of analgesic medications).
      b. Extreme sensitivity: a patient whose response to a medication is more intense than is expected (e.g., severe hypotension from an antihypertensive agent).
      c. Unpredictable adverse reaction: a patient whose medication reaction is substantially different from what would have been predicted and may differ from the usual response in most patients (e.g., an anaphylactic reaction).
      d. Tolerance: a diminished response to a given medication dose that is related to long-term administration of a medication (e.g., fentanyl doses must be increased as the length of therapy increases to achieve the same effects).

e. Tachyphylaxis: a rapidly diminished medication response without a medication dosage change. This may be caused by any of a number of factors, including a limited number of receptor sites or limited numbers of transmitter chemicals (e.g., response to albuterol may diminish if given frequently).

2. Factors that may affect individual medication response are as follows:
   a. Alterations in medication concentration: a change from the expected norm in the amount of medication that reaches the receptor molecule.
   b. Variation in amounts of antagonistic substances: an unusually large or limited amount of antagonistic substances that alter receptor molecule response.
   c. Alterations in numbers or function of receptor molecules: an increased or diminished number of receptor molecules changes the number of potential medication–receptor complexes.
   d. Changes in concentration of molecules other than receptor molecules: if medication response is ultimately dependent on an effect on molecules other than those of the medication–receptor complex, medication response may be limited by the amount of the third molecule type (e.g., prodrugs such as fosphenytoin).

D. Desired versus undesired effects of medications.
1. No medication causes only one effect; all medications have several effects, which can be divided into four groups.
   a. Desired, or therapeutic, effects: those effects that are the desired outcome of the medication administration (e.g., reduction in apnea episodes with caffeine treatment).
   b. Subtherapeutic effect: those effects that are less than the desired outcome of the medication administration (e.g., continued apnea episodes with low caffeine levels).
   c. Side effects: those medication effects that result from medication administration and that are in addition to the desired effects. All medications have some side effects, varying from minor and clinically insignificant to major side effects that are sufficiently adverse to require discontinuation of the medication therapy (e.g., tachycardia with caffeine treatment).
   d. Toxic effects: medication response that results from a medication overdose or unexpected high serum medication concentrations (e.g., caffeine-induced seizures with severe intoxication).
2. It is the responsibility of the health care provider to weigh the benefits of the therapeutic effect against the risk of undesirable side effects and toxic effects or subtherapeutic responses and adjust accordingly.

Pharmacokinetics

A. Principles of medication absorption (Fig. 12.1).
1. General principles of medication absorption.
   a. The movement of a medication from the site of administration to the bloodstream.
   b. Regardless of the route of administration, most medications must cross cell membranes to reach their site of action.
      1) Most medications cross cell membranes by passive diffusion. The physiochemical properties of the medication molecule have a major impact on the ease of diffusion.
      2) Medications can enter the cell through other mechanisms also, such as active transport or facilitated diffusion.
   c. The absorption of a medication is dependent, in large part, on the route of administration. The common sites of administration are as follows:
      1) **Gastrointestinal (GI):** commonly used because of minimal infection risk, decreased cost, and convenience.
         a) Gastric emptying and intestinal transit times: prolonged and irregular; approaches adult values at 6 to 8 months of age. Gastric and intestinal motility are reduced with prematurity, asphyxia, gastroesophageal reflux, and respiratory distress syndrome. Administration of hypocaloric feeds, human milk, or prokinetic agents (e.g., metoclopramide, erythromycin) can increase motility. Prolonged transit times and enterohepatic recirculation may also increase the bioavailability and pharmacologic effect of some substances (Bhosle et al., 2017; van den Anker et al., 2011). However, the bioavailability of the medication may decrease because of increased first-pass loss, increased GI destruction of medication, or shortened transit times from diarrhea or emesis.
         b) GI tract acidity: the presence of marked changes in pH from the stomach through the distal portion of the GI tract may affect absorption. The pH of the GI tract is nearly neutral or slightly alkaline at birth due to the presence of amniotic fluid in the stomach. Gastric acid increases secretion rapidly such that it doubles by 2 months, even in the extremely low birth weight neonate (Kearns et al., 2003; van den Anker et al., 2011). The net effect of GI acidity on the absorption of medications is dependent on the pH characteristics of the medication and preparation.

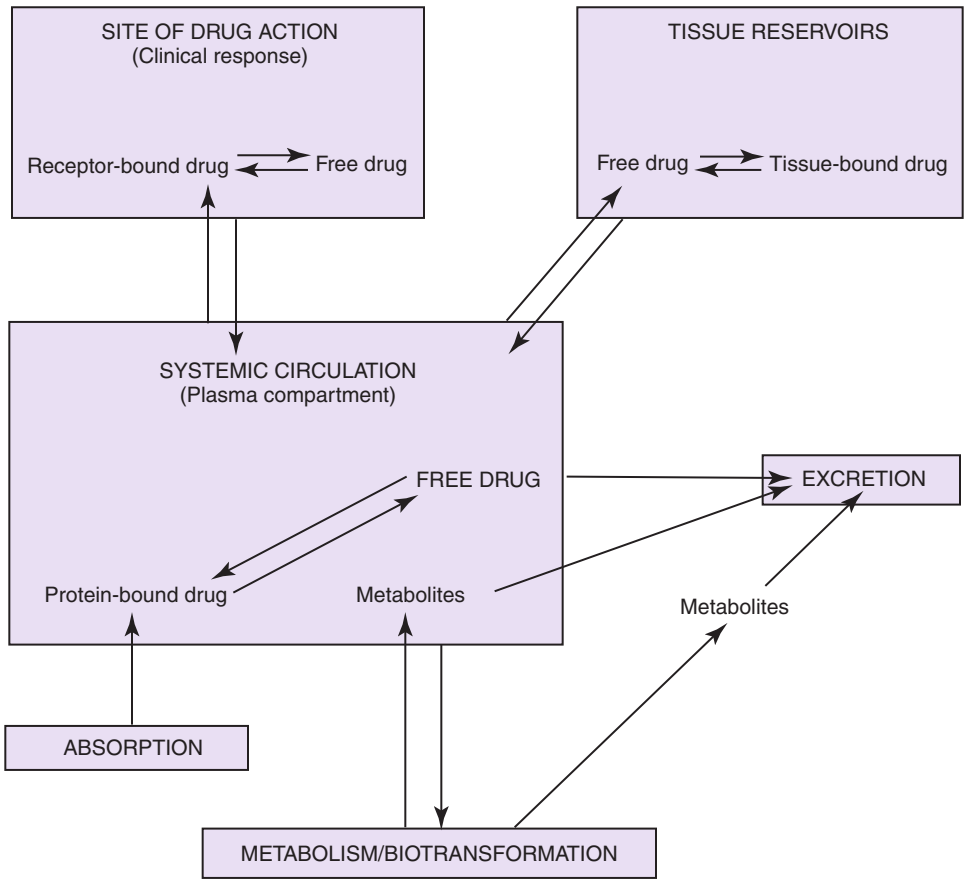

Fig. 12.1 Principles of medication absorption. *(Adapted from McClary, J. D. [2015]. Principles of drug use in the fetus and neonate. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh [Eds.],* Fanaroff and Martin's neonatal-perinatal medicine: Diseases of the fetus and infant *[10th ed.]. Philadelphia, PA: Saunders.)*

Medications that normally may not be absorbed well in the stomach may be absorbed at a higher rate in the neonate because of decreased stomach acidity. The absorption of acidic drugs will be reduced (e.g., phenobarbital, phenytoin) and the absorption of basic drugs will be enhanced (e.g., penicillin, erythromycin) compared with adults (Funk et al., 2012).

c) GI enzyme activity: neonates are deficient in pancreatic enzymes at birth. This deficiency may inhibit absorption of some medications that require pancreatic enzymes for efficient absorption. One compensating mechanism that neonates have is an increased β-glucuronidase secretion. This is an enzyme produced by organisms normally present in the small intestine that are capable of metabolizing some medications. It is present in neonates at up to 7 times the adult amounts (Kearns et al., 2003; van den Anker et al., 2011).

d) Bacterial flora: composition and rate of colonization of the GI tract by the normal bacterial flora may affect both GI tract motility and the metabolism of some medications. Colonization is dependent on oral intake, antibiotic administration, or disease states such as necrotizing enterocolitis or infectious gastroenteritis. Normal colonization in vaginally born term neonates occurs by 4 to 6 days of age. Intestinal flora are required for the production of vitamin K (Bhosle et al., 2017).

e) GI tract perfusion: in very ill neonates, hypoperfusion of the gut may decrease medication absorption.

f) Underlying disease states: underlying disease states such as diarrhea, emesis, or the presence of nasogastric suction may reduce the time available for medication absorption. Diseases of genetic (e.g., cystic fibrosis) or circulatory (e.g., necrotizing

enterocolitis) origin will alter pancreatic enzymes or intestinal mucosa, decreasing GI absorption.

2) **Rectal:** may be a very rapid and efficient means of medication absorption.
   a) Useful when rapid intravenous (IV) access is not available (e.g., patients in status epilepticus in need of anticonvulsant agents).
   b) Serum levels of some medications may be as high as levels obtained through the IV route of administration (Kearns et al., 2003).
   c) Routine administration by the rectal route is discouraged. The relative volume and fragility of the neonatal rectum must be considered.
   d) The retention time is the rate-limiting step.
3) **Inhalation:** useful for gaseous or easily vaporized medications.
   a) Absorption is favored due to the large surface area of the alveolar membranes and the generous blood flow. Medication response may be very rapid.
   b) Medications administered by this route have a particular advantage when the site of desired action is the tracheobronchial tree (e.g., albuterol).
   c) There is a potential for fewer side effects when medications are administered this way, because much of the medication may not be systemically absorbed (e.g., inhaled corticosteroids).
   d) Most frequently used in neonatal intensive care for the administration of various surfactant preparations.
   e) Certain medications (e.g., epinephrine and lidocaine) can be given through the endotracheal tube in emergency situations when IV access is not readily available.
   f) This route may be less effective in a neonate with pulmonary hypertension and poor or abnormally distributed pulmonary blood flow.
4) **Topical/percutaneous:** utility is limited to medications whose absorptive characteristics allow permeation through the skin or mucous membranes. Percutaneous absorption has particular advantages as well as risks in the neonate.
   a) The rate of absorption is inversely related to skin thickness and directly related to skin hydration. With increasing gestational age, skin thickness increases and water content decreases, thus reducing the amount of absorption from this route. Maturation of the epidermis occurs between 23 and 33 weeks of gestation. The stratum corneum forms after 23 to 24 weeks of gestation. Formation of this layer of the skin greatly decreases the permeability of the skin to water and infection (Hoath and Shah, 2017). This allows much more efficient percutaneous absorption of medications in neonates of lower birth weight and younger gestational age. However, this poses a particular hazard in care, because substances that may be safely applied to the skin of a more mature patient may be absorbed in dangerous amounts in the immature neonate (van den Anker et al., 2011).
   b) The ratio of body surface area to body weight is higher in neonates than adults, providing a relatively larger absorptive surface in comparison with body mass.
   c) The absorptive response time is variable and may be limited to the local area of application; however, some topically applied medications (e.g., nitroglycerin) can have a systemic effect. As a result, products that contain alcohol and hexachlorophene skin washes should be avoided. Any treatment with topical steroids should be limited to less than 2 weeks to prevent adrenal suppression. On the other hand, antibiotic ointments will be more readily absorbed to treat infections, povidone–iodine (Betadine) absorption can prevent iodine deficiency, and topical safflower oil may prevent essential fatty acid deficiency.
   d) Occlusive dressings will increase the extent of absorption.
5) **Intramuscular/subcutaneous:** administration into muscle or subcutaneous tissue.
   a) Minimal subcutaneous tissue and muscle mass significantly limit these two routes of administration, particularly in the low birth weight neonate.
   b) These routes are limited to medications that do not cause tissue damage at the administration site and are soluble at physiologic pH.
   c) These routes will achieve slower responses compared with the IV route because of the lag time between administration and achievement of blood concentration.
   d) Response time is dependent on blood flow to muscle and may be greatly delayed in

hypoperfused tissue. Poor peripheral blood flow and low blood pressure are common in neonates. These problems become less common with increasing gestational age but can occur in the presence of many neonatal disease states. Poor cardiac output frequently occurs with many illness states in the neonatal period. Subsequent increases in the peripheral perfusion after resolution of the primary illness states may put the neonate at risk of having an increase in the rate and amount of medication absorption.

e) Diminished muscle activity in the ill neonate decreases muscle perfusion and consequently may limit absorption of medications administered by this route.

6) **IV:** direct administration into the bloodstream.

a) Bypasses all absorptive barriers.

b) Most effective and reliable method of medication administration because the medication is delivered directly to the circulating plasma volume.

c) Significant medication serum concentrations are reached rapidly, allowing for immediate medication response. This includes both desired and undesired or toxic reactions.

d) Adequate and equal distribution to all organs or compartments is not guaranteed. Characteristics of some biological membranes may limit medication distribution to body compartments (e.g., blood–brain barrier).

e) Rapid achievement of potentially dangerous serum medication concentrations may require administration of the IV medication over a prolonged period rather than by IV push (e.g., vancomycin, amphotericin, and aminoglycosides).

B. Principles of medication distribution.

1. **Distribution:** movement of the medication to and through various body compartments. The extent of this movement, the "size" of the compartment, the number and character of the binding sites, and the amount of the medication administered determine the amount of medication at the desired site of action. When medication movement reaches a steady state, the volume of distribution is defined as the hypothetical volume of body fluid that would be required to dissolve the total amount of medication as found in the serum. This volume is sometimes described as apparent volume of distribution. This volume may be larger than the total body volume if the medication is highly protein or tissue bound.

2. **Body compartments.**

a. *Total body water:* as age increases, total body water, as a percentage of total body mass, decreases. Total body water in adults comprises approximately 55% of total body weight; in term infants, it is 75%, and in preterm infants, it is 85% (Funk et al., 2012).

1) As body water increases as a percentage of body mass, water-soluble medications have a larger volume of distribution.

2) Because of increased total body water, a less mature neonate may require a larger per-kilogram dose to achieve the same peak medication concentration and effect as an older patient (e.g., aminoglycosides).

3) In the first several days after birth, total body water decreases, causing the volume of intracellular fluid to be increased relative to the amount of extracellular water (van den Anker et al., 2011). This leads to rapid changes in the volume of distribution for water-soluble medications, in relation to normal physiology and illness states.

4) Body water loss is divided into two main categories: sensible and insensible. Sensible losses can be measured and quantified. In term neonates, insensible losses occur in a strong relationship to metabolism. In extremely premature neonates, insensible losses occur primarily through evaporative loss, independent of metabolic rate. Insensible losses are difficult to quantify (Bhosle et al., 2017).

5) Medications frequently administered to the neonate (e.g., diuretics, indomethacin) may have a major impact on body water volume and, as a side effect, may alter the volume of distribution (Bhosle et al., 2017).

6) Neonates with disease states that alter water excretion (e.g., primary renal disease, syndrome of inappropriate antidiuretic hormone [SIADH], congestive heart failure, capillary leak syndromes) may have expansion of body water as a result of this dysfunction.

7) The preceding alterations make dosing medications that are primarily distributed in body water (e.g., aminoglycosides) difficult.

8) Frequent monitoring of medication levels may be required as the mentioned changes in body compartment volumes occur.

b. *Fat:* wide variability of neonatal values, based on gestational age and intrauterine and postnatal growth patterns. This percentage increases from 1% of body weight at 28 weeks of gestation to approximately 15% in a term neonate (Stewart and Hampton, 1987).

1) Medications with more lipid solubility have affinity for this tissue.
2) Reduced amounts of the percentage of body fat may make the volume of distribution smaller for medications distributed primarily in fatty tissue. Hence, the plasma levels of these medications will be higher because less drug will be bound in the fat tissue, resulting in a greater potential for side effects and toxicity (e.g., morphine, lorazepam).

c. *Blood components:* potential sites for medication binding.
1) Erythrocytes: neonates have 2.5 times more binding sites for digoxin compared with the erythrocytes in adults. This results in the need for much higher doses per total body weight in neonates than adults (Stewart and Hampton, 1987).
2) Plasma protein concentrations: medications may form a complex with large circulating molecules (usually proteins).
a) The amount of medication that binds to these sites has a direct effect on the amount of medication available for the desired pharmacologic effect. This binding may result in a limited medication response because only the unbound medication can be distributed to active receptor sites. When more of the medication is protein bound, less is available for the desired medication effect: serum concentration = protein-bound medication + unbound medication.
b) The primary binding protein for acidic medications (e.g., phenytoin, indomethacin, and furosemide) in the serum is albumin (Bhosle et al., 2017).
c) Serum albumin levels may be markedly decreased in the ill, extremely low birth weight neonate.
d) The primary binding proteins for basic molecules (e.g., lidocaine, propranolol) are lipoproteins, glycoproteins, and β-globulins (Bhosle et al., 2017).
e) *Unconjugated bilirubin:* many neonates have increased plasma unconjugated bilirubin levels. Fetal albumin has an increased affinity for bilirubin and a decreased affinity for medications. This causes the unconjugated bilirubin to displace some medications from the albumin-binding sites, making more free medication available for action. In contrast, some medications (e.g., ceftriaxone, sulfonamides) may displace unconjugated bilirubin from albumin-binding sites. This may lead to the deposition of unconjugated bilirubin in the neonatal brain, causing kernicterus (Kearns et al., 2003). These medications should be avoided if possible in patients younger than 2 months of age or in patients with high unconjugated bilirubin levels.
f) *Free fatty acids:* increased serum free fatty acid concentrations have been shown to displace some medications from plasma albumin–binding sites (Bhosle et al., 2017).
g) *Blood pH:* acidosis is a common finding associated with many neonatal disorders. Changes in blood pH have been shown to change albumin-binding characteristics. This may cause medication displacement from albumin. Changes in blood pH may also cause medications to displace unconjugated bilirubin (see earlier).

d. *Blood–brain barrier:* incomplete in the neonate, causing a greater permeability to lipophilic medications (e.g., phenytoin, benzodiazepines). This incomplete barrier may be beneficial when treating neonatal meningitis because the antibiotics penetrate the cerebrospinal fluid more readily (Stewart and Hampton, 1987).

3. **Medication movement:** an important part of medication distribution involves medication movement from the site of administration to sites throughout the body. It is dependent on the blood flow and medication solubility.
a. *Blood flow:* amount and distribution of blood flow to the target organ or cell affect the delivery of a medication absorbed into the bloodstream. Continued adequate blood flow and serum medication concentration are required to maintain an adequate concentration of the medication at the target organ. Several neonatal conditions affect blood flow:
1) Hypotension: may affect peripheral medication absorption and/or distribution.
2) Distributive shock: caused by inappropriate vasodilation; seen with sepsis. Medication distribution to specific organs may be limited by local hypoperfusion.
3) Pulmonary hypertension: may impede medication delivery to the pulmonary vascular bed.
4) Patent ductus arteriosus: blood flow may be distributed preferentially to either the pulmonary or systemic circulation, depending on the pressure differential.
5) Congestive heart failure: may affect peripheral medication absorption or distribution.

b. *Medication solubility:* in biological tissues, the relative ability of the medication to dissolve in biological fluids.
   1) Medications with low lipid solubility do not distribute well through lipid membranes, though they may be distributed well through the body water spaces. Highly lipid-soluble medications are distributed readily through most lipid membranes but are not distributed well through body water spaces.
   2) The relative medication solubility may make some medication use inappropriate. A medication with low lipid solubility may not reach therapeutic concentrations in an organ that is primarily fat tissue (e.g., aminoglycosides do not readily cross the blood–brain barrier).

C. Principles of medication metabolism.
   1. **General principles of medication metabolism.** Many medications must be converted into more water-soluble compounds before they can be removed from the body. Metabolism (biotransformation) is the *chemical change* of a medication into another form. This transformed medication may be pharmacologically active or inactive. The liver, kidney, GI tract, lung, adrenal gland, blood, and skin are tissues capable of biotransforming certain compounds. Of these sites, the liver is the principal organ for medication metabolism.
      a. Liver.
         1) Metabolic activity is divided into two main types.
            a) Phase I (nonsynthetic) metabolism of medications: primarily oxidation, reduction, hydrolysis, or demethylation reactions, which generally occur in the smooth endoplasmic reticulum of the hepatocyte. The function of these enzymes in the full-term and preterm neonate is approximately 50% to 70% of adult values. Maturation occurs as a function of chronologic rather than postconceptional age, with a wide range of variability. Maturation of nonsynthetic enzyme systems during the first several days of life requires careful monitoring of serum levels of some classes of medications (e.g., anticonvulsants). For instance, at term gestation, neonates have approximately 30% of the adult ability to metabolize phenytoin; hence, the half-life is significantly prolonged. Within several weeks of medication exposure, metabolic enzyme activity for phenytoin surpasses adult activity (Funk et al., 2012; van den Anker et al., 2011).
            b) Phase II (synthetic) metabolism of medications: primarily involves the acetylation, methylation, or conjugation of the medication with another substance. The function of these enzymes is also immature, and they may not reach adult levels in concentration and function until well after the neonatal period.
         2) Hepatic uptake of the medication is dependent on the concentration of the medication in the liver (dependent on hepatic blood flow) and the hepatocyte concentration of ligandin (Y-protein). This protein is responsible for substrate uptake by hepatic cells.
         3) In the first-pass effect, hepatic biotransformation may markedly alter medication availability by directly metabolizing medications absorbed from the GI tract before those medications reach other organs. Slow GI motility may increase the potential for first-pass effect. Prolonged GI transit times may increase the potential for hepatic metabolism and the eventual excretion of orally administered medications.
         4) Certain medications (e.g., phenobarbital) are thought to induce enzyme maturity in the fetus and neonate, resulting in increased rates of medication elimination.
         5) Both hepatic enzyme systems may be vulnerable to hypoxic–ischemic insult.
         6) Maturational changes in medication metabolism can have major clinical significance. Careful monitoring of serum levels of some medication classes (e.g., anticonvulsants) is necessary in the first weeks of life.

D. Principles of medication excretion.
   1. **General principles of medication excretion.** Excretion is the final elimination of medication from the body. The process of excretion begins with administration of the medication and ends when the medication is completely eliminated from the body. There are several important organs of excretion.
      a. **Salivary, sweat, and mammary glands:** small amounts of medication may be excreted through these minor organs. Very limited sweat production makes excretion by this mode insignificant in the neonate.
      b. **Lungs:** the lungs are an important route of excretion of gaseous anesthetics but are relatively less important for other medications. Excretion by the lungs is not well studied in the neonatal population. Because lung disease is common in newborn infants, adult data indicate that this may affect or limit the ability to excrete medications by this method.

c. **GI tract:** the large, lipid-soluble surface of the GI tract allows diffusion of medications into the bloodstream. The limited motility in neonates affects excretion and increases the potential for reabsorption of medications or metabolites back into the circulation.
d. **Liver:** the most important site of medication biotransformation also serves as an important site of medication excretion. The excretion of bile is an important means of medication elimination.
   1) Limited oral intake, long-term parenteral nutrition, or intrinsic hepatic disease may reduce bile flow. This may reduce the efficacy of this route of elimination.
   2) Metabolite or medication elimination in bile is dependent on the solubility characteristics of that substance in bile.
e. **Kidneys:** the most important site for medication excretion.
   1) Renal blood flow.
      a) Clamping of the umbilical cord is a significant event that signals a major increase in renal blood flow.
      b) As a percentage of cardiac output, renal blood flow is limited in neonates compared with older children and adults. Limited renal blood flow as an absolute value and as a percentage of cardiac output restricts medication or metabolite delivery to the kidney for excretion.
      c) Renal blood flow increases with increasing gestational and postnatal age.
      d) High umbilical artery catheter placement may reduce the renal blood flow.
   2) *Glomerular filtration rate (GFR)*: the removal by passive filtration of small unbound medication molecules at the glomerulus. Glomerular filtration is dependent on renal blood flow, the characteristics of the glomerular membranes, and the water solubility of the medication.
      a) The GFR function is extremely limited in neonates (full-term neonates have 30% of adult values per unit of body surface area; adult values are reached by 8 to 12 months of age) (Stewart and Hampton, 1987; van den Anker et al., 2011).
      b) GFR is related to gestational age; the lower the gestational age, the lower the GFR. Neonates born at less than 34 weeks of gestation have fewer glomeruli, with total glomerular mass proportional to gestational age (Stewart and Hampton, 1987). Glomerular filtration has been shown to mature rapidly in the first 2 weeks of life, although GFR in premature neonates remains significantly suppressed compared with full-term neonates (Funk et al., 2012).
      c) GFR can be further compromised with asphyxia, hypoxia, or indomethacin treatment. Limited glomerular filtration reduces the removal of medications or metabolites at the glomerulus.
      d) Medication excretion dependent on glomerular filtration includes indomethacin, digoxin, aminoglycosides, and vancomycin.
   3) *Tubular secretion*: the active secretion of molecules into the tubular urine. Tubular secretion is dependent on the efficiency of tubular function.
      a) Neonates have a relatively small mass of functional tubular cells, as well as an immaturity of tubular function. This functional limitation is thought to be caused in part by a decrease of renal blood flow to the renal tubular region and by shortened renal tubules (Stewart and Hampton, 1987).
      b) The limitation in tubular mass and function causes poor excretion of medications and metabolites removed by this method.
      c) Tubular secretion matures much more slowly than glomerular filtration.
      d) Tubular secretion is also vulnerable to hypoxic–ischemic insult.
      e) Medications dependent on tubular secretion for excretion include penicillins, morphine, and thiazide diuretics.
   4) *Tubular reabsorption*: reabsorption of some medications back into the circulating plasma.
      a) May occur through either passive diffusion or active transport.
      b) Passive diffusion appears to be the most important process.
      c) Tubular reabsorption matures much more slowly than glomerular filtration.
      d) Substances dependent on tubular reabsorption include caffeine, glucose, phosphate, and sodium.
   5) Urinary output.
      a) Because of changes in renal blood flow, glomerular filtration, and tubular secretion in the neonate, urinary output is not a reliable sign of renal excretion of medications.
      b) Blood level monitoring is required to ensure safe serum levels of renally excreted medications.

Medication Categories

ANTIMICROBIAL AGENTS

A. **Introduction.** The use of a larger variety of antimicrobial agents in the neonatal population has occurred in the past several years for several reasons. As the threshold of viability is pushed, the length of stay of NICU infants is increasing. The additional numbers of antibiotic courses, coupled with increasing antibiotic resistance patterns, necessitate more broad-spectrum antibiotic usage, as well as increased use of antifungal agents.

B. **Definitions.**
   1. **Antimicrobial medications:** medications that inhibit the growth of or kill microorganisms such as bacteria, fungi, viruses, protozoa, and amebae.
      a. Bacteriostatic medications: agents that inhibit the growth of microorganisms, thereby allowing normal body defense mechanisms to control spread of the organism (e.g., clindamycin, fluconazole).
      b. Bactericidal medications: agents that kill microorganisms. At lower concentrations, they may be bacteriostatic (e.g., aminoglycosides, penicillin, cephalosporins).
   2. **Minimal inhibitory concentration (MIC):** the lowest concentration of a medication that stops visible organism growth in a laboratory setting. In the body, this cannot be directly measured and is dependent on achieved tissue concentration and bacterial count. This is easily measured in the microbiology laboratory and is used to measure the susceptibility of the microorganism to antimicrobial agents.
   3. **Minimal bactericidal concentration (MBC):** the lowest concentration of a medication that results in a ≥99.9% decline in microbial number, measured in the laboratory setting. It is useful when compared with known potential toxic concentration levels to choose the antimicrobial regimen that does the greatest good with the fewest adverse or toxic effects.
   4. **Resistance:** the ability of microorganisms to counteract the bacteriostatic or bactericidal effects of an antimicrobial agent.
      a. Resistance interferes with the medication's action either through changes in the microorganism's cellular structure or through production of enzymes that reduce antimicrobial activity.
      b. Microorganisms develop resistance by:
         1) Enzymes: microorganisms produce various enzymes to inactivate antimicrobial agents (e.g., β-lactamase inactivates penicillins and cephalosporins).
         2) Decreased cellular penetration: microorganisms alter their cell wall permeability to prevent penetration of antimicrobial agents into the cell (e.g., *Pseudomonas aeruginosa* alters porin channels to limit the entry of ceftazidime, imipenem–cilastatin).
         3) Altered target proteins: microorganisms change target proteins so that antimicrobial agents cannot bind and elicit antimicrobial activity (e.g., *Streptococcus pneumoniae*'s resistance to penicillin).
         4) Efflux pump: microorganisms pump the antimicrobial agent out of the cell before the antimicrobial agent can kill the microorganism (e.g., *S. pneumoniae*'s resistance to erythromycin).

C. Basic principles of antimicrobial use.
   1. Antibiotics must reach the target tissue in a concentration adequate to inhibit the growth of or to kill the desired microorganism. This concentration:
      a. Ideally would be such that it would have limited side effects or toxic effects on target tissues or the patient as a whole.
      b. Must be readily achievable and sustainable for the desired duration of antimicrobial therapy.
   2. The choice of antimicrobial agent(s) must be considered.
      a. Microorganism susceptibility to available antimicrobial agents.
      b. Relative permeability of the target tissue to the agent of choice (e.g., blood–brain barrier).
      c. Bioactivity of chosen antimicrobial agent in target tissue (e.g., bactericidal or bacteriostatic).
      d. Known MIC/MBC in relation to existing body of knowledge concerning side effects and toxic effects in the specific population.
      e. Specific characteristics of the individual patient in relation to the chosen antimicrobial's toxicities (e.g., the blood levels of a nephrotoxic antimicrobial, such as gentamicin, should be closely monitored in patients with impaired renal function).

D. Specific considerations in the neonatal population.
   1. Pharmacodynamics.
      a. Tissue concentration of a medication may be altered by clinical and physiologic conditions that may increase or decrease the bioavailability of the medication in the target tissue (e.g., cerebrospinal fluid penetration by antibiotics may be excellent early in meningitis; as meningeal inflammatory response subsides, penetration into the cerebrospinal fluid diminishes).
      b. Differences in response or potential for toxic effects may result from immaturity and/or illness state.
   2. Pharmacokinetics.
      a. To optimize the probability of response to antibiotics, the unpredictable pharmacokinetic

influences should be minimized; hence, the IV route is preferred for septic patients.

b. Absorption.
   1) Changes in GI tract pH affect absorption of oral medication: may be increased or decreased (e.g., oral penicillin G is absorbed better in neonates than in older infants and children because of increased gastric pH).
   2) Changes in skin permeability in the extremely immature neonate may allow topically applied antimicrobial agents to be absorbed systemically.
   3) Blood flow changes may affect absorption and distribution of antimicrobials administered intramuscularly or subcutaneously (e.g., repeated intramuscular administration of aminoglycosides to premature neonates may result in local tissue damage and unacceptably variable rates of absorption).

c. Distribution: decreasing body water and increasing body fat concentration in more mature neonates affect the volume through which the antimicrobial agent is distributed. This may make dosage adjustments necessary in the first days of life.

d. Metabolism: limited hepatic function, because of immaturity or illness state, may affect dosage regimen of some antibiotics, requiring smaller or less frequent doses of some antibiotics (e.g., nafcillin, erythromycin).

e. Excretion.
   1) Limited renal function with lower gestational age may prolong the half-life of antimicrobials excreted by the kidneys (e.g., aminoglycosides, cephalosporins, penicillins, vancomycin). This limited renal function (GFR and tubular secretion) commonly improves significantly in the first few days of life and with advancing chronologic age. For this reason, serum antibiotic levels must be monitored closely and dosage adjustments made accordingly.
   2) Limited renal function or failure may cause toxic effects as a result of accumulation of medication or metabolites (e.g., nephrotoxicity from aminoglycosides).
   3) Medication may have a direct effect on renal function.
      a) Blood flow to kidney may be diminished (e.g., amphotericin can cause renal artery vasospasms).

CARDIOVASCULAR AGENTS

A. Introduction.
   1. A broad group of medications that affect the regulation, inhibition, or stimulation of the cardiovascular system.
   2. The use of cardiovascular agents is increasing in the care of neonates.

B. Basic principles of cardiovascular medication use.
   1. The wide range of pharmacologic actions of this class of medications requires specific in-depth knowledge about each medication and about concurrent medication therapy.
   2. Knowledge of the pathophysiologic basis of neonatal cardiovascular disease is necessary to ensure proper application of this class of medications.
   3. Many of these medications have overlapping or synergistic effects. This overlap in clinical response makes the optimal choice of a medication and dose difficult.
   4. Extensive knowledge and application of invasive and noninvasive cardiovascular monitoring techniques in the neonatal population are necessary to allow titration of the medication dose to the clinical response.

C. Types of cardiovascular medications.
   1. Inotropic/vasopressive agents.
      a. Includes a broad range of medications that act to improve cardiac output by increasing the heart rate (chronotropic effect), the force of myocardial contraction (inotropic effect), and the vascular tone.
      b. Used both for cardiovascular resuscitation and long-term support of the myocardium.
      c. Specific inotropic agents.
         1) Digitalis glycosides (e.g., digoxin). Inhibit the sodium–potassium pump to increase intracellular calcium, thus increasing myocardial contractility. They also decrease conduction through the sinoatrial and atrioventricular nodes to slow the ventricular rate in tachyarrhythmias.
         2) Sympathomimetic amines (e.g., epinephrine, dopamine, dobutamine, isoproterenol).
            a) Clinical responses stimulated by this group of medications are classified according to their effects on the "receptors" in the body. These receptors are categorized as either α-, β-, or dopamine types.
               (1) α_1-adrenergic receptor response: contractions of vascular smooth muscle and constriction of blood vessels.
               (2) α_2-adrenergic receptor response: activation of central nervous system (CNS) receptors in the brain to suppress outflow of the sympathetic nervous system activity from the brain. Results in decreased motility and tone of intestine and stomach.
               (3) β_1-adrenergic receptor response: increased strength and rate of myocardial contraction.

(4) β_2-adrenergic receptor response: vascular smooth muscle dilation and bronchial muscle relaxation.
(5) Five different dopamine receptors are located in multiple organs and have mixed actions involving motor function, cardiovascular (e.g., vasodilating properties), renal (e.g., intrarenal vasodilator), behavioral, and hormonal (e.g., prolactin secretion) systems. For example, epinephrine increases blood pressure by stimulating the α_1- and β_1-receptors. Dobutamine increases cardiac output by stimulating the β_1-receptors.

b) Response to each of these medications depends on relative amounts of α-, β-, and dopamine receptor effects (Table 12.1).
c) Prolonged administration of sympathomimetic amines may result in diminished clinical efficacy secondary to diminished responses of α- and β-receptors, referred to as tachyphylaxis.

2. Antihypertensives/vasodilators.
   a. Used to normalize blood pressure in patients with hypertension, reduce vascular resistance in patients with poor myocardial function, and reduce pulmonary vascular resistance in conditions associated with pulmonary hypertension.
   b. May be used to inhibit pathophysiologic changes that cause increased blood pressure (e.g., captopril, propranolol) or directly reduce blood pressure through changes in intravascular volume (e.g., diuretics) or vascular resistance (e.g., hydralazine).
3. Antiarrhythmics.
   a. Used to treat cardiac dysrhythmias causing adverse effects on cardiovascular stability (e.g., adenosine, digoxin, or esmolol for the treatment of supraventricular tachycardia).

D. Specific considerations in the neonatal population.
1. Pharmacodynamics.
   a. Specific in-depth knowledge about neonatal cardiovascular physiology and pathophysiology is required to determine the need for these medications.
   b. Cardiovascular medications are commonly used in conjunction with other medications that may affect the neonate's response to the medication regimen (e.g., the digoxin–furosemide combination may result in electrolyte loss with the diuretic, which in turn may potentiate a toxic response to the digoxin).
2. Pharmacokinetics.
   a. Absorption: Many cardiovascular medications cannot be given effectively through any significant absorptive barrier. For this reason, IV administration is necessary in many cases (e.g., pressors, inotropes).
   b. Distribution.
      1) Poor cardiac output/shock states may affect the distribution of medication to all tissues.
      2) Medication administered for a desired response to one target organ may cause an undesirable systemic response (e.g., dobutamine increases cardiac output but may cause decreased blood pressure, furosemide reduces pulmonary edema but may decrease blood pressure).
      3) Some cardiovascular medications are highly albumin-bound; this raises the possibility of unconjugated bilirubin displacement from albumin.
   c. Metabolism.
      1) Hepatic metabolic activity may markedly affect the bioavailability of the medication (e.g., the high rate of first-pass metabolism of oral propranolol causes the IV and oral dosing to be significantly different).

Table 12.1

Vasoactive Agents—Site of Action and Systemic Effects

	Vasoconstriction		Inotrope		Vasodilation		Effects		
Agent	Alpha-1	V-1	Beta-1	PDE-3	Beta-2	D-1	HR	CO	BP
Dobutamine			+++		++		↑	↑	
Dopamine	+ - +++		++			++	↑		↑
Epinephrine	+++		+++		+++		↑	↑	↑
Isoproterenol			+++		+++		↑		
Milrinone				+++				↑	
Norepinephrine	+++		++		+		↑	↑	↑
Vasopressin		+++							↑

BP, Blood pressure; *CO,* cardiac output; *D-1,* dopamine receptor; *HR,* heart rate; *PDE-3,* phosphodiesterase-3 enzyme; *V-1,* vasopressin receptor.

2) Medication metabolites may cause a toxic response (e.g., cyanide liberation as a result of nitroprusside metabolism).
3) Rapid metabolism and serum clearance may require continuous IV infusion (e.g., dopamine, dobutamine).

d. Excretion.
1) Impaired renal function will markedly affect the excretion of some medications (e.g., captopril, furosemide). This requires careful monitoring of the clinical response and serum medication levels if applicable.
2) Medication may have a direct effect on renal function.
a) Urinary output may be diminished (e.g., indomethacin reduces the GFR).

CENTRAL NERVOUS SYSTEM MEDICATIONS

A. Introduction.
1. In adult patients, these are the most widely used group of medications.
2. The value of pain control and mood alteration in the neonatal population has only recently been recognized.
3. Recent increased interest in the use of CNS medications in the neonatal population has caused a recognition that the body of knowledge about these medications is limited.
4. The use of these medications is increasing as neurobehavioral assessment skills increase among neonatal caregivers.

B. Definitions.
1. Analgesic medication: a medication (e.g., morphine, acetaminophen) that provides diminished sensation of pain. These help promote control of undesirable responses to a painful event.
2. Anesthetic medication: a medication that removes pain sensation either through peripheral nerve block (e.g., lidocaine) or through CNS effects (e.g., high-dose fentanyl). Not all anesthetic medications provide pain relief (e.g., inhalation gases, propofol).
3. Sedative–hypnotic medications: medications that provide mood alteration in patients with anxiety. These are divided into two groups: barbiturates (e.g., phenobarbital) and nonbarbiturates (e.g., chloral hydrate, dexmedetomidine, lorazepam). These medications do not provide relief from pain.
4. Addiction: a lifestyle change that occurs in a medication-dependent person. This lifestyle change involves a focus on medication use. This behavior cannot occur in a neonate.
5. Tolerance: a condition that may occur with many types of medications. Tolerance exists when larger doses and higher serum concentrations of the medication are required to achieve the desired response and commonly occurs in conjunction with physical dependence.
6. Dependence: a physiologic state in which the individual requires regular medication administration for continued physiologic well-being. Patients who develop dependence on a medication may need a dosage-tapering regimen rather than abruptly discontinuing the medication to prevent withdrawal symptoms. In neonates, dependence can develop from either placental transfer of medications or iatrogenically due to long-term infusions of sedatives and/or narcotics.

C. Basic principles of CNS medication use.
1. Mechanism of action of most CNS medications is not clearly understood.
2. Assessment of need for these medications must be carefully performed as an ongoing process.
a. Close attention must be paid to differentiation of need for sedation, pain relief, or both.
b. These medications may cause the development of medication tolerance and/or dependence.
3. Consideration must be made for the risks and benefits of the medication in relation to potential side effects or toxicities.
4. The science of the study of neonatal neurologic development is still emerging, and much is yet to be learned. The effect that CNS medications may have on that development is largely unknown.

D. Specific considerations in the neonatal population.
1. Pharmacodynamics.
a. Limited knowledge of CNS development in premature and term neonates mandates a special need for caution in the use of CNS-active medications.
b. Specific physiologic characteristics in the neonatal population require careful observation for harmful side effects or toxicities (e.g., reduction in blood pressure with IV bolus doses of morphine, chest wall rigidity with fentanyl).
c. Narcotic analgesics may cause respiratory depression and may precipitate respiratory failure in neonates. Therefore, the lowest possible dose that relieves the patient's pain should be used.
d. Careful assessment of clinical response is necessary to determine the safest and most effective dose and interval.
2. Pharmacokinetics.
a. Absorption.
1) Poor GI motility and high first-pass clearance may make oral administration highly unpredictable for many medications (e.g., morphine).
2) Oral or rectal absorption of mild analgesics and sedatives is often adequate (e.g., acetaminophen).

b. Distribution.
   1) Because these agents work in the CNS, they must be lipid soluble to cross the blood–brain barrier.
   2) As neonates increase their proportion of body fat, the doses required will increase.
   3) Because these agents are stored in the body fat, patients must be monitored for the accumulation of these agents and hence prolonged effects.
c. Metabolism.
   1) Slower hepatic metabolism may cause a prolonged half-life.
   2) Hepatic disease may markedly increase the risk of toxic effects (e.g., midazolam).
   3) Hepatic metabolism may convert medications to either toxic metabolites or active metabolites (e.g., morphine has an active metabolite).
d. Excretion.
   1) Limited renal function or failure may cause toxic effects as a result of accumulation of medication or metabolites (e.g., seizures from penicillin).

DIURETICS

A. Introduction.
   1. Commonly used in neonatal patients to promote the removal of excessive extracellular fluid.
   2. Site of action of nearly all diuretic agents is the luminal surface of the renal tubular cell.
B. Basic principles of diuretic use.
   1. Use must be based on a thorough understanding of the functions of the various segments of the nephron in the neonatal population.
   2. Diuretic medications whose primary purpose is to cause the excretion of excess extracellular fluid commonly cause a secondary or side effect of loss of electrolytes, along with the desired water loss. Knowledge of the specific action of each diuretic medication will assist the clinician in monitoring electrolytes for undesirable losses.
   3. The pharmacologic response is dependent on the existing level of renal function and the medication's ability to reach the target tissue in amounts adequate to produce the desired diuretic effect.
   4. Any medication or therapy that increases the GFR may have an indirect diuretic effect. Some medications that act on the cardiovascular system to increase cardiac output or increase renal blood flow through vasodilation may cause diuresis (e.g., dopamine). Maximal water and electrolyte excretion usually occurs in the first days of use. Later, decreased GFR and hyperaldosteronism resulting from diuretic-induced hypovolemia limit these losses.
C. Specific considerations in the neonatal population.
   1. Pharmacodynamics.
      a. Many diuretic medications are dependent on reaching the lumen of the proximal tubule to achieve diuresis.
      b. The renal tubular function is limited in all neonates and is more limited in less mature neonates.
      c. The clinical response to diuretic agents is commonly decreased because of existing poor renal tubular absorption. Therefore, a larger dose is needed to achieve the response.
      d. Limited tubular function potentiates electrolyte loss with many diuretic agents (e.g., furosemide, hydrochlorothiazide).
   2. Pharmacokinetics.
      a. Absorption. Oral absorption may be limited, requiring a larger per-kilogram dose compared with the IV dose to achieve the desired effect (e.g., furosemide). Other diuretics (e.g., hydrochlorothiazide, spironolactone) are well absorbed orally.
      b. Distribution. Some diuretic medications are strongly protein-bound. Some concern has been raised over the displacement of bilirubin from albumin-binding sites (e.g., furosemide, spironolactone).
      c. Metabolism. Some diuretics are primarily metabolized by the liver (e.g., spironolactone).
      d. Excretion.
         1) Low renal blood flow and low GFR, along with limited renal tubular function, may delay excretion and limit the effectiveness of the medication (e.g., the plasma clearance of furosemide is prolonged in extremely premature neonates and in neonates with renal failure).
         2) Some diuretics are primarily eliminated unchanged in the urine (e.g., furosemide, hydrochlorothiazide).

IMMUNIZATIONS

A. Introduction.
   1. Vaccines are commonly given to the hospitalized neonatal patient.
   2. Each year in January, the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices publishes an updated version of the recommended immunization guidelines. Each nurse should be familiar with these guidelines (see Chapter 32).
   3. The following documentation is required when vaccines are given:
      a. Name, title, and business address of person administering the vaccine.
      b. Vaccine administered.

c. Manufacturer of the vaccine.
d. Lot number of the vaccine.
e. Expiration date of the vaccine.
f. Date of administration.
g. Site of administration.
h. Route of administration.
i. Documentation that the vaccine information statement (VIS) has been given to the parents/guardians.
j. Documentation of the VIS publication date (the most current version must be used).

B. Basic principles of immunization use.
1. The goal of immunization is to prevent many viral and bacterial diseases and their sequelae.
2. For maximum effectiveness, the immunizations must be given at specific ages before the recipients have been exposed to the diseases.
3. Live-virus vaccines (e.g., measles–mumps–rubella [MMR], rotavirus, varicella) should NOT be administered in the NICU.
4. All adverse events associated with immunization should be reported in detail in the patient's medical record and also on the Vaccine Adverse Event Reporting System (VAERS) form found on the U.S. Food and Drug Administration (FDA) website.

C. Types of immunizations.
1. Active immunization.
a. Involves the administration of all or part of a microorganism or a modified product of that microorganism to evoke an immunologic response mimicking that of natural infection. This usually presents little or no risk to the recipient.
b. Some immunizing agents provide complete protection against disease for life (e.g., polio vaccine), some provide partial protection (e.g., influenza vaccine), and some must be readministered at intervals (booster doses) (e.g., tetanus vaccine).
c. Vaccines may be either live (attenuated) or killed (inactivated). Inactivated vaccines may not elicit the range of immunologic response provided by attenuated agents.
2. Passive immunization.
a. Involves the administration of preformed antibody to a recipient.
b. Most often used when a person exposed to a disease has a high likelihood of complications from that disease and time does not permit adequate protection by active immunization alone.
c. Can be used when a disease is already present with the hope of reducing the reaction to the disease.
d. Accomplished through the use of immune globulin preparations (e.g., hepatitis B immune globulin, palivizumab).
e. There are strict indications for the use of these products (American Academy of Pediatrics [AAP], 2012).

D. Specific considerations in the neonatal population.
1. Pharmacodynamics.
a. Most immunizations are usually given starting at 2 months of age; the immune response to the vaccines may be limited if given before this age. Resistance to certain diseases before this time may be provided from the mother's antibodies that are transferred across the placenta.
b. Preterm infants who are medically stable should receive the immunizations at the recommended chronologic age as long as the following criteria are met:
1) The infant does not require ongoing treatment for serious infections or metabolic disease.
2) The infant does not have acute renal, cardiovascular, or respiratory illness.
3) The infant demonstrates a clinical course of sustained recovery and a pattern of steady growth (AAP, 2012).
c. The dose should NOT be decreased in preterm infants.
d. Antibody titers may be measured to prove adequate immune responses.
2. Pharmacokinetics.
a. Absorption.
1) Injectable vaccines should be administered in sites that limit the risk of neural, vascular, or tissue injury.
2) The preferred site for administration is the anterolateral aspect of the upper thigh.
3) The deltoid area of the upper arm can be used in older infants (>1 year).
4) The upper, outer aspect of the buttocks should not be routinely used because of the possibility of damaging the sciatic nerve and reduced immunogenicity.
5) When necessary, two vaccines can be given in the same limb but should be separated by at least 1 inch if possible so that local reactions are not likely to overlap.
6) The recommended routes of administration are included in the package inserts of the vaccines (e.g., intramuscular, subcutaneous).
b. Distribution. Vaccines should be held when the neonate is on pressor agents because the blood flow to the muscle and subcutaneous tissues may be limited.
c. Metabolism/excretion: Kidney and/or liver failure should not prevent the administration of vaccines.

E. **Misconceptions about vaccine contraindications:** The nurse should be familiar with the specific contraindications listed in the package inserts of the vaccines

so that immunizations are not withheld unnecessarily (AAP, 2012).

Nursing Implications for Medication Administration in the Neonate

There are several areas in which the nursing staff are an invaluable resource for the patient in helping to prevent errors in this fragile patient population.

A. **Correct order-writing policies** should be followed to reduce the potential for error. Unapproved abbreviations should be avoided, trailing zeros should be avoided (e.g., 1.0), leading decimals should be used (e.g., 0.1), and all verbal orders should be read back to the physician for clarification.
B. **Standard concentrations** for IV continuous infusions should be used rather than relying on concentrations based on weight.
C. **Double-check of medication doses** involves recalculating the weight-based doses and comparing prescribed doses with current medication dosing reference books to prevent potential medication dosing errors. In addition, smart pump technology that includes dosing ranges for both intermittent and continuous infusions for IV medications should be used with IV pumps to avoid programmable errors.
D. **Cross-checking** on a regular basis is a nursing responsibility. Because of the very small volumes of medications commonly given to the NICU patient, a system for regular cross-checking of medications' volume accuracy with medication concentration before administration should be established for all medications and especially with high-risk medications.
E. **Monitoring renal function through intake and output measurements** may alert the care team to potential changes in medication metabolism and/or excretion.
F. **Meticulous medication administration and documentation** involves administering the medication at the correct time and at the correct time interval. In addition, documenting the medication administration date, time, dose, route, and interval and the time medication levels are obtained is important in interpreting patient response to therapy.
G. **Facilitation of medication serum-level monitoring with absolute accuracy** makes safe administration of medications—with a narrow margin between effective and toxic levels—possible.
H. **Careful assessment of vital sign parameters and clinical responses** may assist in the evaluation of desirable or undesirable medication responses.
I. **Careful observation of the neonate for therapeutic and toxic medication effects** will allow medication administration to achieve the maximal desired response while minimizing toxic responses.
J. **Medication precautions** must be observed. Any medication or medication preparation known to have a high risk of adverse effects in the neonate should be removed from the patient care area (e.g., concentrated potassium vials) or should be specifically labeled to avoid inadvertent administration.
K. **Facilitation of or participation in clinical trials** designed to evaluate a medication's efficacy does much to advance the body of knowledge related to neonatal pharmacology.
L. **Recognition of established clinical experience with individual medications in the neonatal population is essential.** Because some medications are introduced into the clinical area after only minimal study of specific medication response in the neonate, early observation of potential toxic effects may avert a later disaster.

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CHAPTER 13
Laboratory Testing in the NICU

Patricia Scheans

OBJECTIVES

1. Discuss laboratory testing common to the neonatal intensive care unit (NICU).
2. Review laboratory specimen collection best practices.
3. Review the principles of laboratory values interpretation.
4. Describe iatrogenic sequelae associated with laboratory testing, including strategies to minimize them.
5. Discuss the decision tree for ordering laboratory tests.

Laboratory Testing in the NICU

Newborns in the United States receive at least one laboratory test, typically in the form of screening for jaundice, genetic disorders, and inborn errors of metabolism. In addition, infants admitted to the neonatal intensive care unit (NICU) often require numerous laboratory tests and diagnostic procedures to assess their clinical status. Given the U.S. birth rate of nearly 4 million newborns annually and the average NICU admission rate of 7% of live births, the total number of laboratory tests is staggering (Centers for Disease Control and Prevention, 2017).

Laboratory tests influence nearly 60% to 70% of all medical decisions. In addition, testing contributes to iatrogenic anemia, increased health care costs, and unnecessary downstream testing and procedures (Eaton et al., 2017).

Health care workers in the NICU are involved in obtaining laboratory samples; therefore, an understanding of laboratory testing principles and the impact on patient care and cost is essential. Developing skills in the interpretation of test results is a key element in comprehensive patient care. Laboratory testing in the NICU is multidimensional and is driven by patient history and symptomatology. Selection of specific laboratory tests should maximize patient care, minimize patient risk, and show good stewardship of health care costs (Hiscock et al., 2018). Laboratory testing helps to:

1. Determine the health state of the patient.
2. Monitor the clinical status, trends, and disease severity.
3. Assist in differential diagnosis.
4. Confirm a diagnosis or cure.
5. Screen for common disorders and for disease prevention.
6. Measure the effect(s) of therapy.
7. Assist in the management of disease.
8. Establish a prognosis.
9. Assist in genetic counseling.
10. Evaluate specific events—for example: medication errors, sudden clinical decompensation, medico-legal, research, and postmortem evaluation.

Laboratory tests commonly performed in the NICU include the following (Table 13.1):

A. *Chemistry:* measurement of chemical substances reflects biochemical metabolic processes and disease states in the body. Measuring or monitoring changes in levels aids in diagnosis, planning of care, monitoring of therapy, screening, determining the severity of disease, and response to treatment. The four main categories of chemical analyses include (Crook, 2012):
   1. Hematology: study of the blood and blood-forming tissues of the body, such as the bone marrow and reticuloendothelial system.
   2. Hemoglobin (Hgb) structure, red cell membrane, and red cell enzyme activity.
   3. Blood cells: erythrocytes (red blood cells), leukocytes (white blood cells), and thrombocytes (platelets). Examples: hematocrit (Hct), reticulocyte (Retic) count, platelet (Plt) count, peripheral blood smear, complete blood count (CBC), white blood cell (WBC) count, and WBC differential count.

B. *Plasma proteins, coagulation factors, and immunoglobulins.* Examples include total protein, albumin, fibrinogen (factor I), prothrombin (factor II), thromboplastin (factor III), factors IV through XIII assays, immunoglobulin G (IgG), immunoglobulin A (IgA), and immunoglobulin M (IgM).

C. *Microbiology*: identification of infectious microorganisms. Tests include bacteriology, mycology, virology, parasitology, and serology. Examples include cultures and sensitivities to antibiotics, antigens, and antibodies.

D. *Microscopy:* examination of body fluids and tissues under a microscope. Examples include cell counts, fecal blood, cytology, Apt test (alkali denaturation test), and urinalysis.

Table 13.1

Common Laboratory Tests in the NICU by System

Fluids Electrolytes Nutrition	Respiratory	Cardiac	GI	Renal	Endocrine/Metabolic	Neurologic	Hematologic	Other
Electrolytes (serum)	Blood gas	Iso-enzymes	Alkaline phosphatase	BUN (serum)	Glucose	Phenobarbital level	CBC with differential	Chromosome studies
Calcium (serum)	pH	Digoxin level	Triglyceride levels	Creatinine (serum)	Thyroxine level Thyroid-stimulating hormone level	Dilantin level	Hct/Hgb	Bilirubin Total/indirect/direct
Magnesium (serum)	$Paco_2$		AST (SGOT)	Specific gravity	Cortisol level	Ammonia (serum)	Platelet count Platelet antibody	CRP
Phosphorus (serum)	Pao_2		ALT (SGPT)	Urine sodium	Insulin level	Amino acid (serum)	Reticulocyte count	Drug levels
Alkaline phosphatase	Bicarbonate (HCO_3^-)		GGT (GGTP)	Urine potassium	Growth hormone level	Amino acid (urine)	Direct Coombs' test/ DAT	Urine/meconium/ cordtoxicology screen
Glucose (serum)	Base excess		Bilirubin (total and direct)	Urine osmolality	Testosterone level	Organic acids (urine)	Blood type and Rh	Culture and sensitivity (all sources)
Vitamin levels	Theophylline level		Ammonia (serum)		Aldosterone (serum and urine) level	Glycine (serum and CSF)	G6PD	RPR/VDRL
Serum osmolality	Caffeine level		α_1-antitrypsin	Uric acid (serum)	17-hydroxy corticosteroids	Pyridoxine level	Sedimentation rate	Occult blood (fecal)
Albumin (serum)	Cultures (tracheal/ sputum)		Trypsin (stool)	Urinalysis	Parathyroid hormone level	Lactic acid/ lactate level	Folic acid	PCR (serum)
Total protein			Pyridoxine level	Urine culture/ sensitivity	State blood spot screening		Fibrinogen PT PTT Immunoglobulins Methemoglobin	

ALT (SGPT), Alanine aminotransferase (serum glutamic-pyruvic transaminase); *AST (SGOT)*, aspartate aminotransferase (serum glutamic-oxaloacetic transaminase); *BUN*, blood urea nitrogen; *CBC*, complete blood count; *CRP*, C-reactive protein; *CSF*, cerebrospinal fluid; *DAT*, direct antiglobulin test; *GI*, gastrointestinal; *GGT (GGTP)*, γ-glutamyltransferase (γ-glutamyl transpeptidase); *G6PD*, glucose-6-phosphate dehydrogenase; *Hct*, hematocrit; *Hgb*, hemoglobin; *NICU*, neonatal intensive care unit; *PCR*, polymerase chain reaction; *PT*, prothrombin time; *PTT*, partial thromboplastin time; *RPR*, rapid plasma reagin; *VDRL*, venereal disease research laboratory.

E. *Immunohematology (blood bank, transfusion medicine):* blood donor screening, blood compatibility testing, blood component preparation, and blood and stem cell banking Examples include blood group antibodies and antigens: ABO group, Rh factor, Kell, direct antiglobulin test (DAT)/Coombs test, Kleihauer–Betke.
F. *Immunoassay:* immunologic reaction to detect or quantify a specific substance in blood or body fluid for therapeutic drug monitoring, toxicology screening, detection of plasma proteins, and endocrine testing. Examples include urine and meconium toxicologies, latex agglutination test, and drug levels.
G. *Immunology:* measurement of immune system activity used to diagnose inflammatory responses, immunodeficiency, and autoimmune disorders. Examples include C-reactive protein (CRP), cytokine measurement, complement C3 and C4, IgG, IgM, and IgA.
H. *Cytogenetics*: determination of genetic composition by chromosomal analysis. Examples include karyotyping (blood, amniotic fluid, chorionic villus, tissue, bone marrow, buccal swab), chromosome-specific DNA probes, fluorescence in-situ hybridization (FISH), and advanced array comparative genomic hybridization (aCGH).

Laboratory Specimen Collection Best Practices

Collection of laboratory specimens requires meticulous methodology to ensure accurate results. Proper technique, sample source, specimen quantity, collection tube type, labeling, and laboratory processing maximize the accuracy of results while minimizing blood loss, pain, and costs. Procedural pain management techniques should be employed before and during collection of laboratory specimens (American Academy of Pediatrics, 2017; Hall and Anand, 2014; Johnston et al., 2017).

Point-of-care testing (POCT), alternative-site testing, near-patient testing, and patient-focused testing are done in a variety of settings, often at the bedside. POCT includes blood obtained from arterial, capillary, or venous sources, as well as transcutaneous measurement. It can provide rapid, real-time testing of minimal blood volumes or avoid a blood draw (e.g., transcutaneous). POCT in the NICU includes evaluation of glucose, blood gases, electrolytes, ionized calcium, blood urea nitrogen (BUN), creatinine, hematocrit, Hgb, and transcutaneous bilirubin (Pecoraro et al., 2014).

LABORATORY TEST COLLECTION METHODS IN THE NICU (SEE ALSO CHAPTER 15)

A. *Capillary blood sampling*: admixture of arterial, venous, and capillary blood and tissue fluid. Heel sticks should not be performed if feet are edematous, injured, bruised, infected, or anomalous. NOTE: Finger-stick sampling is contraindicated in infants, because the distance from skin surface to bone is less than 1.5 mm (Eichenwald et al., 2017). NOTE: The Cochrane Database of Systematic Reviews concludes that venipuncture, performed by skilled phlebotomists, appears to be the method of choice for blood sampling in term neonates (Shah and Ohlsson, 2011).
   1. Most common route for obtaining small blood samples in the infant.
   2. Heel stick less than 2 mm in depth; heel-stick devices range from 0.65 to 1 mm, depending on infant size (Fischbach and Fischbach, 2017).
   3. Warming the heel and discarding the initial drops of blood help minimize capillary and venous laboratory value differences (Blackburn, 2018).
   4. Avoid squeezing or milking the site to minimize hemolysis (Eichenwald et al., 2017).
   5. Avoid excessive scooping of blood from nearby skin with the lip of collection tube (Fischbach and Fischbach, 2017).
B. *Venipuncture:* venous blood typically obtained from the hand, arm, foot, leg, or scalp in neonates. Venous blood can also be obtained from an umbilical vein catheter, tunneled central venous catheter, or (in some cases) peripherally inserted central catheter (PICC). In term infants, venipuncture has been shown to be a less painful procedure than heel stick when performed by skilled phlebotomists (American Academy of Pediatrics, 2017; Hall and Anand, 2014).
   1. A tourniquet may be needed to distend peripheral veins. Recommended time for tourniquet application is ≤1 minute, as tourniquet application ≥3 minutes may alter laboratory test results (Fischbach and Fischbach, 2017).
   2. As indicated, long veins may need to be avoided/spared for future intravenous (IV) and PICC sites.
C. *Arterial puncture* (see also Chapter 15): arterial blood typically obtained from an artery stick of the radial, tibial, or temporal arteries in neonates. Brachial artery stick is performed less often due to potential for arteriospasm of the brachial artery supplying the lower arm. Femoral artery stick is rarely performed in the NICU population. Arterial blood can also be obtained from an umbilical artery catheter or percutaneous arterial line.
   1. Allen test (modified) should be done before radial artery stick (Dahan et al., 2016; Eichenwald et al., 2017).
D. *Umbilical cord or placental vessel:* obtained by needle aspiration of umbilical cord artery and/or vein. Examples include blood gases and blood culture (Carroll and Christensen, 2015).

E. *Lumbar puncture* (see Chapter 15): needle aspiration of cerebrospinal fluid (CSF) from the spinal canal can be analyzed for:
   1. Infection.
   2. Hemorrhage.
   3. Demyelinating diseases.
   4. Malignancy.

F. *Urine sampling* (see also Chapter 15): urine obtained by bag collection and/or catheterization can be utilized for:
   1. Chemical analysis.
   2. Bacterial cultures.
   3. Microscopic examination.

G. *Thoracentesis* (see also Chapter 15): needle aspiration or chest tube sampling of fluid (effusion) from the thoracic cavity can be analyzed for:
   1. Microorganisms: cultures, Gram stain.
   2. Chemistries: levels of electrolytes, total protein, albumin, glucose, triglycerides.
   3. Hematology: WBC count, WBC differential count.

H. *Peritoneal tap*: needle aspiration of fluid (ascites) from the abdomen/peritoneal cavity can be analyzed for:
   1. Microorganisms: cultures, Gram stain.
   2. Chemistries: electrolytes, total protein, albumin, glucose, triglycerides.
   3. Hematology: WBC count, WBC differential count.

I. There are several "rights" to laboratory specimen collection: the right test, right patient, right time, right tube, right technique, right amount, right label, and right handling.
   1. Verify diagnostic test order request.
   2. Confirm clinical indication.
   3. Cluster laboratory draws as much as possible.
   4. Confirm patient identification before laboratory sampling per hospital protocol.
   5. Use neurodevelopmental support and procedural pain management techniques (Eichenwald et al., 2017; Johnston et al., 2017).
   6. Observe strict aseptic technique.
   7. Observe Standard Precautions.
   8. Obtain laboratory test using appropriate route, correct collection container/tube, and correct specimen volume. The recommended order is (or per institution protocol):
      a. Blood cultures (to reduce risk of contamination). Note: Blood cultures cannot be obtained via capillary source.
      b. Hematology specimens (to minimize platelet clumping).
   9. Chemistry and blood bank samples (Eichenwald et al., 2017).
   10. Label specimen per institution practice.
   11. Place specimen(s) in biohazard container or bag per institution practice.
   12. Promptly send specimen to laboratory on ice, if indicated.

J. **Laboratory specimen tubes:** standardized, color-coded containers, may contain anticoagulant (Fischbach and Fischbach, 2017).
   1. Whole blood: blood cells suspended in plasma fluid.
   2. Plasma: unclotted blood centrifuged to remove cells; contains fibrinogen.
   3. Serum: by-product of clotted blood, centrifuged to remove the clot and any other cells.
   4. Microtainers: allow use of smaller blood volumes.
   5. Blood culture bottles: prepare and transfer blood per institution practice.
   6. Sterile swabs: bacterial, viral.
   7. Anticoagulant tubes.
      a. Must be filled to the indicated line to properly dilute anticoagulant.
      b. Should be gently inverted, end over end, 7 to 10 times.

Laboratory Test Interpretation Principles

It is important to be familiar with the applications and limitations of laboratory data. Many factors influence blood values and their interpretation in the newborn, including gestational age, postnatal age, placental transfusion, and growth rate (Blackburn, 2018; Eaton et al., 2017; Fischbach and Fischbach, 2017). The following concepts are integral in laboratory interpretation.

A. *Accuracy:* synonymous with "correctness"—how close a test result is to the true value.
   1. Point-to-point variability in test results exists.
   2. Variation in value may be more reflective of an analytic variation of automated chemistry systems than actual patient status.

B. *Precision:* synonymous with "reproducibility"—distribution of results when a sample is analyzed repeatedly.
   1. Imprecision is known as *random error*.
   2. Test precision is a more desirable test characteristic than accuracy in measuring treatment response or clinical changes.

C. *Sensitivity:* ability to correctly identify an individual with disease and avoid falsely testing "healthy." This is a test's ability to generate more true-positive results and fewer false-negative results.
   1. Sensitive tests have a low threshold for abnormality.
   2. Sensitive tests usually have a low specificity.
   3. Certain testing requires sensitivity over specificity. Example: blood bank donors screened for infectious diseases—it is better to err in excluding donors who are falsely positive than include donors who are falsely negative.

D. *Specificity:* ability of a test to identify only those individuals with disease as opposed to individuals testing positive when there is no disease. It refers to a test's

ability to generate more true-negative results and fewer false-positive results.
1. Specific tests have a high threshold for "normal" or negative test results.
2. Specific tests usually have low sensitivity.
3. Certain testing requires specificity over sensitivity. Examples include urine toxicology screen to detect the presence of cocaine and cardiac isoenzymes to rule out a myocardial infarction.

E. *Positive predictive value (yield):* probability that an individual with a positive screening test actually has the disease. It is dependent on the prevalence of the disease in the population being tested.
1. Probability ratio is a percentage based on the population screened.
2. Compare all who test positive with those who actually have the disease to obtain the percentage of probability that the individual who tested positive has the disease.
3. Testing such as state screening programs consider this probability.

F. *Negative predictive value:* probability that an individual with a negative screening test does not actually have the disease.
1. Probability ratio is a percentage based on the population screened.
2. Compare all who test negative with those who actually do not have the disease to obtain the percentage of probability that the individual who tested negative does not have the disease.

G. *Reference range:* established upper and lower boundary levels of a laboratory value. The range of normality (mathematical) is dependent on population subsets such as age, gender, pregnancy, and other patient attributes.
1. Often referred to as "normal" range.
2. The term *normal* is misleading—reference range determined based on specific attributes of a population subset, not due to normalcy.
3. Approximately 5% of "healthy" laboratory results fall outside the reference range.
4. Reference ranges can vary from laboratory to laboratory.

Principles of Test Utilization

Patient management depends on clinical skill, judicious use of laboratory testing, and careful interpretation of laboratory data. **Once a laboratory value is determined and patient clinical status evaluated, the combined information is used to direct treatment. In an effort to optimize care, minimize patient discomfort, and contain health care costs, key principles of test utilization include** (Fischbach and Fischbach, 2017) **the following:**

A. Even under the best of circumstances, no test is perfect.
1. Results can be misleading.
2. Specificity or sensitivity of a test is never 100%.

B. Choice of tests should be based on the probability of the diagnosis being sought, which affects the predictive value of the test.
1. Patient history and examination should precede choice of laboratory tests.

C. History, physical examination, and prevalence of a disease determine the probability of diagnosis.

D. The combination of short-term physiologic variation and analytic error is sufficient to render the interpretation of single determinations difficult when the concentrations are in the borderline range.
1. Despite the high quality of a laboratory, any given laboratory result may be incorrect.
2. Laboratory tests may need to be redone at times by a different laboratory.

E. Reference ranges vary from one laboratory to another.
1. Age, gender, race, size, and physiologic status must be considered.

F. Tables of reference values represent statistical data for 95% of the population; values outside these ranges do not necessarily represent disease.
1. Test results falling within the reference range may be abnormal from the patient's baseline range.
2. Comparing patient laboratory values obtained when not ill often provides a better reference value than "normal" ranges.
3. Some conditions warrant serial testing.

G. Multiple test abnormalities are more likely to be significant than single test abnormalities.
1. Two or more positive tests for a given disease reinforce diagnosis.

H. The greater the degree of abnormality of a test result, the more likely that a confirmed value is clinically significant or represents a real disorder.

I. Patient condition and acuity should dictate testing interval.
1. Tests should be performed only if they will alter the patient's diagnosis, prognosis, treatment, or management.
2. Excessive repetition of tests is wasteful, and the excess burden increases the possibility of laboratory errors.

J. Clerical errors are far more likely than technical errors to cause incorrect results.

K. Medications can produce false-negative and false-positive results. Examples include anticonvulsants, antihypertensives, and antiinfectives.

L. Artifacts can cause spurious values, especially in the face of discrepant laboratory results.

M. Negative laboratory tests (or other tests) do not necessarily rule out a clinical disease.

N. Various disorders or conditions may produce the same combination of laboratory test changes.

Laboratory Interpretation—Decision Tree

Careful laboratory data interpretation is essential in providing accurate therapeutic interventions. Asking focused questions will assist in refining critical thinking skills related to utilization of laboratory values in patient management.

A. Laboratory test result. Is it reliable? Is it believable (Box 13.1)?
   1. Decision tree if *result is too low*.
      a. Is the sample diluted?
         1) A laboratory specimen can be contaminated with or diluted by fluids infusing through indwelling arterial and/or venous lines if the line is not properly cleared.
         2) A laboratory specimen can be diluted by interstitial fluid from the skin tissues if the heel-stick puncture is not fresh, the puncture site is not prewarmed, or the infant is exceedingly edematous.
      b. Was the sample handled correctly?
         1) A serum bilirubin count can be falsely low if obtained while the infant is under phototherapy or if exposed to the daylight or fluorescent light too long before analysis.
         2) A serum glucose level can be falsely low if left in a microtainer and not processed and analyzed promptly.
         3) An overfilled or underfilled hematology sample can precipitate clotting and falsely decrease platelet count.
      c. Was the timing of the test appropriate?
         1) Serum gentamicin, vancomycin, or theophylline level will be too low if drawn too early in the treatment.
         2) Serum glucose or POCT glucose level obtained too soon after feeding the infant may remain falsely low due to lack of digestion.
         3) Electrolyte levels may remain falsely low if obtained too soon after electrolyte replacement.
      d. Was medical therapy not implemented or inadequate?
         1) Blood gas level obtained before weaning the ventilator.
         2) Serum glucose or POCT glucose level obtained before medical intervention for hypoglycemia.
         3) Serum gentamicin, vancomycin, or theophylline level will be too low if the dose is inadequate or dosing interval too long.
         4) Theophylline level may be low because intermittent doses are held as a result of tachycardia in the infant.
      e. Was the specimen site condition a factor?
         1) Capillary blood sample from an edematous infant can be falsely low due to excessive tissue fluid.
         2) Nonwarmed heel can falsely lower a capillary blood gas pH, Po_2.
      f. Was the POCT device calibrated?
         1) POCT device was not calibrated recently.
         2) POCT device was calibrated improperly.
         3) Reagent used for calibration had expired.

Box 13.1

Laboratory Interpretation: Is It Reliable? Is It Believable?

Yes	No
Implement an appropriate clinical intervention, if needed. Consider repeating the laboratory test if the clinical status continues to warrant a laboratory test.	Consider repeating the laboratory test when the appropriate correction is made.
Result Too Low	**Result Too High**
Is the sample diluted? Was the sample handled correctly? Was the timing of the test an issue? Was medical therapy not implemented or inadequate? Was the specimen site condition a factor? Was the point-of-care testing (POCT) device calibrated? Was there interference from a past medical therapy? Was the sample handled correctly? Was medical therapy not implemented or inadequate?	Does the blood gas need to be temperature corrected (as with neuroprotective hypothermia therapy)? Was the laboratory specimen drawn too early?

4) Sample cartridge expired or was not kept at room temperature.

g. Was there interference from past medical therapy?
1) Blood culture result may be falsely negative if mother was treated with antibiotics during labor.
2) Phenobarbital may decrease theophylline concentrations.

2. Decision tree if *result is too high*.
a. Was the laboratory specimen drawn too early?
1) Triglyceride level may be falsely elevated if drawn too soon after lipid infusion.
2) Serum calcium level may be falsely increased if drawn soon after a calcium gluconate bolus.
3) Electrolytes can remain abnormal if drawn too soon after corrective action.

b. Was the sample handled correctly?
1) Serum potassium level may be falsely elevated due to hemolysis from squeezing the heel for capillary sample.
2) Serum protein, potassium level, or lactate may be falsely elevated if a tourniquet is applied too tightly or too long (≥3 minutes).
3) Hematocrit can be falsely elevated if drawn from a poorly perfused heel.
4) Blood gases may need to be temperature corrected during neuroprotective hypothermia therapy.

c. Was medical therapy not implemented or inadequate?
1) Serum bilirubin count can remain elevated if phototherapy is not instituted long enough to measure a change or is not used at effective irradiance levels.
2) P_{CO_2} can remain elevated if ventilator setting changes are not sufficient to correct for the respiratory ailment or the sample is drawn too soon after corrective intervention.

d. Was the source of the laboratory sample not appropriate?
1) Hematocrit can vary with capillary sample versus an arterial or venous sample.
2) Ammonia level can be falsely elevated if hemolyzed, so needs to be drawn via an artery or vein.

e. Was the POCT device calibrated?
1) Result may be unreliable if the POCT device was not recently calibrated or was calibrated improperly, if the reagent for calibration had expired, or the sample cartridge either expired or was not stored properly.

3. Laboratory test result. Is it *reliable*? Is it *believable*? If so:
a. Implement appropriate clinical intervention, if needed.
1) Alert care provider of laboratory result and implement appropriate medical or nursing corrective intervention as needed.
2) Medication dosage change for an out-of-range drug level.
3) Ventilator setting change for underventilation or overventilation.
4) Blood product transfusion for anemia, thrombocytopenia, coagulopathy.
5) Change in IV fluid concentration or rate for electrolyte imbalance or dehydration.
6) Change feeding interval for hypoglycemia.

4. Laboratory test result. Is it *reliable*? Is it *believable*? If not:
a. Consider repeating laboratory test when the appropriate correction is made.
1) Repeat test at an appropriate time for drug-level measurement.
2) Warm heel before obtaining capillary sample.
3) Wait 30 minutes to 1 hour after feeding to test a postprandial serum glucose level.

b. Consider repeating a laboratory test if clinical status continues to warrant laboratory test.
1) Clotted complete blood count (CBC) sample after red blood cell transfusion or after antibiotic therapy: may not require a repeat sample or might wait for redraw until another blood sample is needed.
2) High Hct value from acrocyanotic heel in a hypoglycemic infant might need a central Hct to determine if polycythemia is a cause of hypoglycemia.

B. Laboratory test result. Is it normal? If so (Box 13.2):
1. Consider a change in medical management.

Box 13.2

Laboratory Interpretation: Is It Normal?

Yes	No
Consider a change in medical management.	Institute corrective medical and/or nursing action.
Consider implementing surveillance plans.	Consider calling the laboratory to verify the specimen.
Is the laboratory result in the appropriate reference range?	Consider medication interactions as etiology.
	Review patient care practice at the time of laboratory specimen sampling.

a. Normal electrolyte results in the face of electrolyte replacement may signal a need to decrease or stop the electrolyte supplementation.
b. Normal Hct may warrant cancellation of a projected red blood cell transfusion.

2. Consider implementing surveillance plans.
a. Normal serum calcium, phosphorus, and alkaline phosphatase may need weekly surveillance in very low birth weight infants to monitor for the potential for rickets.
b. Normal electrolytes may need frequent monitoring when initiating diuretic therapy.

C. Laboratory test result. Is it normal? If not:
1. As previously described in this section, with additional interventions described here.
2. Consider calling the laboratory to verify the specimen.
a. Verify that the result is indeed that of the patient in question.
b. Verify correct patient was tested.
3. Is the laboratory result in the appropriate reference range?
a. Critical Hct value differs with age. An Hct of 55% in a newborn is normal compared with an adult.
b. Laboratory methods and equipment vary; confirm laboratory result with the laboratory that analyzed the sample.
4. Review patient care at time of laboratory specimen sampling as previously described in this section.
5. Consider medication interactions as the etiology.
a. Heparin in a blood sample may prolong prothrombin time (PT) and partial thromboplastin time (PTT) (Wyatt et al., 2017).
b. Narcotic sedation may depress respirations and increase P_{CO_2} level.
c. Sulfonamides can increase serum bilirubin.
d. Stool occult blood testing can be falsely positive when receiving iron supplement, indomethacin, potassium preparations, or steroids.
6. Institute corrective medical and/or nursing action as previously described in this section.

D. Laboratory test follow-up—normal test result (Box 13.3).
1. Continue to watch for potential sequelae of treatment.
a. Periodic monitoring of electrolytes while on diuretic therapy.
b. Periodic monitoring of renal function and electrolytes on antifungal therapy.
2. Consider a plan for implementing maintenance laboratory surveillance.
a. Routine weekly monitoring of electrolytes, liver function, and renal function when the infant is on prolonged hyperalimentation.
b. Routine monitoring of skeletal integrity for preterm infants at risk for rickets.

E. Laboratory test follow-up—abnormal test result (see Box 13.3).
1. Consider a change in clinical practice as previously described in this section.
2. Allow time for corrective action, then repeat laboratory test to measure effectiveness of therapy.
a. Weaning from ventilatory support may warrant blood gas analyses every half-hour to every 4 hours for an overventilated infant recovering from primary atelectasis.
b. Repeated serum glucose-level checks every half-hour to every hour may be necessary after a hypoglycemic infant receives an IV dextrose bolus.
c. Weekly or biweekly serum electrolyte tests may be necessary when adjusting oral electrolyte supplementation for infants on diuretics for chronic lung disease.

Laboratory Testing—Iatrogenic Sequelae and Preventive Strategies

The goal of laboratory testing is to diagnose and guide management of disease. Invasive procedures are performed on NICU patients during their stay, with the smallest of infants experiencing the largest number of painful procedures. Inadvertently, the pain of laboratory testing can complicate patient care by creating additional illness, stress, injury, and/or cost. An understanding of the potential sequelae and strategies to minimize them is integral to patient care (Johnston et al., 2017) (see also Chapter 11).

A. *Physiologic stress*: adverse physiologic symptoms triggered by pain and/or sensory stimuli.
1. Tachycardia or bradycardia.
2. Hypertension or hypotension.

Box 13.3

Laboratory Interpretation: Test Follow-Up

Normal Test Result	Abnormal Test Result
Continue to watch for potential sequelae of treatment.	Consider a change in clinical practice.
Consider a plan for implementing maintenance laboratory surveillance.	Allow time for corrective action, then repeat laboratory test to measure effective therapy.

3. Respiratory distress, apnea, cyanosis.
4. Changes in skin color and temperature.

B. Physiologic stress can potentially alter a laboratory sample result.
1. Change in P_{CO_2} and P_{O_2} due to crying.
2. Altered blood pH due to hypothermia.

C. Strategies to minimize sampling-induced physiologic stress include the following (Hall and Anand, 2014):
1. Minimize skin punctures by minimizing or combining laboratory work.
2. Utilize indwelling/central catheters to obtain laboratory samples.
3. Use noninvasive pain management techniques to assist infant in coping with painful stimuli.
4. Use spring-loaded lancets for heel-stick sampling.
5. Apply chemical warming devices to the heel to promote blood flow and improve testing accuracy, thus avoiding repeat laboratory sampling.
6. Careful specimen collection, handling, and labeling decreases repeat draws.

D. *Pain:* unpleasant sensory and emotional experience associated with actual or potential tissue invasion that can cause adverse physiologic stress, including potential central nervous system (CNS) alterations (see also Chapter 16).

E. Strategies to minimize sampling-induced or procedural pain include the following:
1. Minimizing physiologic stress.
2. Use of nonpharmacologic pain management strategies such as swaddling, facilitated tucking, nonnutritive sucking, and skin-to-skin contact.
3. Pharmacologic pain management strategies, for example, 24% sucrose, local anesthetics, opioid and nonopioid analgesics.
4. Topical local anesthesia for venipuncture, lumbar puncture, and IV catheter insertion. This is not effective for heel sticks (American Academy of Pediatrics, 2017; August et al., 2017; Hall and Anand, 2014).
5. Using venipuncture when obtaining blood samples may be less painful and have fewer potential sequelae (i.e., nerve damage, arterial spasm) compared with arterial puncture.
6. Venipuncture may be preferable to the heel-stick procedure in minimizing procedure-related pain in term neonates (American Academy of Pediatrics, 2017).

F. *Skin injury:* alteration in normal barrier function as a result of invasive procedures, adhesives, reaction to antiseptics, and/or disease states. Many laboratory sampling techniques disrupt skin integrity, potentially causing injury and creating a portal for infection (August et al., 2017).

G. Skin injury from obtaining laboratory samples includes:
1. Bruising.
2. Hematoma.
3. Abrasion from antiseptic solutions, friction.
4. Dermal stripping from adhesives and/or tape application.
5. Scarring from multiple punctures.
6. Calcification.
7. Burns secondary to prewarming—use ONLY chemical heel-warming devices.
8. Chemical burns secondary to disinfectant skin-cleansing agents.
9. Infection.

H. Strategies to minimize sampling-induced skin injury from skin puncture include:
1. Minimize laboratory work, combine laboratory draws.
2. Use transcutaneous measurement.
3. Avoid excessive "squeeze" when obtaining capillary blood sample.
4. Apply adequate pressure to puncture sites to minimize bleeding and hematoma.
5. Avoid tape and self-adhering bandages to prevent epidermal stripping.
6. Use nonadhering products to dress puncture site.
7. Thoroughly remove antiseptic solutions with sterile saline or water.
8. Use appropriate skin puncture devices.
   a. Spring-loaded lancets of proper length (<2 mm) and size, ranging from 0.65 to 2 mm, depending on infant size.
   b. Butterfly needle of proper gauge and length for site/size.

I. *Infection:* skin barrier function is disrupted, allowing a portal for infection, including:
1. Bacterial/candidal skin surface infection.
2. Cellulitis.
3. Abscess formation.
4. Septicemia.
5. Osteomyelitis (heel stick too deep, too medial to calcaneus).
6. Urinary tract/bladder infection.
7. Meningitis.

J. Strategies to minimize sampling-induced infection include:
1. Avoid sampling in area of existing skin injury.
2. Avoid sampling from central lines.
3. Meticulous aseptic technique.
4. Use strategies to maintain optimal skin integrity (see Chapter 36).

K. *Organ and/or nerve injury:* needle-incurred injury includes:
1. Nerve and/or tissues in wrist or brachial area from arterial puncture.
2. Lung and/or breast tissue from thoracentesis.
3. Abdominal organs from peritoneal tap.
4. Nerves or tissue of spine from lumbar puncture.
5. Skin.
6. Tissue ischemia from arteriospasm secondary to arterial puncture.

L. Strategies to minimize sampling-induced organ and/or nerve injury include:
   1. Prudent use of laboratory sampling.
   2. Proper technique for needle-stick sampling (see also Chapter 15).
   3. Ultrasound guidance as needed for pleural and peritoneal aspiration.

M. *Anemia*: iatrogenic anemia despite microsampling and conservative laboratory sampling.
   1. Sick infants can lose more than 5 mL of blood per day (Eaton et al., 2017).
   2. Removal of 1 mL of blood from an infant weighing 1 kilogram equals removal of 70 mL of blood from an adult (Blackburn, 2018).

N. Strategies to minimize sampling-induced anemia include:
   1. Judicious use of laboratory sampling.
   2. Microsampling when possible.
   3. Transcutaneous monitoring/testing.
   4. Accurate documentation of blood loss.

O. *False diagnosis:* even under the best circumstances, no test is perfect. Excess repetition of a test increases the possibility of laboratory error.
   1. Strategies to minimize sampling-related false diagnosis include:
      a. Test only when necessary to assist in diagnosis, prognosis, treatment, or management.
      b. Verify spurious laboratory values.
      c. Draw laboratory samples using proper technique and conditions.

P. *Cost:* laboratory testing cost containment is an important aspect of stewardship of health care costs and is incumbent on all health care providers (Hiscock et al., 2018; Sadowski et al., 2017).

Q. Strategies to minimize sampling-related laboratory costs include:
   1. Minimize laboratory sampling.
   2. Prudent medical and nursing decision making regarding laboratory sampling.
   3. Minimizing laboratory errors precipitating repeat sampling.

Decision Questions to Ask Before Obtaining a Laboratory Test

Patient Exemplar: Judicious use of laboratory testing is critical in any setting, particularly in the NICU, where acuity is high. Asking the right questions before ordering and/or obtaining a laboratory sample refines critical thinking skills and improves judicious use of laboratory work (Box 13.4). To illustrate the decision-making process, an exemplar using one presenting symptom—a *jittery infant*—is applied to all phases of critical thinking.

A. Does the patient require the laboratory test?
B. Are the patient examination results abnormal, whereby a laboratory test will help in diagnosis?
   1. Abnormal finding: model–jittery infant.
   2. Possible laboratory tests: glucose, calcium, toxicology screen.
C. Is the medical history helpful in directing which laboratory test to order?
   1. Infant of a gestational, class A1, diabetic mother (IDM-A1)? Might choose to obtain a serum

Box 13.4

Questions to Ask Before Obtaining a Laboratory Test

General questions:

- Are the patient examination results abnormal, whereby a laboratory test will help in diagnosis?
- Is the medical history helpful in directing which laboratory test to order?
- Will the laboratory test requested answer the "so what" question?
- Is the laboratory result integral to the immediate clinical management of the patient?
- Is the laboratory result contributory to a patient's diagnosis?
- Is the laboratory test ordered the "best" test to answer the clinical question?
- Is this the first result or a repeated test (i.e., is there a trend)?

Specific questions:

- Is the laboratory test requested still applicable to the current clinical status?
  - Has the outcome of the patient's clinical examination changed?
  - Has the patient recovered?
- Is the timing of the laboratory test appropriate?
  - When should the laboratory work be obtained?
- Does the laboratory test require too much blood volume?
- Does the potential benefit of the laboratory test outweigh the risk of sequelae in the patient?
- If the laboratory sample is inadequate, faulty, or "lost," is it necessary to redraw?

glucose and/or serum calcium level versus a toxicology screen.
2. Infant with delayed drying of skin after birth and axilla/skin temperature of 96° F? Might choose to place infant under heat source and not obtain laboratory work.
3. Infant 1800 g, IDM-A1, and mother with minimal prenatal care? Might choose to obtain all possible laboratory tests.
4. Otherwise well-looking baby with in-utero opioid exposure? Might choose to send toxicology screen.

D. Will the laboratory test requested answer the "so what" question?
1. Is the laboratory result integral to the immediate clinical management?
2. Hypoglycemia in an IDM-A1 will mandate increasing the carbohydrate intake to treat the problem.
3. Mild hypothermia in an otherwise healthy infant will not require a change in management directed by laboratory work.
4. Opioid exposure will trigger narcotic abstinence scoring, nonpharmacologic and pharmacologic treatment, and social work consultation and will possibly contraindicate breastfeeding.

E. Is the laboratory result contributory to the infant's diagnosis?
1. Serum glucose test result will help diagnose hypoglycemia as a cause of jitteriness.
2. Serum glucose test result will not help diagnose respiratory distress syndrome.

F. Is the laboratory test ordered the "best" test to answer the clinical question?
1. Should the jittery infant have a serum glucose sample sent to the laboratory or by POCT or near-patient testing? A POCT glucose result is available in seconds, allowing for rapid clinical intervention.
2. Should the jittery infant with polycythemia have a serum glucose sample sent to the laboratory or POCT glucose testing? POCT glucose result may not be accurate in the face of polycythemia.

G. Is the laboratory test requested still applicable to the current clinical status?
1. Has the infant's clinical status changed?
   a. An hour-old IDM-A1 whose jitteriness has changed to tonic–clonic movements of extremities—in addition to serum glucose and calcium levels—will need consideration of a urine toxicology screen and electrolytes and potentially other seizure-related diagnostics. Further history is needed, such as perinatal depression.
   b. An hour-old IDM-A1 who breastfed for 20 minutes and is no longer jittery may not require further testing, particularly if the original serum glucose level was normal.
   c. The hypothermic infant who continues to remain hypothermic after 2 hours under heat source may need serum glucose test and sepsis evaluation.
2. Has the infant recovered?
   a. Infant with multiple normal glucose test results may no longer require frequent glucose testing.
   b. Infant no longer jittery after acquiring a normal body temperature—may need to cancel laboratory work ordered to evaluate jitteriness.

H. Is the timing of the laboratory test appropriate?
1. When should the laboratory work be obtained?
   a. IDM-A1 at birth—might wait to check serum glucose level at 30 to 90 minutes of age when the result would reflect the infant's nadir status versus that of the maternal environment.
   b. Jittery infant with normal serum glucose and calcium levels—might obtain specimen(s) for a urine or meconium toxicology screen.

I. Does the laboratory test require too much blood volume?
1. An extremely low birth weight (ELBW—under 1 kilogram birth weight) infant with every-2-hour serum glucose POCT testing requires an average sample size of one drop to 0.1 mL of blood, whereas a serum glucose test requires an average sample size of 0.5 mL.
2. Blood specimen is required for metabolic screening for an ELBW infant: large blood volume loss may not be tolerated; need to prioritize laboratory work and draw in stages based on most common to least common disorders.

J. Does the potential benefit of the laboratory test outweigh the risk of sequelae in the patient?
1. ELBW infant with hypoglycemia: frequent glucose testing needed to monitor treatment; benefit outweighs potential harm of blood loss. POCT use can minimize blood loss.
2. Large-volume blood sample for metabolic screening in ELBW symptomatic infant: potential harm of an acute blood loss outweighs the need to simultaneously obtain all the ordered metabolic screening laboratories.

K. If the laboratory sample is inadequate, faulty, or "lost," is it necessary to redraw?
1. Has the clinical status changed?
2. Has the infant recovered? If the status improves or the infant recovers while waiting for the sample, repeat sampling may not be indicated.

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CHAPTER 14
Radiologic Evaluation

Carol Wiltgen Trotter

OBJECTIVES

1. Define common radiologic terms used to describe an x-ray.
2. Differentiate various densities that are evident on an x-ray.
3. Describe radiologic findings that are commonly seen in neonatal disease states.
4. Differentiate normal from abnormal findings on a chest x-ray.
5. Recognize findings on an x-ray that are consistent with congenital heart disease.
6. Describe an x-ray consistent with necrotizing enterocolitis.
7. Review correct indwelling line and tube placement on an x-ray.

Radiographic medical imaging of abnormalities in a sick newborn infant is an established part of diagnostic evaluation. This evaluation assists the clinician in determining a diagnosis or formulating a differential diagnosis for treatment of the patient. Rarely is a newborn infant admitted to the neonatal intensive care unit (NICU) without having at least one x-ray taken, and frequently several additional films are needed during the course of treatment. Nurses need to become familiar with common x-ray findings to add to the knowledge base on which patient care is founded. This chapter reviews essentials of radiologic interpretation, discusses pathologic findings, and presents x-rays with common findings.

Basic Concepts

A. A radiograph is an image produced when an electromagnetic wave is directed through an object to a photosensitive surface such as an x-ray cassette. The amount of energy reaching the film determines the degree of exposure. Therefore, the image produced on the film is determined by the density of the object that the electromagnetic wave has to pass through.

B. By comparing densities and shapes from the image produced on the film, information can be deduced or inferred regarding anatomy, pathology, and function. Therefore, radiology is referred to as the science of interpreting densities.

C. There are four basic tissue densities.
   1. **Air:** Air is the least dense (radiolucent) substance, allowing the most radiation to pass through to the cassette. Therefore, the radiographic image of air-filled structures will appear black or dark gray or radiolucent.
   2. **Fat:** Subcutaneous fat is denser than air, and therefore, the image appears dark gray on the film.
   3. **Water**: Water-filled organs such as the heart, along with blood vessels, muscle, and tissue masses, have similar density, as they block a significant amount of the x-ray reaching the cassette. Therefore, these images will appear light gray to white, depending on the density.
   4. **Bone/metal**: Bone and metal block most of the x-ray, so these images will appear bright white on the radiograph.

D. Differentiation of densities is the basis for interpretation of an x-ray film. For example, because of the contrast in densities between the fluid-filled heart, which radiographs white, and the air-filled lungs, which radiograph black, the heart can be seen against the lungs. Organs of the same density that are located side by side, such as the heart and the thymus, may be difficult to distinguish from each other. Changes in normal density can indicate a pathologic process, such as severe respiratory distress syndrome. Surfactant-deficient lungs will appear on the film completely white instead of black, indicating areas of alveolar collapse.

Terminology

A. **Air bronchogram:** air in the bronchial tree (black) visualized against a background of generalized alveolar atelectasis (varying shades of gray/white).

B. **Artifact:** an unnaturally occurring silhouette that is artificially reproduced on an x-ray and is not a part of the patient (e.g., electrocardiogram leads, temperature probes).
C. **Cardiothoracic ratio:** computed by dividing the maximum cardiac width by the maximum thoracic width to determine the heart size. The normal cardiothoracic ratio should not exceed 0.6 (Weinert and Martinez-Rios, 2015).
D. **Carina:** bifurcation of the trachea, usually about the level of the third and fourth thoracic vertebrae. Used in determining the location of the endotracheal tube.
E. **Exposure:** amount of radiation used, producing a film ranging from light to dark. An underpenetrated (underexposed) film causes images to appear lighter gray or whiter (more radiopaque) than if the film was normally penetrated. Overpenetration (overexposure) causes the film to be dark and to lack contrast (more radiolucent), in comparison with an appropriately penetrated and exposed film.
F. **Gray (Gy):** replaces the rad as the current unit of measurement for the absorbed dose of ionizing radiation (1 Gy = 100 rad) (Davis and Frush, 2019).
G. **Inspiratory/expiratory film:** Ideally, chest x-rays are taken during full inspiration. Counting ribs that are visible above the diaphragm is often used to define the degree of inspiration or expiration. However, according to Swischuk (2004), this is not accurate in the infant. Swischuk explains that because physiologically lung expansion occurs in all directions, especially in the very pliable thoracic cage of the neonate, a two-dimensional radiograph does not always capture the full degree of inspiration. Despite this caveat, many practitioners use the following definitions:
    1. **Expiratory film:** obtained when the infant is in expiration; lungs appear hypoexpanded, which may falsely increase the cardiothoracic ratio and accentuate lung markings.
    2. **Hyperexpanded lungs:** lungs expanded to greater than the ninth rib above the diaphragm.
    3. **Hypoexpanded lungs:** lungs expanded to less than the seventh rib above the diaphragm.
    4. **Inspiratory film:** obtained when infant is in full inspiration and the lungs project to the eighth rib above the right diaphragmatic dome.
H. Interlobar fissure: separations between the lung lobes, which are lined by visceral pleura; more visible on radiograph when there is accumulation of fluid within the fissures; may appear as a distinctive white/light gray line.
I. Perihilar: pertaining to the radiographic area surrounding the hilum, which is where the major bronchi and pulmonary vessels exit the mediastinum and intersect each lung.
J. Pleural effusion: abnormal collection of fluid in the pleural space.
K. Radiolucent: pertaining to substances with varying degrees of transparency.
L. Radiopaque: pertaining to substances that are dense and nonpenetrable to x-rays.
M. Rad: previous unit of measurement for the absorbed dose of ionizing radiation (replaced by the gray) (Davis and Frush, 2019).
N. Roentgen: "A unit of exposure to ionizing radiation named after Wilhelm Rontgen, the scientist who discovered x-rays in 1895" (Davis and Frush, 2019, p. 6).
O. Rotation: turned from the midline. Chest structures closest to the beam are magnified, making their shadows appear enlarged and distorted.
P. Skinfold: the most common artifact seen in the neonate. Manifests as a straight line of variable length that can travel across or outside the chest or across the diaphragm and into the abdomen. Results from folding of excessive skin; may mimic the appearance of a pneumothorax. However, the obliquity of the line produced by a skinfold is opposite to that produced by the edge of the lung in pneumothorax.
Q. Proper technique: signifies correct exposure, positioning, collimation, and timing in relation to inspiration and proper labeling of a film.
R. X-ray: a form of electromagnetic radiation with short wavelengths that can penetrate most structures (Eklund et al., 2018).

X-Ray Views Commonly Used in the Newborn Infant (Fig. 14.1)

A. **Anteroposterior view.** The infant is lying supine with the x-ray tube positioned above the infant's chest, with the x-ray beam passing through from front to back. Most common view used in the neonate.
B. **Posteroanterior view.** The infant is lying prone on the cassette with the x-ray tube positioned above the infant's back. This approach may be preferable in an unstable infant who is lying prone to avoid moving the infant.
C. **Cross-table lateral view.** The infant is lying supine and the x-ray beam passes horizontally through the infant. Used for general assessment, assessment of free air, and to verify line placement.
D. **Lateral decubitus view.** The infant is lying on his or her left or right side with the film on the infant's back. The infant is facing the x-ray tube with the arms positioned above the head and out of the field of view. For a left-sided pneumothorax, the infant is placed in the right lateral decubitus position. Free air will rise to the highest portion of the thorax if a pneumothorax is present. If an intestinal perforation is present, the

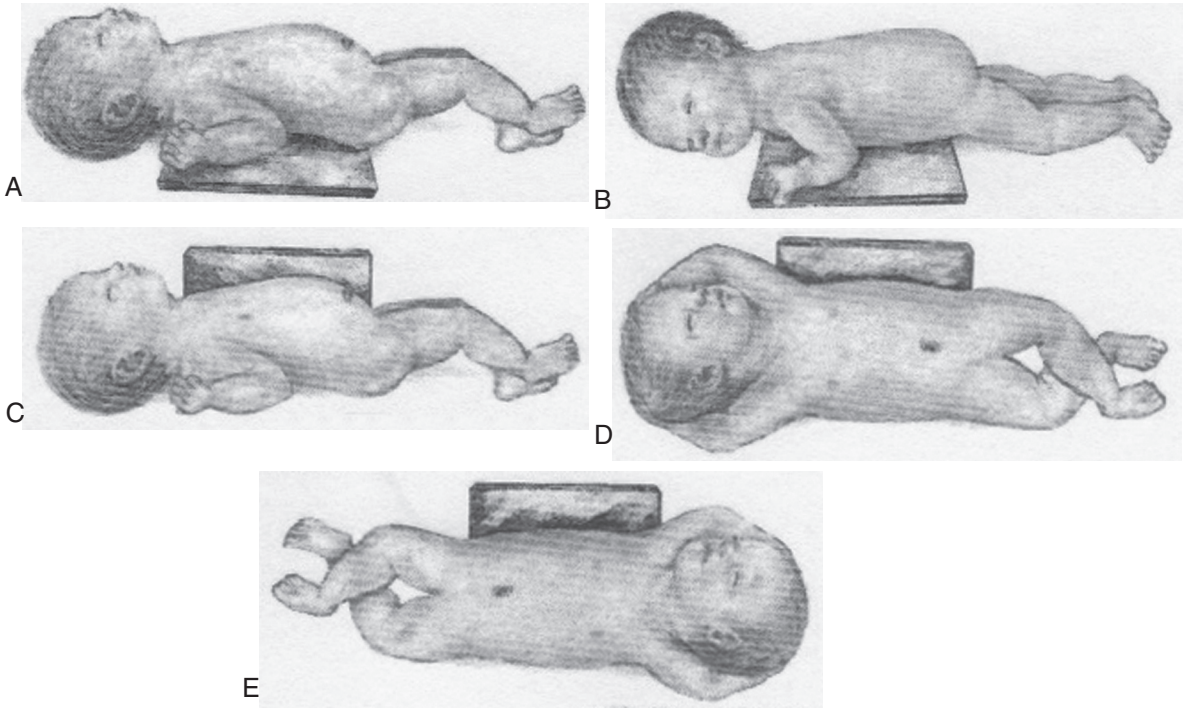

Fig. 14.1 X-ray views commonly used for the newborn infant. **A,** Anteroposterior view. **B**, Posteroanterior view. **C,** Cross-table lateral view. **D,** Lateral decubitus view: right-lateral decubitus view. **E,** Left lateral decubitus view. *(From Eklund, M., Swift, C., & Hill, J. [2018]*. Neonatal imaging. *The National Certification Corporation.)*

infant is placed in the left lateral decubitus position, and free peritoneal air will rise and layer above the liver.

Risks Associated With Radiographic Examination in the Neonate

A. Radiation effects and risks.
   1. Ionizing radiation is a known carcinogen; adverse biologic effects occur as a result of damage to DNA (Davis and Frush, 2019).
   2. Infants are most sensitive to ionizing radiation, possibly due to greater cell division in rapidly growing and developing tissues (Davis and Frush, 2019).
   3. Infants have longer life expectancy, so effects of radiation exposure may be more significant.
   4. Computed tomography (CT) scans have a higher radiation dose than other imaging studies (Davis and Frush, 2019).
   5. Ultrasound does not use radiation (Davis and Frush, 2019).
   6. Radiation protection: two basic principles when considering radiation exposure are justification (the examination is warranted) and optimization (appropriate technique is used) (Davis and Frush, 2019).
   7. Specific recommendations (Wallingford and Rubarth, 2017).
      a. Limit radiation exposure during x-rays to the area needed.
      b. Provide gonadal shielding.
      c. Consider use of ultrasound over x-ray.
      d. CT scan and fluoroscopy as appropriate.
      e. Avoid artifacts and incorrect positioning of the infant to limit repeat x-rays.
      f. Avoid "routine/surveillance" x-ray orders.

B. Risks to personnel in the area, when studies and technique are properly done, are low.

Approach to Interpreting an X-ray

A. Avoid tunnel vision. Develop a systematic approach and a definite order for assessing a film to ensure that no pathology is missed.
B. Labeling. Note name or identification of the patient, date and time of the film, and radiographic labeling on right or left side of the film.
C. Assess technique and quality of the film.
   1. Evaluate quality of the film.

Part 2

a. Compare to previous films if available.
b. Exposure.
c. Adequate inspiration for chest films.

2. Evaluate rotation and infant positioning.
a. Evaluate clavicles, ribs, and location of heart.
b. Symmetry: spine placement in center with equal rib lengths.

3. Clarify artifacts: may interfere with view.
a. Monitor leads and probe patches.
b. Incubator holes.
c. Skinfolds: linear markings but extend outside lung fields.

D. Assess any bony structures that are visible.
1. General skeletal assessment. Assess for symmetry, size, continuity, intactness, and abnormalities.
2. Rotation of chest or shoulder elevation will distort view of clavicles and ribs.
3. Fractures of long bones, clavicles, ribs, and skull. A dark line or separation is seen along any portion of a fractured bone.

E. Assess soft tissue.
1. Edema.
2. Hard to evaluate if film is overpenetrated.

F. Assess location of all indwelling tubes.
1. Position of endotracheal tube, gastric tubes, chest tubes.
2. Umbilical catheter placement.
3. Central venous line placement.

G. Assess chest: lung fields, heart and mediastinum, thymus, diaphragm.
1. Lung fields.
a. Symmetry of lung fields, densities or areas of lucency.
1) Densities: infiltrates, atelectasis, lobar collapse, masses, pleural effusions, fluid in fissures.
a) Infiltrate descriptors: diffuse/focal, symmetrical/asymmetrical, fluffy, coarse, streaky.
b) Lucencies: pneumothorax, pneumatocele, blebs.
b. Lung expansion/volume: eight ribs projecting above the diaphragm with the trachea in midline position and diaphragm slightly rounded.
c. Locate tracheal air column and carina and note if air bronchograms are present.
d. Pulmonary vascularity: vessels branching from the lung root (hilum) and decreasing in size, with extension into the lung fields. Vascularity will be increased or diminished, depending on pathologic state.

2. Heart and mediastinum.
a. Cardiovascular
1) Heart size: normal CT ratio 0.6.
2) Location: dextrocardia or other pathology.
3) Shape: may indicate pathologic change—for example, boot-shaped heart in tetralogy of Fallot and egg-shaped heart in transposition of the great vessels.
4) Pneumopericardium: air within pericardial sac.
5) Pulmonary vascular markings: may be significantly diminished, as in pulmonary atresia, or increased, as in congestive heart failure (CHF).
b. Mediastinum: contains heart, great vessels, trachea, and mainstem bronchi.
1) Pneumomediastinum.

3. Thymus.
a. Composed of two asymmetric lobes, variable appearance, wavy borders.
b. Present in most newborns, sits within mediastinum, overlies heart.
c. Can be large at birth, regresses at 24 to 48 hours.
d. Stress in utero may cause thymus to regress before delivery.
e. Pneumomediastinum: air within mediastinum may lift lobes of thymus, producing sail sign on radiograph (triangular densities in upper lobes).

4. Diaphragm.
a. General pattern: two smooth, curved shadows on either side of the heart, taking off from the midline. Position on chest radiograph depends on degree of inspiration.
b. Contour: possibly flattened with lung overdistention or elevated if expiratory film or if there is abdominal distention.
c. Diaphragmatic hernia: abdominal contents passing through a defect in the diaphragm.
d. Eventration: herniation of bowel and liver against a weakened hemidiaphragm. The diaphragm remains intact but is abnormally elevated.

H. Assess abdomen.
1. Understand gastrointestinal anatomy and sections of small and large intestine.
2. Stomach bubble location and orogastric (OG) tube placement.
3. Normal bowel gas pattern.
a. Gas normally present by 24 hours of age.
b. Gas in rectum signifies movement of air through intestines.

4. Abnormalities.
a. Ileus pattern: large amount of gas with dilated loops.
b. Calcifications may signify in-utero bowel perforation.
c. Pneumatosis intestinalis: linear or curvilinear gas collections within bowel wall.
d. Pneumoperitoneum: free air within the peritoneum, best x-ray view left lateral decubitus and/or cross-table lateral.
e. Gastrointestinal (GI) obstructions, fistulas, tumors, and lesions.

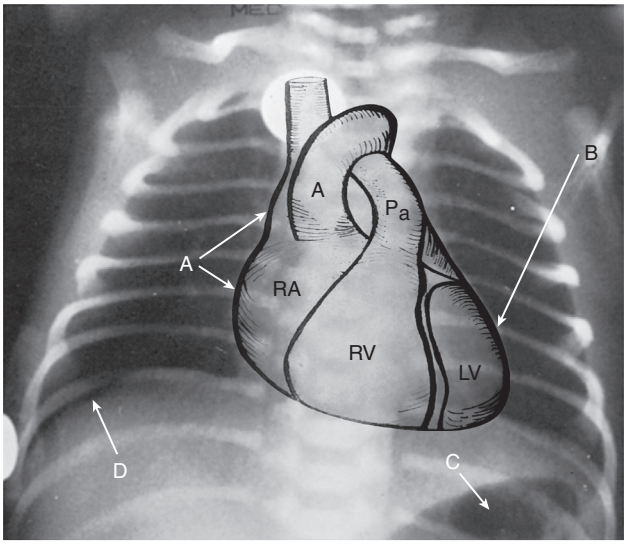

Fig. 14.2 Normal appearance of chest on x-ray film. **A**, Right perihilar area. **B,** Left heart border. **C,** Stomach air bubble. **D,** Edge of right diaphragm below eighth rib.

Respiratory System

A. The normal chest and lung pattern (Fig. 14.2).
   1. Uniform radiolucent appearance. Similar/symmetrical density between right and left lung fields and upper and lower lobes.
   2. Hilar and perihilar regions show some increased density because of vascular, bronchial, and hilar structures.
   3. Periphery shows few, if any, markings.
   4. Fluid in the various interlobar fissures represents a normal variation right after birth as lung fluid is cleared.
   5. Residual fluid may be present in the alveoli after delivery. Early films (<6 hours after delivery) may show increased bronchovascular markings because of this fluid.

B. Thymus.
   1. Occupies the anterior part of the superior portion of the mediastinum and consists of right and left lobes (Swischuk, 2004).
   2. Appears as a smoothly rounded or wavy outline superior to the cardiac shadow and blending imperceptibly with the cardiac silhouette.
   3. Definite notch visible in some cases at the junction of the cardiac silhouette and the thymus.
   4. Generally more prominent on the right.
   5. Shape may alter markedly with degree of inspiration.
   6. Regresses after birth with rapid involution during times of stress.
   7. Aplasia of the thymus (DiGeorge syndrome).
   8. Creation of "sail sign" when mediastinal air lifts the thymus upward.

C. Trachea.
   1. Trachea is normally displaced slightly to the right by the left aortic arch.
   2. Deviated trachea supports a mediastinal shift.
   3. On inspiration, the trachea dilates and lengthens.
   4. On expiration, the trachea constricts and shortens.
   5. On deep inspiration, the trachea and major bronchi are well distended and are easily identifiable.

Pulmonary Parenchymal Disease

A. Respiratory distress syndrome (Figs. 14.3 and 14.4).
   1. Depending on degree of ventilation, pronounced under aeration. Fewer than eight ribs expand on inspiration on anteroposterior film, with doming of the hemidiaphragms on lateral view.

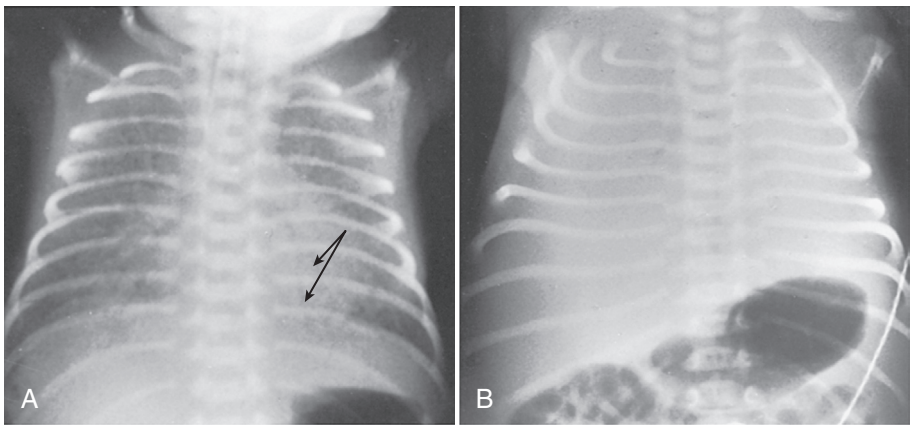

Fig. 14.3 **A,** Hyaline membrane disease. Note reticulogranular lung pattern and air bronchograms (*arrows*). Heart borders very "shaggy" indicating increased atelectasis and increased vascularity, particularly on the right. **B,** Severe hyaline membrane disease. Note "white-out" appearance of both lung fields consistent with severe atelectasis.

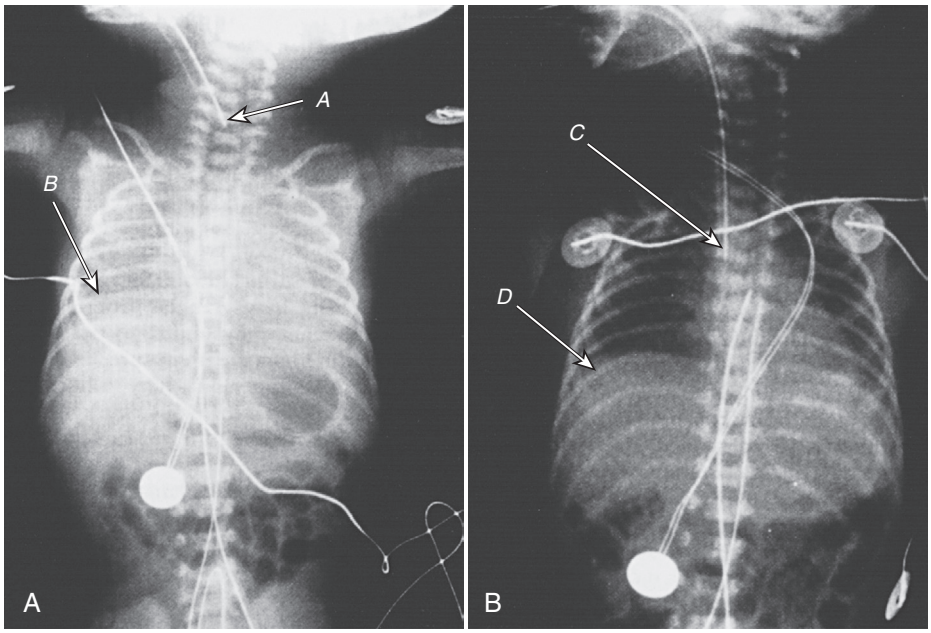

Fig. 14.4 Hyaline membrane disease. **A,** Before administration of surfactant. Endotracheal tube (ETT) high above thoracic inlet (*A*) and edge of diaphragm at T6 (*B*) indicating poor inspiration contributing to underventilation. **B,** Significant improvement in aeration after surfactant administration and repositioning of ETT, which is now at T3 (*C*)**.** Better inspiration noted by edge of diaphragm at seventh rib (*D*)**.**

2. Bilateral diffuse alveolar infiltrates. Reticulogranular (ground-glass) appearance is due to microatelectasis of the alveoli.
3. Homogeneous pattern throughout both lung fields.
4. Air bronchograms. Air-filled bronchi (black) are contrasted against the more radiopaque (whiter) lung fields.
5. With severe disease, a generalized opacity, or frank "white-out" appearance.
6. Reticulogranular pattern and air bronchograms. May resemble those seen in group B streptococcal pneumonia and may be impossible to distinguish from respiratory distress syndrome.
7. X-ray findings after surfactant administration.
   a. Improvement in pulmonary aeration on x-ray.
   b. Asymmetrical distribution of surfactant, showing areas of improved lung alternating with areas of unchanged respiratory distress syndrome (RDS).

B. Transient tachypnea of the newborn (retained fetal lung fluid, wet lung disease) (Fig. 14.5).
1. More common in neonates born via cesarean section due to lack of thoracic compression with vaginal delivery. Results in retained lung fluid (Eklund et al., 2018).
2. Fine interstitial opacities throughout lung and small pleural effusions due to increased interstitial and alveolar fluid (Eklund et al., 2018).
3. Mild to moderate overaeration of the lungs and streaky appearing densities, particularly in perihilar region.

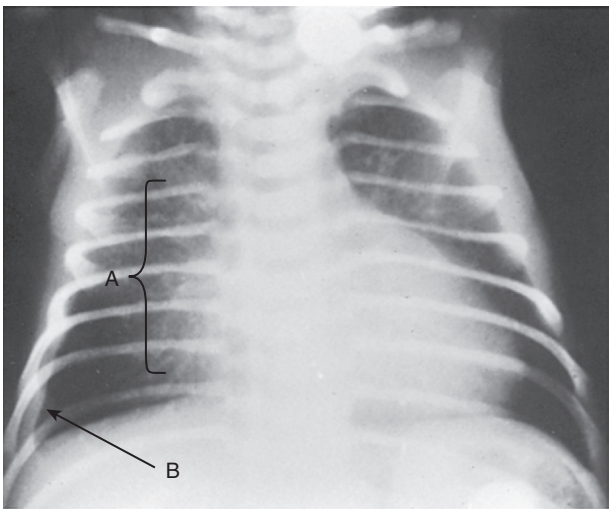

Fig. 14.5 Transient tachypnea of the newborn. Note increased perihilar vascular markings and congestion on right **(A)**, hyperexpansion to the ninth rib, and small effusion on the right **(B)**.

4. Possible fluid in minor (or horizontal) fissure and major (or oblique) lobar fissure.
5. Mildly enlarged cardiothymic silhouette.
6. Lung fields begin to clear in 24 to 48 hours.

C. Bronchopulmonary dysplasia (BPD) (Fig. 14.6).
1. Occurs secondary to lung injury from positive pressure ventilation and oxygen toxicity. Initial

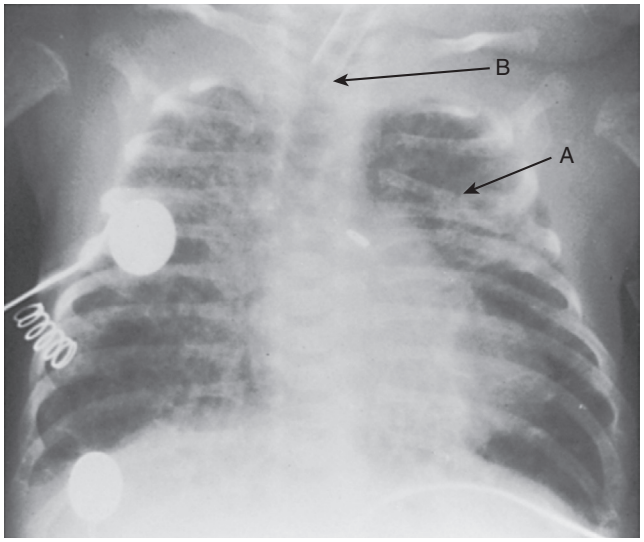

Fig. 14.6 Bronchopulmonary dysplasia. Note ill-defined heavy densities bilaterally, rib fracture upper left chest **(A)**, and pale-appearing ribs. The endotracheal tube is high **(B)** at the thoracic inlet just below the clavicles.

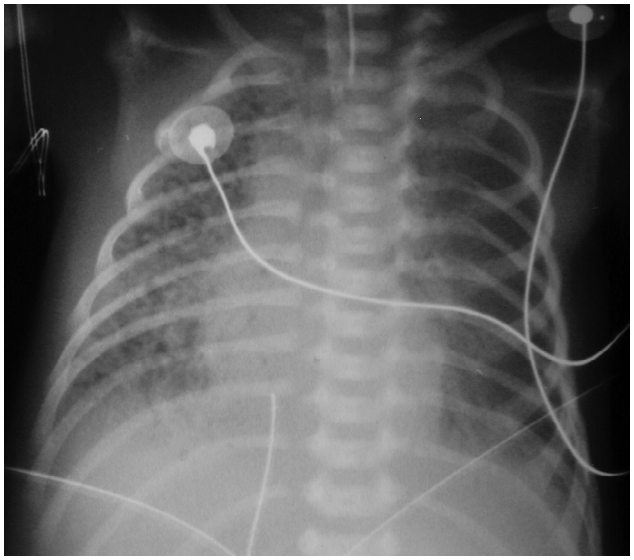

Fig. 14.7 Pulmonary interstitial emphysema (PIE) throughout the right lung field. Note small cystic-like lucencies. The left lung is hyperexpanded with areas of cystic lucencies along the mediastinal and heart borders indicating PIE progression to the left lung.

radiograph shows primary lung disease (e.g., RDS, meconium aspiration syndrome).

2. Radiologic appearance and course of BPD have changed since Northway and Rosan (1968) described their four stages. BPD diagnosis now based more often on clinical course rather than specific x-ray features.
3. X-ray features: coarse, interstitial markings; scattered small, cystic lucencies; hyperinflation (Eklund et al., 2018).

D. Pulmonary interstitial emphysema (Fig. 14.7).
   1. Alveolar overdistention is most often due to assisted ventilation, visualized as multiple small, cystlike radiolucencies that can be bilateral, unilateral, or localized.
   2. Condition may lead to a pneumothorax or other air leak.

E. Meconium aspiration syndrome (Fig. 14.8).
   1. Mild cases may show a normal lung pattern to mild infiltrates with overexpanded lungs.
   2. Bilateral asymmetrical areas of atelectasis and/or alveolar hyperaeration secondary to air trapping from meconium debris; flattened hemidiaphragms with overdistention.
   3. Possible air leaks (pneumothorax or pneumomediastinum) resulting from overdistention and rupture of the alveoli.

F. Pneumonia.
   1. Occasionally asymmetrical, patchy, or streaky bilateral interstitial infiltrate. A nodular pattern may predominate in hazy lungs, and a pleural effusion may be present.

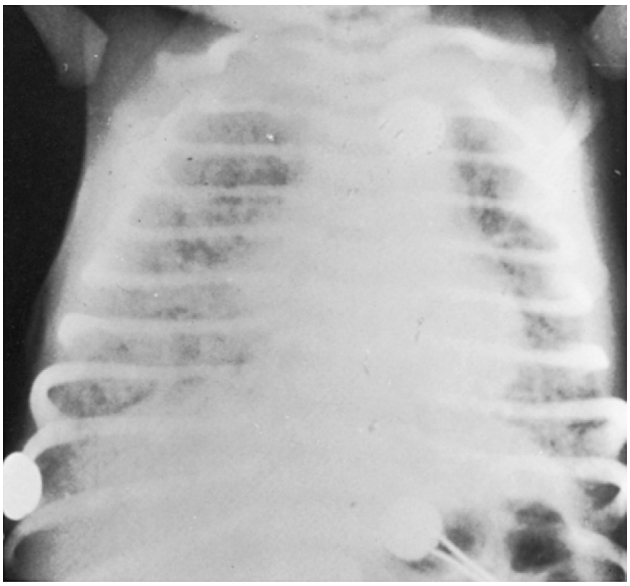

Fig. 14.8 Meconium aspiration syndrome. Note diffuse coarse, patchy infiltrates and overall very poor aeration.

   2. Reticulogranular pattern similar to that of RDS. Some alveoli contain inflammatory exudate, which will appear more opaque on x-ray than those filled with air.
   3. Group B streptococcal pneumonia is often difficult to diagnose on x-ray due to variable lung volumes and variable densities. May be indistinguishable from RDS (Fig. 14.9).

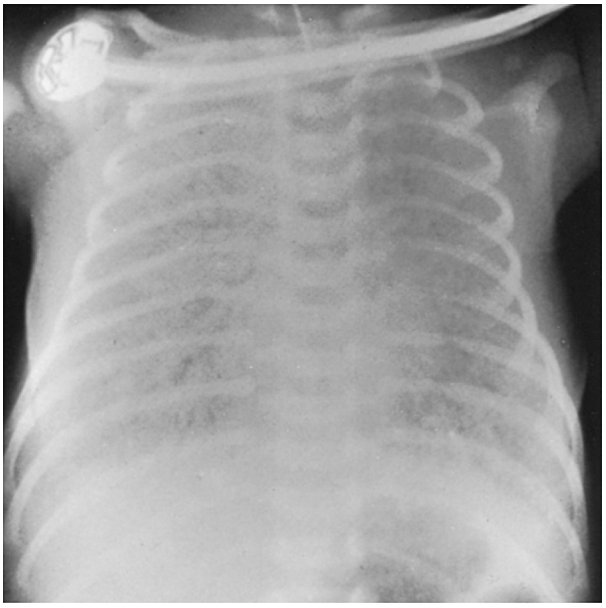

Fig. 14.9 Group B streptococcal pneumonia. Note dense reticulogranular pattern similar to hyaline membrane disease (HMD). Heart borders hard to discern secondary to significant infiltrates.

Pulmonary Air Leaks

A. Pneumothorax (Fig. 14.10).
   1. Accumulation of air in the pleural space. Air can outline the lung circumferentially or can accumulate.
   2. Mediastinal shift of structures away from the affected side as air accumulates (tension pneumothorax).
   3. Outline of the collapsed lung, with a band of hyperlucency between the chest wall and the underlying lung.
   4. Other findings related to pneumothorax.
      a. Pneumothorax not under tension will not exhibit a mediastinal shift.
      b. Air that has accumulated in the anterior or posterior pleural space and not along the lung margin may present as a more lucent lung field rather than as a more obvious shift or dark vertical collection of air.
      c. Diaphragm on affected side of a pneumothorax under tension may be flattened because of

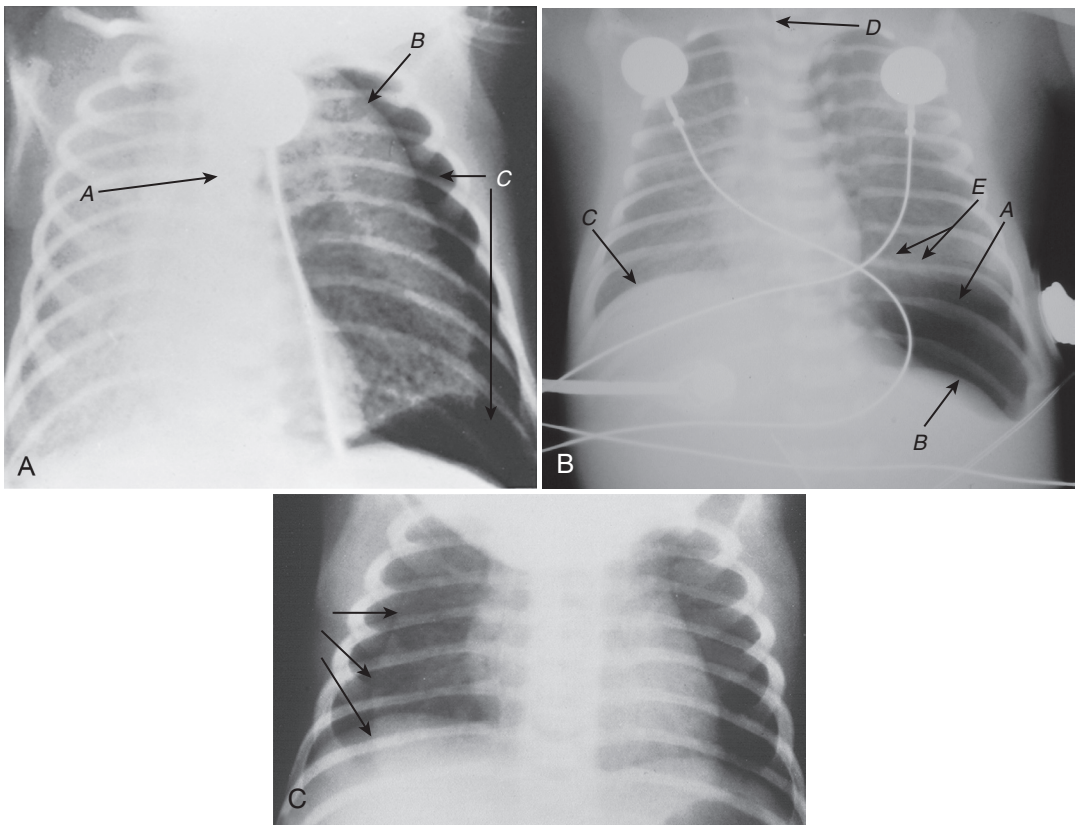

Fig. 14.10 **A,** Left tension pneumothorax with mediastinal shift to the right (*A*)**.** Note left lung edge (*B*) collapsed to the right and free air, which is dark surrounding left lung lobes (*C*). **B,** Left lower lobe pneumothorax in infant with hyaline membrane disease (HMD). Note well-defined hyperlucent area starting at ninth rib (*A*). Diaphragm depressed below rib 11 (*B*). Right diaphragm overinflated to rib 9 (*C*). Endotracheal tube at T1 slightly to right of spinal column (*D*) and heart appears shifted, but this is due to infant rotation. Air bronchograms noted on left (*E*). **C**, Note skinfold on right (*arrows*) extending beyond chest and over diaphragm. Skinfolds can be mistaken for pneumothorax.

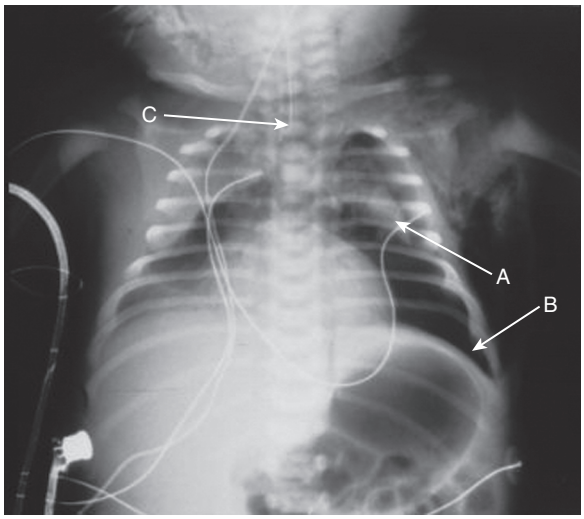

Fig. 14.11 Pneumomediastinum with sail sign. Air in the mediastinum lifts the triangular lobes of the thymus **(A)**. There is also a left lower lobe pneumothorax **(B)** and subcutaneous air noted over the left shoulder. This is apparent when comparing the right and left shoulder. The left shoulder has a "mottled" appearance. The endotracheal tube tip is at T1 **(C)**.

tension placed on it by air accumulation superior to it.

d. Skinfold may mimic a pneumothorax (see Fig. 14.10, C).

B. Pneumomediastinum (Fig. 14.11).
   1. Mediastinal air collection, which produces irregular gas collections within the soft tissues of the superior mediastinum, with air frequently outlining the undersurface of the thymus gland and thus creating a "sail sign."
   2. Can accompany a pneumothorax.
   3. On cross-table lateral film, a radiolucent area of hyperlucency in the superior retrosternal space.

C. Pneumopericardium (Fig. 14.12).
   1. Radiolucent halo of free air surrounds the heart as air accumulates within the pericardial space. To distinguish from pneumomediastinum, air within the pericardial space extends below the heart but not above the level of the great vessels (Walker and Shannon, 2017).
   2. Width of air around the heart is proportional to the amount of air present. Air is limited to the pericardium and cannot extend beyond the origins of the aorta and pulmonary artery.
   3. Decreased cardiac size may indicate cardiac tamponade.
   4. Other pulmonary air leaks and/or pulmonary interstitial emphysema are generally present.
   5. Pneumopericardium is rare in the absence of assisted ventilation.

Fig. 14.12 Pneumopericardium. Note air completely encircles heart. Bilateral chest tubes are also in place.

Miscellaneous Causes of Respiratory Distress

A. Diaphragmatic paralysis (phrenic nerve injury) (Fig. 14.13) (Mangurten et al., 2015).
   1. Elevation of diaphragm; mediastinal structures may be shifted away from affected diaphragm.
   2. Usually unilateral and associated with brachial plexus injury.
   3. Bilateral areas of atelectasis may be present.
   4. Real-time ultrasound may be beneficial to document abnormal diaphragm movement.

B. Eventration of the diaphragm (Fig. 14.14).
   1. Weakness of the hemidiaphragm, allowing upward movement of abdominal organs against diaphragm (Swischuk, 2004).

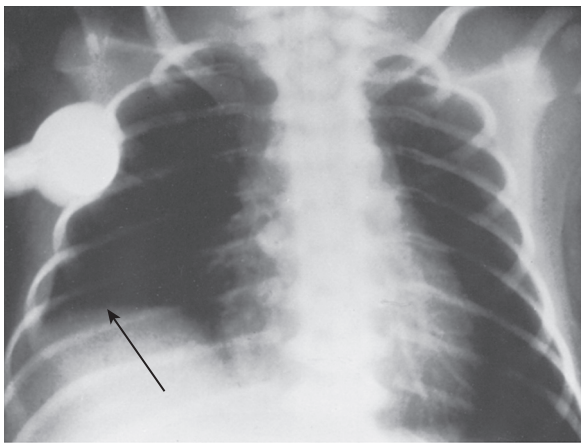

Fig. 14.13 Paralysis of right side of diaphragm demonstrated by a domed and markedly elevated right diaphragm with edge between ribs 6 and 7 (*arrow*).

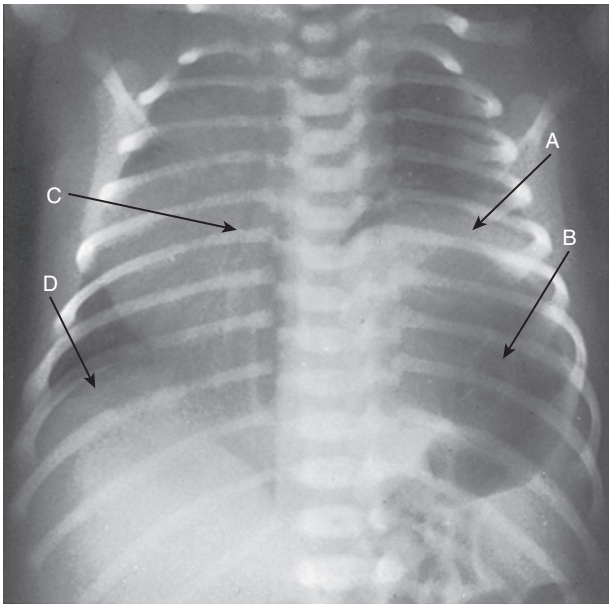

Fig. 14.14 Eventration of the left diaphragm **(A)**. Note the large air-filled stomach pushing up against the diaphragm into the left chest **(B)**. The structures of the mediastinum have been shifted to the right **(C)**. The right diaphragm is positioned normally at the level of the eighth rib **(D)**.

2. Radiograph demonstrates smooth bulge up into lung field blending with the diaphragm on affected side (Swischuk, 2004).

C. Pulmonary edema (Fig. 14.15).
1. When a neonate experiences increased alveolar permeability, the appearance of the chest radiograph can range from diffuse haziness of the lungs to a complete white-out.

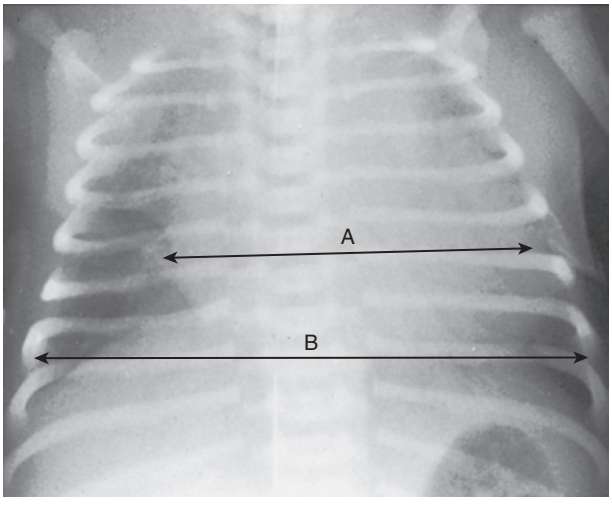

Fig. 14.15 Pulmonary edema with cardiomegaly. Note hazy lung fields with fuzzy heart borders. The cardiac size **(A)** is approximately 68% of the chest diameter **(B)**.

2. May occur with excessive fluid intake as a result of a clinically significant patent ductus arteriosus (PDA) or BPD.
3. Common with certain congenital heart defects due to increased pulmonary blood flow (coarctation of the aorta, hypoplastic left heart syndrome).

Thoracic Surgical Problems

A. Congenital diaphragmatic hernia (Fig. 14.16).
1. Herniation of abdominal contents through defects in the diaphragm into the thoracic cavity, most commonly through the foramen of Bochdalek (Crowley and Stork, 2015).
2. The majority occur on the left side.
3. Hemithorax filled with loops of bowel, and possibly the stomach and liver, displaces the mediastinal structures away from the affected side.
4. Radiograph demonstrates mass-like structure on herniated side with the hemithorax opacified until gas enters the stomach and bowel; mediastinal structures deviated away from herniated bowel contents.
5. May result in pulmonary hypoplasia.
6. Abdomen may be scaphoid on physical examination.
7. Contralateral pneumothorax possible with assisted ventilation or as a result of pulmonary hypoplasia on the unaffected side.

B. If the stomach has herniated into the chest, on x-ray, a gastric tube will be observed within the thoracic cavity.

C. **Congenital lobar emphysema** (Fig. 14.17) (Crowley, 2015).
1. Air trapped within one or more lung lobes at birth from multiple causes, resulting in obstructive emphysema.
2. Overdistended affected lobe, with mediastinum shifted to contralateral side.
3. Radiograph may initially show opaque mass and subsequent hyperlucent, overexpanded lung segment with atelectasis of adjacent lobes.
4. May mimic pneumothorax.

D. Cystic adenomatoid malformation (Crowley, 2015).
1. Five types with varying embryologic origins.
2. Most often unilateral; both lungs equally affected; preference for lower lobes (Crowley, 2015).
3. X-ray findings: multiple air-filled cysts with overdistention, mediastinal shift, and compression of opposite lung.

E. Pulmonary lymphangioma (Fig. 14.18),
1. A congenital abnormality of lymphatic vessel development that may present as a mass in the lungs.

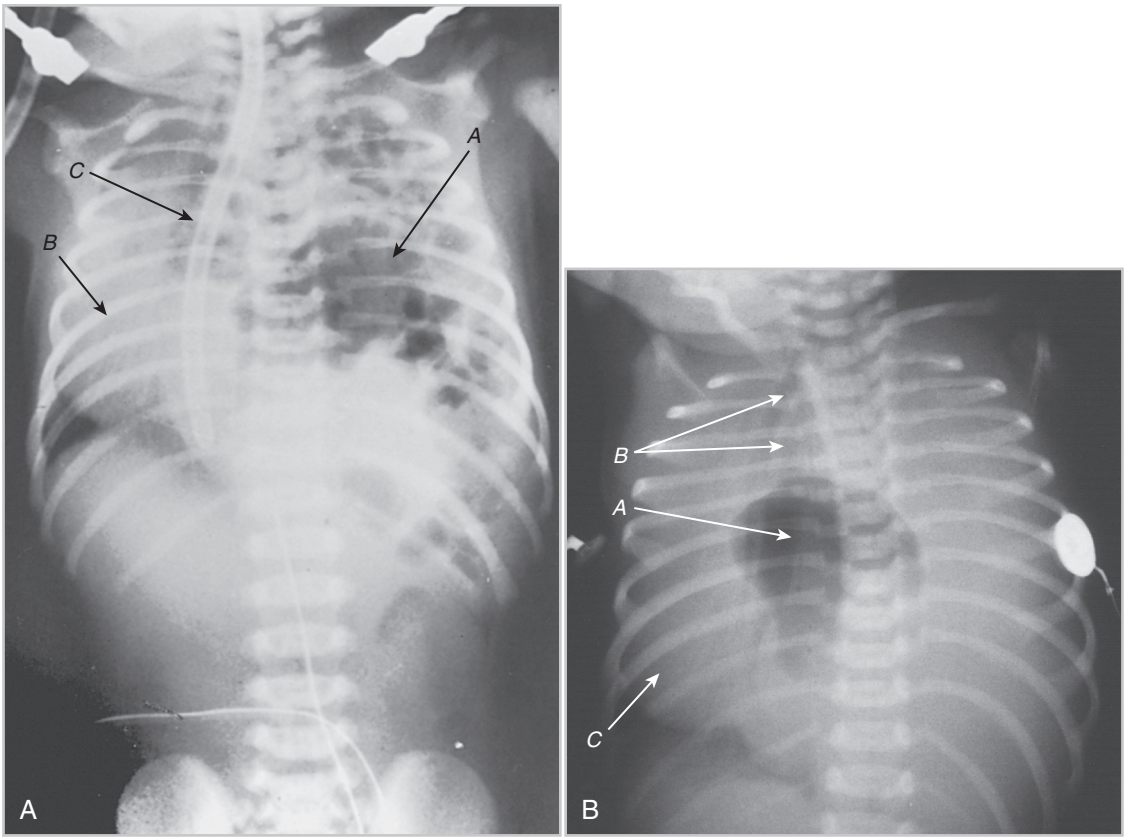

Fig. 14.16 **A,** Left diaphragmatic hernia. Note presence of bowel in left chest (*A*) and lack of bowel in the abdomen. There is a significant shift of the mediastinum to the left, including the heart (*B*) and esophagus as illustrated by the deviated gastric tube (*C*). **B,** Left diaphragmatic hernia before much air has entered the bowel, and therefore lung fields are mostly gasless with the exception of a large dark collection of air in the center. This most likely represents a gas-filled stomach (*A*). The esophagus, trachea, and mainstem bronchi are shifted and compressed to the right (*B*) along with the heart (*C*).

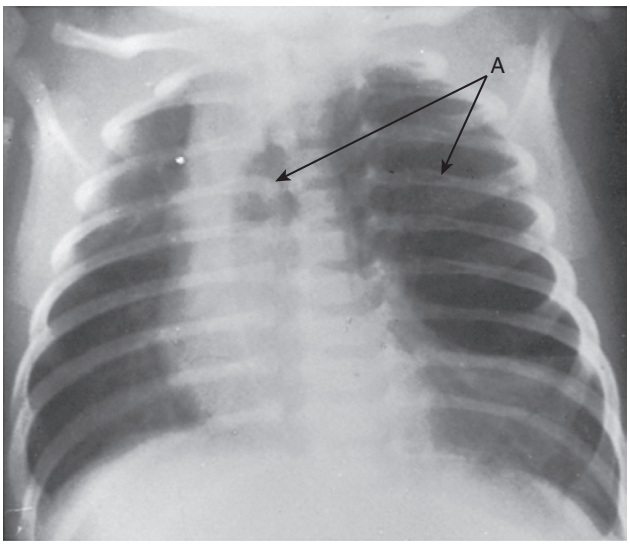

Fig. 14.17 Congenital lobar emphysema. Note hyperlucency in left upper lobe with extension across the midline **(A)** and shift of mediastinal structures to the right.

Cardiovascular System

A. Size of the heart.
   1. May be difficult to assess on anteroposterior film right after birth in the presence of a large thymus and poor inspiration. Lateral film assessing a specific chamber enlargement may be more useful.
   2. Enlargement suggested by cardiothoracic ratio greater than 60% (Weinert and Martinez-Rios, 2015) (Fig. 14.19).
   3. Cardiac apex is normally left-sided with stomach bubble visible on same side.
   4. Malpositioning: may represent cardiac displacement, developmentally abnormal cardiac position, or ambiguous rotation or site.

B. Pulmonary vascularity.
   1. Normal vascular markings extend from the perihilar region to the middle one third of the lung fields (Fig. 14.20A).

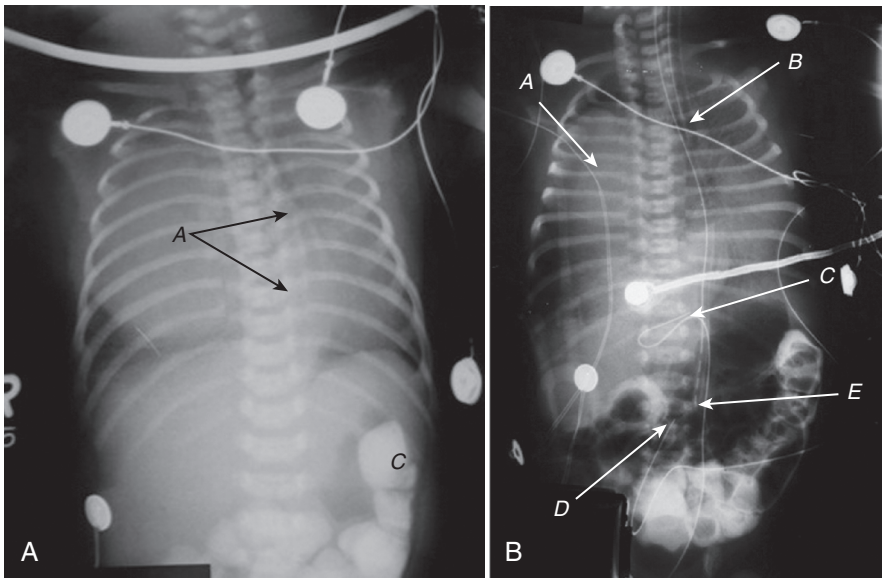

Fig. 14.18 **A,** Congenital lymphangioma. Admission film of term infant with respiratory distress. Lymphatic vessel mass in right chest causing shift of mediastinum and airways to left (*A*). Contrast material noted in normally placed intestinal tract to rule out diaphragmatic hernia (*C*). **B,** Congenital lymphangioma at 6 hours of age after increased respiratory distress. Note better defined lymphangioma (*A*), endotracheal tube shifted to left secondary to mediastinal shift from mass (*B*). UVC coiled in liver (*C*) and UAC at top of L4. **D,** Nasogastric tube (*E*) needs to be pulled back so tip lies within body of stomach.

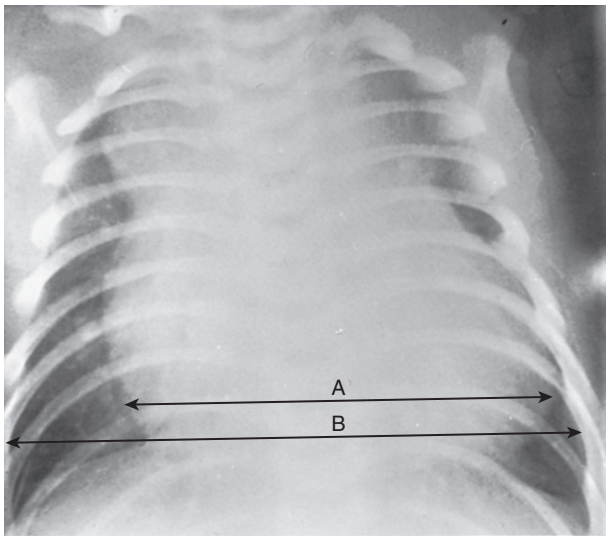

Fig. 14.19 Cardiomegaly. The ratio of heart diameter to chest diameter is approximately 74%.

2. Decreased vascular markings occur with obstruction along the right ventricular outflow tract of the heart and are manifested as hyperlucency in both lung fields (Fig. 14.20B).
3. Increased pulmonary vascularity occurs when excess blood flow causes congestion in the blood vessels and is manifested as increased perihilar streakiness, hazy lung fields, and increased densities as the condition worsens.

C. **General principle**: Radiographs are helpful but may be nonspecific when considering congenital heart disease in the newborn. Echocardiography is frequently required to better define anatomy.

D. **Positional anomalies of the heart (Bansal and Snyder, 2015).**
   1. Types of malposition are as follows:
      a. Dextrocardia: mirror image of its normal position with apex pointed to the right.
      b. Mesocardia: apex of heart is in the midline.
      c. Extrathoracic: heart develops outside the thoracic cavity, as in ectopia cordis.
   2. Position of other organs in relation to the heart is also incorporated into the definition of cardiac malposition. Positions of the abdominal organs are as follows:
      a. Situs solitus: normal location of atria and abdominal organs.
      b. Situs inversus: right atrium on left, stomach and spleen on right, liver on left. Dextrocardia with situs inversus (mirror image dextrocardia) is usually associated with normal cardiac anatomy (Fig. 14.21).
      c. Situs ambiguous: variable atrial position, but liver and stomach midline; condition associated with other intracardiac anomalies.

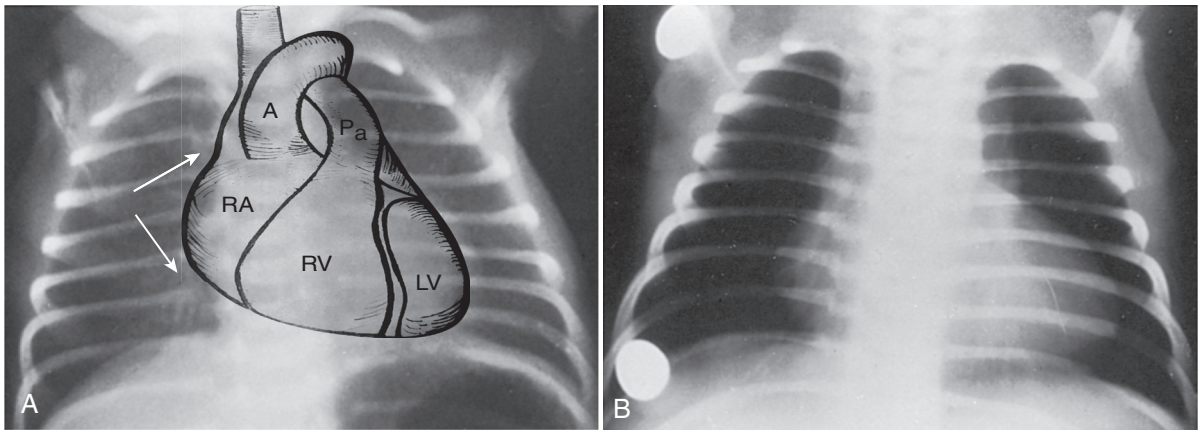

Fig. 14.20 **A,** Normal pulmonary vascularity. Note presence of vascularity radiating from perihilar region (*arrows*). **B,** Hyperlucent lung fields secondary to decreased pulmonary blood flow. Note lack of pulmonary vascularity and very dark lung fields when compared to figure 14-20A.

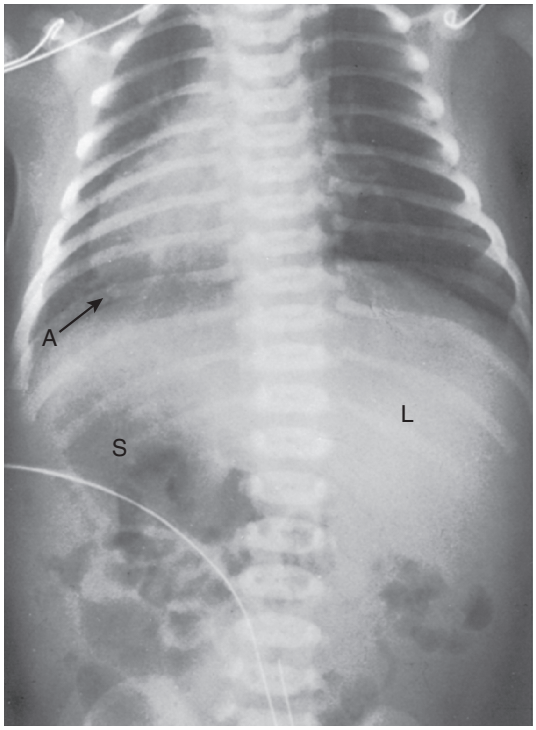

Fig. 14.21 "Mirror image" dextrocardia. Note left ventricle and apex of heart pointing to the right **(A)** with the stomach on the right (S) and liver on the left (L).

3. Cardiac malposition caused by shift of the heart within the thorax must be differentiated from extracardiac causes, such as pneumothorax, hypoplastic lung, diaphragmatic hernia, and lung mass.

E. Lesions with increased pulmonary vascularity.
1. Left-to-right shunt or intracardiac mixing.
   a. Transposition of the great vessels. Most common cyanotic heart defect in the first week of life. Classic radiograph may show egg-shaped heart and increased pulmonary vascularity, but this is variable in the newborn period (Ashwath and Snyder, 2015). Pulmonary vascularity depends on the presence or absence of a ventricular septal defect or a PDA.
   b. Total anomalous pulmonary venous return. Chest x-ray may show pulmonary edema secondary to pulmonary venous obstruction. There may be cardiomegaly and increased pulmonary vascular markings. There may be widening of the superior mediastinum secondary to dilated mediastinal veins. This produces a "snowman" appearance of the heart that may be hidden by the thymus gland (Ashworth and Snyder, 2015).
   c. Atrioventricular canal defect (endocardial cushion defect). Pulmonary vascular resistance usually remains high enough to delay the onset of CHF until after the first 1 to 2 weeks, after which marked cardiomegaly and vascular congestion are evident on x-ray.
   d. Truncus arteriosus. Chest x-ray shows cardiomegaly with increased pulmonary vascularity secondary to pulmonary overcirculation (Ashworth and Snyder, 2015). As CHF develops, pulmonary vessels become indistinct and obscured by pulmonary edema.
   e. Atrial septal defect. Chest x-ray may be normal, with small defects. With large left-to-right shunts, there are moderate cardiac enlargement and increased pulmonary vascularity.
   f. Ventricular septal defect. With small defects, the heart size and vascularity may be normal. With moderate-sized defects, heart size may be enlarged, with increased pulmonary vascular markings. With large defects and increased blood flow, cardiomegaly is evident because of

right and left ventricular enlargement. Pulmonary vascularity is markedly increased. Signs of CHF may be present, including interstitial edema and alveolar fluid.

g. PDA. With clinically significant PDA, chest x-ray shows increased pulmonary vascularity and increasing heart size. Pulmonary edema throughout lung fields as left-to-right shunt increases.

2. Left-sided obstruction. Obstruction to outflow of blood from the left side of the heart or return of blood from the lungs.
   a. Hypoplastic left heart syndrome (aortic atresia, mitral atresia). Chest x-ray may appear normal until significant cardiac decompensation occurs when ductus arteriosus starts to close. This results in pulmonary edema, and the chest x-ray demonstrates cardiomegaly and increased pulmonary vascular markings followed by significant pulmonary congestion.
   b. Coarctation of the aorta. Chest x-ray usually normal. If cardiomegaly is present, this may be associated with other lesions or ventriculomegaly after ductal closure. Ductal closure will also result in increased pulmonary vascularity secondary to pulmonary venous congestion.
   c. Aortic stenosis. Normal cardiac size and vasculature with mild stenosis of the aortic valve. With moderate to severe aortic stenosis cardiomegaly, pulmonary venous congestion and pulmonary edema may be noted on x-ray.
3. Lesions with decreased pulmonary vascularity. All these lesions involve some form of obstruction to the normal flow of blood through the right outflow tract. They can be located anywhere from the tricuspid valve to the pulmonary artery.
   a. Ebstein's anomaly. Chest radiograph shows massive cardiomegaly secondary to right atrial enlargement (Merrow and Hariharan, 2018).
   b. Pulmonary valve atresia with intact ventricular septum. Cardiomegaly often present secondary to right atrial dilatation (Ashwarth and Snyder, 2015). Pulmonary vascularity is reduced or normal, depending on alternative sources of pulmonary blood flow, such as a PDA. Closure of the ductus arteriosus and obstruction of the right ventricular outflow tract cause decreased pulmonary blood flow. Pulmonary vessels are underfilled and appear small and thin, which results in dark, hyperlucent lung fields and decreased pulmonary vascular markings.
   c. Tricuspid atresia. Tricuspid valve has complete atresia, and the right ventricle and right outflow tract are underdeveloped. Chest x-ray may be nonspecific with a normal or small heart and decreased pulmonary vascular markings in severe cases (Ashwath and Snyder, 2015).
   d. Tetralogy of Fallot. Cardiac size and shape are frequently normal. Pulmonary vascular markings may be decreased depending on the degree of pulmonary stenosis/atresia (Ashwath and Snyder, 2015). A "boot-shaped" contour may occur from a small, concave pulmonary artery and a prominent cardiac apex as a result of right ventricular hypertrophy.
   e. Pulmonary stenosis. In mild cases the chest x-ray is generally normal with or without a mild decrease in pulmonary vascular markings. In more severe cases there is significantly decreased pulmonary vascularity along with cardiomegaly as a result of right heart enlargement (Fig. 14.22).

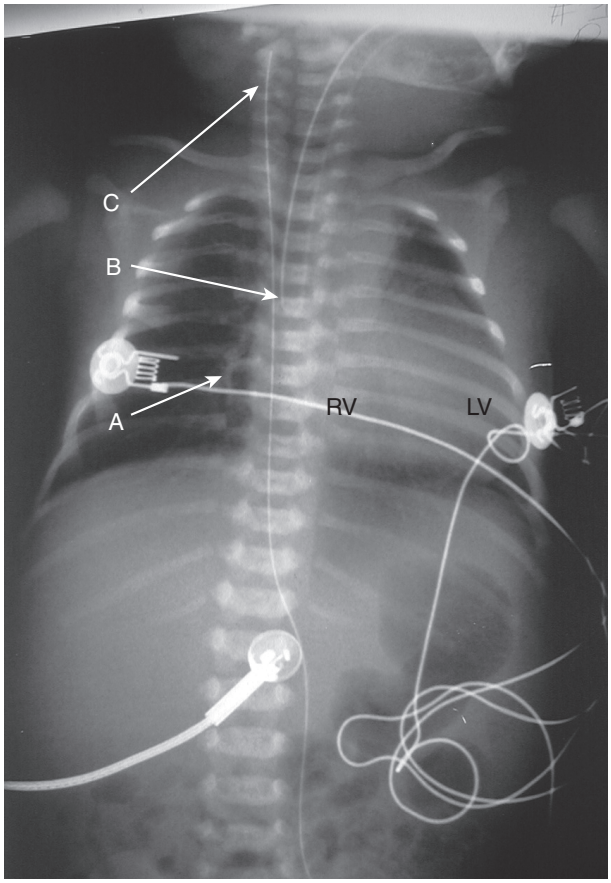

Fig. 14.22 Pulmonic stenosis with normal pulmonary vascularity **(A)**. Infant is rotated, so cardiac silhouette lies more to the left; however, right ventricular hypertrophy is present (RV). Right ventricular hypertrophy causes the left ventricle (LV) and apex to appear upturned, producing the oval-shaped heart. Of note, the endotracheal tube is at the carina and needs to be pulled back **(B)**. The UVC has entered the right atrium and passes through to the superior vena cava **(C)**. This needs to be pulled back to the level of the diaphragm.

Gastrointestinal System

A. Normal characteristics (Fig. 14.23A).
   1. Air is usually present in the stomach immediately after birth because of respiratory movement of the thorax and swallowing of air. By 24 hours of life, air should move throughout the bowel and be observed on x-ray in the distal colon and rectum (Eklund et al., 2018).
   2. Stomach normally visible directly beneath the left diaphragm. Often appears large in neonate due to dilation from air.
   3. A gasless abdomen may be seen in infants with decreased swallowing or obstruction, decreased GI motility (i.e., with intubation or chemical paralysis), vomiting, or gastric decompression from suctioning.
   4. Resuscitation with positive pressure ventilation may increase the amount of bowel gas seen on an x-ray (Fig. 14.23B).

B. Esophageal abnormalities.
   1. Esophageal atresia (EA) (Fig. 14.24). The upper or proximal esophagus ends in a blind pouch and is not connected to the stomach via the lower esophagus.
      a. On x-ray a radiolucent, air-filled, distended esophageal pouch is present. Unless there is a connection to the trachea, the stomach and bowel are gasless because no air can enter. The pouch can be identified by passing a radiopaque tube and obtaining a chest film. The tube will not advance and may be observed at the level of the thoracic inlet or may coil in the pouch. Air may be injected into the tube and will accumulate in the proximal pouch, which can be observed on x-ray.
      b. Aspiration pneumonitis of the upper lobes, especially the right upper lobe, is a common finding, as secretions will accumulate in the esophageal pouch and are easily aspirated.
   2. Four variants of EA with tracheoesophageal fistula (TEF) (Parry, 2015).
      a. EA with fistulous connection *between distal esophagus and trachea:* most common type (85%).
         1) Radiograph may demonstrate excessive dilation of the stomach and/or small bowel as a result of air from the lungs entering the stomach through the TEF.
         2) Chest film should be obtained with a radiopaque tube in place. The tube will not advance into the stomach, and air will be present in the GI tract.
      b. TEF with no EA (H type of fistula).
         1) Difficult to identify without a contrast study.
         2) Fistula is angled downward with the esophageal end lower than the tracheal end.
         3) Widespread pulmonary infiltrates are commonly present because of constant aspiration through the fistula into the lungs.

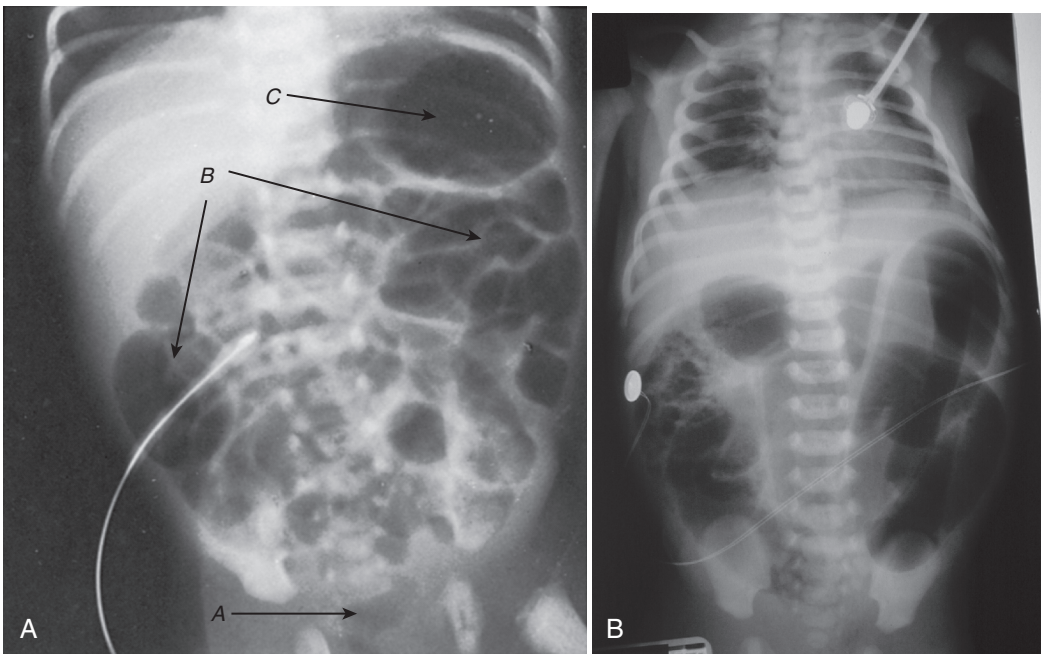

Fig. 14.23 **A,** Generous amount of bowel gas with air in rectum (*A*). Generally, normal-appearing bowel gas with some areas of mild dilation (*B*) and distended, gas-filled stomach (*C*). **B**, Large dilated loops of bowel and abdominal distention from face mask ventilation at delivery. Although this mimics a large-bowel obstruction, there was no obstruction and the gaseous distention resolved spontaneously. Note poor lung expansion from abdominal distention.

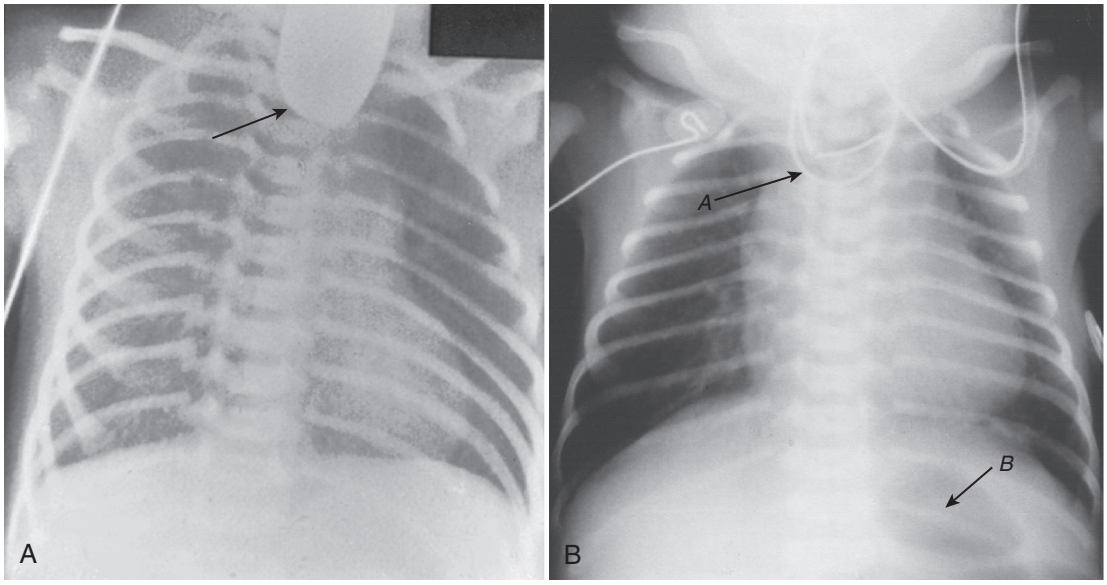

Fig. 14.24 **A,** Esophageal atresia. Contrast medium outlines esophagus, which ends in blind pouch (*arrow*). **B,** Esophageal atresia with tracheoesophageal fistula. The gastric tube is coiled in the esophageal pouch (*A*). Air in the stomach (*B*) confirms the presence of a fistula between the trachea and the esophagus.

   c. The rarest forms are proximal TEF with distal EA and double fistula.

C. Abnormalities of the stomach.
   1. Pyloric sphincter abnormalities (Parry, 2015).
      a. Hypertrophic pyloric stenosis: acquired condition causing gastric outlet obstruction. Typical patient is male 3 to 6 weeks of age. Real-time ultrasound is imaging study of choice. Plain films may demonstrate a distended stomach with disproportionately less gas in the small bowel.
      b. Pyloric atresia: congenital partial or complete obstruction between stomach and duodenum. Atresias are apparent in the first few days of life. Radiograph demonstrates large gastric air bubble with little or no gas in the bowel.
   2. Gastric perforation.
      a. Uncommon, but may result from gastric ulcers, hypoxia-induced focal necrosis, gastric tubes, or indomethacin therapy for closure of ductus arteriosus.
      b. Possible overinflation due to distal obstruction, as with mechanical ventilation.
      c. Common x-ray finding of free air (pneumoperitoneum) with absence of gastric gas.

D. Duodenal abnormalities.
   1. Duodenal atresia and stenosis.
      a. Infants with duodenal atresia present with vomiting in the first few hours of life. Those with stenosis present at variable times, depending on the degree of stenosis.
      b. X-ray demonstrates dilation of the stomach and proximal duodenum, producing the characteristic "double-bubble" pattern. No air is present distal to the duodenum (Fig. 14.25).
   2. Annular pancreas.
      a. Congenital abnormality where pancreas grows in the form of an encircling ring around the duodenum. Frequently occurs along with intrinsic abnormalities of duodenum (Parry, 2015).
      b. Presentation is similar to that of duodenal atresia or stenosis.

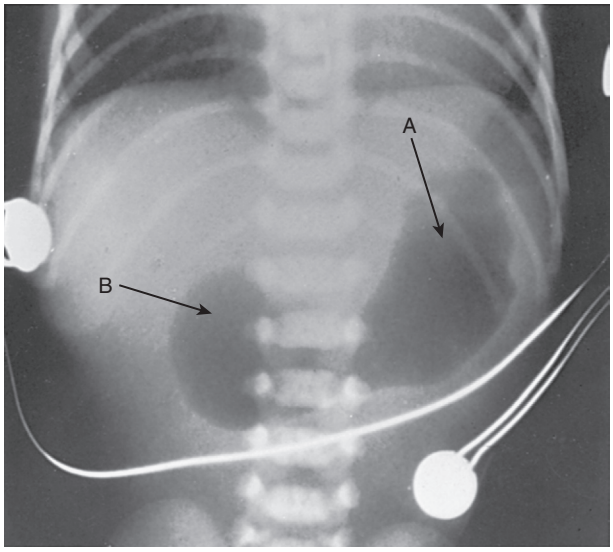

Fig. 14.25 Duodenal atresia with classic "double-bubble" pattern. This pattern is created by the dilated air-filled stomach **(A)** and the dilated proximal duodenum **(B)**. Gas does not move past the duodenal obstruction, which results in a gasless abdomen.

c. X-ray findings are generally indistinguishable from duodenal atresia/stenosis.

E. Abnormalities of the small bowel.
1. Small-bowel atresia and stenosis.
a. Single or multiple areas of atresia or stenosis may exist.
b. Clinically, abdominal distention and bile-stained vomiting are apparent early on.
c. Types of small-bowel atresia.
1) High jejunal obstruction: one or two loops of bowel are visible on x-ray.
2) Midjejunal obstruction: more dilated loops are visible on x-ray.
3) Distal ileal atresia: many dilated loops are visible on x-ray.
2. Midgut volvulus (Parry, 2015).
a. Obstruction is at the level of the duodenum. Caused by twisting and spiraling of the gut around the superior mesenteric artery, resulting in vascular compromise, necrosis, perforation, and gangrene. Emergency surgery is essential for preservation of bowel.
b. May be difficult to determine on x-ray because findings are variable, from a normal abdomen to one suggesting a gastric outlet obstruction, partial obstruction of the duodenum, or small-bowel obstruction.
c. Fluoroscopy may have bird's-beak appearance or a spiral/corkscrew appearance if the duodenum is partially obstructed (Parry, 2015).
d. Ultrasonography and barium enema may also be helpful in diagnosis.

F. Abnormalities of the colon.
1. Hirschsprung's disease (aganglionosis of the colon) (Fig. 14.26) (Merrow and Hariharan, 2018).
a. Functional obstruction due to lack of peristalsis from aganglionosis.
b. Typical clinical presentation is vomiting, distended abdomen, and failure to pass meconium within the first 24 hours of life.
c. Plain films show numerous loops of dilated bowel.
d. Contrast enema demonstrates rectosigmoid ratio less than 1 and transition zone from distal colon to dilated proximal colon.
2. Neonatal small left colon syndrome (see "Meconium Plug Syndrome").
3. Imperforate anus (Merrow and Hariharan, 2018; Parry, 2015).
a. Wide range of severity.
b. May have rectal fistula to urinary tract or other perineal structures.
c. May be associated with malformations of the lower spine as well as thoracic and lumbar hemivertebrae.
d. X-ray evaluation should include the spine to evaluate for anomalies. Abdominal x-ray will demonstrate many dilated bowel loops and air in rectum.

G. **Meconium syndromes**: intestinal obstruction from thick, tenacious meconium.
1. Meconium ileus.
a. Almost always associated with cystic fibrosis.
b. Usually obstructs at the level of the distal jejunum or proximal ileum.
c. Radiograph shows small-bowel dilatation above obstruction and soap bubble appearance caused by air bubbles in the thick meconium (Fig. 14.27).
2. Meconium plug syndrome.
a. More common in preterm infants and occurs in colon frequently as a result of poor motility.
b. Abdominal radiograph shows multiple distended bowel loops.

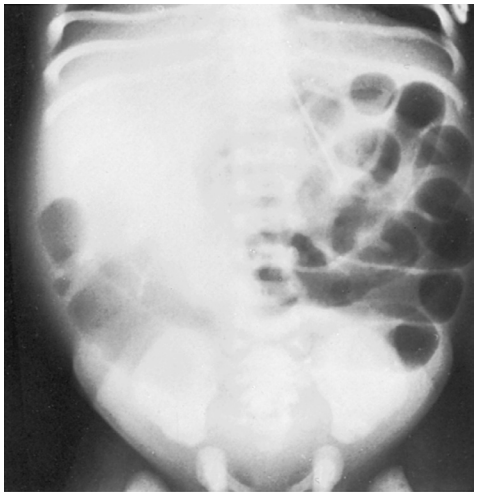

Fig. 14.26 Hirschsprung's disease. Note abdominal distention with dilated loops of bowel and lack of air present in distal portion of bowel.

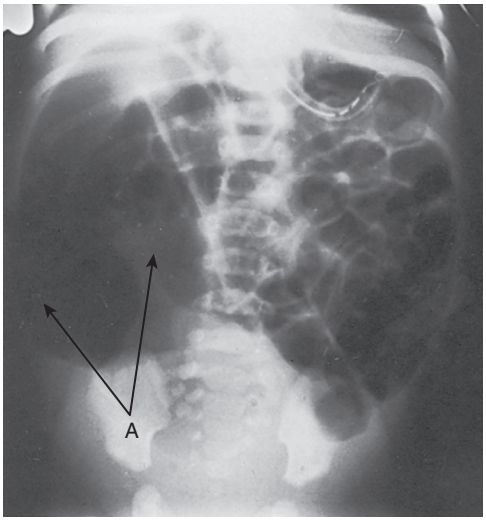

Fig. 14.27 Meconium ileus with perforation. Dilated loops of bowel on left and free intraperitoneal air **(A)**. No gas is noted in the rectum.

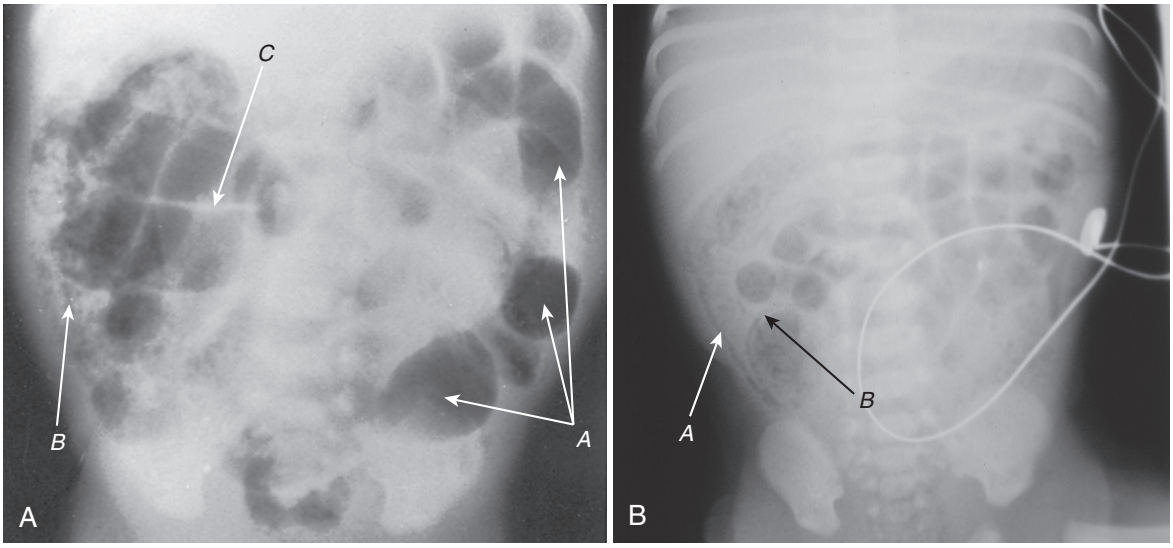

Fig. 14.28 **A,** Necrotizing enterocolitis. Note presence of dilated loops of bowel (*A*), mottled-looking bowel consistent with pneumatosis intestinalis (*B*) and thickened bowel walls (*C*). **B,** Necrotizing enterocolitis. Note linear collection of intramural air in bowel wall (*A*) and surrounding bowel loop (*B*) diagnostic for pneumatosis intestinalis.

c. Water-soluble contrast enema illustrates microcolon distal to obstruction. The water-soluble contrast agent draws large amounts of fluid into the intestine and lubricates the meconium, allowing it to pass without surgical intervention.

3. Meconium peritonitis.
   a. Meconium escapes into peritoneum during the fetal period from a variety of causes.
   b. There may be intestinal necrosis along with inflammation, calcifications, and scarring.
   c. In-utero perforations may seal before delivery.
   d. Postnatal radiographs may demonstrate calcifications, meconium ascites, or bowel obstruction from scarring (Parry, 2015).

H. **Necrotizing enterocolitis** (NEC) (Fig. 14.28) (Eklund et al., 2018).
1. Ileum and right colon most commonly involved.
2. Abdominal radiographs are obtained every 6 to 8 hours to follow the progression of the disease in the acute phase. A left lateral decubitus view or cross-table lateral view should be obtained to detect free air.
3. Variations in x-ray presentation, from nonspecific to diagnostic.
4. Nonspecific finding on abdominal radiograph: dilated bowel loops, thickened bowel walls, fixed bowel gas loops that are present on serial films, paralytic ileus (static bowel loops on serial films), and ascites.
5. Specific x-ray findings include pneumatosis intestinalis, portal venous gas, and pneumoperitoneum from bowel perforation.
6. Pneumatosis intestinalis: small lucent air bubbles present along the bowel wall. Appear overlying the bowel or typically in curvilinear appearance. When present, diagnostic for NEC.
7. Portal venous gas: small branching lucencies in the right upper quadrant, which represent air that has escaped the bowel into the portal venous system.
8. Pneumoperitoneum (see next section).

I. **Pneumoperitoneum** (see Fig. 14.27).
1. Presents with abdominal distention and respiratory distress, or abdominal wall erythema and tenderness.
2. Abdominal flat plate x-ray findings: generalized lucency over upper abdomen; football sign, which is air outlining the falciform ligament; Rigler's sign, which is the appearance of air on both sides of the bowel wall; and continuous diaphragm sign, which is peritoneal air adjacent to the lower edge of the diaphragm (Eklund et al., 2018; Rampton, 2004).
3. Because the dense liver and abdominal contents provide an excellent contrast to the lucent free air, a cross-table lateral or left lateral decubitus film should be obtained if a pneumoperitoneum is suspected. A left lateral decubitus film (left side down) allows peritoneal air to rise and layer out over the liver, clearly demonstrating free air. In a cross-table lateral film with the infant lying on the back, free air will rise to the anterior abdominal cavity and layer out above the organs below the abdominal wall.

J. Abdominal ascites (Fig. 14.29).
1. Causes include fetal hydrops, GI obstruction with perforation, NEC, and peritonitis.
2. Abdominal radiographs demonstrate a distended and uniformly dense abdomen or gasless or

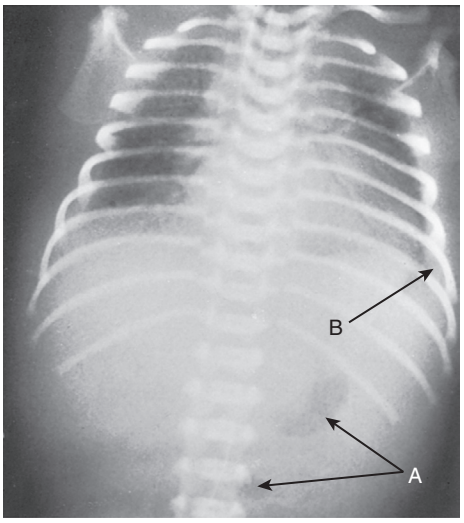

Fig. 14.29 Abdominal ascites depicted by dense appearance of abdomen and small collections of centralized gas representing compressed loops of bowel **(A)**. Bilateral pleural effusions present at right and left costophrenic angles **(B)**.

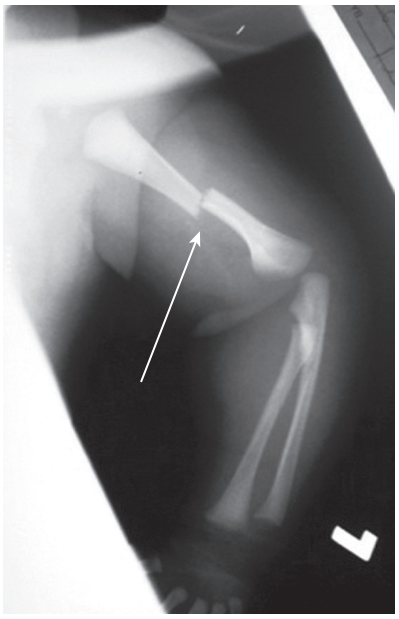

Fig. 14.31 Fractured left humerus.

centralized bowel gas pattern as loops of bowel are compressed by the intraperitoneal fluid. There may be evidence of body wall edema in infants with fetal hydrops.

Skeletal System

A. **Fractures:** occur most often during delivery, with an increased incidence during breech deliveries. In breech deliveries, fractures can occur in both upper and lower extremities (Figs. 14.30 and 14.31).
   1. Clavicle: most common injury to skeleton in newborn, caused by difficult vaginal delivery. Fractures occur at the midclavicle most commonly. More common in large infants with shoulder dystocia (Swischuk, 2004).
   2. Rib fractures: may occur at delivery or related to performance of compressions and be asymptomatic. With multiple fractures, the infant may show signs of respiratory distress and pain. Premature infants may have rib fractures as a result of osteopenia of prematurity. These bones are fragile and will fracture with handling and chest physiotherapy.
   3. Metabolic bone disease/osteopenia of prematurity/rickets of prematurity (Abrams and Tiosano, 2015).
      a. Occurs secondary to immature bone mineralization, inadequate postnatal nutrition, and use of drugs that increase calcium loss.
      b. Bone demineralization is difficult to evaluate on radiograph; fractures may be preceded by a thin, "washed out" appearance to the ribs or long bones; radiographs at 4 to 5 weeks can identify fractures and can be part of routine assessment.
   4. Skull fractures (Mangurten et al., 2015).
      a. Uncommon in neonates because skull bones are less mineralized and membranous sutures allow for mobility during vaginal delivery.
      b. Usually results from pressure with forceps or from forceful contact of fetal skull with maternal bony structures during a difficult and prolonged vaginal delivery.
      c. Fractures can be linear or depressed, may underly a cephalohematoma.
      d. Linear fractures on radiograph present with lines and strips of decreased density.
      e. Depressed skull fractures are visible as an indentation in one of the skull bones. Radiographs may demonstrate dense lines and/or inward buckling of the bone.
      f. CT may be helpful to delineate injury to underlying structures.

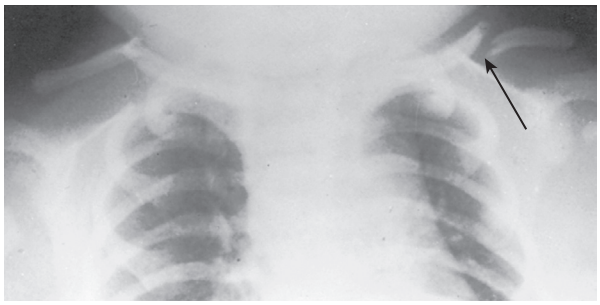

Fig. 14.30 Fractured left clavicle.

B. Skeletal dysplasias: skeletal survey is advised when an infant presents with a suspected skeletal dysplasia. A skeletal survey includes radiographs of the skull and spine, anterior and posterior views of the upper and lower leg and arm bones, hands, feet, pelvis, and abdomen (Weinert and Martinez-Rios, 2015).
   1. Osteogenesis imperfecta (see Chapter 35).
   2. Dwarfism.
      a. Achondroplasia: the most common type of short-limbed dwarfism with autosomal-dominant inheritance. X-ray appearance: shortened humerus and femur, flaring of the metaphyses, short ribs, vertebral bodies are short with other anomalies, making the infant more prone to spinal stenosis. Iliac bones are short in height with flat, acetabular roofs. Skull is enlarged (Merrow and Hariharan, 2018; Towbin, 2017).
      b. Thanatophoric dwarfism (Fig. 14.32): micromelia with shortened humerus and short curved femurs, short ribs, and enlarged skull. Thorax is small and narrow, with pulmonary hypoplasia. Condition is uniformly fatal in the perinatal period (Morrison et al., 2015).

C. **Postnatal infection/osteomyelitis**: most common pathogens are staphylococci, streptococci, and *Candida*. Initial radiographs in early stages of infection may just demonstrate soft tissue swelling. Ill-defined lucency of the metaphyses and bony destruction may occur at approximately 7 to 10 days. Radiography is not as sensitive as magnetic resonance imaging (MRI) in early detection of osteomyelitis (Weinert and Martinez-Rios, 2015).

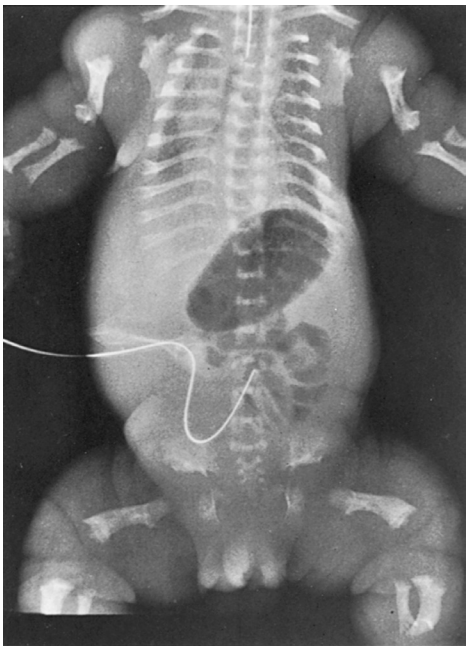

Fig. 14.32 Thanatophoric dwarf. Note small, narrow thorax and shortness of long bones.

D. **Intrauterine infection**: cytomegalovirus infection and congenital rubella are associated with lesions of the metaphyses, including vertical striations, which have been compared with a celery stalk. Metaphyseal lesions are also apparent in congenital syphilis (Weinert and Martinez-Rios, 2015).

E. **Congenital spine abnormalities** (Son-Hing and Thompson, 2015).
   1. Congenital scoliosis is secondary to a failure of formation of the vertebral bodies or abnormal development or both.
   2. Radiograph will demonstrate hemivertebrae and lateral curvatures.
   3. May occur in isolation but also as part of other syndromes or conditions. A careful review of other areas is necessary to rule out additional abnormalities.
   4. Lumbosacral agenesis is apparent on radiograph if the lower lumbar spine is absent. Sacral agenesis may be complete or partial failure of development.
   5. Ultrasound and MRI are helpful in evaluating the extent of spinal cord involvement.

F. Developmental dysplasia of the hip (DDH) (Son-Hing and Thompson, 2015).
   1. Ultrasonography avoids exposure of neonate to ionizing radiation but requires experienced ultrasonographer.
   2. X-ray examination: radiologist takes line measurements to determine anatomic relationship between femoral head and acetabulum; limited accuracy secondary to lack of ossification of femoral head.

G. Malformations or absence of skeletal parts (Morrison et al., 2015).
   1. Limb reduction anomalies: radiograph demonstrates absence of skeletal part.
   2. Amniotic band syndrome can cause limb amputations or truncation of a digit or extremity.
   3. Deformities of the feet, such as clubfeet, can be delineated with a radiograph.

Indwelling Lines and Tubes

A. **Endotracheal tube** (Figs. 14.33 and 14.34).
   1. Placement should be below the thoracic inlet and above the carina. When evaluating the position on chest radiograph, the endotracheal tube should be at or below T1, which is at the level of the first rib and just below the clavicles. The carina is at T4, so the tip should be at T3 or above.
   2. Head position: head flexion will advance the tube, and head extension will pull the tube away from the carina; therefore, head position should be considered when determining position of the endotracheal tube (ETT) tip.

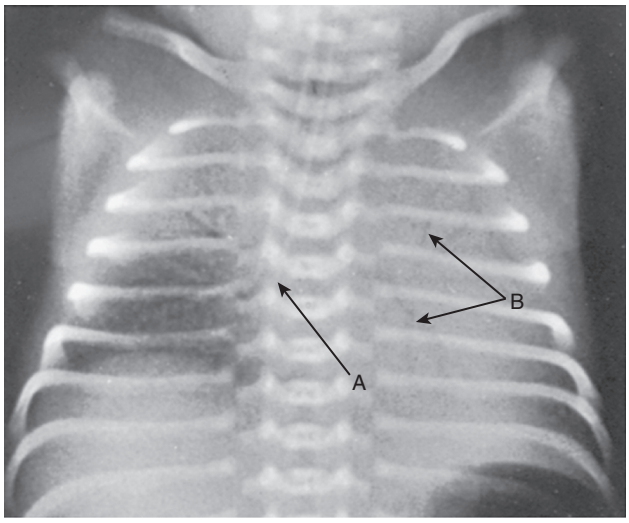

Fig. 14.33 Endotracheal tube is below T4 **(A),** entering the right mainstem bronchus, causing atelectasis of the right upper lobe and the left lung. Air bronchograms are apparent on the left against the dense underaerated left lung **(B)**.

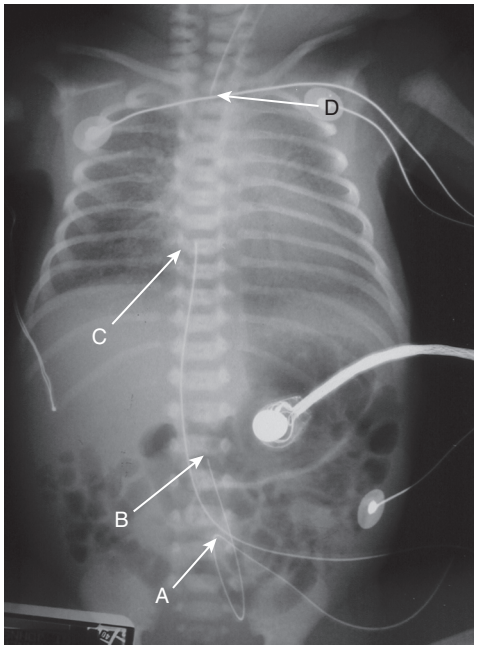

Fig. 14.34 Umbilical artery catheter courses down after entering the umbilicus **(A)** and then courses cephalad. Tip location bottom of L3 **(B)**. UVC passes cephalad to the right of the spinal column. UVC tip location **(C)**, entering right atrium and needs to be pulled back to the level of the diaphragm. The endotracheal tube is in a good position just below the clavicles **(D)**.

3. Placement beyond the carina results in occlusion of a bronchus (usually the right mainstem bronchus), with subsequent atelectasis and clinical deterioration.

B. **Umbilical artery catheter (see Fig. 14.34).** Proceeds from the umbilicus down toward the pelvis, making an acute turn into the internal iliac artery and common iliac artery and advancing into the abdominal aorta.
   1. Low placement: at third and fourth lumbar vertebrae, which is below mesenteric vessels, renal and celiac arteries.
   2. High placement: at sixth through ninth thoracic vertebrae, which is above the diaphragm and celiac arteries.

C. Umbilical venous catheter (UVC) (see Fig. 14.34).
   1. Proceeds from the umbilicus cephalad to the inferior vena cava (IVC) bypassing the liver through the ductus venosus.
   2. Correct placement is just above the diaphragm in the IVC below the junction of the IVC and right atrium.
   3. Caution: it is imperative that the UVC tip is advanced beyond the liver and does not enter the portal venous system or other pathways (splenic vein) or the right atrium (see Fig. 14.18B).

D. Chest tube (see Fig. 14.12).
   1. X-rays are obtained to determine placement and effectiveness in air and fluid removal and reinflating the lung.
   2. Lateral chest radiograph will determine anterior or posterior placement within the pleural space. For air evacuation, anterior placement with the infant in the supine position is desirable. For fluid evacuation, posterior placement with the infant in the supine position is most effective.
   3. Anteroposterior chest radiograph: correct placement will show the tube in the midclavicular line with the distal chest tube hole inside the thoracic space.

E. Peripherally inserted central venous catheters (PICCs) (Trotter, 2009).
   1. PICC placement radiographs: recommendations for timing and use of contrast.
      a. On insertion with water-soluble contrast, note arm and leg position.
      b. Any time catheter is adjusted (withdrawn) or inadvertently dislodged/moved.
      c. 24 hours after insertion to ensure tip has not moved.
      d. Weekly intervals.
      e. Any time infant clinically deteriorates, suspect PICC-related injury and check catheter tip location. Contrast media will help identify the location of the PICC tip and if the infusate is entering the aberrant venous system.
      f. Contrast media also important in the presence of significant lung disease or if a pleural effusion is present, as the density of the diseased lung fields and surrounding tissues may obscure the view of the catheter.
   2. Upper extremity catheters (Figs. 14.35 and 14.36).
      a. An anteroposterior chest radiograph is obtained. The catheter will travel from the insertion site through the subclavian vein and brachiocephalic veins to the superior vena cava.
      b. The tip of the catheter should be located in the superior vena cava and is considered central once it crosses the midclavicular line past the subclavian vein and enters the brachiocephalic vein and/or upper superior vena cava. The

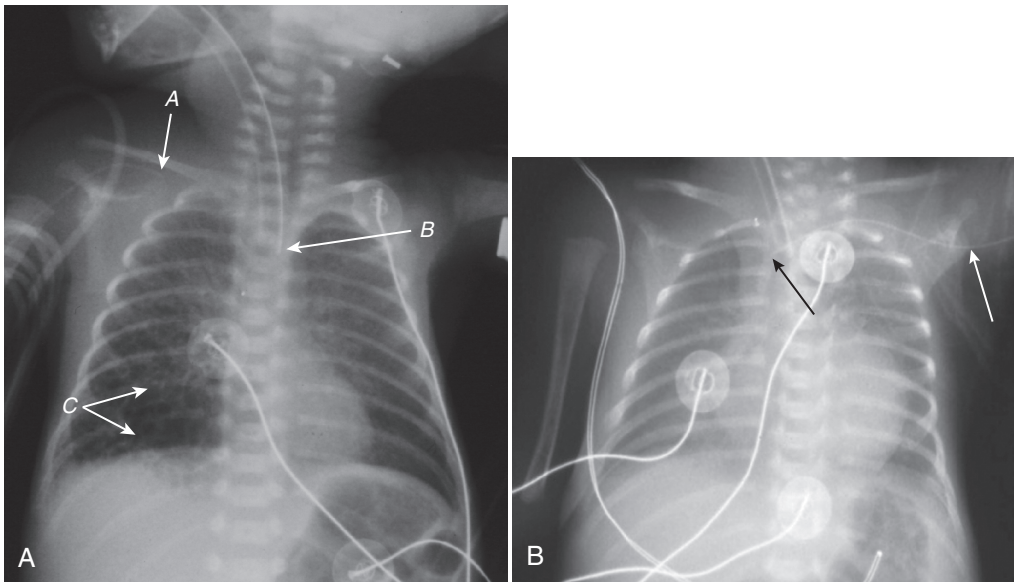

Fig. 14.35 **A,** Peripherally inserted central venous catheter inserted in right arm. Tip location within subclavian vein at midclavicular line (*A*). This is not considered a central venous location. The endotracheal tube is just below T3 (*B*). The circular lucency in the right lower lobe is a pneumatocele that developed secondary to barotrauma (*C*). **B,** Peripherally inserted central venous catheter inserted in left arm. The catheter passes through the left subclavian vein to the left brachiocephalic and terminates close to the brachiocephalic–SVC junction *(arrow)*.

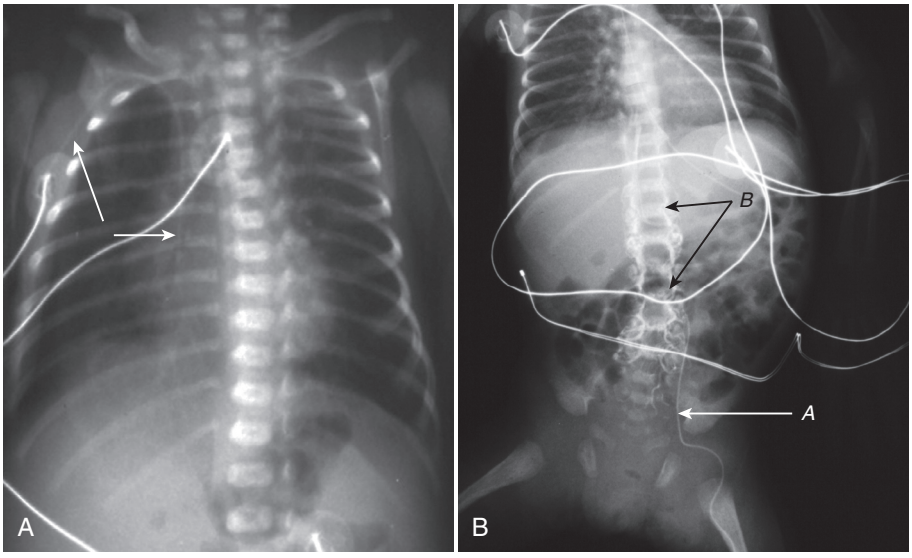

Fig. 14.36 **A,** Peripherally inserted central venous catheter inserted into right arm *(upper arrow)*. Tip location is in right atrium and needs to be pulled back to the SVC *(lower arrow)*. Cather tips located near or within the right atrium can cause injury and pericardial tamponade. Intracardiac tip locations may also result in cardiac arrhythmias. **B,** Catheterization of the ascending lumbar vein. The PICC (*A*) entered the ascending lumbar vein, which arises from the common iliac vein before the inferior vena cava. After contrast injection, the infusate was noted to enter the vertebral venous plexus (*B*). If left in this location, neurologic injury may occur.

catheter tip should lie above the junction between the superior vena cava and right atrium in an effort to prevent catheter tip migration into the heart.

3. Lower extremity catheters.
   a. An anteroposterior chest and abdominal radiograph is obtained. The catheter usually passes from the saphenous vein through the iliac and femoral veins into the IVC.
   b. Ideally, the tip reaches the level of the diaphragm below the IVC right atrial junction. If placed in a lower extremity, the line should be positioned in the IVC and is considered central once it crosses to the pelvic cavity and rests

below the right atrium of the heart. The catheter tip should lie below the junction between the IVC and the right atrium in an effort to prevent catheter tip migration into the heart.

4. Important considerations.
   a. There are many alternative venous pathways that the catheter can take, so it is imperative that the clinician monitors for correct position to prevent complications of an incorrect tip position (see Fig. 14.35).
   b. PICC tips can migrate after insertion; therefore, it is important to monitor catheter tip location by radiograph at regular intervals *and* any time the infant exhibits an unexpected clinical deterioration.

Diagnostic Imaging

A. Ultrasound.
   1. Uses sound waves to depict anatomic and functional motion of tissue. The sound waves reflect back to a transducer, which displays the echogenicity of the images. Images are stored digitally. The degree of echogenicity is determined by the varying density of tissues, the movement of tissue, and blood flow. The sound waves can be directed in a variety of planes and angles. Color Doppler ultrasound is used to depict the direction of vascular flow. Imaging terminology include the following terms (Merrow and Hariharan, 2018):
      a. Hyperechoic: bright or white images.
      b. Hypoechoic: dark or black images.
      c. Anechoic: no reflection of sound waves, black, seen with simple fluid.
   2. Ultrasound is commonly used to evaluate brain parenchyma and ventricular size, myocardial function and structure, urinary tract anatomy and pathology, pelvic masses, liver anatomy, and blood flow in major vessels.
   3. Benefits/advantages of ultrasound:
      a. Unlike conventional radiography, ultrasound does not emit radiation.
      b. Ultrasound is less expensive than CT or MRI, is portable, and is therefore more convenient for the evaluation of the unstable patient.
      c. Ultrasound is painless and generally does not require sedation. The procedure is performed at the bedside, and the infant's environment is minimally disrupted.
   4. Poor imaging technique, presence of bone and air in the imaging area, and patient position adversely affect the quality of the examination. Infant should be supine for cranial imaging, and the head should be in midline position.
   5. The nurse's role during an ultrasound examination is to correctly position the infant, offer comfort measures if necessary, and monitor vital signs and the infant's tolerance of the procedure.

B. CT.
   1. Obtains cross-sectional images of structures by emitting multiple x-ray beams through tissue. High-quality two-dimensional (2D) images in varied shades of gray are produced. The different densities of the image slices help depict the tissues and fluids (Merrow and Harharan, 2018).
   2. Use of CT has decreased due to concerns over increased radiation and availability of other imaging modalities (Merrow and Harharan, 2018).
   3. CT provides a 2D visualization of anatomy and can be further enhanced by the use of a radiographic contrast agent. Contrast enhancement can assist in the evaluation of blood flow and help define pathologic abnormalities.
   4. CT can distinguish changes in density in very small areas of tissue and allows identification of a variety of soft tissues. This allows for superior anatomic detail and precise clarity of tissue structure.
   5. CT requires the infant to be transported to the radiology department, so the infant's environment is disrupted. CT is painless but may require sedation depending on the infant's state.
   6. Utilized to evaluate structure, function, malformation, and extent of disease process. Used commonly in the NICU to evaluate brain anatomy; intraventricular hemorrhage and extent of parenchymal disease; and subgaleal, subarachnoid, and subdural bleeds. Also used to evaluate tumors and masses and organ-system anomalies of the chest, abdomen, and pelvis.
   7. The nurse's role in caring for an infant undergoing a CT examination is to swaddle the infant to decrease movement while in the scanner, thus diminishing artifacts from scan. The nurse must also provide comfort measures, evaluate the need for sedation, and monitor vital signs and infant's tolerance of procedure.

C. **MRI** (Merrow and Hariharan, 2018; NIH, n.d.).
   1. Noninvasive method that produces three-dimensional images while avoiding ionizing radiation.
   2. Images are created utilizing magnets that produce a strong magnetic field, resulting in the production of magnetized hydrogen protons. These protons within specific tissues are then agitated with radiofrequency energy pulses. This process results in a signal that is emitted and ultimately is converted into an image. Because hydrogen protons respond differently depending on their environment, high-quality images are produced that define the appearance of the tissues scanned. The image quality is excellent,

and the increased sensitivity allows for more precise imaging of even the smallest structures.
3. Intravenous contrast media can be used to enhance visibility of a specific area.
4. Best for imaging nonbony parts or soft tissues, including the brain, spinal cord, nerves, muscles and tendons, and tumors.
5. Is costly and has limited availability. The magnetic field can interfere with monitoring devices and may restrict the availability to unstable infants.
6. Requires that the infant be transported to the MRI department, so the infant's environment is disrupted. MRI is painless, but sedation may be required for an optimal study, which may require mechanical ventilation.
7. The nurse's role in MRI includes swaddling the infant and positioning in the scanner. The infant must be placed on a monitor designed to function within a magnetic field; specialty ventilators are also available for use with MRI. The nurse provides comfort measures and sedation as ordered, as well as monitoring vital signs and infant's tolerance of procedure.

D. Echocardiogram (ECHO).
1. Noninvasive diagnostic tool to evaluate cardiac structure and function.
2. High-frequency sound waves send vibrations through the heart, which reflect energy, which is transmitted into a visual image.
3. Poor imaging technique and infant movement adversely affect ECHO quality. It is portable and therefore available for even the unstable infant.

E. Barium enema.
1. Used to evaluate the structure and function of the large intestine and diagnose disorders such as Hirschsprung's disease, malrotation, and meconium plug syndrome.
2. A water-soluble contrast solution is instilled, and a series of x-rays is taken under fluoroscopy. A series of follow-up x-rays may be taken at timed intervals to evaluate the evacuation of the solution from the bowel.

F. Upper GI series with small-bowel follow-through.
1. Used to evaluate the structure and function of the upper GI tract. The three main areas examined are the:
   a. Esophagus (for size, patency, reflux, and presence of fistula or swallowing abnormalities).
   b. Stomach (for abnormalities and motility).
   c. Small intestine (for strictures, patency, and function).
2. A water-soluble contrast solution is swallowed, and a series of x-rays is taken under fluoroscopy. A series of follow-up x-rays is obtained to evaluate emptying ability of the stomach, intestinal motility, and for potential obstruction. Complications include reflux of the contrast solution, vomiting, and potential for aspiration.

G. Voiding cystourethrogram (VCUG) (Vogt and Dell, 2015).
1. Used to evaluate the structure and function of the kidneys, bladder, and lower urinary tract.
2. The infant's bladder is catheterized and then filled with a radiopaque contrast solution. A series of x-rays is taken during and at the end of voiding to evaluate the anatomy and for vesicoureteral reflux.
3. The infant should be monitored for hematuria and signs of infection related to a contaminated catheterization.

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CHAPTER 15
Common Invasive Procedures

Teresa B. Bailey and Heather Lynn Maltsberger

OBJECTIVES

1. Understand the indications for common procedures performed in the neonatal intensive care unit (NICU), such as endotracheal tube (ETT) intubation and suctioning, vascular access methods, blood sampling methods, bladder catheterization, bladder aspiration, thoracentesis, and lumbar puncture.
2. Know the equipment and supplies needed to perform common fundamental and advanced invasive procedures in the neonate.
3. Identify pertinent anatomic landmarks for commonly performed invasive procedures in the NICU.
4. Describe the precautions and contraindications for each invasive procedure.
5. Describe potential complications associated with each invasive procedure.

Approximately 250,000 to 350,000 newborn infants are admitted into the neonatal intensive care unit (NICU) in the United States annually and undergo hundreds of diagnostic and/or therapeutic procedures during their hospitalization. This chapter incorporates many of the diagnostic and therapeutic interventions that are commonly performed in the NICU. These procedures are crucial to the infant's survival; however, they expose the infant to pain and stress that can result in harmful long-term consequences. Therefore, pain management is essential when performing interventions in the NICU.

In many NICUs today, qualified registered nurses or advanced practice nurses, rather than physicians, perform invasive procedures. Before performing any procedure, it is essential that one have knowledge of the indications, precautions, and complications associated with each procedure. Infants are extremely vulnerable; therefore, the ability to perform the procedure proficiently is a major requirement to prevent harm.

The details pertaining to each of the covered procedures comprise this chapter. Aspects that are common to each include the crucial issues listed here:

- Always practice within your scope of practice and know your institution's protocols about the qualifications needed to perform any procedure.
- Know your institution's protocols about any specific ways in which procedures differ from the descriptions included here.
- Obtain informed consent whenever required for an invasive procedure. Discussion with family is key, even if signed informed consent is not required.
- Always use standard infection control precautions and implement aseptic technique whenever indicated.
- Provide for pain and comfort control before, during, and after the procedure.
- Developmentally supportive positioning and principles should be implemented to minimize pain and distress frequently associated with common neonatal procedures.
- Monitor the patient's clinical status during the procedure. Minimally, monitoring will include oxygenation, ventilation, temperature, and reaction to the procedure, including pertinent vital signs.
- Make written documentation about pertinent aspects of the procedure, and enter this into the medical record.
- Perform time-out before procedure to ensure patient safety.
- Evidence-based care bundles should be reliably implemented when available to improve procedural processes and patient outcomes and to decrease harm to hospitalized neonates.

Airway Procedures

ENDOTRACHEAL TUBE SUCTIONING: FUNDAMENTAL PROCEDURE

A. Indications.
   1. Facilitate oxygenation and ventilation.
   2. Maintain patent airway.
   3. Clear tracheobronchial secretions.
   4. Obtain tracheal aspirate specimens.

B. Contraindications.
   1. Recent surgical procedure to area.
   2. Recent surfactant administration.
   3. Pulmonary hemorrhage—suction only if needed to maintain tube patency.

C. Precautions.
   1. Suctioning should be done only when the infant's condition indicates and not on a routine schedule. Suctioning frequently or on a preset schedule has not been shown to decrease adverse events and may expose the infant to pain, hypoxia, and alterations in cerebral blood flow (Gardner and Shirland, 2009; Kaiser et al., 2008).
   2. Maintain aseptic technique.
   3. Monitor vital signs and for adverse responses to procedure, such as bradycardia and oxygen desaturations.
   4. Avoid hyperoxygenation, hyperinflation, and hyperventilation techniques if possible. Hyperoxygenation in preterm neonates is discouraged, due to risk of retinopathy of prematurity (ROP). If the infant easily becomes hypoxic or oxygenation status is critical, oxygen can be increased by 10% to 20% above baseline to maintain adequate oxygenation. Hyperinflation should be avoided, as this places the neonate at risk for air leaks. The effect of hyperventilation alone in neonates is unclear and therefore discouraged (Davis and Rosenfeld, 2005).
   5. Consideration should be given to suction catheter systems on an individual unit basis. Closed-system (in-line) suction catheter kits are available that remain attached to the endotracheal tube (ETT) adapter and should be used per the manufacturer's recommendations. Increased loss of lung volume and hypoxia can be associated with open catheters versus closed catheters. Although closed systems may have positive benefits on nursing time and staffing (Evans et al., 2014; Garner and Shirland, 2009; Tingay et al., 2007), insufficient evidence from large trials exists that demonstrate improvement in infection rates or a significant difference in physiologic parameters with closed versus open catheter systems (Cardoso et al., 2015; Taylor et al., 2011).
   6. Keep infant's head midline during suctioning to prevent jugular vein distention, which can increase intracranial pressure (ICP).
   7. Pulmonary hemorrhage may be exacerbated by suctioning. However, suctioning may be needed to clear the blood from the airway or tube.
   8. Always suction ETT before suctioning mouth.
   9. When feasible, use two caregivers to perform endotracheal suctioning if the closed (in-line) system is not in use. This may minimize adverse responses and shorten procedure time.
   10. Shallow suctioning technique is the preferred method. Deep suctioning should be avoided, as this has been shown to cause tissue damage and inflammation. The suction catheter should not extend beyond the length of the ETT (Gardner and Shirland, 2009).
   11. Routine normal saline (NS) irrigation is not recommended, as there is insufficient evidence to support benefit, and it may worsen bradycardia and prolong recovery (American Association for Respiratory Care [AARC], 2010; Garner and Shirland, 2009).

D. Equipment and supplies.
   1. Sterile gloves.
   2. Choose the appropriate-sized catheter (Table 15.1).
   3. Resuscitation bag with 100% oxygen source, oxygen blender, and manometer.
   4. Suction source with vacuum control setting.
   5. Stethoscope.
   6. Specimen trap (if applicable).

E. Procedure.
   1. Determine the need to suction and suction only when indicated.
      a. Falling oxygen saturations.
      b. Increasing oxygen requirements.
      c. Diminished breath sounds.
      d. Changes in vital signs.
      e. Changes in blood gases.
      f. Changes in respiratory rate and pattern.
      g. Agitation.
      h. Visible secretions in ETT.
      i. Pattern change in ventilator graphics.
      j. Loss of or poor chest wall excursion with ventilator breaths.

Table 15.1

Suction Catheter, Blade, and ETT Size by Weight

Weight	Gest. Age	Laryngoscope Blade	ETT Size	Suction Catheter
<1000 g	24 to 28 weeks	00	2.5 mm	5F to 6F
1001 to 2000 g	28 to 34 weeks	0	3.0 mm	6F to 8F
2001 to 3000 g	34 to 38weeks	0	3.5 mm	8F
3001 to 4000 g	>38 weeks	0	3.5 to 4 mm	8F
≥4000 g	>38 weeks	1	4.0 mm	8F

2. Wash hands and ensure that equipment is in working order.
3. Gather supplies.
4. If using a commercially prepared suction kit, open package and maintain sterility of contents. Remove and don sterile gloves, then remove catheter. If using separate gloves and catheter supplies, open suction catheter package, maintaining sterility of catheter, then open and don gloves. Continue to maintain aseptic technique and remove catheter from package.
5. While maintaining aseptic procedure, attach suction catheter to suction tubing with nondominant hand (now considered contaminated). With sterile dominant hand, hold suction catheter and maintain sterility of catheter.
6. Release suction tubing from nondominant hand and remove infant from ventilator. Provide oxygen and ventilation at necessary levels to maintain the heart rate and provide adequate oxygen saturation. Infant may be ventilated by hand or by providing manual breaths from ventilator. If manual breaths are provided by the ventilator, use caution to avoid hyperinflation and to allow adequate exhalation times.
7. Suction at 60 to 100 mm Hg or with just enough suction to extract secretions through catheter.
8. Advance catheter only to a predetermined distance—length of the ETT plus end adapter. If a cough reflex is initiated, catheter distance is too far.
9. Apply suction only when withdrawing catheter, and limit suction duration to 5 to 10 seconds. Allow patient to recover between suction passes while monitoring vital signs, oxygen saturation, and chest wall movement.
10. Limit the number of suction passes. Suction until secretions are removed or infant shows signs of intolerance. Clear suction catheter with NS between suction passes. Most secretions can be cleared in one or two passes.
11. If obtaining tracheal specimen, attach sterile specimen trap to suction catheter and suction tubing for specimen before general suctioning.
12. Return infant to previous oxygen requirement as tolerated, if applicable.
13. Label and send tracheal specimen to laboratory, if applicable.
14. Document patient's tolerance, character of secretions (amount, color, and consistency), and breath sounds.
15. If using a closed-system (in-line) catheter device, change per manufacturer's recommendation or per institution's policy if sooner.

F. Complications.
1. Hypoxia.
2. Bradycardia.
3. Apnea.
4. Accidental extubation or malpositioning of tube.
5. Trauma to trachea or bronchi and formulation of granulation tissue.
6. Hemorrhage.
7. Atelectasis and loss of lung volume.
8. Infection/pneumonia.
9. Pneumothorax.
10. Increased ICP and alterations in cerebral blood flow.
11. Bronchial stenosis.

ORAL ENDOTRACHEAL INTUBATION: ADVANCED PRACTICE PROCEDURE

A. Indications.
1. To perform resuscitation.
2. Bag-and-mask ventilation is ineffective or undesirable.
3. Need for mechanical ventilation.
4. To obtain sterile tracheal aspirate specimen.
5. Protection of the airway is required.
6. Diaphragmatic hernia is present.
7. Administration of exogenous surfactant.
8. To relieve critical upper airway obstruction.

B. Precautions.
1. Endotracheal intubation is a procedure with a low frequency but high risk of complications. Experienced providers generally can successfully intubate in shorter time frames and with fewer number of attempts. A simulation program that gives inexperienced providers the opportunity to gain competence in intubation is essential to providing high-quality neonatal care.
2. Patient's heart rate and oxygen saturation should be monitored continuously during the procedure and stabilized with bag-and-mask ventilation if possible before intubation and between attempts.
3. Use free-flow oxygen held near the mouth and nose of any infant with respiratory effort to maximize oxygenation during the procedure.
4. Limit intubation attempts to 30 seconds.
5. Have all equipment necessary for intubation prepared and in working order before initiating procedure.
6. For nonemergent intubations, infant pain management coupled with sedation or careful muscle relaxation is recommended before procedure using institutional protocol (Allen, 2012; Hatch et al., 2016).
7. Maintain thermal homeostasis and developmental care.

C. Equipment and supplies.
1. Pediatric laryngoscope handle.
2. Laryngoscope blade with functioning secure bulb. See Table 15.1 for blade and ETT size. A Miller straight blade is preferred (American Academy of Pediatrics [AAP] and American Heart Association [AAH], 2016); however, video laryngoscopes can be helpful in teaching intubation and improving intubation success (Assaad et al., 2016; Grgurich et al., 2016).

3. Stylet (though use is optional, it should be available).
4. Suction catheters (size 4F to 10F) and suction source set at 60 to 100 mm Hg of negative pressure.
5. Resuscitation bag and mask of appropriate sizes. Alternatively, availability of infant ventilation device, such as a T-piece resuscitator (i.e., NeoPuff).
6. 100% oxygen source with blender providing an appropriate Fio_2 for the patient, minimally at a flow rate of 5 to 10 L/min, with attached manometer.
7. Tape and other supplies to secure ETT according to hospital policy.
8. Cardiorespiratory monitor and oxygen saturation monitor.
9. Stethoscope.
10. Meconium aspirator, if applicable.
11. End-tidal CO_2 ($EtCO_2$) detector, colorimetric device such as the Pedi-Cap to confirm intubation.
12. Devices for difficult intubation—ideally, a difficult airway should be identified before intubation. The following devices should only be used by personnel with extensive training and experience, such as a neonatologist, otolaryngologist, or anesthesiologist. If this is not possible, arrangements should be made for transfer to a center where personnel and equipment are available (Kumar et al., 2010).
    a. Laryngeal mask airway (LMA) should be available at all intubations in the event intubation is unsuccessful (Kumar et al., 2010).
        1) All personnel who are trained in neonatal intubation should also be trained in the use of LMA.
        2) This is not an acceptable long-term airway; however, it may be used while preparations are made for a secure airway.
    b. Specialized stylets such as lighted and fiberoptic stylets, intubating introducers such as the gum elastic bougie, and fiberoptic flexible bronchoscopes.
    c. Indirect rigid laryngoscopes.
    d. Video laryngoscopes.

D. Procedure.
1. Gather ancillary personnel and ensure that all equipment is in working order (i.e., stethoscope, bag, and mask at bedside; suction on and functioning; laryngoscope with secured working light source; etc.).
2. Wash hands and verify patient and procedure to be performed.
3. It is recommended that an analgesic be given before all nonemergent intubation and use of a vagolytic be considered. Premedication can decrease adverse effects of intubation, such as bradycardia, hypoxia, and increased ICP, by treating pain and calming a patient during an uncomfortable procedure (Kumar et al., 2010). When writing a unit policy for preintubation medications, consider the use of agents that are rapid onset with the shortest possible duration of action. See Table 15.2 for common medications used in intubation.
    a. Analgesics: Preferred AAP analgesic is fentanyl, with morphine and remifentanil listed as acceptable.
    b. Sedative–hypnotic (optional): Due to limited data and side effect profile, there are no AAP-preferred sedative–hypnotic agents. Acceptable agents are thiopental and propofol in preterm and term infants, and midazolam is acceptable in term infants. A sedative alone without analgesia should not be used (Kumar et al., 2010).
    c. Neuromuscular blocking agents (optional): Muscle relaxants are contraindicated in situations where intubation may be difficult, such as micrognathia and cleft lip/palate or with health care providers with limited neonatal intubations. Sensation remains intact with neuromuscular blockade, and thus, analgesia must be used in combination.
    d. Vagolytics: These drugs may help prevent reflex bradycardia during intubation. Atropine is the AAP-preferred vagolytic, but glycopyrrolate may be used as a second option.
4. Select ETT of the appropriate size.
5. Insert stylet (optional) and shape the ETT as desired. The stylet must be secured so that its tip does not extend below the tip of the ETT and so the stylet cannot advance during the procedure. Keep the tube and stylet as clean as possible.
6. Determine ETT insertion depth. A variety of methods has been reported for predicting insertional length, such as nasal–tragus length, sternal length, foot length, and weight. The AHA Neonatal Resuscitation Program uses the 7-8-9 Rule (AAP and AHA, 2016).
    a. 6 plus the weight in kilograms (e.g., in a 2-kg neonate, the ETT should be inserted to the 8-cm marking: 2 kg + 6 = 8 cm).
    b. The 7-8-9 Rule has been associated with overestimated depth insertion in infants weighing less than 750 g (Peterson et al., 2006).
7. Aspirate gastric contents and suction the oropharynx.
8. Position the patient supine on a flat surface with the head midline and the neck slightly extended (optional: place a soft flat roll under neck) in a "sniffing" position. The person performing intubation must have easy access to the airway and equipment while positioned at the patient's head.
9. Hold the laryngoscope in the left hand between the thumb and first finger, with the blade pointing away. The laryngoscope is designed to be held with the left hand only.
10. Open the patient's mouth with the fingers of the right hand and gently slide the blade into the right side of the mouth.
11. Stabilize the left hand against the left side of the patient's face, advance the blade tip to the base of the

Table 15.2

Medications for Use With Intubation

Medication	Onset of Action	Duration of Action	Dose	Considerations
Analgesics				
Fentanyl (preferred)	Almost immediate IV, 7 to 15 minutes IM	30 to 60 minutes IV, 1 to 2 hours IM	1 to 4 mcg/kg IV or IM	Give slowly (over 1 to 2 minutes minimally), as rapid infusion may cause thoracic and skeletal muscle rigidity. May cause apnea, hypotension, and CNS depression; reversed with naloxone.
Remifentanil	Almost immediate	3 to 10 minutes	1 to 3 mcg/kg IV	Give slowly (over 1 to 2 minutes minimally), as rapid infusion may cause thoracic and skeletal muscle rigidity. May cause apnea, hypotension, and CNS depression.
Morphine	5 to 15 minutes IV, 10 to 30 minutes IM	3 to 5 hours IV or IM	0.1 to 0.3 mg/kg IV or IM	May cause apnea, hypotension, and CNS depression; reversed with naloxone.
Sedative–Hypnotic				
Thiopental	30 to 60 seconds	5 to 30 minutes	2 to 6 mg/kg IV	May cause apnea, hypotension, and bronchospasm.
Propofol	Within 30 seconds	3 to 10 minutes	1 to 2.5 mg/kg	May cause apnea, hypotension, bronchospasm, bradycardia, and pain at injection site.
Midazolam	1 to 5 minutes IV, 5 to 15 minutes IM	20 to 30 minutes IV, 1 to 6 hours IM	0.05 to 0.1 mg/kg IV or IM	Has not been established as safe for use in very preterm infants due to risk of benzyl alcohol toxicity. May cause apnea, hypotension, and CNS depression. Effects reversed with flumazenil.
Neuromuscular-Blocking Agents				
Succinylcholine	30 to 60 seconds IV, 2 to 3 minutes IM	4 to 6 minutes IV, 10 to 30 minutes IM	1 to 2 mg/kg IV, 2 mg/kg IM	Do not use in neonates with hyperkalemia, suspicion of muscular dystrophy, increased ICP, or a family history of malignant hyperthermia; monitor for bradycardia (pretreatment with atropine minimizes bradycardia).
Vecuronium	2 to 3 minutes	30 to 40 minutes	0.05 to 0.10 mg/kg IV	Minimal cardiovascular side effects; however, decrease in heart rate and blood pressure has been observed when used concurrently with narcotics. Reversed with neostigmine and atropine.
Rocuronium	1 to 2 minutes	20 to 30 minutes	0.5 mg/kg IV	May cause hypertension or hypotension, tachycardia, arrhythmias, and bronchospasm.
Pancuronium	1 to 3 minutes	40 to 60 minutes	0.05 to 0.10 mg/kg IV	May cause hypertension, tachycardia, bronchospasm, and excessive salivation; reversible with atropine and neostigmine.
Vagolytics				
Atropine	1 to 2 minutes	0.5 to 2 hours	10 to 20 mcg/kg IV or IM	May cause tachycardia and dry skin.
Glycopyrrolate	1 to 10 minutes	≈6 hours	5 mcg/kg IM	May cause tachycardia, arrhythmias, and bronchospasm.

CNS, Central nervous system; *ICP*, intracranial pressure; *IM*, intramuscularly; *IV*, intravenously.

Adapted from Allen, 2012; Kumar et al. and Committee on Fetus and Newborn, Section on Anesthesiology and Pain Medicine, 2010.

tongue, and move the blade to the midline, pushing the tongue to the left.

12. Expose the pharynx by lifting the entire blade upward in the direction in which the handle is pointing. Do not rock the tip of the blade upward or use the upper gum as a fulcrum, as this may damage the gums.
13. If unable to see the glottis, apply gentle external tracheal pressure (cricoid pressure) with the fifth finger of the left hand or have an assistant perform this and withdraw the blade slowly until the glottis is visible.
14. Remove any secretions that interfere with visualization by suctioning. Direct suctioning under laryngoscopy is ideal.

15. Identify anatomic landmarks.
    a. Epiglottis is uppermost.
    b. Glottis is anterior, with vocal cords closing side to side.
    c. Esophagus is posterior.
16. After identifying the vocal cords, and with the cords in clear view, place the ETT into the right side of the patient's mouth with the right hand.
17. Keeping the cords in view, pass the ETT between the cords 1 to 2 cm into the trachea on inhalation (level of the vocal cord guide mark on the ETT). This should position the tip of the tube midway between the thoracic inlet and the carina, approximately at the second and third thoracic vertebrae. If the vocal cords are closed or will not open, wait for spontaneous breath, or stimulate a breath by stroking the soles of the feet.
18. With the right index finger, firmly hold the ETT against the roof of the mouth, stabilize the right hand against the patient's face, and carefully remove the laryngoscope with the left hand.
19. Carefully remove the stylet, if used, from the ETT.
20. Attach the resuscitation bag and $EtCO_2$ detector, if applicable, and assess tube placement.
    a. Auscultate both sides of the chest for the presence and intensity of breath sounds.
    b. Assess chest movement with inflationary breaths.
    c. Auscultate over the epigastrium and visually assess for distention.
    d. Check for condensation in tube during exhalation.
    e. Check for color change on CO_2 detector, which should be considered in conjunction with the earlier factors and improving vital signs.
    f. Limitations of neonatal colorimetric $EtCO_2$ detection devices (AAP and AHA, 2016).
        1) Decreased perfusion—adapter may not change color quickly, if at all, when the neonate has little to no perfusion.
        2) Inadequate ventilation—adapter may not change color if there is not enough exhalated CO_2.
        3) Detector contamination—detector may be contaminated with bodily fluids or medications, limiting its ability to display color change. False-positive color change has been reported with atropine, epinephrine, calfactant (Infasurf), and naloxone (Narcan) (Hughes et al., 2007).
        4) Defective device—check color when device is removed from package, and discard if it is already yellow.
21. After confirmation of successful intubation, attach ETT to bag or special ventilation device such as a T-piece resuscitator and deliver breaths.
22. If the tube is in too far and placed in a right or left mainstem bronchus, auscultation may reveal unilateral or unequal breath sounds. The tube should be withdrawn very gradually and assessed until equal bilateral breath sounds are auscultated. If the tube is in the esophagus:
    a. Air may be heard entering the stomach with inflationary breaths.
    b. The stomach may become distended.
    c. A strong cry or cough may be noted.
    d. No breath sounds will be heard on auscultation of the chest during inflationary breaths, though air movement may be heard, especially over the lower portion of the chest.
    e. No color change with $EtCO_2$ detector.
    f. Remove the ETT and discard it and hand ventilate with bag and appropriate-sized mask.
23. In very small infants, breath sounds may seem audible even with an ETT in the esophagus.
24. When the tube is assessed to be in good position, note the markings and secure the tube to the face according to hospital policy.
25. To confirm ETT position:
    a. Obtain chest x-ray in anteroposterior (AP) view with head midline and not in a flexed position.
    b. Tip of ETT should lie approximately 0.5 to 1 cm above the carina.
26. After confirming tube placement by chest radiograph, any length of tube that extends more than 4 cm beyond the lip should be cut off to limit dead space and to prevent kinking.
27. Document according to hospital policy: date, time, ETT size, centimeter marking at lip, $EtCO_2$ results, chest radiograph, and patient's tolerance of procedure. Medications given, if any, should also be documented.

E. Complications.
1. Hypoxia during the procedure or due to misplacement of tube.
2. Bradycardia due to hypoxia or due to vagal stimulation from the laryngoscope, ETT, or suction catheter.
3. Increased risk for intraventricular hemorrhage in low birth weight infants (Wallenstein et al., 2016).
4. Infection.
5. Perforation of esophagus or trachea.
6. Trauma/edema to oropharyngeal and laryngeal tissues.
7. Vocal cord injury.
8. Subglottic stenosis associated with long-term (>3 to 4 weeks) intubation.
9. Misplacement of tube into esophagus or bronchus.
10. Interference of oral development caused by oral ETT.
11. Ingestion/aspiration of laryngoscope bulb.

12. Tube obstruction or kinking.
13. Pain, agitation, or discomfort.

THORACENTESIS: ADVANCED PRACTICE PROCEDURE

A. Indications.
   1. Emergency evacuation of pneumothorax.
   2. Emergency evacuation of pleural fluid.
B. Equipment and supplies.
   1. Skin antiseptics according to hospital policy.
   2. Over-the-needle intravenous (IV) catheter (18 to 24 gauge).
   3. Three-way stopcock.
   4. Syringe, 10 to 30 mL.
   5. Local anesthetic, tuberculin (TB) syringe with small-bore needle, if medical condition permits.
C. Procedure.
   1. Position the infant supine and restrain limbs if necessary.
   2. Provide pharmacologic pain management if medical condition permits.
   3. Identify entry site. For evacuation of a pneumothorax, use second or third intercostal space along the midclavicular line. The fourth intercostal space at the anterior axillary line can also be used. If thoracentesis is being done because of pleural fluid or effusion, the thorax should be punctured between the fifth and sixth intercostal spaces, midaxilla.
   4. Prepare skin with antiseptic as per hospital policy.
   5. Infiltrate the area with 1 mL of local anesthetic using a TB syringe and 25- to 27-gauge needle.
   6. Puncture skin at 45-degree angle, angling over third or fourth rib, and advance needle/catheter at a 90-degree angle. Inserting the catheter over the top of the rib will avoid blood vessels and nerves that run along the bottom of the rib. Remove needle from IV catheter while sliding the catheter into the pleural space.
   7. Attach catheter hub to stopcock and syringe. The stopcock allows for aspiration of free air or fluid into the syringe and emptying of the syringe while maintaining a closed system.
   8. When free air or fluid is obtained, stabilize the catheter and continue to aspirate until preparation for chest tube insertion is complete or until the air leak or fluid accumulation is evacuated.
   9. Document according to hospital policy: date, time, catheter size, location, amount of air/fluid evacuated, patient's tolerance of procedure. Pharmacologic interventions performed should also be documented.
D. Complications.
   1. Hemorrhage.
   2. Infection.
   3. Injury to lung or adjacent structures.
   4. Damage to breast tissue.
   5. Pain.

Circulatory Access Procedures

PERIPHERAL INTRAVENOUS LINE PLACEMENT: FUNDAMENTAL PROCEDURE

A. Indications.
   1. Administration of medications.
   2. Administration of fluids, volume expanders, or blood products.
   3. Administration of parenteral nutrition.
B. Precautions.
   1. Avoid areas of infection or loss of skin integrity near selected puncture site.
   2. Use caution in infants with coagulation disorders, which may result in bleeding into surrounding tissues.
   3. Padded armboard is to be used only if necessary to maintain line placement and must be of an appropriate size for gestational age.
   4. Choose an access site based on patient's condition, prescribed therapy, and inserter's experience (Alexander and Infusion Nurses Society [INS], 2016).
      a. Consider conserving areas that may later be needed for central line placement, such as the basilic, cubital, cephalic, and saphenous veins.
      b. The inserter should be familiar with anatomic characteristics and acceptable venipuncture sites.
      c. Recommended for short-term IV therapy (<6 days).
      d. Avoid infusion of hyperosmolar fluids (<600 mOsm/L), dextrose (>10%), and acidotic (pH <5) or alkalotic (pH >9) fluids because of the risk of injury (Wycoff and Sharpe, 2015).
C. Equipment and supplies.
   1. 22- to 24-gauge over-the-needle safety catheter.
   2. Tape and dressing supplies as per hospital policy.
      a. Catheter stabilization device if available.
      b. Transparent semipermeable membrane to allow visualization of insertion site.
   3. Skin antiseptics as per hospital policy.
   4. Tourniquet (a sanitized rubber band will suffice).
   5. NS flush solution in a 3-mL syringe.
   6. Transilluminator, if necessary to visualize vessels.
   7. Small scissors or safety razor, if necessary.
   8. Appropriately sized, padded armboard, if necessary.
   9. Nonsterile gloves.
   10. Additional tubing and infusate as indicated per hospital policy.
   11. Pain/developmental management: pacifier, sucrose pacifier, blankets for developmental swaddling, eye protection from bright lights.
D. Procedure.
   1. Verify order from licensed health care provider for placement of a vascular access device.

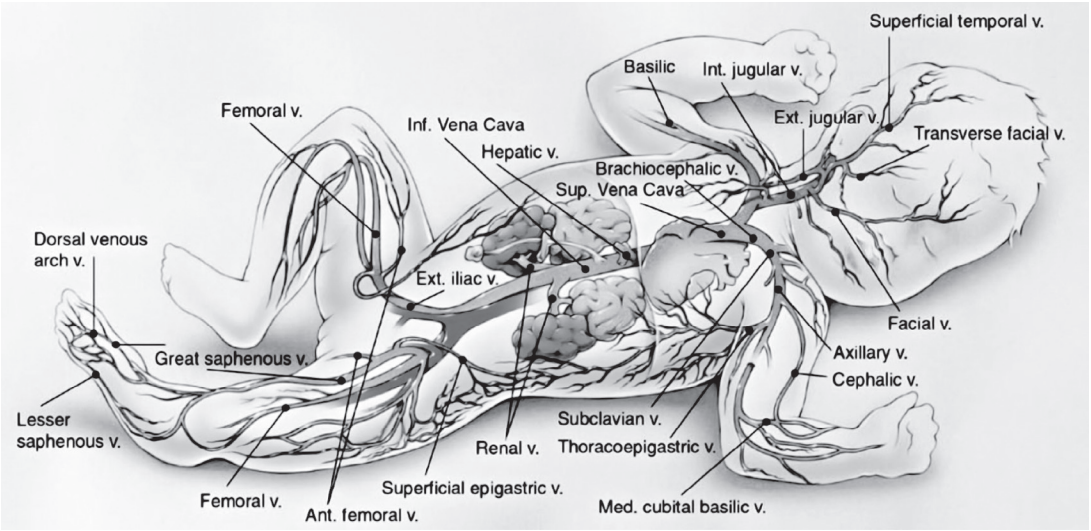

Fig. 15.1 The major veins that may be used for peripheral intravenous line placement in young infants. (Courtesy and copyright Becton Dickinson and Company.)

2. Gather supplies, use hand hygiene as indicated by hospital policy, and don gloves.
3. Provide pain management such as pacifier for non-nutritive sucking, sucrose pacifier, and/or developmental care with facilitated tucking or swaddling. Shield eyes from bright lights.
4. Flush connecting tubing with NS flush solution.
5. Determine vein for cannulation (Fig. 15.1). Accomplish distention of the vessel by applying a gentle tourniquet proximal to the selected insertion site. Alternatively, an assistant may encircle the proximal extremity with hand/fingers and apply direct pressure for the same effect.
   a. Transilluminate to locate vein, if necessary (use caution to avoid skin burns from heated device).
   b. Apply warm compress for 5 minutes if needed to help dilate veins and make them more visible.
   c. If a scalp vein will be cannulated, trim hair with scissors rather than shaving to help visualize and secure IV tubing.
6. Choose appropriate-sized catheter for patient's size and vein.
7. Prepare skin at selected puncture site with antiseptic as per hospital policy, using aseptic technique.
8. Position and stabilize puncture site, keeping skin taut.
9. Beginning a few millimeters distal to the anticipated site of the vessel puncture, insert the needle bevel-up, at a 10- to 20-degree angle, depending on location of vein. Puncture skin in the direction of blood flow and advance needle in 1- to 2-mm increments.
10. If resistance is met or vein is not punctured, withdraw needle slowly to just below the level of the skin, relocate vein, and advance the needle again.
11. If a hematoma develops or bleeding occurs, occlude the vessel with pressure just proximal to the puncture site, remove tourniquet, withdraw the needle or catheter, and apply pressure until hemostasis has occurred.
12. If cannulation appears to be successful (i.e., flashback of blood in hub), remove the tourniquet and catheter needle (if using over-the-needle catheter), connect the tubing to the catheter hub, and inject some of the flush solution gently to evaluate patency of the catheter. If flush solution infiltrates the tissues surrounding the catheter tip, occlude the vessel with pressure just proximal to the puncture site, withdraw the needle or catheter, and apply pressure until hemostasis has occurred.
13. Each inserter should attempt access no more than 2 times to limit damage to future access sites and patient pain. Access attempts should be limited with considerable thought given to alternative treatments or access should attempts continue to be unsuccessful.
14. If cannulation was successful and flush solution infuses without complications, connect T-connector and IV tubing with appropriate fluid to catheter, if applicable.
15. Tape catheter in position that is developmentally appropriate and per hospital policy. Tape, dressing, and restraint must allow for easy inspection of insertion site, circulation of the distal extremity, and patency of the IV tubing. Avoid occlusion of the IV tubing with the tape or dressing.
16. Activate safety device upon removal of needle and dispose of needle(s) in appropriate sharps container.
17. Document date, time, catheter size, site location, and patient's tolerance of procedure, according to

hospital guidelines. Pain management interventions should also be documented.

18. Monitor for tissue infiltration or device dislodgment. If signs of infiltration are present, stop infusion immediately. Adverse signs may include:
    a. Redness, blanching, or discoloration at or near IV insertion site.
    b. Edema or swelling of extremity.
    c. Blistering at site.
    d. Pain with flushing.
    e. Resistance with flushing.
    f. Leaking at site.
    g. Coolness of skin around insertion site/extremity.
19. Treatment for infiltration/extravasation (Fox, 2011; Sawatzky-Dickson and Bodnaryk, 2006; Thigpen, 2007).
    a. Immediately stop all infusion of fluids and/or medications.
    b. Remove any constricting bands that may interfere with blood flow.
    c. Consider elevation of affected extremity.
    d. Use of cold or warm compresses is controversial; further evidence is needed to demonstrate benefit.
    e. Notify physician or advanced practice nurse immediately.
    f. Assess and document appearance of infiltrated area, including size, areas of blanching or erythema, pulses, perfusion, and estimated amount of infusate. Determine stage of extravasation (Sawatzky-Dickson and Bodnaryk, 2006; Thigpen, 2007).
        1) Stage 1: IV difficult to flush, pain at site without redness or swelling.
        2) Stage 2: Slight swelling and redness at site, pain, good pulse and normal perfusion below site.
        3) Stage 3: Moderate swelling and blanching at site, pain, good pulse and normal perfusion below site, skin cool to touch.
        4) Stage 4: Severe swelling and blanching at site, pain, decreased pulse and prolonged or absent capillary refill below site, skin cool to touch with evidence of breakdown or necrosis.
    g. Pharmacologic intervention.
        1) Hyaluronidase (Vitrase)—indicated for the treatment of stage 3 and 4 injuries. For best results, use hyaluronidase within 1 hour of infiltration but may be given up to 3 hours after infiltration. Reconstitute product with NS. The recommended dose is 15 units/mL. After cleaning the area with an antimicrobial agent, inject five 0.2-mL injections subcutaneously around the periphery of the infiltration (do not inject directly into affected area), using a different 25- to 27-gauge needle for each injection. Not recommended for IV use.
        2) Phentolamine (Regitine)—indicated for treatment of infiltration of α-adrenergic drugs such as dopamine, epinephrine, norepinephrine, and phenylephrine. For best results, use within 12 hours of infiltration. Dilute the available 5-mg/mL product to a concentration of 0.5 mg/mL. Inject subcutaneously into the area of infiltration using multiple small injections of 0.2 mL with a 25- to 27-gauge needle, changing the needle between each skin entry. Use cautiously in hemodynamically unstable infants. Monitor for hypotension.
        3) Nitroglycerin 2%—apply 4 mm/kg to affected area. Use with caution in neonates ≤34 weeks postmenstrual age who are not older than 21 days of age because of enhanced absorption through the thin immature skin, which may put them at risk for overdosage and toxicity. Apply only to intact skin. Monitor heart rate and blood pressure, as it may cause tachycardia and hypotension.
    h. Multiple puncture technique.
        1) To be used to express fluid in extreme infiltrations (stage 4) to reduce pressure and prevent skin necrosis.
        2) Prepare skin at site with antiseptic technique as per hospital policy.
        3) Provide pain management with swaddling, sucrose pacifier, and/or pain medication.
        4) Use a large-bore (18-gauge) sterile needle and make multiple perforations over the greatest area of swelling with strict aseptic technique.
        5) Allow for free flow of infiltrated fluid. May gently massage affected area.
        6) Cover skin with room-temperature, saline-soaked dressing and elevate affected extremity.

E. Complications.
    1. Hematoma.
    2. Infection.
    3. Air, clot, or particle embolus.
    4. Tissue injury (phlebitis, infiltration) and possible necrosis after infiltration of infused solutions and/or medications.
    5. Injury to extremity from restraint.
    6. Compromised distal circulation.
    7. Pressure necrosis over bony areas.
    8. Limb deformity after prolonged immobilization.
    9. Pressure injury of peripheral nerves.
    10. Inadvertent arterial line placement.
    11. Blood loss from inadvertent catheter or tubing dislodgment.
    12. Pain from infiltration or ruptured blood vessel from unsuccessful cannulation.

PERIPHERALLY INSERTED CENTRAL CATHETER AND MIDLINE CATHETER: ADVANCED PRACTICE PROCEDURE

Peripherally inserted central catheters (PICCs) are central catheters inserted in an extremity or the scalp of an infant that can be used as a reliable method of delivering long-term IV therapy, fluids, and nutrition. Their use has been shown to be beneficial and cost-effective when compared with peripheral IV access in extremely low birth weight infants and infants requiring more than 6 days of IV therapy (Wycoff and Sharpe, 2015).

A midline catheter (MLC) is a peripherally inserted catheter that dwells deeper in the vein than those used for standard peripheral IV therapy but never enters the abdominal–thoracic cavity. MLCs are a form of intermediate IV therapy and should not be used in infants who require the use of a PICC. The Centers for Disease Control and Prevention (CDC) recommends insertion of an MLC or PICC if IV therapy is expected to exceed 6 days (CDC, 2011). Insertion of an MLC is the same as for a PICC (i.e., use of strict aseptic technique, need for continuous heparinized carrier fluid); however, their use is strictly that of a peripheral IV device. Newer products are available in shortened lengths for use as an MLC (Chenoweth et al., 2018). An MLC can remain in place for 2 to 4 weeks. Studies in neonates have reported MLC mean dwell times from 6 to 10 days (Wycoff and Sharpe, 2015). The longer MLC dwell time therefore minimizes the frequent painful IV insertions and costs associated with standard peripheral IV lines (Chenoweth et al., 2018). It is important to note that although MLCs have established safety, studies have shown significantly higher rates of nonelective removal with noncentrally placed catheters (Colacchio et al., 2012; Goldwasser et al., 2017; Jain et al., 2013). The most common indication cited for nonelective removal of noncentral catheters is infiltration (Colacchio et al., 2012). If a central placement is not possible, the catheter may be retracted and position confirmed outside the abdominal–thoracic cavity (Wycoff and Sharpe, 2015).

NOTE: Catheters with a stylet are available. A stylet may make advancing a catheter easier, and there is no evidence to support concerns that the stylet will damage or perforate vessels when used with care (Wycoff and Sharpe, 2015). Hospital-stock choice of catheter size, lumen, and manufacturer should be based on the evidence, patient population need, and cost-effectiveness. The stylet should not extend past the tip of the catheter and should never be trimmed. Follow the manufacturer's recommendations regarding trimming and flushing catheters with stylets before insertion.

A. Indications.
   1. Intermediate or long-term IV therapy (>6 days).
   2. Parenteral nutrition (strongly consider use of PICC, especially if anticipated dextrose or osmolarity requires central placement).
   3. Antibiotic or other medicinal therapy.
   4. Difficult venous access.
   5. Irritating drug therapy (strongly consider central placement).

B. Contraindications.
   1. Use in active bacteremia or sepsis is controversial. Consider deferring placement for at least 24 to 48 hours after antibiotic dosing is started; however, this access may be needed to deliver antibiotics.
   2. Inadequate vessel for cannulation.
   3. Anatomic irregularities in infant's extremities or chest that could interfere with proper insertion.
   4. Fracture in an extremity can alter the vessels surrounding the bone (Wycoff and Sharpe, 2015).
   5. Avoid insertion in the right arm of infants with congenital heart defects resulting in decreased blood flow to the subclavian artery.
   6. Extremities with edema or other conditions that may make assessment for infiltration difficult.
   7. The infant can be adequately treated with a peripheral IV access.
   8. Parental refusal.

C. Precautions.
   1. Avoid areas of infection or loss of skin integrity near selected puncture site.
   2. Avoid placement of a PICC in an extremity with inadequate or poor circulation.
   3. Obtain parental informed consent for PICC insertion before the procedure per institutional policy.
   4. Use caution in infants with coagulation disorders or a history of thrombosis. An MLC should not be used in these infants at all (Alexander and INS, 2016).
   5. Avoid use of MLC in infants with decreased venous blood flow to the extremities or in conditions where preservation of peripheral veins is desired (Alexander and INS, 2016).
   6. Use caution with high-frequency ventilation, as pressure changes within the chest may lead to catheter migration, particularly with upper body insertions.
   7. Do not measure blood pressure or perform venipuncture on the extremity containing the PICC/MLC.
   8. Use aseptic technique during insertion and care of PICC/MLC.
   9. Ensure attention to pain management, developmental care, and thermal homeostasis.
   10. Infuse medication via infusion pump; avoid "pushes."
   11. Use larger-bore syringes (>10 mL) that generate less pressure.
   12. Avoid tension on catheter and tubing.
   13. Never pull the catheter back through the hollow needle introducer because of the risk of damage or shearing of the catheter.

14. Monitor for bradycardia and hypoxia during procedure.
15. Follow manufacturer's recommendations regarding infusion of blood products or obtaining blood specimens from a PICC or MLC.
16. When infusing fluids via MLC, follow the same precautions as with peripheral IV to avoid damage to noncentral vessels.

D. Equipment and supplies.
1. Commercially prepared catheter insertion kit or the following:
   a. Antiseptic per hospital policy. If it is institutional policy to use chlorhexidine, use with care in premature infants or infants under 2 months of age, as these products may cause irritation or chemical burns. An alternative of povidone–iodine may be considered (Alexander and INS, 2016). No antiseptic has been determined as best for all infants. Use caution and clean the extremity well after placement (Chapman et al., 2013; Wycoff and Sharpe, 2015).
   b. Nontoothed forceps.
   c. Sterile measuring tape.
   d. Sterile gown and gloves, mask, and surgical cap.
   e. Sterile flush solution per institutional policy.
   f. Sterile gauze pads.
   g. Sterile drapes and towels.
   h. Sterile tourniquet (optional with preterm infants).
   i. Sterile 5- to 10-mL syringes, as recommended by manufacturer.
   j. Transparent, semipermeable dressing.
   k. Sterile adhesive strips.
   l. Extension set per hospital policy.
   m. Select a neonatal percutaneous catheter of appropriate size. Catheter sizes include single-lumen 1F to 5F and single- or double-lumen 1.9F to 3F. Usually, lumens of 1.1F to 3F are used in neonates (Wycoff and Sharpe, 2015).
   n. Select an introducer of appropriate size to accommodate the catheter.
      1) Different types of catheter introducers are available, depending on manufacturer.
         a) Breakaway needle—the vessel is cannulated and the catheter advanced through the needle to the premeasured distance. The needle is then retracted and broken along its longitudinal axis and discarded. These needles may be smaller in diameter than introducer-type devices, yet catheter shearing or damage may occur if the catheter is retracted through the needle.
         b) Peel-away plastic cannula—the vessel is punctured and the needle is removed, leaving the plastic cannula in the vessel for catheter insertion. Advance the catheter to the premeasured distance, then retract the plastic cannula from the vessel and pull the catheter apart along its longitudinal axis and discard.
         c) A device with a safety needle retractor should be used to avoid needle-stick injury.
   o. Catheter trimming device per manufacturer's recommendation.

E. Procedure.
1. Verify order for PICC/MLC.
2. Check to ensure informed consent is obtained per institutional policy.
3. Gather equipment and supplies.
4. Provide pain management (Wycoff and Sharpe, 2015).
   a. Developmentally supportive positioning, swaddling, and pacifier use.
   b. Consider premedication with sedative.
   c. Consider use of topical lidocaine cream if appropriate.
5. Maintain thermoregulation.
6. Provide environmental support by protecting infant's eyes from bright lights.
7. Select vein (see Fig. 15.1).
   a. Most common sites for neonates include the cephalic, basilic, and greater saphenous veins. Other sites include popliteal, temporal, and axillary veins.
   b. Ultrasound evaluation of vessels may assist in identifying appropriately sized vessels, decrease number of attempts, and improve success. The use of this technology requires a trained provider (Johnson et al., 2016; Katheria et al., 2013; Wycoff and Sharpe, 2015; Zaghloul et al., 2018). When using ultrasound, a catheter less than 45% of the vein diameter should be chosen (Alexander and INS, 2016).
8. Position infant so selected vein is accessible. Restrain infant if necessary to prevent contamination of sterile field.
9. Measure length of catheter to be inserted.
   a. For PICC (central venous access) insertion (Wycoff and Sharpe, 2015):
      1) Upper body insertion: Tip should be in the superior vena cava.
         a) Measure from insertion site along the course of the vein to the third intercostal space, with the arm at a 90-degree angle for upper extremity placement.
      2) Lower body insertion: Tip should be in the inferior vena cava above the L4–L5 vertebrae or iliac crest and below the right atrium.
         a) Measure from insertion site to xiphoid process for lower extremity placement.
   b. For MLC (peripheral venous access) insertion:
      1) Upper body insertion: Tip should end in the upper arm, distal to the head of the humerus.

a) Measure from the insertion site to the desired site of catheter tip.
2) Lower body insertion: Tip should end in the upper leg distal to the head of the femur.
a) Measure from the insertion site to the desired site of catheter tip.

10. Don mask and cap and perform a 3-minute scrub.
11. Don sterile gown and gloves. Set up sterile field and open catheter kit, maintaining sterility of contents. Assemble equipment using an aseptic technique.
12. Trim catheter to predetermined length per manufacturer's recommendations and institution's policy.
13. Attach flush-syringe and prime catheter.
14. Prepare insertion site with antiseptic per hospital policy and allow to dry.
15. Change into new sterile gloves if contamination occurs.
16. Drape infant with sterile towels.
17. Apply sterile tourniquet (optional) and stabilize vein.
18. Take introducer and puncture vessel at an approximately 5- to 15-degree angle for shallow veins and approximately 15 to 30 degrees for deeper veins. After skin puncture, pause and let infant relax to prevent vasoconstriction. Entry into the vessel is signaled by blood leaking from puncture site or from the introducer needle/cannula.
19. Loosen tourniquet (if applicable) after advancing catheter a short distance. Remove needle, leaving peel-away plastic cannula in place if using this method.
20. Advance flushed catheter with forceps in 0.5- to 1-cm increments to predetermined distance. Catheter should advance smoothly and slowly to avoid vasospasm.
21. Once catheter is advanced 7 to 8 cm or to the predetermined distance, remove introducer. Catheter may be pulled out slightly during splitting technique and may need to be advanced slightly when complete. Gentle pressure with finger distal to puncture site may reduce blood loss.
22. Remove stylet (if present) slowly.
23. Aspirate on catheter to confirm blood return. If blood is obtained, flush catheter.
24. Temporarily secure catheter with sterile adhesive strips and obtain radiographic confirmation of catheter placement while maintaining sterile field and aseptic technique.
    a. Confirming placement is central before any infusions. Radiographic confirmation is historically standard practice. Pull back or advance catheter, if necessary, to appropriate distance. Check for blood return and obtain another chest radiograph to confirm satisfactory position.
        1) For upper extremity PICCs, the tip should be in the lower half to one-third of the superior vena cava above the right atrium (Alexander and INS, 2016; Wycoff and Sharpe, 2015).
        2) For lower extremity PICCs, the tip should reside in the inferior vena cava above the diaphragm (Wycoff and Sharpe, 2015).
    b. If a lower extremity PICC is placed, consider performing a lateral abdominal radiograph in addition to AP view to verify that the catheter is in the inferior vena cava and not the ascending lumbar vein. As an alternative, 0.3 mL of contrast medium may be injected into the catheter with the AP view to verify central venous placement and avoid an additional radiograph (Sharpe et al., 2013; Trotter, 2009).
    c. Bedside ultrasonography is an accepted method for identifying vessels, aiding and confirming PICC placement with a trained provider (Johnson et al., 2016; Katheria et al., 2013; Wycoff and Sharpe, 2015; Zaghloul et al., 2018).
25. Remove antiseptic from surrounding skin with sterile water.
26. Secure and dress catheter per hospital policy.
    a. Use of skin closure or Steri-Strips over the body of the catheter is contraindicated, due to risk of catheter shearing (Wycoff and Sharpe, 2015).
    b. INS recommends a product-specific catheter securement device, if available (Alexander and INS, 2016).
27. Document procedure, including:
    a. Indication for placement.
    b. Parental education and consent.
    c. Site preparation.
    d. Catheter size, manufacturer, and lot number.
    e. Catheter length if trimmed.
    f. Presence of stylet.
    g. Location and insertion distance.
    h. Location of catheter tip on radiograph.
    i. Pain management provided and patient tolerance.
    j. Complications.
    k. Type of dressing.
    l. Name of clinician.

F. **Modified Seldinger technique**—this technique provides for central catheter placement using a peripheral IV catheter of smaller gauge than a standard PICC introducer (Fig. 15.2). Use of a smaller gauge may allow the inserter to access a smaller vessel and minimizes vessel and surrounding nervous tissue trauma and hematoma formation. This procedure is now standard practice in adult and pediatric patients and is recommended by the INS to minimize damage to vessels (Alexander and INS, 2016; Wycoff and Sharpe, 2015).
1. Supplies.
    a. All supplies previously described for PICC insertions.
    b. 24-gauge peripheral IV catheter.

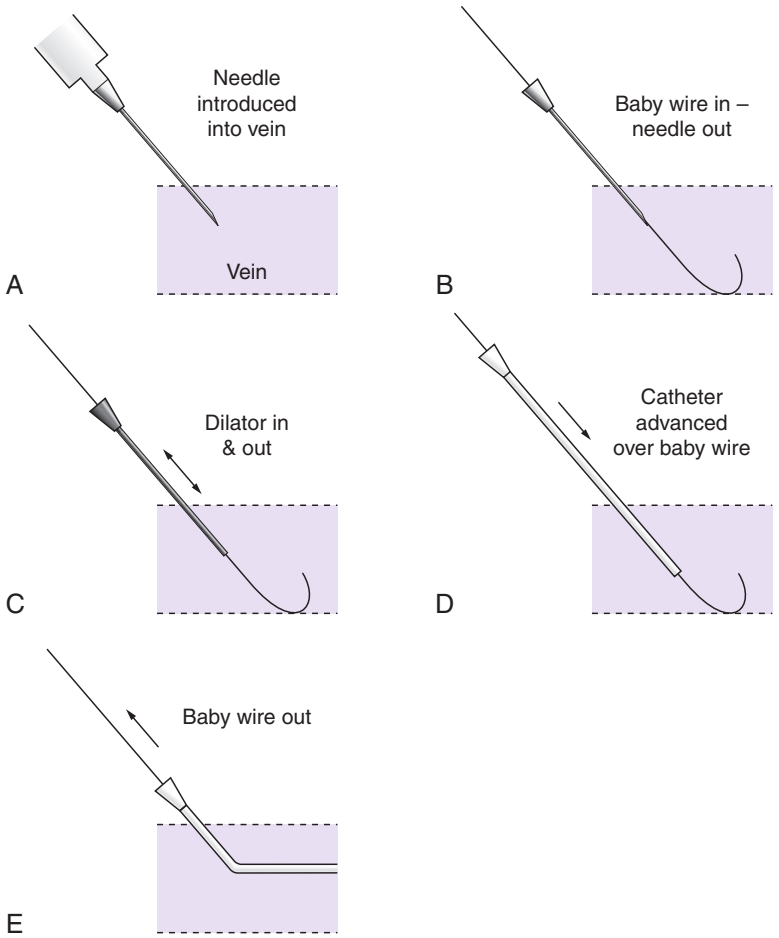

Fig. 15.2 The modified Seldinger technique for PICC insertion. *(From Al-Shaikh, B., & Stacey, S. [2013].* Essentials of anaesthetic equipment *[4th ed.]. London, UK: Churchill Livingstone.)*

c. Guidewire.
   1) 0.012 or 0.018 inch.
   2) 15 to 20 cm.
d. No. 11 scalpel blade or straight needle.

2. Procedure.
   a. Identify vessel, trim catheter, and prepare the insertion site as previously described for PICC insertion.
   b. Apply tourniquet as needed.
   c. Perform venipuncture with 24-gauge peripheral IV catheter.
   d. When flashback of blood is noted, advance catheter into vein and remove inner needle.
   e. Thread guidewire through catheter into the vein, approximately 3 cm beyond the tip of the catheter.
      1) Take caution to advance gently; do not apply force, as this may perforate the vessel.
      2) Do not advance the guidewire past the infant's shoulder if placed in the arm.
   f. Remove the IV catheter while holding the guidewire in place. Take care to firmly stabilize the guidewire to prevent removal or embolization.
   g. Enlarge the insertion site by 1 to 2 mm.
      1) Consider use of 1% lidocaine injected intradermally or topical lidocaine cream, or a systemic analgesic such as fentanyl.
      2) Use forceps to gently dilate the insertion site.
      3) Alternatively, thread a 20-gauge needle over the guidewire, and move side to side in the insertion site.
      4) Alternatively, use a scalpel blade to make a dermatotomy or small nick in the insertion site, taking care to avoid damaging the vessel.
   h. Slowly thread a plastic peel-away PICC introducer over the guidewire past the insertion site into the vessel. If the introducer cannot be advanced into the vein, the insertion site may need to be further dilated.
   i. Remove the guidewire, leaving the introducer in the vein.
   j. Remove tourniquet if applicable.
   k. Thread the catheter into the vein as previously described to premeasured depth.

l. Follow steps described for PICC placement earlier to verify blood return, assess proper placement of catheter, and apply dressing.
m. Document procedure, including method of insertion, any additional steps taken, catheter length, patient tolerance, and any complications.

G. Complications.
1. Cardiac arrhythmias.
2. Pericardial effusion with cardiac tamponade.
3. Atrial perforation with cardiac tamponade.
4. Intravascular catheter shearing, followed by embolization of catheter fragment.
5. Thrombus formation.
6. Infection: local or systemic.
7. Nerve damage.
8. Air embolism.
9. Rupture of catheter from using excessive infusion pressure (e.g., from using small-bore syringes).
10. Infiltration/extravasation for MLC.
11. Hemorrhage.
12. Vascular perforation.

H. Catheter maintenance.
1. INS and NANN recommend an evidence-based catheter care policy to include all aspects of insertion, care, and infusion with tracking of outcome measures (Alexander and INS, 2016; Wycoff and Sharpe, 2015). This may reduce infection rate and improve patient safety.
2. Dressing changes only whenever damp, soiled, or nonocclusive is associated with decreased incidence of catheter-related bloodstream infections (CLABSI) (Wycoff and Sharpe, 2015).
a. If gauze is used in the dressing, it must be changed every 48 hours.
3. Monitor for infiltration or extravasation.
a. Redness.
b. Edema.
c. Difficulty with flushing or fluid infusion.

REMOVAL OF PERIPHERALLY INSERTED CENTRAL CATHETER: FUNDAMENTAL PROCEDURE

A. Indications.
1. No longer needed or indicated.
2. Septicemia, especially fungal.
3. Malfunctioning.

B. Precautions.
1. Avoid catheter disruption.
2. Venospasm (if resistance is met, do not force catheter; apply warm compress for 20 to 30 minutes and reattempt).

C. Equipment and supplies.
1. Sterile gauze.
2. Measuring tape.
3. Transparent dressing.
4. Nonsterile gloves.

D. Procedure.
1. Verify order for removal.
2. Wash hands and don gloves.
3. Remove securing tape and dressing carefully to avoid skin trauma.
4. Change gloves.
5. Cleanse site with povidone–iodine or antiseptic per hospital policy and allow to dry.
6. Slowly and carefully retract catheter 1 cm at a time, grasping the catheter near the insertion site until the catheter has been removed. Do not apply pressure over insertion site during catheter removal.
7. Apply sterile gauze over insertion site as withdrawal is complete.
8. Continue to apply pressure if needed with gauze until hemostasis is obtained. Once hemostasis is confirmed, cover site with petroleum-based ointment and sterile occlusive dressing (Wycoff and Sharpe, 2015). Dressing should remain in place for at least 24 hours.
9. Measure and inspect removed catheter and compare catheter length with the recorded insertion depth.
a. If any part has broken off during removal or the length of the catheter differs from the recorded insertion length, place a tourniquet on the affected extremity above the insertion site, such as upper arm or upper leg, to prevent advancement of the catheter piece into the right atrium. Check for pulses. If the extremity is dusky or there is no pulse, loosen the tourniquet. Place the infant on the right side and immediately notify health care provider, as catheter embolization is an emergency and may require removal via cardiac catheterization or via surgery (Wycoff and Sharpe, 2015).
10. Document date, time, site location, measurement of catheter removed in comparison to recorded insertion depth, patient's tolerance of procedure, and any complications according to hospital guidelines.

E. Complications.
1. Shearing of catheter inside patient before complete removal.
2. Dislodgment of thrombus from tip.

UMBILICAL VESSEL CATHETERIZATION: ADVANCED PRACTICE PROCEDURE

A. Indications.
1. Arterial catheterization.
a. Frequent arterial blood sampling.
b. Continuous arterial blood gas monitoring.
c. Continuous arterial blood pressure monitoring.
d. Vascular access for IV fluids when other sites are not available or suitable.
e. Exchange transfusion.
f. Cardiac catheterization.

2. Venous catheterization.
   a. Emergency administration of drugs.
   b. Emergency measurement of P_{CO_2} and pH.
   c. Fluid administration (hypertonic solutions or inadequate peripheral access).
   d. Exchange transfusion.
   e. Central venous pressure monitoring.
   f. Blood sampling.

B. Contraindications.
1. Abdominal wall defects.
2. Necrotizing enterocolitis (controversial).
3. Vascular compromise below level of umbilicus.
4. Omphalitis.
5. Peritonitis.

C. Precautions.
1. Maintain thermal homeostasis.
2. Monitor heart rate and oxygen saturation throughout the procedure.
3. Maintain aseptic technique.
4. Dilate artery before attempting vessel cannulation.
5. Do not force catheter past obstruction.

D. Equipment and supplies.
1. Commercially prepackaged sterile umbilical catheter tray or sterile instrument tray for umbilical catheterization to include:
   a. 4 × 4 gauze pads.
   b. Sterile drapes.
   c. Small container for antiseptic solution.
   d. Scissors.
   e. Umbilical tape.
   f. Measuring tape.
   g. Syringes, 10 mL.
   h. No. 11 scalpel with handle.
   i. Mosquito hemostats (2).
   j. Curved, nontoothed iris forceps (2).
   k. Toothed iris forceps (1).
   l. Needle holder.
   m. Umbilical catheter of either polyurethane or silicone material. Silicone catheters may be more difficult to insert due to their lack of rigidity.
   n. Determine appropriate-sized catheter with either a single, double, or triple lumen or as desired by medical staff. Various sizes of catheters are available ranging from 2.5F to 8F. Generally, the following guidelines apply:
      1) Size 3.5F for infants weighing less than 1500 g.
      2) Size 3.5F, 4.0F, or 5.0F for infants weighing more than 1500 g.
      3) A 2.5F polyurethane catheter is available for use in the extremely premature infant.
   o. 3-0 silk suture.
   p. 4-0 silk suture with curved needle.
   q. Three-way Luer-Lock stopcock.
   r. Dressings for securing (clear occlusive dressing and a hydrocolloid skin barrier).
   s. Sterile heparin-flush solution (1 unit/mL).
2. Sterile antiseptic solution.
3. Mask, surgical cap, and sterile gown and gloves.
4. Standardized premeasurement graph or access to a formula to determine insertion depth.

E. Procedure.

UMBILICAL ARTERY CATHETERIZATION

NOTE: *Low position*, catheter tip placed between the third and fourth lumbar vertebrae (L3–L4). *High position*, catheter tip placed between the sixth and tenth thoracic vertebrae (T6–T10). Either position is accepted practice currently. Consult your institution's guidelines for desired positioning of umbilical artery catheters (UACs).

1. Inspect lower extremities for bruising and palpate pulses.
2. Assess umbilical cord to rule out umbilical anomaly, such as a small omphalocele.
3. Place infant supine and restrain limbs.
4. Calculate insertion depth.
   a. Measure shoulder-to-umbilical distance (adding length of umbilicus stump) and multiply by 0.66 to arrive at insertion depth for a "low" placement (L3–L4).
   b. 2.5 times body weight in kilograms plus 9.7 cm (2.5 × weight + 9.7) for a "high" placement (T6–T10).
5. Don mask and cap and perform a 3- to 5-minute scrub.
6. Don sterile gown and gloves.
7. Have assistant hold heparin-flush vial and draw up flush into sterile syringe.
8. Prepare catheter by attaching Luer-Lock stopcock to catheter and connect flush-filled syringe to stopcock and flush catheter.
9. Turn stopcock off to catheter.
10. Have assistant hold umbilical cord up and out of procedure area while cord is prepped with antiseptic solution. Scrub in a circular manner, moving from the cord to approximately 5 cm in radius on surrounding abdomen. Do not let antiseptic drip down infant's side or pool on abdomen because this may cause skin damage, especially in extremely premature infants.
11. Drape procedure area with sterile towels.
12. Tie umbilical tape using a single-hand knot tight enough to prevent bleeding at the base of the cord, not on the skin. Umbilical tape may have to be loosened to advance catheter or tightened to control bleeding.
13. Using a scalpel, cut through the umbilical cord 1 to 1.5 cm from skin.
14. Identify cord vessels.
   a. Arteries: two small, thick-walled, and white constricted vessels that may stick out slightly and are typically located at the 4 and 8 o'clock positions.

   b. Vein: single, large, thin-walled vessel, often open and typically located at the 12 o'clock position.
15. Stabilize cord stump.
   a. Grasp portion of cut edge of cord with hemostat and apply gentle traction.
   b. Apply hemostats to opposite sides of the cord and roll them away from each other, causing the arteries to protrude from the cut surface of the cord.
16. Dilate artery.
   a. Insert one tip of curved iris forceps into selected artery and probe gently to a depth of about 0.5 cm; withdraw forceps tip.
   b. With tips of forceps together again, gently probe artery to a depth of about 0.5 cm.
   c. Gently spread forceps apart and then slowly withdraw forceps from artery, dilating lumen as forceps is withdrawn.
   d. Continue to dilate lumen (approximately 15 to 60 seconds) until forceps can easily be inserted to a depth of about 1 cm.
17. Insert catheter.
   a. Insert catheter into dilated artery.
   b. Thread catheter to predetermined depth.
   c. If resistance is met, do not force catheter. Apply gentle, steady pressure to catheter while applying gentle traction on cord.
   d. If catheter cannot be advanced to the desired distance, discontinue attempts and catheterize second artery.
   e. Observe for blanching of legs, toes, and/or buttocks.
18. Aspirate blood to ensure placement in vessel after catheter advanced approximately 5 cm. If blood is obtained, clear catheter by injecting 0.5 mL flush solution. If blood cannot be aspirated, remove catheter and attempt catheterization of second artery.
19. Confirm catheter position.
   a. Historically radiograph has been the standard for confirming tip placement below the right ventricle and above the diaphragm. More recent studies have noted that bedside ultrasound has equal accuracy in identifying tip location when done by a trained provider (Fleming and Kim, 2011; Zaghloul et al., 2018).
   b. If the catheter tip is too high, pull the catheter back to its proper position and obtain another radiograph/ultrasound.
   c. If the catheter tip is too low for "high position," pull back to "low position" if your institutional guidelines allow this.
   d. If catheter tip is too low for "low position," it should be adjusted to an acceptable position. Keep in mind that a catheter that is no longer sterile should not be advanced.
20. Suture catheter in place.
   a. Place purse-string suture around cord. Avoid piercing the vessels and catheters. Secure to umbilical skin or cord depending on your institution's guidelines.
   b. Knot suture securely in cord close to catheter per manufacturer's recommendations.
   c. If suture is around catheter, it must be tight to prevent catheter from sliding, but not so tight that flow through catheter is obstructed.
21. Loosen umbilical tape.
22. Remove antiseptic as soon as possible from the skin to prevent irritation or breakdown.
23. Secure catheter per hospital policy. The following are various techniques used to secure catheters:
   a. Commercially manufactured securing devices.
   b. "Bridge" or "goalpost" taping technique.
   c. Hydrocolloid skin barrier applied to umbilical area with clear occlusive dressing.
24. Document procedure according to hospital policy, noting type of catheter; catheter size; distance catheter threaded; location of catheter tip on radiograph/ultrasound; adjustments made to catheter to correct malpositioned catheter; and assessment of color, pulses, and perfusion to lower extremities.

UMBILICAL VEIN CATHETERIZATION

NOTE: Equipment for umbilical vein catheterization is the same as that for UAC insertion, with the exception that an 8F catheter may occasionally be used for infants weighing more than 3500 g.

1. Maintain aseptic technique.
2. Prepare cord as for UAC and identify the thin-walled vein.
3. Grasp the base of the cord with curved hemostats or toothed forceps, hold upright, and dilate vessel with the tip of iris forceps.
4. Insert the catheter to predetermined distance.
   a. Emergency placement (temporary catheter, "low position"): Insert 2 to 3 cm into vessel until blood is obtained. Once emergency medications and fluids have been administered and the infant is stabilized, remove the catheter.
   b. Indwelling umbilical venous catheter.
      1) Measure shoulder-to-umbilical distance and multiply by 0.75 to arrive at insertion depth.
      2) Alternatively, calculate insertion depth with the formula 1.5 times body weight in kilograms plus 5.6 cm ($1.5 \times \text{weight} + 5.6$).
5. If resistance is met, withdraw the catheter 2 to 3 cm and attempt to reinsert. If cannulation remains unsuccessful, remove the catheter.
6. If cannulation is successful, connect and secure catheter and confirm position by radiograph or bedside ultrasound by a trained provider. Correct

radiographic position is 0.5 to 1 cm above the diaphragm.
7. Secure catheter per hospital policy.
8. Document procedure according to hospital policy, noting type of catheter, catheter size, distance catheter threaded, location of catheter tip on radiograph/ultrasound, and adjustments made to catheter to correct malpositioned catheter.

F. Complications of using umbilical catheters.
1. Vasospasm, embolism, thrombosis, and distal ischemia.
   a. Blanching, cyanosis, and mottling of skin.
   b. Sloughing of skin.
   c. Necrosis of extremities, possibly leading to loss of toes.
   d. Paraplegia.
   e. Intestinal necrosis and perforation.
2. Infection.
3. Mechanical complications.
   a. Perforation of vessels.
   b. Perforation of peritoneum.
   c. False aneurysm.
   d. Knot in catheter or breaking of catheter.
4. Malpositioned catheter.
   a. Cardiac arrhythmias.
   b. Pericardial effusion.
   c. Cardiac tamponade.
   d. Hydrothorax.
5. Necrotizing enterocolitis (controversial).
6. Perforation of colon.
7. Hepatic necrosis.
8. Skin burns from antiseptics.
9. Hemorrhage, exsanguination.
10. Portal hypertension.
11. Death.

PERIPHERAL ARTERY CATHETERIZATION: ADVANCED PRACTICE PROCEDURE

A. Indications.
1. Need for frequent blood sampling and umbilical artery catheterization cannot be done or UAC has been removed.
2. Need for continuous blood pressure monitoring.

B. Precautions.
1. Avoid areas of skin breakdown or infection.
2. Use caution in infants with coagulopathy, who may bleed excessively.
3. Inadequate collateral artery blood flow precludes placement in the radial or ulnar artery.
4. Limb malformation.

C. Equipment and supplies.
1. 22- to 27-gauge over-the-needle IV catheter.
2. Antiseptic solution per institution policy.
3. 0.25 to 0.5 NS flush.
4. Occlusive dressing and tape per institution policy.
5. Transilluminator (optional).
6. Appropriately sized, padded armboard.
7. Arterial pressure transducer and extension tubing per institution policy.
8. Nonsterile gloves.
9. 4-0 sutures if needed per institution policy.
10. T-connector as needed per institution policy.
11. Pain/developmental management: pacifier, oral sucrose, blankets for swaddling, and eye protection from bright lights.

D. Procedure.
1. Select site for catheterization. Radial artery is the most common site, but posterior tibial artery, ulnar artery, and dorsalis pedis artery are reasonable alternatives. The following method describes radial artery catheterization but can be adapted for other sites.
   a. Palpate radial artery pulse.
   b. Transillumination may assist in identifying vessel.
2. Take care not to hyperextend wrist, as this will occlude arterial flow.
3. Perform modified Allen test to ensure adequate collateral circulation.
   a. Elevate hand.
   b. Occlude both radial and ulnar arteries.
   c. Massage the palm toward wrist to blanch hand.
   d. Release pressure on the ulnar artery.
   e. Perfusion to hand should return in less than 10 seconds; if longer than 15 seconds, do not puncture artery.
4. Position and secure wrist as shown in Fig. 15.3.
5. Provide pain management and developmental support.
6. Prepare site with antiseptic solution per institution policy.

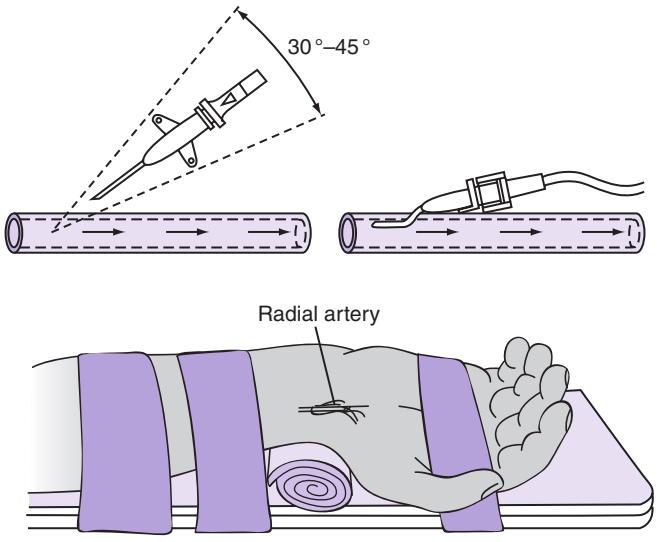

Fig. 15.3 Peripheral arterial line insertion. (From Gomella, T. L. [2013]. *Neonatology: Management, procedures, on-call problems, diseases and drugs* [7th ed.]. New York, NY: Lange Medical Books/McGraw-Hill.)

7. Puncture the skin proximal to the wrist crease with the needle at a 30- to 45-degree angle (a deeper angle may be needed for larger babies).
8. Cannulate the artery using one of the following methods.
   a. Puncture both walls of the artery with the needle bevel up (blood return may be delayed). Remove the stylet and withdraw the catheter until blood return is noted. When blood return is seen, advance the catheter into the artery and flush. Flushing while advancing may stabilize the catheter and make advancing easier.
   b. Puncture the anterior wall of the artery until blood return is seen; at this point the catheter is in the artery. Advance the catheter while simultaneously withdrawing the stylet and flush.
9. Secure cannula with sutures or tape per institution policy.
10. Attach T-connector per institution policy and flush line. Luer-Lock connections are preferred if they do not interfere with patency of the catheter.
11. Secure line with armboard and dressing per institution policy. Ensure visibility of insertion site and all fingers.
12. Attach pressure transducer and extension tubing per institution policy and ensure unobstructed flow of fluids by pump. Secure all connection sites to avoid backflow of blood into line.
13. Maintain patency of catheter with heparinized fluids per institution policy.
14. Dispose of needle in designated sharps container.
15. Document date, time, location, catheter size, distal perfusion, pain response, and management to placement of catheter.
16. Monitor site for extravasation or leakage of fluids and/or blood.
17. Monitor digits for adequate perfusion.

E. Complications.
1. Arteriospasm.
2. Infection.
3. Extravasation of fluids.
4. Hematoma or hemorrhage.
5. Embolism or thrombus formation leading to tissue ischemia or necrosis and possible loss of hand, foot, or digits.
6. Damage to surrounding tissues or structures.

Blood Sampling Procedures

CHOICE OF METHOD FOR BLOOD SAMPLING

A. Amount of blood needed.
1. Capillary sampling is indicated for small amounts of blood, generally less than 1 mL.
2. It may be easier to obtain large amounts of blood (>2 mL) from venipuncture or an arterial puncture.

B. Type of testing indicated.
1. Newborn metabolic screens in well newborns are primarily drawn via heel stick.
2. Some laboratory results may be affected by hemolysis, clotting, or clumping of the blood, and a large-volume, free-flowing specimen may be easier to obtain by venipuncture or arterial puncture (Folk, 2007; Milcic, 2010).
   a. Chemistry levels.
   b. Platelet levels.
   c. Hematocrit.
   d. Coagulation studies.
3. Collection of blood for cultures requires sterile technique, and blood should be collected via venous or arterial puncture (Folk, 2007).
4. Blood gas values will differ based on arterial, capillary, or venous sources. As exchange of oxygen for CO_2 occurs in peripheral tissues, CO_2 levels will be lowest in arterial blood and highest in venous blood, and oxygen levels will be highest in arterial blood and lowest in venous blood. Po_2 cannot be accurately measured with capillary blood. Blood pH will also vary, being lower in arterial and higher in venous sources. An arterial sample may be helpful to ascertain accurate pH, Pao_2, and $Paco_2$ levels.

C. Pain of procedures.
1. Studies have shown venipuncture to be less painful than other sampling methods when drawn by a skilled phlebotomist (Folk, 2007). However, consideration should be given to preserving future IV sites in sick infants.
2. Laboratory samples should be drawn with as few invasive procedures as possible to minimize pain. Consider the total volume of blood needed when choosing a sampling method, and try to cluster laboratory draws to avoid multiple punctures. For infants needing frequent blood draws, consider placement of an arterial catheter.

CAPILLARY BLOOD SAMPLING: FUNDAMENTAL PROCEDURE

A. Indications.
1. Small amount of blood is needed (<1 mL) (Folk, 2007).
2. Venous or arterial blood sample is not possible or necessary.
3. Collection of blood specimen for blood gas sampling, routine laboratory sampling, state newborn metabolic screens.

B. Contraindications.
1. Impaired circulation in selected limb or at puncture site.
2. Infection near puncture site.

C. Precautions.
   1. Consider venipuncture if impaired skin integrity noted at selected puncture site (edema, bruising, multiple puncture marks).
   2. Consider venipuncture as an alternative to capillary sampling in term neonates, as it may be less painful (Shah and Ohlsson, 2011).
   3. Hyperviscous blood may render sampling difficult. Consider venipuncture in infants with polycythemia.
   4. Use caution in infants with coagulation disorders.
   5. Do not puncture the back of the heel; this may cause damage to the calcaneus bone.
   6. Avoid finger, great toe, and earlobe sticks.
   7. Avoid excessive squeezing that may cause hemolysis.

D. Equipment and supplies.
   1. Sterile alcohol swabs or other antiseptic, as per institutional guideline.
   2. Automated heel-lancing incision device based on infant size.
   3. Sterile gauze pad.
   4. Warm compress. Studies have suggested that warming the heel may not be needed (Folk, 2007). When warming heels, use a warm compress manufactured for use with infants, no warmer than 40° C.
   5. Nonsterile gloves.
   6. Appropriate specimen collection containers.
   7. Pain management: pacifier, oral sucrose, and blankets for developmental swaddling.

E. Procedure.
   1. Select puncture site on the lateral or medial aspect of the heel. Avoid other areas because of the possibility of nerve damage or osteomyelitis (Fig. 15.4).
   2. Warm heel with compress for 5 to 10 minutes if desired.
   3. Provide pain management.
      a. Pacifier for nonnutritive sucking.
      b. Consider 24% sucrose solution applied to pacifier or nipple 2 minutes before procedure, if patient age and status allow (Folk, 2007).

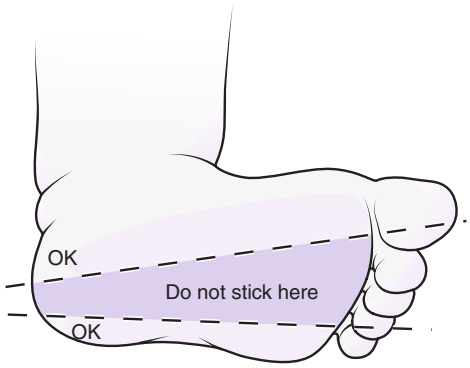

Fig. 15.4 Use shaded areas when performing heel stick in infant. (From Roberts, J. R. [2014]. *Roberts and Hedges' clinical procedures in emergency medicine* [6th ed.]. Philadelphia, PA: Elsevier Saunders.)

      c. Dim and quiet environment.
      d. Skin-to-skin holding and/or blanket swaddling with selected extremity exposed.
   4. Gather supplies, wash hands, and don gloves.
   5. Prepare area selected for skin puncture with antiseptic or alcohol and allow to dry.
   6. Puncture heel perpendicular to the skin.
   7. Wipe away first drop of blood with sterile gauze pad.
   8. Collect specimen from free-flowing drops at puncture site.
      a. Blood flow is increased if the puncture site is dependent relative to the extremity.
      b. Gentle "pumping" of the extremity above the puncture site may encourage blood flow.
   9. After specimen is collected, elevate foot and apply pressure with sterile gauze pad until hemostasis has occurred.
   10. Dispose of lancet in appropriate sharps container.
   11. Label specimen per institutional policy.
   12. Document the heel-stick procedure, specimen obtained, date and time, pain management, and patient's tolerance.

F. Complications.
   1. Bruising or loss of skin integrity.
   2. Infection.
   3. Scarring.
   4. Calcified nodules.
   5. Cellulitis.
   6. Osteomyelitis.
   7. Nerve damage (Folk, 2007).
   8. Pain.
   9. Erroneous laboratory values may result from the following:
      a. Contamination of specimen with tissue fluid.
      b. Contamination of specimen with alcohol.
      c. Inadequate warming or poor circulation at puncture site.
      d. Hemolysis of specimen.

VENIPUNCTURE (PHLEBOTOMY): FUNDAMENTAL PROCEDURE

A. Indications.
   1. Large quantity of blood required.
   2. Arterial sample not possible or necessary.
   3. Capillary sample not possible or sufficient.
   4. Sterile collection for blood culture.
   5. Specific laboratory tests requiring venous sampling.

B. Contraindications.
   1. Inadequate or impaired circulation in selected limb.
   2. Infection or loss of skin integrity near selected venipuncture site.

C. Precautions.
   1. Use caution in infants with coagulation disorders.
   2. Utilize distal sites first and avoid sites that may be needed for possible central venous cannulation.
   3. Differentiate between arteries and veins.

D. Equipment and supplies.
   1. Antiseptic skin preparation per hospital policy.
   2. 23- to 25-gauge butterfly needle or hypodermic needle attached to syringe.
   3. Syringe(s) for specimen collection.
   4. Appropriate specimen collection tubes.
   5. Sterile gauze pad.
   6. Tourniquet or rubber band.
   7. Nonsterile gloves.
   8. Transilluminator or vein finder (optional).
   9. Pain management: pacifier, oral sucrose, blankets for swaddling leaving venipuncture site accessible, and/or cloth to protect eyes from bright lights.

E. Procedure.
   1. Gather supplies, wash hands, and don gloves.
   2. Choose vein to be used. Accomplish distention of the vessel by applying a gentle tourniquet proximal to the selected insertion site. Alternatively, an assistant may encircle the proximal extremity with his or her hand or fingers and apply direct pressure for the same effect.
   3. Provide pain-relieving measures and developmentally position/swaddle infant with selected venipuncture site accessible.
   4. Stabilize and position the selected puncture site to allow puncture in direction of blood flow.
   5. Prepare skin at selected puncture site with antiseptic per hospital policy.
   6. Puncture skin at a 15- to 45-degree angle, with needle bevel up, just distal to anticipated vessel entry site, using shallow angle for smaller infants or superficial vessels.
   7. Advance needle until blood appears in the tubing.
      a. If resistance is met or vessel is not punctured, withdraw needle slowly to just below level of the skin, relocate vessel, and advance the needle again.
      b. If a hematoma develops or bleeding occurs, occlude the vessel with pressure just proximal to the puncture site, remove the tourniquet, and withdraw the needle. Apply pressure until hemostasis has occurred.
   8. On entrance of blood into tubing, attach syringe and gently aspirate to obtain specimen. If a hypodermic needle with an intact hub was used, blood specimen may drip into laboratory collection container.
   9. After specimen is obtained, using a gauze pad just proximal to the puncture site, occlude vessel with pressure over entry site while removing tourniquet and withdrawing needle.
   10. Apply pressure to site until hemostasis has occurred.
   11. Dispose of needle in appropriate sharps container.
   12. Label specimens per institution policy.
   13. Document date, time, site location, specimen collected, amount of blood removed, nonpharmacologic interventions, patient's tolerance of the procedure, and any complications.

F. Complications.
   1. Hematoma.
   2. Infection.
   3. Hemorrhage.
   4. Needle injury to adjacent structures.
   5. Pain.

RADIAL ARTERY PUNCTURE: ADVANCED PRACTICE PROCEDURE

A. Indications.
   1. Venous and/or capillary sites are not satisfactory.
   2. Arterial blood gas sampling.
   3. Need to sample large quantities of blood.

B. Precautions.
   1. Avoid area of infection or loss of skin integrity near selected puncture site.
   2. Use caution in infants with coagulation defects.
   3. Consider need to preserve arterial site for possible cannulation.
   4. Avoid extremity with inadequate collateral circulation distal to the selected puncture site.
   5. Use of small-gauge needle reduces potential complications.

C. Equipment and supplies.
   1. Antiseptic supplies to prepare for arterial puncture per hospital policy.
   2. 23- to 25-gauge butterfly needle or 23- to 25-gauge needle attached to a 3-mL syringe.
   3. Extra syringes.
   4. Sterile gauze pad.
   5. Arterial blood gas syringe, other applicable laboratory specimen containers.
   6. Transilluminator (optional).

D. Procedure.
   1. Determine puncture site.
      a. Transillumination may assist in vessel location.
      b. Extend wrist; do not hyperextend, which may occlude vessel.
      c. Palpate artery at distal crease of wrist.
   2. Perform modified Allen test to assess collateral circulation.
      a. Elevate hand.
      b. Apply pressure to occlude both radial and ulnar arteries.
      c. Massage the palm to blanch hand.
      d. Release pressure on ulnar artery.
      e. If color returns to hand in less than 10 seconds, adequate collateral circulation is suggested. If color returns in more than 15 seconds, do not puncture artery because of poor collateral circulation.
      f. Doppler-flow evaluation of ulnar, radial, and palmar circulation can also help determine adequacy of collateral flow.
   3. Provide pain management such as nonnutritive sucking, oral sucrose, and/or developmental care with facilitated tucking or blanket swaddling.

4. Position and stabilize extended wrist to allow puncture against direction of arterial flow.
5. Prepare area with antiseptic for skin puncture (middle to outer third of wrist) per hospital policy.
6. Puncture skin with needle (bevel up) at a 15- to 45-degree angle, using shallower angle for smaller infants or more superficial arteries.
7. Advance needle slowly to puncture artery.
   a. If resistance is met or blood is not obtained, withdraw needle slowly to just below skin level, palpate artery, and advance needle again in the direction of the artery.
   b. If hematoma or bleeding develops, occlude artery with gauze and pressure just proximal to the puncture site, withdraw needle, and apply pressure until hemostasis has occurred (approximately 5 minutes of direct pressure).
8. If arterial cannulation is successful, when blood enters the butterfly tubing, attach syringe and aspirate gently to obtain sample.
9. Apply firm, but not occlusive, pressure to artery with gauze just proximal to puncture site and withdraw needle. Apply pressure to site for 5 minutes or until hemostasis has occurred.
10. Ensure distal circulation after puncture.
    a. Evaluate color and temperature.
    b. Check capillary refill time.
    c. Palpate arterial pulse.
11. Document the following: date, time, site location, Allen test result before procedure, pain management interventions, tolerance to procedure, specimen obtained, amount of blood drawn, hemostasis, distal circulation, and any complications if encountered.

E. Complications.
1. Hematoma.
2. Hemorrhage.
3. Infection.
4. Thrombosis, embolism.
5. Arteriospasm, tissue necrosis, possibly leading to loss of hand.
6. Needle injury to adjacent structures.
7. Pain.

Miscellaneous Procedures

BLADDER CATHETERIZATION: FUNDAMENTAL PROCEDURE

A. Indications.
1. To obtain urine specimen for culture.
2. To precisely monitor urinary output.
3. To monitor bladder residuals.
4. To relieve urinary retention.
5. To accomplish genitourinary testing such as cystogram or voiding cystourethrogram.

B. Contraindications.
1. Some genital anatomic malformations; catheterization may be indicated after consultation with surgeon or urologist.
2. Pelvic fracture or urethral trauma.

C. Precautions.
1. Use caution in infants with coagulation disorders.
2. Maintain an aseptic technique.
3. Do not force the catheter, as this may lead to trauma to the urethra and bladder.
4. Remove catheter as soon as possible to minimize infection.
5. Use the smallest-diameter catheter to avoid trauma.

D. **Equipment and supplies.** NOTE: All equipment is sterile and is available in commercially prepared kits.
1. Urethral catheters.
   a. Size 3.5F urinary catheter for infants weighing less than 1000 g may be used.
   b. Size 5F urinary catheter for infants weighing more than 1000 g may be used.
2. Urinary catheter tray.
   a. Sterile gloves.
   b. Povidone–iodine solution swabs.
   c. Sterile drapes.
   d. Lubricant.
   e. Sterile specimen container or closed urinary drainage system.

E. Procedure.

MALE CATHETERIZATION

1. Place infant supine and restrain legs or have assistant hold legs.
2. Consider oral sucrose solution and nonpharmacologic measures to minimize pain.
3. Don sterile gloves.
4. Clean penis.
   a. Hold the penis perpendicular to the body with the nondominant hand (which is now considered contaminated).
   b. Starting at the meatus and moving down the penis, clean with povidone–iodine solution swabs 3 times, using a new swab each time.
5. Drape sterile towels across infant's lower abdomen and across legs.
6. Apply sterile lubricant to appropriately sized catheter tip with the sterile dominant hand.
7. Place the catheter (held by the sterile dominant hand) into the meatus while maintaining perpendicular position of the penis with the nondominant hand. Advance catheter along the urethra until urine appears. Slight resistance may be felt as the catheter passes through the external bladder sphincter. Steady, gentle pressure is usually needed to pass beyond this area; however, never force the catheter (Fig. 15.5).

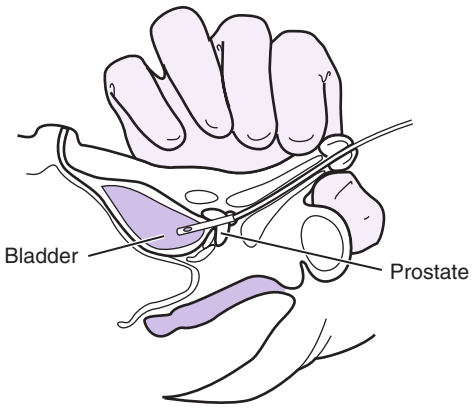

Fig. 15.5 Male bladder catheterization. (From Gomella, T. L. [2013]. *Neonatology: Management, procedures, on-call problems, diseases, and drugs* [7th ed.]. New York, NY: Lange Medical Books/McGraw-Hill.)

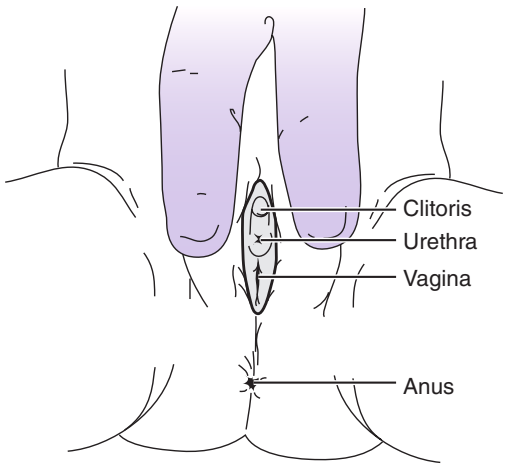

Fig. 15.6 Landmarks used in female bladder catheterization. (From Gomella, T. L. [2013]. *Neonatology: Management, procedures, on-call problems, diseases, and drugs* [7th ed.]. New York, NY: Lange Medical Books/McGraw-Hill.)

8. Advance catheter slightly past the point where urine flow began. Inflate the balloon per hospital policy and manufacturer's recommendations, if applicable. Usually the catheter will function satisfactorily if simply taped in place. Balloon inflation may injure the urethra if the catheter is not properly positioned in the bladder.
9. If catheter is to remain indwelling, tape it to lower abdomen or to penile shaft.
10. Collect urine specimen in the sterile container and send to the laboratory or attach to a closed urinary drainage system.
11. Document procedure, catheter type and size, nonpharmacologic pain measures, patient's tolerance, quantity and characteristics of sample obtained, and any difficulties encountered.

FEMALE CATHETERIZATION

1. Place infant on back and secure legs in frog-leg position. You may secure with restraints or have an assistant hold the legs.
2. Consider oral sucrose solution and nonpharmacologic measures to minimize pain.
3. Don sterile gloves.
4. Separate the labia with the nondominant hand (which is no longer sterile). With the sterile dominant hand, clean the area around the meatus with the povidone–iodine solution swabs, using front-to-back strokes, repeating with three separate swabs.
5. Drape sterile towels across infant's lower abdomen and across legs.
6. Spread the labia and identify the meatus and urethra (Fig. 15.6).
7. Apply sterile lubricant to an appropriately sized catheter tip using the sterile dominant hand.
8. Insert the catheter into the urethra and advance until urine appears.
9. Advance catheter slightly past the point where urine flow began. Inflate balloon per hospital policy and manufacturer's recommendations, if applicable. Usually, the catheter will function satisfactorily if simply taped in place. Balloon inflation may injure the urethra if the catheter is not properly positioned in the bladder.
10. If catheter is to remain indwelling, secure to inner thigh.
11. Collect urine specimen in the sterile container and send to the laboratory or attach to a closed urinary drainage system.
12. Document procedure, catheter type and size, nonpharmacologic pain measures, patient's tolerance, quantity and characteristics of sample obtained, and any difficulties encountered.

F. Complications.
   1. Infection.
   2. Hematuria.
   3. Trauma to urethra.
   4. Stricture of urethra or at meatus.
   5. Possible knotting of catheter.
   6. Pain.

LUMBAR PUNCTURE: ADVANCED PRACTICE PROCEDURE

A. Indications.
   1. To obtain cerebrospinal fluid (CSF) to diagnose central nervous system (CNS) disorders such as infections or subarachnoid hemorrhage.
   2. To monitor the efficacy of antibiotic therapy in the presence of CNS infection (rare).
   3. To drain CSF in communicating hydrocephalus associated with intracranial hemorrhage.
   4. To administer medication.

5. To assist in the diagnosis of certain metabolic disorders.

B. Contraindications.
1. Evidence of increased ICP. Performance of the procedure could cause cerebral herniation.
2. Lumbosacral anomalies.
3. Uncorrected thrombocytopenia or coagulopathies.
4. Severe cardiorespiratory instability.
5. Skin or tissue infection at the puncture site.

C. Precautions.
1. Avoid areas of infection or loss of skin integrity at puncture site.
2. Monitor for and be prepared to respond to cardiorespiratory instability.
3. Avoid flexion of the neck and ensure that a patent airway is maintained.
4. Always maintain aseptic technique.
5. Always use a needle with a stylet to avoid development of intraspinal epidermoid tumor.
6. To prevent traumatic tap caused by overpenetration, insert the needle slowly while removing the stylet at frequent intervals to detect CSF as soon as the subdural space is entered.
7. Never aspirate CSF with a syringe. Even a small amount of negative pressure can increase the risk of subdural hemorrhage or herniation.
8. Palpate landmarks accurately to prevent puncture above the L3 interspace.

D. Equipment and supplies:
1. Prepackaged lumbar puncture kit.
2. If a prepackaged kit is not available, gather the following supplies:
   a. Sterile gloves, gown, mask, and surgical cap.
   b. Sterile cup with povidone–iodine.
   c. Sterile gauze pads.
   d. Sterile towels or transparent aperture drape.
   e. Spinal needle with short bevel and stylet (22-gauge needle).
   f. Three or more sterile specimen tubes with caps.
   g. Adhesive bandage.
3. Cardiorespiratory monitor, pulse oximeter, and emergency equipment such as suction and oxygen source.
4. Analgesic agents and/or sedatives.
5. Pressure-monitoring equipment, if planning to obtain CSF pressures.

E. Procedure.
1. Obtain informed consent per institution's policy.
2. Gather equipment and supplies.
3. Provide anxiety/pain management by considering the following:
   a. Oral sucrose solution to minimize pain (Leef, 2006).
   b. Topical anesthetics such as EMLA, Ametop, or LMX4 over puncture site in term newborns per institution's policy and manufacturer's recommendations (Kaur et al., 2003; O'Brien et al., 2005). Use of topical local anesthetic has been shown to increase success rates (Baxter et al., 2006).
   c. Nonnarcotic relief such as acetaminophen.
   d. Local anesthesia: 1% lidocaine drawn up in a 1-mL syringe with a 27- to 25-gauge needle for injection.
   e. Opioid (fentanyl or morphine) or a benzodiazepine (midazolam not recommended in premature infants).
4. Examine and determine puncture site.
   a. Grasp both iliac crests at their highest points and following an imaginary line that passes across the level of the fifth lumbar vertebra, palpate the interspace of the spinous process that falls immediately above or below the imaginary line drawn between the iliac crests (Fig. 15.7).
   b. The preferred puncture site is between L3–L4 and L4–L5 (MacDonald and Ramasethu, 2013).

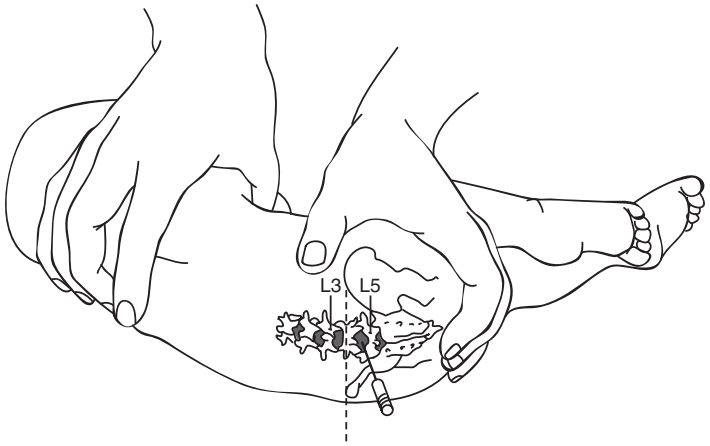

Fig. 15.7 Lumbar puncture positioning and landmarks. (From Gomella, T. L. [2013]. *Neonatology: Management, procedures, on-call problems, diseases, and drugs* [7th ed.]. New York, NY: Lange Medical Books/McGraw-Hill.)

c. The puncture site can be marked by making a small nail print impression or using a surgical marker.

5. Don mask and cap and perform a 3-minute scrub, and then don gown and sterile gloves.
6. Have an assistant open tray while maintaining the sterility of its contents.
7. Have assistant restrain the infant with hips flexed and back arched in the lateral decubitus (knee–chest) or sitting position, with spine flexed. An intubated infant must be positioned in the lateral decubitus position. Avoid flexion of the neck, and ensure that a patent airway is maintained.
8. Clean the lumbar area 3 times with antiseptic using a new swab each time.
   a. Begin at the desired interspace, using a circular motion from puncture site outward to up and over the iliac crests.
   b. Allow antiseptic to dry.
9. If used, inject a wheal of local anesthetic at the puncture site. After several minutes, infiltrate the deeper tissues also.
10. Place one sterile drape under the infant and another that covers the infant, with the exception of the puncture site and the infant's face. Transparent aperture drapes are available and recommended because they permit better observation of the infant.
11. Relocate the desired interspace and insert the needle in the midline.
    a. Hold a finger on the vertebral process above or below the interspace to aid in locating the puncture site if the infant moves.
    b. Angle slightly cephalad to avoid the vertebral bodies.
    c. If resistance is met, withdraw the needle slightly and redirect more cephalad.
12. Advance the needle slowly to a depth of approximately 1.0 to 1.5 cm, depending on infant's size, in small increments (2 to 3 mm) to avoid puncture of posterior wall.
    a. Remove the stylet frequently to observe the needle hub for fluid. Always replace the stylet before readvancing the needle.
    b. A pop may be felt when the ligamentum flavum and dura are penetrated. Penetration of the dura may also be detected when a loss of resistance is met.
    c. Once fluid is noted in the needle hub, patiently wait for CSF, which may be slow.
13. Obtain pressure measurement reading, if desired.
    a. Opening pressure measurements are difficult and often unreliable, but possible in a quiet infant in the lateral decubitus position. If measuring pressure, attach the manometer and wait for the fluid oscillations to stabilize in the tube before recording the pressure. Normal mean lumbar CSF pressures in term neonates and preterm infants are 100 and 95 mm H_2O, respectively (Marra et al., 2004).
14. Allow CSF to collect dropwise into the collection tubes; never aspirate with a syringe.
15. If no fluid is obtained, try gently rotating the needle. If no fluid is obtained after repositioning the needle, replace the stylet, remove the needle, and try one interspace above or below, using a new needle for each attempt.
16. Allow the CSF to drop from the needle hub to collect 0.5- to 1-mL aliquots of CSF in three or four of the specimen tubes for the following diagnostic studies:
    a. Tube 1: culture, Gram stain, and sensitivity studies.
    b. Tube 2: protein and glucose.
    c. Tube 3: cell count and differential.
    d. Tube 4: other diagnostic studies such as Venereal Disease Research Laboratory (VDRL) and/or viral studies.
    e. NOTE: If a traumatic (bloody) tap was performed, send the clearest specimen for cell count and differential. Bloody CSF can be differentiated from venous blood by dropping a sample onto filter paper. Bloody CSF will form a "water ring" around a central patch of erythrocytes.
17. Once specimens have been obtained, replace stylet and remove needle–stylet unit in a single outward motion to prevent injury to the spinal cord and nerves.
18. Apply local pressure to the puncture site for 3 to 5 minutes to minimize the risk of CSF leakage. Then place an adhesive bandage over the puncture site.
19. Remove the surrounding antiseptic with sterile water to avoid skin injury.
20. Document procedure according to hospital policy, noting position of the patient during procedure, needle size used, complications or difficulties encountered, CSF characteristics, pain management interventions, patient's tolerance, and specimens sent to laboratory for analysis.

F. Complications.
   1. Infection from nonsterile conditions.
      a. Use of poor sterile technique.
      b. Bacteremia if blood vessel punctures during procedure, having passed through infected CSF.
   2. Intraspinal epidermoid tumor from lack of stylet use.
   3. Spinal cord and/or nerve damage if puncture performed above L4.
   4. Cerebral herniation.
   5. Intraprocedure apnea, bradycardia, and/or hypoxia.
   6. Spinal cord or epidural abscess.
   7. Spinal or intracranial subdural hematoma.
   8. Spinal or intracranial subarachnoid hematoma.
   9. Spinal fluid leakage into epidural space.

10. Vertebral body osteomyelitis.
11. Persistent bleeding, especially in patients with an underlying coagulopathy.
12. Pain.

Simulation

In the high-risk environment of the NICU, there are many delicate procedures that require proficiency, precision, and great skill. Opportunities for training in these skills are essential, as competence is critical to reducing patient harm and improving patient outcomes (see Chapter 18).

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CHAPTER 16

Pain Assessment and Management

Marlene Walden

OBJECTIVES

1. Review the physiology of acute pain in preterm neonates.
2. Discuss the current standards for assessing and managing pain in neonates.
3. Identify behavioral and physiologic responses that are indicative of pain in the neonate.
4. Select a valid and reliable composite measure for assessment of pain in neonates.
5. Discuss the evidence base for nonpharmacologic and pharmacologic approaches to the management of pain in neonates.

Advances in neonatal care during the past several decades have led to the increased survival of extremely preterm and sick neonates who regularly are subjected to numerous diagnostic and therapeutic procedures that are painful but medically necessary to their care. The prevention of pain in these critically ill neonates not only is an ethical obligation but may also minimize the immediate and cumulative effects of repeated painful experiences on the developing brains of these vulnerable neonates. Despite impressive gains in the knowledge related to the assessment and management of pain in neonates over the last several decades, a large gap still exists between routine clinical practice and scientific evidence. This chapter will review pain pathways, identification of pain, and interventions to alleviate pain in the neonate.

Definition of Pain

A. The International Association for the Study of Pain (IASP) defines pain as "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (IASP Subcommittee on Taxonomy, 1979, p. 250). The IASP definition implies that the meaning of pain must be learned through experience and articulated within the context of verbal language. This conceptualization of pain perpetuates the misconception that infants, who lack linguistic skills, do not experience pain (Anand and Craig, 1996). In neonates, physiologic, behavioral, and hormonal indicators provide objective and quantifiable information about the location, intensity, and duration of painful stimuli. These responses can be used in conjunction with other contextual indicators to infer the existence of pain.

B. Although chronic pain in neonates has been acknowledged, there is no consensus on the definition of prolonged, persistent, or chronic pain in the newborn (Anand, 2017). Pain experts have hypothesized that chronic pain in the newborn is characterized by pain that is not proximate to a procedure or event, occurs over a period of time, has no clear endpoint in sight, and often is not associated with a specific cause (van Ganzewinkel et al., 2014). The lack of a clinically useful definition and nonspecific signs and symptoms may limit caregivers' ability to accurately assess and manage chronic pain in the neonatal intensive care unit (NICU), leading to impaired growth, prolonged hospitalization, altered pain perception, and impaired cognitive and behavioral development in newborns (van Ganzewinkel et al., 2014).

Neonatal Intensive Care Unit Procedures That Cause Pain

A. **Many activities and interventions in the NICU cause pain. The most frequently occurring painful procedures include heel lance, suctioning, venipuncture, and insertion of peripheral venous catheters** (Cruz et al., 2016). Despite advances in neonatal pain management over the past decade, pharmacologic and nonpharmacologic interventions (e.g., mechanical spring-loaded lancets, venipuncture over heel stick, oral sucrose with pacifier before procedures, swaddling and facilitated tucking, skin-to-skin contact with mother) continue to be inconsistently utilized before invasive procedures to prevent neonatal pain (Cruz et al., 2016).

B. **Frequency of invasive procedures is inversely related to gestational age and severity of illness** (Cruz et al.,

2016). **Therefore, smaller and sicker neonates are subjected to the greatest number of painful procedures.**

1. Studies found that neonates experienced on average between 7.5 and 17.3 painful procedures per day during the first 14 days of admission (Cruz et al., 2016).

C. **The number of procedures encountered by infants in the NICU is partially due to a substantial number of failed attempts.**
   1. Roofthooft and colleagues (2014) found the failure rates for placement of peripheral arterial catheters and venipunctures were 63% and 9.1%, respectively.
   2. Carbajal et al. (2008) noted some of the most painful procedures needed as many as 10 to 15 attempts for completion.

D. **Despite safe, effective pharmacologic and nonpharmacologic interventions to prevent or minimize pain and distress, many painful procedures in the NICU are performed without analgesia.**
   1. Simons et al. (2003) found that many of the procedures were rated by physicians and nurses to be painful (>4 on a 10-point scale); however, very few infants received any pharmacologic or nonpharmacologic procedural pain management.
   2. Johnston and colleagues (2011) reported that 46% of tissue-damaging procedures (e.g., heel lance, venipuncture, lumbar puncture, endotracheal intubation, and ophthalmologic examination) and 57% of non–tissue-damaging procedures (e.g., endotracheal suctioning, tape removal, nasogastric tube insertion, catheter removal) were performed without analgesic interventions.
   3. A descriptive survey of nurses and physicians noted that, rather than lack of knowledge, the most common reasons for withholding analgesia were related to fear of adverse drug reactions, absence of a unit pain policy, inadequate staffing, poor interdisciplinary communication about timing of procedures, forgetfulness, and taking advantage of the fact that "babies cannot protest" (Akuma and Jordan, 2012).
   4. Johnston and colleagues (2011) found parental presence predicted the use of sweet-taste analgesia or nonpharmacologic interventions for tissue-damaging procedures.

E. **Procedural pain guidelines are available to help clinicians choose the most effective and safe pain control measures based on best evidence (Anand and International Evidence-Based Group for Neonatal Pain, 2001; Lago et al., 2009; Spence et al., 2010).**
   1. Heel stick.
      a. Pain resulting from the heel-stick procedure is caused not only by the lancing procedure but also by the squeezing of the heel to obtain the blood sample.
      b. Spring-loaded mechanical lancets result in less bruising, less need for repeat punctures, and fewer behavioral and physiologic signs of pain.
      c. Heel warming has no effect on facilitating blood flow during the heel-stick procedure.
      d. Use of EMLA cream (eutectic mixture of local anesthetics, lidocaine, and prilocaine) is not effective for management of pain associated with the heel-stick procedure.
      e. Evidence-based interventions include pacifier with sucrose, swaddling, containment, facilitated tucking, breastfeeding, and skin-to-skin contact with mother.
   2. Venipuncture.
      a. May be preferable to heel stick in minimizing procedure-related pain in full-term infants. However, frequent venipuncture for blood sampling is not feasible for most infants in the NICU, necessitating the continued use of heel sticks.
      b. Use smallest-gauge trocar cannula whenever possible.
      c. Evidence-based interventions include swaddling, facilitated tucking, pacifier with sucrose, and topical anesthetic cream in infants ≥37 weeks of gestation.
   3. Lumbar puncture.
      a. Avoid extreme flexion of the neck and knees toward the chest, as this may cause significant hypoxemia.
      b. Evidence-based interventions include sucrose, pacifier, and topical anesthetic cream in infants ≥37 weeks of gestation.
   4. Chest tube insertion.
      a. If procedure is not urgent, apply topical anesthetic cream in infants ≥37 weeks of gestation. If urgent, infiltrate site with 1% subcutaneous lidocaine.
      b. If infant is intubated and ventilated, administer a slow IV opiate bolus such as fentanyl before the procedure.
   5. Endotracheal intubation (Kumar et al., 2010. Reaffirmed May 2018).
      a. Awake intubations should only be performed during resuscitation in the delivery room or after acute deterioration or critical illness.
      b. Premedication with analgesic agents alone or in combination with vagolytic agents, muscle relaxants, or sedatives should be given.
      c. Using appropriate analgesia and sedation reduces potentially harmful physiologic fluctuations and pain, decreases the time and number of attempts, and minimizes the potential for intubation-related airway trauma.
   6. Ophthalmologic examination screening for retinopathy of prematurity.

a. Evidence-based interventions include the use of a pacifier, sucrose, containment, and local anesthetic eyedrops.
b. Retinal surgery should be considered major surgery, and opiates should be provided.

F. **Technician expertise, such as the skill of the operator, influences pain responses in infants and should be monitored. Ensuring staff competence to perform required procedures may reduce the number of painful procedures to which an infant is exposed by reducing the number of failed attempts** (Simons et al., 2003)**.**

Postoperative Pain

A. Pediatric anesthesiologists and anesthetists are responsible for initiating postoperative analgesia in collaboration with the neonatal health care team.
B. Postoperative analgesia should be selected based on the developmental age of the infant, surgical procedure, and pain assessment scores.
C. Pain after surgery is usually most severe in the first 24 to 72 hours but may persist for days to weeks, depending on the surgical procedure performed (Association of Paediatric Anaesthetists of Great Britain and Ireland, 2012). Postoperative analgesia should be provided as long as pain assessment scores, along with nursing judgment, indicate ongoing pain.
D. Regular postoperative pain assessments using a valid and reliable tool should be used to assess the neonate's level of pain and pain relief after pharmacologic and nonpharmacologic comfort measures.
E. **In the early postoperative period, analgesia should be given regularly around the clock and then as required according to pain assessments** (Association of Paediatric Anaesthetists of Great Britain and Ireland, 2012).
F. Opioids remain the mainstay of postoperative pain relief in newborn infants (Hall and Anand, 2014).
G. The use of low-dose continuous infusions of opioid analgesics provides more constant, effective pain relief with less medication than repeated, intermittent scheduled doses of opioids (Spruill and LaBrecque, 2017).

Physiology of Acute Pain in Preterm Neonates

A. **An understanding of the physiology of acute pain in preterm neonates is essential for optimal pain management in the NICU. Pain responses exhibited by neonates are the result of a concurrent set of reactions within the peripheral nervous system, spinal cord, and higher centers involved at the supraspinal/integrative level, including the thalamus and cerebral cortex** (Melzack, 1996)**.**

1. Peripheral nervous system (Evans, 2001).
   a. Fully mature and functional by 20 weeks of gestation.
   b. Consists of two types of neuronal afferent fibers.
      1) Delta fibers: thinly myelinated, rapid-conducting fibers associated with sharp pain or "first pain" (e.g., sharp, localized, pricking).
      2) C fibers: polymodal, unmyelinated, slow-conducting fibers associated with aching, burning, poorly localized, or "second pain."
   c. Density of nociceptors is equal to or greater than that in adult skin.
   d. Local tissue injury, such as heel stick or venipuncture, activates nociceptors of sensory afferent fibers to:
      1) Transmit pain impulses to spinal cord and central nervous system (CNS).
      2) Release biochemical mediators such as substance P and prostaglandins, which results in hyperalgesia (increased sensitivity to painful stimuli) or allodynia (pain caused by a stimulus that ordinarily does not cause pain). This decreased pain threshold may persist for days or weeks.
      3) Cause dendritic sprouting and hyperinnervation that result in hypersensitivity and lower pain threshold that may persist into adulthood.
2. Spinal cord (Evans, 2001).
   a. During the first postnatal week, weak linkages exist between the peripheral nervous system and the dorsal horn, resulting in either prolonged pain responses or no reaction to the painful stimuli.
   b. Receptive fields of the dorsal horn cells are larger than those of adults and begin to diminish 2 weeks after birth.
   c. Local spinal cord response to pain impulses from peripheral afferent fibers stimulates efferent somatomotor neurons in the anterior horn and produces reflex withdrawal.
   d. Afferent fiber neurotransmitters stimulate *N*-methyl-D-aspartate and tachykinin receptors in the dorsal horns, producing central sensitization (increased excitability of dorsal horn neurons that spreads to several adjacent segments of the spinal cord), "wind-up" phenomenon (perceived increase in intensity or duration of painful stimuli), or secondary hyperalgesia (hypersensitivity elicited by both painful and nonpainful stimuli that extends to areas beyond the site of injury).
   e. Increases in autonomic responses, such as heart rate and respiratory rate, and facial responses,

such as brow bulge, eye squeeze, and nasolabial furrow, in response to heel-stick procedures provide evidence of maturity of ascending pathways by 20 weeks of gestation.

f. Preterm infants have a limited ability to modulate pain. Dopamine and norepinephrine are not available to modulate pain before 36 to 40 weeks of gestation. Serotonin is first released at approximately 6 to 8 weeks after birth.

3. Supraspinal/integrative level (Evans, 2001).
   a. Cerebral cortex has a full complement of neurons by 20 weeks of gestation.
   b. Cerebral cortex is functionally mature by 22 weeks of gestation and bilaterally synchronous by 27 weeks of gestation.
   c. Somatosensory evoked potentials are slow and simple before 29 weeks of gestation, but short and complex by 40 weeks of gestation.
   d. Cortical cell migration is complete at approximately 24 weeks of gestation. However, the support structure of the germinal matrix remains highly vascular until 28 weeks. Therefore, the neonate is vulnerable to intraventricular hemorrhage related to increases in blood pressure associated with pain.
   e. Maximum number of cortical neurons is reached at 28 weeks of gestation, and then approximately 70% of cortical neurons are lost before birth through apoptosis.
   f. Neonates as early as 27 weeks of gestation can differentiate touch (sham heel stick) from a noxious stimulus (heel stick) as evidenced by physiologic and facial response patterns.
   g. Neurologic connections are in place for the perception of, reaction to, and memory of pain on the cortical level as evidenced by mature visual and auditory response patterns on electroencephalogram in infants younger than 30 weeks of gestation and by measurements of in-vivo cerebral glucose in the sensory areas of the brain.

B. **Repetitive, unrelieved pain can lead to serious and adverse consequences for neonates.**
   1. Short-term physiologic consequences of painful procedures include decreased oxygen saturations and increased heart rates that can place increased demands on the cardiorespiratory system.
   2. Pain can cause elevation in intracranial pressure, thereby increasing the risk of intraventricular hemorrhage in preterm neonates.
   3. Pain and stress may also depress the immune system and contribute to increased susceptibility of neonates to infections.
   4. The long-term effects of pain in animals are clear, with changes observed in pain thresholds, social behaviors, stress responses, and pain responses to nonpainful stimuli (Fitzgerald and Anand, 1993; Plotsky et al., 2000; Reynolds et al., 1997; Ruda et al., 2000). Early pain experiences may impair brain development and alter future pain responses (Bouza, 2009; Brummelte et al., 2012). Johnston and Stevens (1996) reported that neonates who were born at 28 weeks of gestation and were hospitalized in the NICU for 4 weeks (32 weeks of postconceptional age) had decreased behavioral response and significantly higher heart rate and lower oxygen saturation during a heel-stick procedure compared with newly born neonates at 32 weeks of gestation. In another study, Taddio and colleagues (1995) reported that males circumcised within 2 days of birth had significantly longer crying bouts and higher pain intensity scores at immunization at 4 or 6 months of age than males who were not circumcised.

Standards of Practice

A. **Organizations that support the importance of optimal pain assessment and management in hospitalized neonates include the National Association of Neonatal Nurses (Walden and Gibbins, 2012) and the American Academy of Pediatrics (2016). There is considerable consistency in the recommendations set by these professional organizations. Core principles contained within these guidelines and standards that are applicable to pain assessment and management in the NICU include:**
   1. Assess education and competency in pain assessment and management of new and current employees.
   2. Regularly assess and reassess pain using a valid and reliable multidimensional pain assessment instrument.
   3. Use both nonpharmacologic and pharmacologic approaches to prevent and/or manage pain.
   4. Health care team members should collaborate together and with the infant's family in developing an approach to pain assessment and management.
   5. Documentation should facilitate regular reassessment and follow-up intervention.
   6. Policies and procedures should be established to provide consistency and quality of pain assessment and management practices.
   7. Data should be collected to monitor the appropriateness and effectiveness of pain management practices.

B. **The clinical challenge remains in how to implement these standards in various institutional settings based on patient types, frequently occurring clinical procedures performed, and current staffing patterns.**

Pain Assessment

A. **Pain assessment has been advocated as the "fifth vital sign" and should be assessed routinely.**
B. **The golden rule of pain assessment must be: What is painful to an adult is painful to an infant until proven otherwise** (Franck, 1989)**. This rule, along with the use of valid and reliable tools, must be used for the assessment of and intervention for pain.**
C. **Pain instruments developed to assess acute pain in neonates may not accurately capture pain in neonates with persistent, prolonged, or chronic pain. These infants may completely shut down or present with more subdued responses when pain exceeds the infant's ability to respond** (Anand, 2019)**.**
D. **Pain assessment is an essential prerequisite to optimal pain management.**
E. **Behavioral responses.**
   1. Facial activity offers the most specificity as an indicator of pain, namely brow bulge, eye squeeze, and nasolabial furrow.
   2. Acoustic and temporal characteristics of pain cries are different than other cry types in both preterm and full-term infants, including increases in peak fundamental frequency (pitch), peak spectral energy, cry duration, and intensity. However, differences in cry types are difficult to discriminate in the clinical setting.
   3. Many preterm infants do not cry in response to a noxious stimulus. The absence of response may only indicate the depletion of response capability and not lack of pain perception.
   4. Healthy full-term newborns use swiping motions by the unaffected leg to the lanced foot, as if trying to push away the noxious stimulus.
   5. Preterm infants demonstrate an increase in motor extension patterns, including finger splay, "saluting," and "sitting on air" during painful clinical procedures. These hyperextension motor patterns are quickly replaced with flaccidity in infants at younger postconceptional ages.
F. **Physiologic responses.**
   1. Preterm infants respond to noxious stimuli in patterns similar to those of full-term neonates, including increases in heart rate and decreases in oxygen saturation.
   2. Although physiologic measures provide greater objectivity in the assessment of pain, they also reflect the body's nonspecific response to stress and thus are not specific to pain (Ranger et al., 2007). Therefore, physiologic measures should be converged with behavioral measures that have been demonstrated to be more consistent and specific to pain in neonates.
   3. Physiologic measures should be used to assess pain in infants who are paralyzed for mechanical ventilation or who are severely neurologically impaired. Increases in heart rate and blood pressure during handling generally indicate the need for more analgesia and/or sedation in the pharmacologically paralyzed infant.
   4. If the infant is sedated, variability in heart rate and blood pressure decreases. However, it is important to remember that although sedatives may mask physiologic and behavioral signs of pain, sedatives do not provide pain relief.
G. **Contextual factors modifying pain responses.**
   1. Developmental maturity, health status, and environmental factors may all contribute to an inconsistent, less robust pattern of pain responses between infants and even within the same infant over time and situations. Therefore, contextual factors that have been demonstrated to modify the pain experience must be considered when assessing for the presence of pain in neonates.
   2. Infants in awake or alert states demonstrate a more robust reaction to painful stimuli than infants in sleep states.
   3. Research examining facial as well as bodily activity has demonstrated that the magnitude of infant response has been observed to be less vigorous and robust with decreasing postconceptional age. Craig and colleagues (1993) suggested that the less vigorous responses demonstrated by preterm infants "should be interpreted in the context of the energy resources available to respond and the relative immaturity of the musculoskeletal system" (p. 296).
   4. Less mature behavioral responses to noxious stimuli are also noted with increased number of painful procedures to which the infant is exposed, increased postnatal age of the infant at time of observation, and shorter length of time since last painful procedure (Ranger et al., 2007).
   5. When pain stimuli or pain persists for hours or days without intervention, the infant exhibits a decompensatory response. The sympathetic nervous system, or the "fight-or-flight" mechanism, can no longer compensate. As a result, the physiologic parameters return to baseline (Hummel and van Dijk, 2006). Return to baseline does not indicate that pain is no longer felt or is tolerated, but it does make the infant's pain more difficult to evaluate.

Pain Assessment Instruments

A. Presently there is not a single, universally adopted pain instrument considered the gold standard for assessment of pain in neonates (Anand, 2019).
B. Given the multifaceted nature of pain, select a multidimensional instrument that incorporates both

Table 16.1

CRIES: Neonatal Postoperative Pain Measurement Score*

	SCORE			
	0	1	2	Tips for Scoring CRIES
Crying	No	High pitched	Inconsolable	Score 0: no cry or cry not high pitched Score 1: high-pitched cry, but consolable Score 2: high-pitched cry, inconsolable
Requires O_2 for saturation >95%	No	<30%	>30%	Score 0: no oxygen required from baseline Score 1: oxygen requirement <30% from baseline Score 2: oxygen requirement >30% from baseline
Increased vital signs	HR and BP ≤ preoperative values	HR or BP <20% of preoperative values	HR or BP ≥20% of preoperative values	Score 0: HR and BP are both unchanged or at less than baseline Score 1: HR or BP is increased by <20% Score 2: HR or BP is increased by >20% *Note:* Measure BP last so as not to wake the infant.
Expression	None	Grimace	Grimace/grunt	Score 0: no grimace Score 1: grimace only is present Score 2: grimace and inaudible grunt present *Note:* Grimace consists of lowered brow, eyes squeezed shut, deepening nasolabial furrow, and open lips and mouth.
Sleepless	No	Wakes at frequent intervals	Constantly awake	Score 0: continuously asleep Score 1: awakens at frequent intervals Score 2: awake constantly *Note:* Based on infant's state during previous hour.

BP, Blood pressure; *HR*, heart rate.

* Neonatal pain assessment tool developed at the University of Missouri–Columbia.

From Krechel, S., & Bildner, J. (1995). CRIES: A new neonatal post-operative pain measurement score: Initial testing of validity and reliability. *Paediatric Anaesthesia*, *5*(1), 53–61.

physiologic and behavioral measures of pain. Caregivers should select instruments with tested reliability, validity, and clinical utility. Infant population, setting, and type of pain experienced should also guide selection of a pain instrument (Duhn and Medves, 2004)**.**

C. Pain scores should direct pain management decisions. If pain interventions are performed, the neonate should be re-evaluated following nonpharmacologic comfort or pharmacologic measures to assess for pain relief. However, clinical judgment should always be used for interpreting and managing pain in neonates, who may not respond to pain with clear signals.

D. CRIES: a postoperative pain tool (Table 16.1) (Krechel and Bildner, 1995)**.**

1. Acronym for five behavioral and physiologic parameters: C = crying; R = requires oxygen to maintain saturation at greater than 95%; I = increased vital signs; E = expression; and S = sleeplessness.
2. Developed to assess postoperative pain in infants between 32 and 60 weeks' gestation.
3. Concurrent validity (Spearman rank correlation coefficient between objective pain scale and CRIES [0.73; $p < 0.0001$]); discriminant validity (decreased pain scores following analgesics); interrater reliability (r 0.72, $p < 0.0001$).
4. Tool scoring system, 0 to 10, is structured in the same fashion as the Apgar score and was designed to make the tool easy to use and remember.
5. A score between 0 and 4 may indicate mild pain, and nonpharmacologic comfort measures should be considered. A score of 5 or greater is consistent with moderate to severe pain and should receive pharmacologic intervention in conjunction with comfort measures.

E. **The Premature Infant Pain Profile (PIPP)** (Stevens et al., 1996)**.**

1. Developed to assess procedural pain in infants between 28 and 40 weeks' gestation and has been validated in over 62 studies (Stevens et al., 2010).
2. Seven-item, 4-point multidimensional scale. Two physiologic indicators (heart rate, oxygen saturation), three facial behaviors (brow bulge, eye squeeze, and nasolabial furrow), and two contextual modifiers of pain expression (gestational age and behavioral state).
3. Content validity (experts and literature), construct validity (scores between pain and no pain situations

[paired t-test = 12.24, two-tailed $p < 0.0001$]), internal consistency (0.71).

4. Total pain score of 7 to 12 indicates mild pain, and infant may benefit from use of nonpharmacologic comfort measures. Total pain score greater than 12 indicates moderate to severe pain and requires pharmacologic intervention in conjunction with comfort measures.
5. The PIPP was revised in 2013 to enhance validity and feasibility (Stevens et al., 2014). In the revised (PIPP-R) (Table 16.2), the decimal points in oxygen saturation were rounded to the nearest whole number and the scoring of facial features was changed from a percentage to the absolute duration of time the indicator was observed in the 30-second block. Instructions related to baseline behavioral state were clarified and made more specific.

F. **Neonatal Infant Pain Scale (NIPS)** (Lawrence et al., 1993) (Fig. 16.1).

1. Developed to assess procedural pain in infants between 26 and 47 weeks' gestation.
2. Six-item scale. Five behavioral items (facial expression, crying, arms, legs, and state of arousal) and one physiologic indicator (breathing pattern). Each behavior except cry has descriptors for the two possible scores of 0 and 1. Cry is scored on a 3-point scale (0, 1, 2).
3. Interrater reliability (Pearson's r 0.92 to 0.97), internal consistency (Cronbach's alphas 0.87 to 0.95), content validity (survey), concurrent validity (r 0.53 to 0.84 compared with Visual Analogue Scale).
4. Total score can range from 0 to 7. Although no scoring guidelines are given to direct pain management, scores of 4 or greater may indicate moderate to severe pain requiring pharmacologic intervention in conjunction with comfort measures.

G. **Neonatal Pain Agitation and Sedation Scale (N-PASS)** (Hummel et al., 2008; Hummel et al., 2010) (Fig. 16.2).

1. Developed to assess both procedural pain and pain/agitation and sedation in ventilated and/or postoperative infants between 23 and 42 weeks' gestation and between 0 and 100 days of life.

Table 16.2

The Premature Infant Pain Profile: Revised

	INDICATOR SCORE				
Infant Indicator	**0**	**+1**	**+2**	**+3**	**Infant Indicator Score**
Change in Heart Rate (bpm) Baseline: _____	0 to 4	5 to 14	15 to 24	>24	
Decrease in Oxygen Saturation (%) Baseline: _____	0 to 2	3 to 5	6 to 8	>8 or increase in O_2	
Brow Bulge (Sec)	None (<3)	Minimal (3 to 10)	Moderate (11 to 20)	Maximal (>20)	
Eye Squeeze (Sec)	None (<3)	Minimal (3 to 10)	Moderate (11 to 20)	Maximal (>20)	
Nasolabial Furrow (Sec)	None (<3)	Minimal (3 to 10)	Moderate (11 to 20)	Maximal (>20)	
			*Subtotal Score:		
Gestational Age (Wk + Days)	>36 wk	32 wk to 35 wk, 6 days	28 wk to 31 wk, 6 days	<28 wk	
Baseline Behavioral State	Active and Awake	Quiet and Awake	Active and Asleep	Quiet and Asleep	
			†Total Score:		
SCORING INSTRUCTIONS					
Step 1: Observe infant for **15 seconds at rest** and assess vital sign indicators [highest heart rate (HR) and lowest O_2 saturation (O_2 SAT)] and behavioral state.					
Step 2: Observe infant for **30 seconds after procedure** and assess **change** in vital sign indicators (maximal HR, lowest O_2 SAT, and duration of facial actions observed).					
If infant requires an increase in oxygen at any point before or during procedure, they receive a score of 3 for the O_2 SAT indicator.					
Step 3: Score for corrected gestational age (GA) and behavioral state (BS) if the subtotal score is greater than 0.					
Step 4: Calculate total score by adding **Subtotal Score + BS Score.**					

* Subtotal for physiological and facial indicators. If subtotal score is greater than 0, add GA and BS indicator scores.

† Total Score: Subtotal Score + GA Score + BS Score.

From Stevens, B. J., Gibbins, S., Yamada, J., Dionne, K., Lee, G., Johnston, C., & Taddio, A. (2014). The premature infant pain profile-revised (PIPP-R): Initial validation and feasibility. *Clinical Journal of Pain*, *30*, 238–243.

	Before Time		During Time					After Time		
	1	2	1	2	3	4	5	1	2	3
Facial expression 0—Relaxed 1—Grimace										
Cry 0—No cry 1—Whimper 2—Vigorous										
Breathing patterns 0—Relaxed 1—Change in breathing										
Arms 0—Relaxed/restrained 1—Flexed/extended										
Legs 0—Relaxed/restrained 1—Flexed/extended										
State of arousal 0—Sleeping/awake 1—Fussy										
Total										

Note: Time is measured in 1-minute intervals.

Fig. 16.1 Neonatal Infant Pain Scale. (From Lawrence, J., Alcock, D., McGrath, P., Kay, J., MacMurray, S. B., & Dulberg, C. [1993]. The development of a tool to assess neonatal pain. *Neonatal Network*, *12*[6], 59–66.)

N-Pass:
Neonatal Pain, Agitation, & Sedation Scale

Assessment Criteria	Sedation		Sedation/Pain	Pain / Agitation	
	–2	–1	0/0	1	2
Crying Irritability	No cry with painful stimuli	Moans or cries minimally with painful stimuli	No sedation/ No pain signs	Irritable or crying at intervals Consolable	High-pitched or silent-continuous cry Inconsolable
Behavior State	No arousal to any stimuli No spontaneous movement	Arouses minimally to stimuli Little spontaneous movement	No sedation/ No pain signs	Restless, squirming Awakens frequently	Arching, kicking Constantly awake or Arouses minimally / no movement (not sedated)
Facial Expression	Mouth is lax No expression	Minimal expression with stimuli	No sedation/ No pain signs	Any pain expression intermittent	Any pain expression continual
Extremities Tone	No grasp reflex Flaccid tone	Weak grasp reflex ↓ muscle tone	No sedation/ No pain signs	Intermittent clenched toes, fists or finger splay Body is not tense	Continual clenched toes, fists, or finger splay Body is tense
Vital Signs HR, RR, BP, SaO_2	No variability with stimuli Hypoventilation or apnea	<10% variability from baseline with stimuli	No sedation/ No pain signs	↑10–20% from baseline SaO_2 76–85% with stimulation - quick↑	↑ >20% from baseline SaO_2 ≤75% with stimulation - slow ↑ Out of sync/fighting vent

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Premature Pain Assessment +1 if <30 weeks gestation/corrected age

Fig. 16.2 N-PASS: Neonatal Pain, Agitation, and Sedation Scale. (From © Hummel & Puchalski [Rev. 8/14/01] Loyola University Health System, Loyola University Chicago, 2000.)

2. Five-item scale. Four behavioral items (crying/irritability, behavior state, facial expression, extremities/tone) and one physiologic indicator (vital signs).
3. Psychometrics.
   a. Heel-stick study (2010): Construct (discriminate) validity (compared heel stick and sham procedures ($Z = 6.429$, $p < 0.0001$), convergent validity (correlation with PIPP scores (Spearman rank correlation coefficient 0.75 and 0.72), interrater reliability (0.86 to 0.93, $p < 0.0001$), internal consistency (Cronbach's alpha 0.84 to 0.89), test–retest reliability (recorded videos [Spearman's rho correlation, 0.87, $p < 0.0001$]).
   b. Prolonged pain/mechanical ventilation study: interrater reliability (intraclass coefficients 0.85 to 0.95, $p < 0.001$ to 0.0001), convergent validity (correlation with the PIPP scores [Spearman's rank correlation coefficient 0.83 at high pain scores, 0.61 at low pain scores]), internal consistency (Cronbach's alpha with pain scores 0.82 and with sedation scores 0.87), construct validity (compared N-PASS scores before and after pharmacologic intervention pain scores $p < 0.0001$ and sedation scores $p < 0.0001$).
4. Total pain scores range from 0 to +10. Derived from the PIPP, pain scores are adjusted for gestational age to account for the preterm infant's limited ability to mount a robust pain response due to immaturity. Total pain scores vary depending on the infant's gestational age, but scores greater than 5 usually signify pain requiring nonpharmacologic comfort measures and/or pharmacologic pain intervention.
5. Sedation scores range from 0 to −10. The sedation portion of the N-PASS requires an assessment of response to stimuli and can be useful in titrating opioid requirements based on level of sedation required. Scores of −10 to −5 are considered deep sedation, whereas light sedation scores range from −5 to −2.
   a. Hillman and colleagues (2015) reported that the N-PASS sedation score was significantly correlated with nursing bedside assessment.
   b. Giordano and researchers (2014) found that the N-PASS reliably detected oversedation but failed to differentiate between levels of adequate sedation and undersedation.
   c. Further research is needed to determine optimal levels of sedation in order to maximize the ventilator benefits of the right sedation, while reducing the negative impact of oversedation on clinical outcomes.

Echelle Douleur Inconfort Nouveau-Né, Neonatal Pain and Discomfort Scale (EDIN) (Debillon et al., 2001) (Fig. 16.3)

A. Developed to assess prolonged pain in infants between 25 and 36 weeks' gestation who:
   1. Required assisted ventilation for respiratory distress syndrome.
   2. Required prolonged assisted ventilation for bronchopulmonary dysplasia.
   3. Developed necrotizing enterocolitis.
   4. Was postoperative after closure of a patent ductus arteriosus.
B. Five-item scale. Five behavioral items (facial activity, body movements, quality of sleep, quality of contact with nurses, and consolability). No physiologic indicators are included in the EDIN, as physiologic measures are not specific for prolonged pain in the neonate. Infants with persistent pain often are passive with limited or no body movements, have a flaccid face, and demonstrate reduced heart and respiratory rate variability and decreased oxygen consumption (Anand, 2019).
C. Interrater reliability (coefficients 0.59 to 0.74), internal consistency (Cronbach's alphas 0.86 to 0.94), construct validity (compared scores during pain and no pain [$p = 0.0009$], and before and after analgesic treatment [$p < 0.0001$]).
D. Total score can range from 0 to 10. The total score is summed after the infant is observed for several hours during and between caring and feeding and the infant's response to consoling. Although no scoring guidelines are given to direct pain management, scores of 5 or greater may indicate moderate to severe pain requiring pharmacologic intervention in conjunction with comfort measures.

Nursing Care of the Infant in Pain

Skilled observation, assessments, and interventions are the responsibility of the care providers. Pain intervention may be provided by both nonpharmacologic and pharmacologic methods.

A. **Nonpharmacologic approaches to pain management.**
   1. **Goals.**
      a. **To help minimize pain and stress while maximizing the infant's ability to cope with and recover from clinical procedures.**
      b. **To provide additive or synergistic benefits to pharmacologic therapy.**
   2. Preventive measures.
      a. **Reduce the total number of painful procedures to which the infant is exposed.**
         1) Evaluate all aspects of caregiving.

Indicator	Description	Result
Facial activity	0. Relaxed facial activity 1. Transient grimaces with frowning, lip purse and chin quiver or tautness 2. Frequent grimaces, lasting grimaces 3. Permanent grimaces resembling crying or blank face	
Body movements	0. Relaxed body movements 1. Transient agitation, often quiet 2. Frequent agitation but can be calmed down 3. Permanent agitation with contraction of fingers and toes and hypertonia of limbs or infrequent, slow movements and prostration	
Quality of sleep	0. Falls asleep easily 1. Falls asleep with difficulty 2. Frequent, spontaneous arousals, independent of nursing, restless sleep 3. Sleepless	
Quality of contact with nurses	0. Smiles, attentive to voice 1. Transient apprehension during interactions with nurses 2. Difficulty communicating with nurses. Cries in response to minor stimulation 3. Refuses to communicate with nurses. No interpersonal rapport. Moans without stimulation	
Consolability	0. Quiet, total relaxation 1. Calms down quickly in response to stroking or voice, or with sucking 2. Calms down with difficulty 3. Disconsolate. Sucks desperately	
		TOTAL SCORE: /15

Fig. 16.3 EDIN Scale. (From Debillon, T., Zupan, V., Ravault, N., Magny, J. F., & Dehan, M. [2001]. Development and initial validation of the EDIN scale, a new tool for assessing prolonged pain in preterm infants. *Archives of Disease in Childhood. Fetal and Neonatal Edition*, *85*[1], F36–F41.)

2) Evaluate the number and grouping of laboratory and diagnostic procedures.
3) Schedule clinical procedures based on medical necessity versus a routine schedule.
4) Use minimal amounts of tape/adhesives and use skin barrier products when possible.
5) Ensure proper premedication before invasive procedures.
6) Use noninvasive monitoring devices when possible.
7) Establish central venous/arterial access, when appropriate, to minimize skin-breaking procedures.
8) Involve parents in caregiving by teaching signs and symptoms of pain and comfort techniques that they can provide.

b. Painful procedures should not be performed at the same time as other, nonemergency routine care (e.g., taking vital signs, changing a diaper), as this can cause sensory hypersensitivity (referred to as "wind-up" phenomenon) causing nonnoxious stimuli to be perceived as painful (Bouza, 2009; Holsti et al., 2005).
c. Handling and immobilization in preparation for painful procedures should be minimized before a painful procedure, as this may heighten activity in nociceptive pathways and accentuate the infant's pain responses.
d. Use environmental interventions, such as reduced lighting and noise levels, to minimize infant stress.

3. Behavioral measures.
a. Facilitated tucking (hand-swaddling technique that holds the infant's extremities flexed and contained close to the trunk) during a painful procedure may significantly reduce pain responses in preterm infants (Hartley et al., 2015; Obeidat et al., 2009; Pillai et al., 2015).

b. Blanket swaddling after a painful procedure may help reduce physiologic and behavioral pain and distress in preterm neonates (Pillai et al., 2015).
c. Nonnutritive sucking (NNS) (Pillai et al., 2015).
   1) NNS is thought to modulate the transmission or processing of nociception through mediation by the endogenous nonopioid system (Hall and Anand, 2014).
   2) The efficacy of NNS is immediate but appears to terminate almost immediately upon cessation of sucking.
   3) Pain relief is greater in infants who receive both NNS and oral sucrose (Gao et al., 2018).
d. Breastfeeding may be used to alleviate procedural pain in term neonates undergoing a single painful procedure (Benoit et al., 2017; Shah et al., 2012).
e. Skin-to-skin contact (also known as *kangaroo care*) has been shown to significantly reduce pain responses in term newborns and preterm neonates greater than 28 weeks' gestational age during heel-stick and single painful procedures (Johnston et al., 2017). Although the mechanism of action for skin-to-skin contact is unclear, it has been suggested that the effects observed are related to the neonate's enhanced ability to self-regulate and to hear the maternal heartbeat (Hall and Anand, 2014).

B. **Pharmacologic approaches to pain management.**
   1. **Pharmacologic therapy should maintain a balance between pain relief and adverse effects of analgesics.**
   2. Pharmacologic therapy to manage neonatal pain consists of oral sucrose, systemic analgesics, nonsteroidal/antiinflammatory medications, and topical anesthetic agents.
      a. Oral sucrose.
         1) Administration of oral sucrose with and without NNS is commonly used to provide pain relief for neonates during minor to moderately painful procedures.
         2) Sucrose should be considered a medication and prescribed and tracked accordingly (AAP Committee on Fetus and Newborn and Section on Anesthesiology and Pain Medicine, 2016).
         3) Sucrose has been demonstrated to be effective in reducing pain from single procedures performed in the NICU, including heel sticks, venipunctures, and intramuscular injections, in term and preterm neonates. Inconclusive evidence exists for newborn pain relief for other commonly performed procedures, such as arterial puncture, insertion of feeding tubes, urinary catheterizations, and eye examinations (Stevens et al., 2016).
         4) Sucrose is most effective when combined with other nonpharmacologic interventions such as NNS.
         5) Mechanism of action is the endogenous opioid release triggered by the sweet taste of sucrose (Blass, 1994).
            a) To activate the endogenous opioid system, Blass and Shah (1995) reported in term healthy newborns that sucrose should be optimally administered 2 minutes before a heel-stick procedure, which has been adopted as the standard of practice in NICUs worldwide.
            b) Findings from a more recent study conducted with preterm and critically ill neonates suggest that pain intensity is not correlated with the length of time between sucrose administration and a heel-stick procedure; therefore, suggesting waiting 2 minutes after sucrose administration is unnecessary (Meesters et al., 2017).
         6) Inconclusive evidence exists on the optimal dose of sucrose according to a recent Cochrane review, where solutions ranged from 0.05 mL of 24% sucrose to 2.0 mL of 50% sucrose (Stevens et al., 2016). A more recent randomized controlled trial found the minimally effective dose of 24% sucrose for procedural pain of a single heel stick in neonates was 0.1 mL (Stevens et al., 2018).
         7) The safety and efficacy of repeated doses of sucrose for the reduction of procedural pain in very low birth weight infants have not been confirmed; therefore, caution is advised before widespread use of repeated doses in preterm and critically ill neonates.
            a) Gao and colleagues (2016) conducted a systematic review and reported that repeated doses of sucrose were effective in reducing behavioral pain responses and composite pain scores but was inconclusive for reducing physiologic pain responses.
            b) The effect of repeated sucrose on long-term neurodevelopmental outcomes are unknown (Stevens et al., 2016). Johnston and colleagues (2002) reported that preterm infants less than 31 weeks postmenstrual age who received repeated doses of sucrose for painful procedures showed poorer neurodevelopmental scores at 36 and 40 weeks. However, a later study failed to demonstrate significant differences on neurobiologic risk-status outcomes between preterm infants who received sucrose plus pacifier, water plus pacifier, or the standard care group (Stevens et al., 2005).
         8) No major adverse events have been reported after sucrose administration. Minor adverse

events (e.g., gagging, choking) of sucrose administration have been reported (Stevens et al., 2016; Stevens et al., 2018), but all resolved spontaneously or with minimal caregiver interventions.

b. Systemic analgesics.
   1) **Systemic analgesics should be used when moderate, severe, or prolonged pain is assessed or anticipated.**
   2) Intravenous (IV) opioids remain the most common class of analgesics administered in the NICU, particularly morphine sulfate and fentanyl citrate (Table 16.3).
   3) Systemic opioids induce analgesia by acting at various levels of the CNS.
      a) Spinal cord: opioids impair or inhibit the transmission of nociceptive input from the periphery to the CNS.

Table 16.3

Commonly Used Drugs for Analgesia in Neonates

DRUGS	Dosing	Adverse Effects	Special Considerations
Opioid Analgesics			
Morphine	**Analgesia** Oral 0.08 mg/kg/dose every 4 to 6 hours IV, IM, SQ Initial: 0.05 to 0.1 mg/kg/dose every 4 to 6 hours Continuous IV Infusion Initial: 0.01 mg/kg/hour (10 mcg/kg/hour); Maximum: 0.03 mg/kg/hour (30 mcg/kg/hour) **Endotracheal Intubation (Nonemergent)** IM, IV: 0.05 to 0.1 mg/kg **Neonatal Abstinence Syndrome** Oral: Initial: 0.04 mg/kg/dose every 3 to 4 hours Increase by 0.04 mg/kg/dose if symptoms are not controlled Maximum: 0.2 mg/kg/dose	Respiratory depression Hypotension Bradycardia Transient hypertonia Ileus Delayed gastric emptying Urinary retention Tolerance and dependence Seizures	Analgesia Notes • Titrate doses carefully to appropriate effect • Oral dose is approximately one-half as effective as parenteral dose • Lower infusion rates may be needed due to decreased elimination, increased CNS sensitivity, and adverse effects • Higher doses may be needed in neonates who develop tolerance • Use caution in neonates with hypotension due to potential for increased adverse neurologic outcomes Procedural Notes • Allow at least 5 minutes for onset of analgesia Neonatal Abstinence Syndrome Notes • Dose and weaning schedule should be individualized based on signs and symptoms of withdrawal and/or withdrawal scores • Once withdrawal symptoms are controlled, maintain dose for 48 to 72 hours, then taper dose usually by 10% to 20% every 2 to 7 days
Fentanyl	**Analgesia (Opioid-Naïve)** Intermittent doses Slow IV push: 0.5 to 3 mcg/kg/dose every 2 to 4 hours Continuous IV infusion 0.5 to 2 mcg/kg/hour **Continuous Analgesia/Sedation (Mechanically Ventilated)** Initial IV bolus: 1 to 2 mcg/kg, then 0.5 to 1 mcg/kg/hour. **Continuous Analgesia/Sedation (ECMO)** Initial IV bolus: 5 to 10 mcg/kg slow IV push over 10 minutes, then 1 to 5 mcg/kg/hour **Endotracheal Intubation** IV: 1 to 4 mcg/kg slow IV push	Respiratory depression Chest wall rigidity Tolerance and dependence Urinary retention	Analgesia Notes • Titrate dose to appropriate effect • Lower initial doses are recommended for nonventilated patients • Tolerance may develop rapidly requiring higher doses

Continued

Table 16.3

Commonly Used Drugs for Analgesia in Neonates—cont'd

DRUGS	Dosing	Adverse Effects	Special Considerations
Nonsteroidal Antiinflammatory Medications			
Acetaminophen	Oral • GA 28 to 32 weeks: 10 to 12 mg/kg/dose every 6 to 8 hours; maximum daily dose: 40 mg/kg/day • GA 33 to 37 weeks or term neonates <10 days: 10 to 15 mg/kg/dose every 6 hours; maximum daily dose: 60 mg/kg/day • Term neonates ≥10 days: 10 to 15 mg/kg/dose every 4 to 6 hours; do not exceed 5 doses in 24 hours; maximum daily dose: 75 mg/kg/day IV *Loading:* 20 mg/kg/dose *Maintenance dose* • PMA 28 to 32 weeks: 10 mg/kg/dose every 12 hours; maximum daily dose: 22.5 mg/kg/day • PMA 33 to 36 weeks: 10 mg/kg/dose every 8 hours; maximum daily dose: 40 mg/kg/day • PMA ≥37 weeks: 10 mg/kg/dose every 6 hours; maximum daily dose: 40 mg/kg/day	Liver toxicity Rash Fever Thrombocytopenia Leukopenia Neutropenia	• Use IV preparation with caution in premature neonates <32 weeks PMA • Routine prophylactic use of acetaminophen at the time of vaccination is not recommended because of a potential reduction in antibody response
Topical Anesthetic Agents			
EMLA	Circumcision (major dermal procedure) GA ≥37 weeks: Topical cream: Apply 1 to 2 g to prepuce Topical local anesthetic (minor dermal procedures [e.g., IM injection, IV access, venipuncture]) *GA* <37 weeks: 0.5 g per site *GA* ≥37 weeks and weighing <5 kg: Apply up to 1 g per site (typically 10 cm^2 area)	Methemoglobinemia Redness Blanching Transient purpuric lesions	• Apply and wrap with occlusive dressing • Remove and clean before procedure to avoid systemic absorption • Maximum application time is 60 to 90 minutes for circumcisions and 60 minutes for other minor dermal procedures
LMX 4%	Topical cream *Full-term neonates (Circumcision)* Apply 2 g of cream to foreskin and penis; occlude with plastic wrap	Redness	• Cover with plastic wrap • Leave on for 20 to 30 minutes before circumcision • Has faster onset of action than EMLA and no risk of methemoglobinemia • Contains an excipient of benzyl alcohol that is known to cause serious respiratory compromise, gasping respirations, metabolic acidosis, and death

CNS, Central nervous system; *ECMO*, extracorporeal membrane oxygenation; *EMLA*, eutectic mixture of local anesthetics; *GA*, gestational age; *IM*, intramuscular; *IV*, intravenous; *LMX*, liposomal lidocaine cream; *PMA*, postmenstrual age; *SQ*, subcutaneous.

Data from Lexicomp Online, Pediatric and Neonatal Lexi-Drugs Online, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2018; May 24, 2018.

b) Basal ganglia: opioids activate a descending inhibitory system.
c) Limbic system: opioids alter the emotional response to pain, making it more tolerable.

4) Special considerations in neonates.
a) Longer dosing intervals are often required in neonates less than 1 month of age because of longer elimination half-lives and delayed clearance of opioids compared with adults or children greater than 1 year of age.
b) Neonates should be monitored closely during opioid therapy and for several hours after opioids have been discontinued, because enterohepatic recirculation

in preterm and full-term neonates may result in higher plasma concentrations of opioids for longer periods compared with older children.

c) Because of immature descending pain pathways, preterm infants may require significantly higher opioid concentrations to achieve adequate analgesia compared with older children (Evans, 2001).

d) Efficacy of opioid therapy should be assessed using a valid and reliable neonatal pain scale. Sedation level should also be assessed regularly, monitoring for the attainment of desired sedation level or inadvertent oversedation.

e) Opioid-induced cardiorespiratory side effects in neonates are uncommon.

5) Managing opioid tolerance and dependence.

a) Tolerance is decreasing pain relief with the same dosage over time and is exhibited by increased wakefulness and increased sympathetic responses, such as high-pitched crying and tremors when handled or disturbed. Tolerance to opioids is usually managed by increasing the dose, although adjunctive analgesics or sedatives may also be clinically beneficial.

b) Neonates who require opioid therapy for more than several days should be weaned slowly to prevent withdrawal symptoms, such as signs of neurologic excitability, gastrointestinal dysfunction, autonomic signs, poor weight gain, and skin excoriation due to excessive rubbing.

c) The prevalence of opioid withdrawal is greater in infants who have received fentanyl as opposed to morphine. Similarly, infants who receive higher total doses or longer duration of infusion are significantly more likely to experience withdrawal (Dominguez et al., 2003).

d) **Data are insufficient to determine the optimal weaning rate of opioids to prevent withdrawal symptoms in neonates on opioid therapy** (Hudak et al., 2012).

(1) Ducharme and colleagues (2005) reported that adverse withdrawal symptoms in children who received continuous infusions of opioids and/or benzodiazepines could be prevented when the daily rate of weaning did not exceed 20% for children who received opioids/benzodiazepines for 1 to 3 days, 13% to 20% for 4 to 7 days, 8% to 13% for 8 to 14 days, 8% for 15 to 21 days, and 2% to 4% for more than 21 days.

(2) A weaning scale such as the modified Neonatal Abstinence Scoring System should be used to manage opioid withdrawal in neonates exposed to prolonged opioid therapy (Finnegan, 1990) (see Chapter 3).

6) Minimal evidence exists regarding the efficacy of intranasal drug delivery for short-term procedural sedation and analgesia in infants in the NICU (Ku et al., 2018; McNair et al., 2018).

c. Nonsteroidal antiinflammatory medications.

1) Acetaminophen is the most common nonopioid analgesic administered in the NICU.

2) See Table 16.3 for dosing recommendations based on gestational age.

3) Although acetaminophen may be effective for short-term management of mild to moderate pain, it has not been demonstrated to be effective for acute procedure-related pain.

4) A synergistic effect is noted when IV acetaminophen is administered concurrently with opioid analgesia. This paired dosing allows for a reduction in dosages of both drugs, thereby resulting in fewer adverse side effects (Menon et al., 1998; Ohlsson and Shah, 2016).

d. Topical anesthetic agents.

1) The most common topical application of local anesthetics for procedure-related pain in the NICU includes EMLA cream and liposomal lidocaine cream (LMX 4%).

2) Although EMLA has the strongest evidence base for use in neonates, LMX has a faster onset of action without the risk of methemoglobinemia.

3. Other considerations.

a. Sedatives suppress the behavioral expression of pain and have no analgesic effects.

1) Sedatives should only be used when pain has been ruled out.

2) When administered with opioids, sedatives may allow more optimal weaning of opioids in critically ill, ventilator-dependent neonates who have developed tolerance from prolonged opioid therapy. However, no research has been done to determine the safety or efficacy of combining sedatives and analgesics for the treatment of pain in infants.

3) The two most commonly used sedatives in neonates are midazolam and chloral hydrate.

b. Neuromuscular blocking agents.

1) Chemical paralysis is often used in severely ill neonates to maximize oxygenation and ventilation.

2) Because the use of paralytic agents masks the behavioral signs of agitation and pain, sedatives or analgesics should be used in conjunction with paralytics.
3) Although not readily available at the bedside, emerging technologies such as near-infrared spectroscopy (NIRS), amplitude-integrated electroencephalography, functional magnetic resonance imaging (fMRI), skin conductance, and heart rate variability assessment are being explored for efficacy in assessing pain in infants who are receiving moderate to heavy sedation or paralytic agents (Hall and Anand, 2014; Holsti et al., 2011; Mele, 2018).

Pain Management at End of Life

A. **Neonates at end of life (EOL) deserve a good death free of pain and suffering. A good death has been defined as "one that is: free from avoidable distress and suffering for patients, families, and caregivers; in general accord with patients' and families' wishes; and reasonably consistent with clinical, cultural, and ethical standards" (Committee on Palliative and End-of-Life Care for Children and Their Families; Board on Health Sciences Policy; Institute of Medicine, 2003, p. 40).**
B. Although no pain scale exists that specifically assesses pain in neonates at EOL, use of a pain scale is a clinical standard, provides an objective approach to assessing pain, and may allow for better symptom control (Carter and Jones, 2013).
C. **As it is often difficult to accurately assess pain in neonates at EOL, caregivers should consider risk factors for pain and use physiologic measures to guide pain management decisions.**
D. Although dying adults commonly receive opioids to relieve suffering at EOL, opioids are not routinely administered to critically ill or dying infants when life support is being withdrawn or withheld (Partridge and Wall, 1997).
E. Opioid doses well beyond those described for standard analgesia are often required for infants who are in severe pain or who have developed tolerance after the prolonged use of opioids (Partridge and Wall, 1997). Therefore, continuous infusions of opioids should be titrated to desired clinical response (analgesia).
F. Nonpharmacologic comfort measures (e.g., reduction of noxious stimuli, organization of caregiving, and positioning and containment strategies) should be used in conjunction with pharmacologic interventions to palliate pain and distress in infants at EOL.
G. Palliative care services may provide additional support to parents and health care providers caring for an infant at EOL (Currie et al., 2016).

Parents' Role in Pain Assessment and Management

A. Parents have many concerns and fears about their infant's pain and about the interventions used in the treatment of pain (Franck et al., 2005; Gale et al., 2004). Parents may fear the effects of pain on their child's development. They may also fear that their infant may become "addicted" to the analgesics (Franck et al., 2004).
B. Parents and health care professionals must talk openly and honestly about acute and chronic pain associated with medical diseases, as well as about pain associated with operative, diagnostic, and therapeutic procedures.
C. Parents should receive accurate and unbiased information about the risks and benefits of (as well as alternatives to) analgesia and anesthesia so that they can make informed treatment choices (Harrison, 1993).
D. Parents' cultural and religious beliefs about pain should be taken into consideration when determining a pain management plan.
E. **Parents should be taught to observe how their infant expresses pain through physiologic and behavioral cues.**
F. **Parents should be educated and engaged as partners on how they can assist caregivers in providing nonpharmacologic comfort measures, such as facilitated tucking, to their infants during minor painful procedures** (Axelin et al., 2006; Axelin et al., 2009; Axelin et al., 2010; Marfurt-Russenberger et al., 2016; Palomaa et al., 2016).

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CHAPTER 17
Families in Crisis

Carole Kenner and Marina Boykova

OBJECTIVES

1. Define the concepts of crisis, grief, and bonding.
2. Describe assessment strategies for families in crisis.
3. Identify nursing interventions to support families.
4. Identify characteristics of adolescent parents.
5. Identify strategies for families experiencing perinatal or neonatal end-of-life issues.

With current technological advances, the most acutely ill or premature infant, even one born as early as 23 weeks' gestation, has a good chance of surviving and going home. Although technological advances are increasing the odds of having a neonate live, it may come with a price. When a newborn infant requires intensive care at birth because of illness, prematurity, congenital malformations, or lethal disease, the effects of these unexpected events on the parents can be overwhelming. The families of these infants may experience multiple crisis events during the infant's hospitalization and after discharge. This situation and stress can be exacerbated if the parent is an adolescent. The focus of this chapter is on the psychosocial and environmental aspects of supporting parents who are coping with stressful events. The emphasis is placed on creating a supportive environment for parents of sick or premature newborn infants.

A. Definitions.
   1. Crisis. Crisis is defined as a temporary disequilibrium that occurs when people face an important problem or transitional phase so stressful that they are unable to effectively cope by using their customary problem-solving resources (Howland, 2007). This crisis will continue until new ways of coping can be developed and maintained (Caplan et al., 1965; Kaplan and Mason, 1960).
   2. Bonding. Bonding is a gradual, reciprocal process that begins with acquaintance. It is a unique and specific relationship between two people and endures across time. Bonding occurs on a different timetable for mothers than fathers. Although mothers experience a sharp increase in bonding around the fifth month of pregnancy and have intensifying feelings throughout the pregnancy, the father's feelings usually tend to develop more slowly than the mother's and become congruent after birth when infant caregiving begins (McGrath, 2014).
   3. Attachment. Attachment is the quality of the bond, or affectional tie, between parents and their infant, which begins early in the prenatal period, appears to increase when fetal movement is felt, and is intensified with interaction between the parent and the infant after birth.

Grief

A. Grief is the response of sadness and sorrow to the loss of a valued object (Kenner, 2014).
   1. Anticipatory grief is grieving that occurs before an actual loss.
   2. Chronic grief is unresolved or blocked grief, frequently seen in the parents of a child with a disability when there is a constant reminder of the loss of an ideal "healthy" child.
   3. Signs of grief reaction include sadness and despair, denial, numbness, shock, disbelief, and anger, as well as fatigue and sleep disturbances (Golish and Powell, 2003).
   4. Uncomplicated grief resolves through stages: shock and disbelief, awareness of the loss, and eventual recovery in the form of reestablishment of well-being (Teel, 1991).

B. Crisis and the birth of the sick or premature infant. Pregnancy and transition to parenthood are exciting yet stressful events that are referred to as *developmental or maturational stressors.* These major life changes are expected, and some difficulties with life adjustments are anticipated. In contrast, the birth of a premature or sick infant or the death of an infant are unexpected life events; such events are referred to as *situational or accidental stressors* for which a person or family is often psychologically unprepared (Watson, 2011). When such maturational and situational stressors occur

simultaneously, the resulting pressure can overwhelm a person's usual coping resources and support system, thus leading to crisis. Several psychological tasks and phases have been identified that the mother/father and family must accomplish to cope with the crisis of a premature birth or the birth of a sick infant.

1. **Failure to deliver a term infant.** Parents, and especially mothers, often struggle with feelings of guilt and failure related to the loss of an "ideal" infant (Golish and Powell, 2003; Shah et al., 2011). Family members may also be, or be perceived as, blaming the mother for giving birth to a premature infant. Family members may also feel guilty as if they, too, have contributed to the infant's condition and, in some instances, blame the mother for the infant's problem.
2. **Grief.** Unfortunately, not all pregnancies result in a healthy term infant. When adverse neonatal events occur, the parents might be overwhelmed by grief (Dyer, 2005; Golish and Powell, 2003). As the parents realize that their newborn is "less than perfect" and not the infant of their fantasies, acute grief reactions occur. Grief is also related to the loss of imagined parenting activities (e.g., hospital birth with infant admitted to the newborn nursery) and the absence of symbolic rituals (e.g., baby shower). With neonatal death, the parents also grieve for the lost opportunity to parent the child. Because uncertainty about infant outcomes is often present, the loss can be ambiguous, making parents emotionally and physically exhausted (Boykova et al., 2014; Golish and Powell, 2003; Kenner et al., 2015).
3. **Possible loss of the infant and uncertainty about infant's health outcomes**. Parents often consider the possibility of death or disability of the infant while simultaneously hoping for the infant's survival (Lasiuk et al., 2013). The uncertainty about outcomes influences parent–child relationships and parental well-being, leading to increased levels of anxiety and depression (Brandon et al., 2011; Rogers et al., 2013).
4. **Developing relationships with the infant in a stressful environment**. Parents who have an infant born ill or premature may have difficulty bonding and developing their parental identity. In the beginning, parents struggle to develop secure relationships in the unfamiliar and stress-provoking settings of the intensive care unit (Bozzette, 2007; Bozzette and Holditch-Davis, 2015; Gibbs et al., 2015; Korja et al., 2012; Spinelli et al., 2016). When an event occurs that affects the attachment between a parent and infant, parents are potentially placed in a state of increased anxiety, leading to difficulties in establishing a nurturing relationship with the infant. Opportunities for parents to learn to interpret their infant's unique needs and to develop reciprocal interaction through sensitivity to behavioral cues are also interrupted (Boykova et al., 2014). Environmental stressors of the neonatal intensive care unit (NICU) (e.g., lights, noise, and equipment) influence parental perception of the infant, parental role development, and parental interactions with the infant (Holditch-Davis et al., 2011; Miles et al., 2011). The relationship between earlier parent–infant attachment and later parenting behaviors has been well established (Borghini et al., 2006; Forcada-Guex et al., 2011; Korja et al., 2012). Once the threat of the infant's loss has passed, parents begin to make efforts to participate in the infant's care and gain more confidence in their caregiving abilities.
5. **Preparing for taking the infant home** is another task for parents (Smith et al., 2009; Smith et al., 2012). Parents might have difficulty understanding the special needs and characteristics of the premature or sick infant and the necessary precautions that must be taken. The negative psychological impact of having a sick infant often continues after discharge, resulting in parental psychological distress (Boykova, 2016b; Boykova and Kenner, 2012; Hall et al., 2015; Smith et al., 2013).

C. **Consequences of crisis.**

One of the most difficult tasks parents face when their newborn infant is sick or preterm deals with resolving the discrepancy between the idealized and the real infant. A family in crisis expends most, if not all, of their energy trying to resolve the crisis of unanticipated birth complications. Thus, little energy is left to interact with their newborn. Alteration in the parental role related to the infant's sickness and hospitalization might lead to diminished parental attachment to the infant and decreased parental confidence in their own abilities to give care to and keep their infant safe (Holditch-Davis et al., 2011; Miles et al., 2011). Alteration in parental role may be caused by the fear of the NICU equipment surrounding their infant and their inability to provide infant care while he or she is in critical condition (Boykova, 2016a, 2016b; Bozzette, 2007; Korja et al., 2012; Meijssen et al., 2011). The psychological impact of having a sick infant often continues after a successful discharge, resulting in elevated parental worries during the transition to home (Boykova, 2016a; Boykova and Kenner, 2012; Boykova et al., 2014). Maladaptive and overprotective parenting may result in the vulnerable child syndrome (VCS) and compensatory parenting (Greene et al., 2017; Kokotos and Adam, 2009; Miles and Holditch-Davis, 1995). Conversely, parental outcomes might include emotional disengagement and deprivation and low adherence to follow-up recommendations in the postdischarge period (Ballantyne et al., 2012; Ballantyne et al., 2014) that, in turn, might affect infant development and growth.

During the crisis period (and often afterward), parents often display signs of anxiety, depression, increased levels of stress, fear, and powerlessness (Harris et al., 2018; Hynan and Hall, 2015; Solberg et al., 2011). They also may exhibit symptoms of posttraumatic stress disorder (PTSD), as well as physical or cognitive problems such as short-term memory problems, confusion, and inability to multitask (Hynan et al., 2013; Jubinville et al., 2012; Vanderbilt et al., 2009).

During the crisis period, parents are more receptive to overtures of help from other family members, friends, and the health care team. Coping mechanisms are intimately tied to social and health care professional support, as well as available resources (Boykova, 2016a; Jones et al., 2009; Pinelli et al., 2008). Cultural values and beliefs, and spirituality in some instances, also affect the perception of stressful situations and influence coping styles (Brooks et al., 2016; Heidari et al., 2012). Often, parents search for causes of the infant's condition; they also intensely search for all possible health outcomes when having a vulnerable child. This searching for answers, coupled with fatigue, anxiety, and symptoms of PTSD, may lead to tensions and decreased communication between parents. The breakdown of the family at a time the couple needs support may exacerbate the crisis.

D. Specific populations of parents: Adolescents.

Parents who are adolescents have some unique needs. Adolescence is a turning point or a change period. It moves a child from childhood toward the maturation of the adult; physical appearance changes, and the adolescent is capable of childbearing. Some developmental tasks of this period are (1) independence from adults; (2) role identification; (3) need for a stable, realistic, and positive sense of self; (4) preparation for financial security; (5) identification of one's own moral/ethical values; and (6) development within a social context. Adolescents often strive to have an identity unique from those of other family members. They are developing their self-concept and self-esteem. The peer group becomes important for validation of the attitudes, values, and beliefs. Adolescent parents may have engaged in other risky behaviors besides being sexually active. She or he may smoke, drink, or use drugs. She or he might be at risk of having human immunodeficiency virus (HIV) infection and other sexually transmitted infections (STIs). These risks are not unique to adolescents, but such behaviors are more likely to occur because of the feelings of invincibility that accompany this age. Moreover, a female adolescent may have sought pregnancy as a way to have someone need her. She may not seek prenatal care or may try to hide the pregnancy by limiting weight gain. These actions may put her health and her infant's health at risk.

Adolescence is a time of constant change and turmoil and a period of maturational changes. It is a period of vulnerability to a crisis occurrence should a traumatic event be added to the developmental transitional state. Adolescence is the time when childbearing becomes a potential reality for most individuals. In addition to dealing with the usual developmental tasks, adolescents undergo the crises of early parenthood and of having an infant in the NICU. Sometimes adolescents' developmental tasks can be in conflict with their tasks/needs as new parents, creating elevated levels of stress, anxiety, anger, and distancing from family or friends. The nurse must be aware of these conflicts and realize the unique blending of needs and tasks. As health professionals, we often make assumptions of what adolescents need or what type of parents they will be. The reality is they need to be assessed for their knowledge, level of crisis, and available supports. It has been shown that adolescents often underestimate the severity of their infant's illness (Boss et al., 2010; Farnell et al., 2012; Grassley, 2010) and require increased levels of informational and esteem/appraisal supports (Logsdon and Koniak-Griffin, 2005; Phipps et al., 2013). Adolescents should not be treated as bad parents or judged to be immature in their actions.. Health professionals must evaluate parental needs of adolescents certainly within the context of their developmental stage but also with consideration of their personal, individualized needs (Riesch et al., 2010). Events that stimulate the occurrence of a crisis for teenage parents can originate from being in a transitional state (such as moving from adolescence to adulthood and moving from childhood to parenthood), violating customs or cultural norms embedded in the social-cultural structure (such as having a newborn and being a teenager), role confusion (being a child and a parent at the same time), lack of experience with parenthood, and giving birth to a sick newborn infant. When teens become pregnant, they often experience the following:

1. **Loss of peer group support.** Adolescents' peers often separate from their peer that is pregnant or has a child, leaving the new mother or father without their usual peer group support. Feelings of social isolation may result. Often, teenage parents are tied down to taking care of a newborn or having to arrange for child care at a time when peers are freely going to sports, games, and dances and having fun.
2. **Disruption of family ties.** The pregnant adolescent and her boyfriend often bring on direct conflict with their parents. The essence of this conflict is that, in many cultures, the parents of the adolescents believe that adolescence is an inappropriate time to start a family and that the adolescents need to live by the parental house rules. At the same time, the adolescent parents may be trying to take on adult responsibilities while feeling that they are being treated as children. Such conflict diminishes the levels of possible positive social support,

making development of adolescent parenting identity more complicated. It also disrupts the levels of caregiving confidence in underage parents when the adolescents' parents try to make decisions regarding the coming/newly born infant. Once a teenage girl delivers a baby, she is considered an emancipated minor who can make independent decisions for herself and her child. However, this legal status does not mean that developmentally she may feel ready to take on critical health care decisions about her infant.

3. **Emotional distress.** The pregnant adolescent may be emotionally immature and may react inappropriately to the birth of an infant, for instance, expressing arrogance and denial of the severity of the situation or expressing very unrealistic expectations of an infant and of herself or himself as a parent. Adolescents also might interrupt her or his education to bear and raise a child, jeopardizing their personal and family future. She or he may be forced into a marriage due to cultural values specific for her or his ethnic or racial group. Cultural characteristics must be considered as well. In some cultures, she will have full rights to determine the future for her child without consultation with the father or other family members. But in other cultures, the father must make the decisions about the family—no matter what the marital status may be. These decisions are not always congruent with the legal rights afforded by society to the mother. The pregnant teen may be excluded from decisions regarding whether to keep the child, the placement of the child after birth, visitation rights, and other formal or informal ties. In addition, the infant can be at risk of having faulty or negative parent–infant interactions, caused by the parents' lack of understanding of the normal growth and developmental process due to their own immaturity and educational level. An infant who is premature may be more irritable, feed poorly, have poor self-regulatory behaviors, and be difficult to console. This seeming lack of responsiveness to parenting efforts often reinforces the adolescent parents' poor self-esteem and poor self-concept, which often accompany adolescent pregnancy. The infant may also be at risk of experiencing abuse or neglect.

E. **Assessment of families in crisis.**
Understanding the origins of a crisis and the links with the normal "ups and downs" of life is crucial to successful assessment and intervention.

1. **Determine the parents' understanding of the situation** (i.e., realistic vs. distorted). The parents' ability to resolve the crisis depends on their realistic perception of their situation: they need to be fully informed about their infant's condition and expected progress/outcome. An inability to comprehend the crisis may be related to low socioeconomic status, educational level, or cultural values and beliefs. Parents of a lower socioeconomic status or educational level may not fully understand what to expect of their infant or their role because they may lack good role models for themselves. Older mothers may have difficulty in coping, as they are used to being in control of their situations. They may actually blame the health professionals for the adverse outcomes of their pregnancy and delivery. Cultural values and beliefs also may play a role because different cultures view the infant in relationship to parents in different ways, and these parents' view of health and death may be different from the typical U.S. views (Callister et al., 2011; Obeisat and Hweidi, 2014; Zauderer, 2009). Whereas in Western culture, people crave control over the environment, other cultures may view this as fate (Cone, 2007). When crucial conversations are necessary, the family's cultural values must be considered.
2. **Determine the parents' grief response**. The extent to which parents are experiencing grief must be determined. Grief responses to death, premature birth, or the birth of an infant with a malformation are similar; however, the grief responses do not necessarily occur in the same sequence for all people. Sequence of stages of grief such as shock, denial, anger, and acceptance may or may not be followed. Grief is very individualized and may be in the form of anticipatory grief because the parents fear the infant might die, even though the physical condition does not appear to warrant this fear. Consider this within the cultural context of the family because in some cases, it may not be acceptable for parents to express grief or worries to outsiders. Grief reactions are mediated by cultural beliefs and values as well as the parents' developmental stage (Whitaker et al., 2010). In addition, the responses may overlap and recur.
3. **Determine the parents' willingness to participate in caregiving.**
Parents may be fearful that they cannot provide care or that their care might do more harm than good.
4. **Identify the development of attachment behaviors.** Mothers' activity with their infants has been found to be indicative of the initial adjustment to the infant, important past and present interpersonal relationships, and involvement in taking care of the infant. Examples of attachment behaviors include the following:
   a. Touching: typical maternal progression of touching the premature infant is from fingertip touching of the infant's extremities to palmar stroking of the infant's trunk, to holding and embracing the infant. This progression of touch

usually occurs during a period of several visits to the NICU.
   b. Looking en face: aligning the head with the infant's head in the same plane to make eye-to-eye contact with the infant.
   c. Talking to the infant, calling it by name.
   d. Bringing pictures, toys, and/or clothes to the hospital.
   e. Participating in caregiving activities such as feeding, bathing, and clothing the infant.
5. **Evaluate parent–infant bonding and attachment**. Positive behaviors include the parent visits frequently, has named the infant, makes positive comments when talking to or about the infant, demonstrates increasing skill in caregiving/holding the infant, and displays increasing eye and body contact (i.e., kissing, fondling, stroking, nuzzling) (Mercer, 1977). Behaviors of concern include the parent is overly optimistic, appears unconcerned about the infant's condition, does not ask questions, is passive or indifferent, avoids close body contact by holding the infant at a distance, and attributes inappropriate characteristics to the infant, such as "she's lazy and stubborn just like her father." Make sure these areas of concern are considered within the context of the culture of the parents. Different cultures approach parenthood and parent–infant interaction in different ways. In some cultures, only male offspring are valued, and girl babies are dismissed as nonessential; in some cultures, the birth of an infant that has been hospitalized in an NICU leads to stigmatization (Heidari et al., 2012); touching an infant's head is seen as threatening by some Southeast Asians, Buddhists, and native Hawaiians (Cone, 2007). In addition, the ongoing patterns of parental behaviors should be assessed rather than viewed as isolated incidents.
6. **Note the pattern of parental visiting to the NICU, duration of visits, and frequency of phone calls.** This pattern, if abnormal, is predictive of maternal parenting difficulties. If parents are not visiting frequently, be careful to determine the reasons (e.g., cultural practices after childbirth, conflicting obligations between work and family roles, or lack of transportation to the hospital) before assuming that the parents are unconcerned or that parenting difficulties exist.
7. **Determine the parents' adaptation to and coping with the stressful event**. Assess the parents' ability to maintain their relationship with one another. Activities of daily living should be assessed in parents, such as personal grooming, eating, appropriate clothing, etc. Assess whether parents can maintain the lifestyle they led before the crisis. For instance, ask if they are returning to work, able to do housekeeping activities, care for any other children in the household, or have financial issues. Single parents might require additional assessments to determine what social supports or help they have or any unique concerns they are facing.
8. **Determine what support systems exist** for the parents and whether they are being used. It is also important to determine whether these supports are positive. Find who the significant others in the lives of parents are; consider biologic kinship (family) and/or emotional kinship (friends). Determine if any professional/peer support is available (psychologist, counseling, parent support group). Address cultural specifics; for example, Latinos value the inclusion of the extended family and view illness/death as having associated rituals (Cone, 2007).
9. **Determine the parents' preparedness to go home.** Most hospitals have a discharge checklist that indicates what the parents have been taught, such as cardiopulmonary resuscitation (CPR), car seat safety, feeding schedules, and any medications that the infant may require. Assess, too, if they have a safe place to stay and whether there are any concerns, such as heat, running water, public or other transportation, and support people to help them.
10. **Determine the access to the primary care postdischarge**. Check to see if referrals have been made to early intervention (e.g., zero to three programs, high-risk follow-up clinics), and ensure that a primary care practice is identified.

F. **Management of crisis and grief.**

Because nurses work directly with parents, they are in a key position to anticipate a family crisis and to promote positive coping and effective use of social supports. Nurses are the primary health care providers who help parents overcome a crisis. The assessment skills of a nurse and appropriate nursing interventions are of vital importance to the well-being of the family. The nurse is the advocate for the family who has the most continual interactions with parents.

Whereas most of the current research focuses on the maternal role and the mother's level of distress, fathers must be considered too. The father's perception of a crisis is just as important as the mother's, and interventions to ease his distress must be part of the preparation for taking an infant home (Garfield et al., 2014; Kim, 2018; Tooten et al., 2013). Facilitation of parent–infant interaction and attachment is a vital component of nursing care for parents of high-risk infants. The development of a warm and nurturing relationship between infant and parent is essential for a healthy psychological outcome to the family (Hall et al., 2015). "The parent 'at risk' cannot resolve a crisis surrounding birth of his/her infant and simultaneously establish warm attachment bonds while retaining his or her self-esteem without the support of others in the social system" (Mercer, 1977, p. 5). When interventions are put into

place to promote effective coping, the crisis will resolve, and psychological equilibrium, a necessary step toward the establishment of a healthy parent–child relationship and family well-being, will be restored. The Creating Opportunities for Parent Empowerment (COPE) program has demonstrated decreased stress, shortened length of stay, and increased coping by involving parents in their infant's care (Melnyk et al., 2006; Melnyk et al., 2008; Melnyk and Feinstein, 2009). A positive environment can be created by adopting the philosophy of family integrative care. In 2015, the National Perinatal Association published "Psychosocial Program Standards for NICU Parents" (Hynan and Hall, 2015) that promote evidence-based recommendations to provide integrative care. Before these recommendations can be enacted, the following factors that influence the family must be considered:

1. Promoting parental understanding of the infant's health problem and the need for NICU care.
2. Promoting parental understanding of the importance of their parental role.
3. Resolving/lessening of the family's grief and guilt reactions related to the birth of an unwell infant and their need for NICU care.
4. Involving parents in caregiving activities as partners in care.
5. Using positive coping mechanisms and social supports (Boykova et al., 2014; Purdy et al., 2017).

Many of the strategies and interventions are the same for all groups of parents because they represent parenting needs. Cultural influences must also be considered. Following are some interventions and strategies that can help alleviate the pressure of NICU hospitalization for parents.

Interventions for Facilitating Crisis Resolution

A. **Be present with the physician or nurse practitioner at the initial meeting with the parents.** The first encounters parents have with health professionals are important. Knowing the caregivers who provide care for their infant helps decrease parental anxiety and stress. During the family's first visit, ensure that the nurse assigned to the infant stays at the bedside to explain the equipment and the infant's condition and to answer questions, provide emotional support, and provide encouragement to touch the infant.

B. **Use consistent caregivers for the premature or sick infant to establish a rapport with the parents.**

C. **Talk with the mother and father together whenever possible.** Consider the cultural values of each family. In some cultures, the father must receive the information first (Kenner, 2014). Give families the opportunity to share their feelings; listening to concerns (conducting "listening visits") helps families combat depression and anxiety (Purdy et al., 2017; Siewert et al., 2015).

D. **Address the parents' perceptions of the infant's condition.** Talk with the parents to learn about their concerns and perceptions. As health professionals, we often follow our own perceptions and discuss issues we deem important without validating whether the views are shared by the parents. Avoid power struggles with parents by defining their role and recognizing that they are the parents and that the infant is theirs, not the staff's.

E. **Be consistent with information given to parents.** If the infant is hospitalized in a NICU where the physicians or nurse practitioners rotate frequently, be sure to explain any changes that may result from provider preferences in care management. If parents do not understand the basis of these changes or are not told when their infant's condition really changes, then mistrust begins (Boykova et al., 2014). Convey a positive, realistic attitude about the infant rather than a negative or fatalistic viewpoint, which may alienate the parents and impair attachment (Boykova et al., 2014).

F. **Do not overload parents with detailed information about their infant during their initial visits to the NICU**. Provide the basic facts and allow the parents to have some time to process the information. Help parents to understand the information given by repeating information that is either given verbally or written. Often parents do not hear all of what is said due to their stress. Give them information on the disease process their infant is experiencing so they know what to expect.

G. **Periodically assess the parents' understanding of their infant's condition and their interpretation of the information given to them**. Information must be reinforced throughout the hospital stay. Whenever anyone is anxious, little information is actually heard or retained.

H. **Address the grief response.** Males and females express their grief in different ways. However, most, if not all, parents experience some form of grief by just having an infant who requires specialized care (Boykova et al., 2014). This reaction must be assessed throughout the hospital stay. Sometimes the response is directly tied to their understanding of the infant's condition. At other times, it is related to cultural beliefs and values.

I. **Acknowledge any feeling of guilt that might be expressed about the unexpected birth outcome**. Let the parents know that these feelings are normal (Gardner et al., 2016). Be a very good, attentive listener; observe body language; and help parents verbalize their feelings (Gardner et al., 2016).

J. **Give parents the freedom to express negative feelings without being judged.** Fear and frustration over the inability to control their infant's circumstances are often the basis for parental anger displaced to staff. Remember that situational control is not acceptable in

all cultures, so it is important to ask what is making parents uncomfortable. In addition, a positive way to approach and possibly decrease their anger is to ask them what would help them feel more comfortable.

K. **Encourage the parents to keep a journal concerning their experience of delivering a premature or sick infant.** This action can assist families to work through their feelings, as well as having memories to review what happened and reflect on issues that have been or have not been resolved (Howland, 2007).

L. **Facilitate adaptation of the parents' new role.** If at all possible, show the infant to the parents in the delivery room and allow them to touch the infant, if only for a few moments, to facilitate bonding. This also helps establish the reality of the infant for the parents (Boykova et al., 2014). Allow time for the parents to get used to the infant's appearance; start involving parents in the care with small tasks (such as holding the hand, holding the pacifier, propping the bottle). Write notes from the infant to the parents concerning the infant's status (e.g., equipment, feedings, oxygen concentration) and, if the parents wish, take pictures of the infant periodically. A notebook containing the notes and pictures can be kept at the infant's bedside for the parents. These can be memory books or scrapbooks that become especially important if the child dies. This intervention should be individualized because not all parents want this form of "communication." However, for some parents this is one strategy that promotes positive attachment (Gardner et al., 2016).

M. **Give positive reinforcement to parents as they interact with their infant.** For example, say that "He seems to calm down when you talk with him" or "She really seems to sleep better after you have held her" (Kenner and McGrath, 2010). Assisting parents to recognize positive changes in the infant in response to their caregiving has a strong impact on the parents and increases their feelings of success.

N. **Encourage parents to participate in the care as they desire.** Parents need to understand their role and develop themselves as parents. If professionals provide all the care, a clear message is conveyed to the parents that they are not capable of helping their infant. With help and encouragement from nurses, parents are the best caregivers. The role of parents in an NICU has changed (Thomas, 2008), and now parents are a part of the health care team. Taking part in their infant's care helps parents to ease the crisis, decrease guilt and grief, increase parental attachment to a baby, and increase the psychological well-being of parents. Allow the parents to provide "kangaroo care" (or skin-to-skin contact, done by placing the naked infant next to the parent's naked chest with a blanket or gown draped over the parent and infant) and to participate in comfort care and feeding their infant (Bigelow et al., 2012; Neu and Robinson, 2010; Skene et al., 2012; Welch et al., 2012). Explain to parents of very premature infants the relationship between neurologic maturity and the capacity for handling stimulation (Holditch-Davis and Blackburn, 2014).

O. **Give the mother the opportunity to provide breast milk for the infant should she so desire and support her in this endeavor**. However, be careful not to overemphasize the importance of breastfeeding. The rationale is that if she should be unsuccessful or decide to stop breastfeeding, feelings of guilt or disappointment may occur if breastfeeding has been touted as the only ideal infant feeding method.

P. **Model nurturing parenting behavior, such as stroking, touching, and talking to the infant, for parents who may need assistance in developing positive parenting behaviors** (Welch et al., 2012). Assist the parents with holding and cuddling their infant as soon as possible, taking into consideration the infant's condition and the parents' readiness (e.g., assist in managing respiratory and monitoring equipment and intravenous lines). Identify and address situations in which there are difficulties in parent–infant interaction or problems in the family's functioning.

Q. **Encourage the parents to visit their infant, but do not refer to the parents as visitors**. Parents are not visitors. They are partners in care, as well as an integral part of the infant's care and thus should be a focus of nursing care too. Before the first visit to the nursery, prepare the parents for what to expect by giving them written information about the unit, describing the atmosphere of the nursery (i.e., noise, high activity level, infants attached to various kinds of equipment), and discussing the positive aspects of their infant's health/appearance as well as deviations. If the mother is unable to visit due to her own health conditions, the father can be given pictures of the infant for the mother (consider cultural preference in each case). In addition, the mother should be given the phone number of the nursery and encouraged to call as often as desired. Encourage opportunities for siblings to engage with the infant by drawing pictures for the baby or visiting the infant in the NICU according to visitation guidelines.

R. For the parents of an infant born with a malformation, encourage the parents to see the infant together as soon as possible, but do not force them to interact. Point out to the family the normal qualities of the infant, as well as the abnormalities (Boykova et al., 2014).

S. **Promote a developmentally supportive environment for the family.** Use of individualized family-centered care is important if the family is to be helped through this crisis (Kenner and McGrath, 2010). For example, kangaroo care, dimmed lights or cycled lights, private areas for parent interaction with the infant, and

swaddling or cuddling of the infant promotes positive development of the infant and family (McGrath, 2014). It is important to include not only mother but the father as well. Encourage parental stays within a more homelike environment, and include parents as an integral part of the health care team (Kenner and McGrath, 2010). Identify infants who are at risk of having developmental difficulties (Kenner and McGrath, 2010) and address the parents' needs regarding their infant's development.

T. **Determine the parents' social support networks and encourage parents to attend a parent support group if they desire**. The social support network may include family, friends, clergy, and health professionals. Also determine whether the level of support is adequate from the parents' and the health professionals' standpoint. Online and telephone-based peer support and parent support groups are examples of strategic interventions for parents with an infant in the NICU who require increased levels of social support (Ardal et al., 2011; Liu et al., 2011; Morris and Bertram, 2013). Involvement in a parent support group has been demonstrated to facilitate parental grieving, reduce fears, and increase feelings of parental competence. The interventions must be culture specific. In some cultures, it is not acceptable to discuss family problems openly.

U. **Identify the unique needs of the parent with lower socioeconomic status**. Parents may want to provide the best possible care to the infant but may either not know how to do so (poor role models) or may not have the means to provide for the infant's perceived needs.

V. **Encourage parents to share their concerns and fears with each other.** Often it is not until the infant is discharged that parents share their feelings with each other. This is another area where culture plays a role. In some cultures, expressions of concern are acceptable within the family unit but not with others. Health professionals may be viewed as authority figures and not ones to whom fears should be confided. It is important to find out what this illness and hospitalization mean to the family and to what degree they are viewed as stressors (Howland, 2007).

W. **Assist parents in maintaining their relationship with one another**. Reinforce with them that they must take time for themselves as a couple. If the mother is single, encourage her to maintain ties with other family members and her friends.

X. **Assist parents in maintaining their relationship with the infant's siblings by helping them recognize the needs of the other children and identify how the needs can be met**. For example, using coloring and activity books may help the young siblings express their feelings.

Y. **Suggest that the parents or siblings bring something for the infant, such as a small toy, pictures of the family members to be taped on the infant's bed, and/or a tape recording of the parents' voices to be played for the infant**. Share personalized information about the infant with the parents. This information can include statements such as, "She really enjoys sucking on her pacifier" or "He was really active while I was giving him a bath," to assist the parents in individualizing and accepting the infant.

Z. **Assist adolescent parents in developing their parental role**. Provide guidance and help them to learn infant care, recognize parental responsibility, and learn how to talk with their own parents. Role-model caregiving techniques—one on one, if possible.

AA. **After the mother's discharge from the hospital, maintain communication with the parents by providing them with the phone number of the unit**. For parents of transported infants, sending pictures and cards from their infant to show current status, arranging for transportation assistance through social service agencies for parents who lack means of travel, and maintaining frequent phone contact with parents can be helpful in promoting parent–infant attachment.

BB. **Provide a list of primary health care providers available**. Where appropriate also list social or early intervention services that might help the parents take care of their infant.

CC. **Be sensitive to cultural values and practices that may influence parent–infant behaviors and facilitate strong bonding and attachment**. Assess the cultural needs of minority parents—be culturally sensitive to what the parenting role means in that culture and then gear the interventions toward these cultural values and beliefs.

Interventions for Facilitating Grief Resolution

A. **Listen**. Parents need to be given the opportunity to express their feelings.

B. **Acknowledge the pain of their loss**. This gives the parents the opportunity to talk about their loss and provides support for acknowledging and working through their grief.

C. **Convey an attitude of acceptance, openness, and availability to the family**. Grieving people need permission to experience their feelings, regardless of how uncomfortable or unpleasant.

D. **Help the parents understand the individuality of the grieving process**. Mothers and fathers usually have "incongruent grieving"—they do not grieve at the same pace. This incongruence frequently leads to marital discord because of misconceptions about feelings and an inability to communicate.

E. **Refer to counseling/psychological assistance as needed.**

Interventions for Parents Experiencing a Perinatal Loss

Nurses are integral to preparing parents for a potential loss through clear communication. Advocate for a team/family meeting to discuss the plan of care, including neonatal/perinatal hospice.

A. **Encourage the family to see, hold, and spend time with the infant before and after death** (Catlin and Carter, 2002; Kenner, 2014). Consider cultural values in each case; seeing and holding a baby might help some parents with closure, but not other parents. It also may be appropriate to help the parents actively plan the care of their yet-to-be-born or dying infant through use of an advance directive (Catlin, 2005). Much like in the adult, the advance directive during either the prenatal or the neonatal period allows the parents to say what they wish to be done and whether they want to "allow a natural death," a term much more acceptable than a do-not-resuscitate order.

B. **Be sensitive to individual and cultural differences in rituals of saying goodbye**.

C. **Physically bring the family together and offer privacy**. Some hospitals have a neonatal hospice program in which the family is involved with the infant's care (Catlin and Carter, 2002; Kenner, 2014).

D. **Provide the parents with mementos if culturally acceptable.** Give parents photographs of the infant, identification bracelet, footprints, completed crib card, blanket, wisp of hair, and birth certificate. Keep these mementos in a file in the nursery for future retrieval should the parents choose not to take the items at the time of the infant's death. This intervention must be individualized according to the needs and desires of each family (Catlin and Carter, 2002; Kenner, 2014). This is a very culturally sensitive topic and must be explored with the family.

E. **Provide information about support groups and/or grief counseling**. Consideration for individual family wishes is important. Not all families want or would benefit from support groups. Family follow-up, even if just a phone call from an NICU nurse or hospice nurse a few weeks after the loss, is very helpful to many families.

F. **Encourage the parents to name the infant (again, consider cultural issues).** This task is very important for many parents. Dressing the infant in a diaper or loose clothing can allow the parents to have at least one image of their child as a baby and not a dying infant. Because the birth of a premature or a physically or neurologically challenged infant creates a sense of loss from the expected picture of their infant, the parents must resolve their grief before attachment with their infant can be fully achieved.

G. **Offer palliative care to parents.** This form of care provides pain management and psychological and spiritual support (Kenner et al., 2015). Provide a booklet about perinatal loss for the parents and siblings. Pediatric hospice and palliative care programs have a number of resources for parents and the left-behind siblings. There are many age-appropriate books and videos. A good resource is Children's Hospice International: www.chionline.org; 1101 King Street, Suite 360, Alexandria, VA 22314; phone: 800-2-4-CHILD.

H. **Discuss options for autopsy, disposition of the body, and a memorial or funeral service**. It is important to ask parents what they need and what they would like. Some parents wish to be an active participant in the plans; other families want these arrangements to be done for them. Rituals surrounding death are culturally driven; for example, taking pictures after death is not acceptable to Native Americans, Eskimos, Amish, Russians, Hindus, and Muslims. It is the family's choice (Kenner, 2014).

I. **Offer the option for the infant to be baptized**. This option is not acceptable in all cultures.

J. **Assist parents in understanding the importance of informing siblings about the death of the infant**. Suggest that they use simple statements based on the children's level of understanding. Many times, the siblings take the death much better than adults expect. Allowing them to see the infant after death may make the infant real to them. Of course, parental wishes should always be the guiding principle for how the siblings are informed of the death and what part they play in the rituals following the death. Again, this is a culturally sensitive issue, and beliefs must be explored with the family.

K. **Assist families of dying infants to tell you what they need.** End-of-life care issues are never easy but are especially difficult for new parents when celebration of a birth was the expectation. Ask the family to tell you what they need during these difficult times. Find out if parents want siblings and extended family, clergy, or spiritual healers involved. Asking them about what they think constitutes a good death is another important aspect of helping families cope (Kenner, 2014). Use of consistent information and the same message from all health care providers is important too. The use of a palliative care protocol is one method to ensure more consistency (Catlin, 2005; Catlin and Carter, 2002). Consideration of cultural differences once again is important (McGrath, 2014).

L. **Talk with parents about possible responses from family and friends, who often minimize the infant's death in an attempt to offer comfort**. Encourage them to delegate or give tasks to those who call. Simple tasks that can be delegated to others who truly want to help but do not know what to do may include doing laundry or buying groceries. More information on end-of-life care can be obtained through the joint project of the American Association of Colleges of

Nursing (AACN) and the City of Hope End-of-Life Nursing Education Consortium (ELNEC).

M. **Positive predictors of parenting outcomes** (Boykova et al., 2014).
   1. Anxiety level is moderate to high: Parent worries about the infant's chances of surviving, the possibility of abnormality, and competence as a mother or father.
   2. Seeks information about the infant.
   3. Demonstrates warmth toward infant and in other relationships.
   4. Has a support system (i.e., father of the infant, her mother, friends).
   5. Has had a previous successful experience with a premature infant (i.e., previous child, a sibling, other relative), which enables the parent to feel more experienced and confident.
   6. Recognizes positive attributes of the child (i.e., smiling).
   7. Views self positively.
   8. For an adolescent: has a centralized locus of behavioral control.
   9. Exhibits effective caregiving.
   10. Makes positive eye contact with the infant.

N. **Negative predictors of parenting outcomes** (Boykova et al., 2014).
   1. Exhibits an inappropriately low anxiety level.
   2. Demonstrates passivity—does not actively seek out information related to infant's condition.
   3. Has limited verbal interaction.
   4. Visits infrequently and for short periods in the NICU. (Remember that sometimes infrequent visits are due to a lack of transportation and not self-determined parenting problems.)
   5. Is unaware of the infant's needs.
   6. Has unrealistic expectations of the infant or the parenting role.
   7. Personalizes the infant's behavior as a lack of ability to parent or characterizes infant's behavior as "bad."
   8. During pregnancy, expressed little desire to have a child.
   9. Is more likely to express disappointment about the sex of the infant.
   10. Has no support system.
   11. Is an adolescent with little or no social supports.
   12. Exhibits role confusion.

O. **Summary of the key messages to support parents.**
   1. Help the mother/father reconceptualize her or his image of an "ideal" infant to the image of their premature, acutely ill, or malformed infant.
   2. Help parents to deal with feelings of guilt.
   3. Help parents develop relationships and affectionate ties with the infant by involving them in the infant's care and by helping them learn how to read the infant's behavioral cues.
   4. Assist parents in gaining confidence in parenting by encouraging them to participate in caregiving tasks.
   5. Promote communication between the parents and, if desired, extended family members.
   6. Be sensitive to the unique needs of the individual families.
   7. Assist families in preparing for the transition to independent care at home after discharge.
   8. Provide support for parents during the transition phase after their infant's discharge from the NICU.
   9. Assist parents in dealing with neonatal death in a personally meaningful way.
   10. Provide the parents the opportunity to talk about their cultural beliefs and values in relationship to parenting to understand their views of their infant and their role as parents.

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CHAPTER 18
Patient Safety

Joan Renaud Smith and Ann Donze

OBJECTIVES

1. Define the roles of culture and the learning system in maintaining a safe, reliable, and effective health care system.
2. Discuss the essential role families have in promoting patient safety.
3. Discuss the human factors systems approach and the relation to common errors.
4. Discuss specific strategies designed to decrease errors in health care.
5. Describe processes for responding when an error occurs.
6. Describe specific neonatal errors and recommended improvement strategies.
7. Describe the importance of discharge teaching to promote patient safety at home.

Patient safety is the prevention of errors and adverse effects to patients that are associated with health care (World Health Organization, 2018). Patient safety is a national priority, and improvement in patient safety has accelerated since the Institute of Medicine's (IOM) (now known as the National Academy of Medicine) report concluded that up to 98,000 lives are lost annually in U.S. hospitals as a result of error (Kohn et al., 1999). More recent estimates project nearly 200,000 deaths per year, which means medical errors kill 4 times more Americans annually than motor vehicle accidents (American College of Healthcare Executives [ACHE], Institute for Healthcare Improvement [IHI]/National Patient Safety Foundation [NPSF], and Lucien Leape Institute [LLI], 2017; James, 2013). Health care is one of the most complex industries in the world, and elimination of harm to patients and the workforce is both a moral and ethical obligation (ACHE, IHI/NPSF, and LLI 2017). Additionally, when patients experience harm, clinicians are often negatively affected—including risk for self-harm, depression, and isolation (ACHE, IHI/NPSF, and LLI, 2017). Yet nearly two decades later, only small-scale incremental and sustainable improvements to keep patients and the workforce safe have resulted. It is imperative that health care organizations strive to provide a healthy work environment for both workers and patients (LLI, 2013; Smith, 2017). Executive leaders must focus on patient and workforce safety as not only key improvement initiatives but also as core values that are embedded throughout the organization (ACHE, IHI/NPSF, and LLI, 2017).

The neonatal intensive care unit (NICU) is highly complex, involving many systems and subsystems; the reliability of these systems is in part due to the limitations in human performance (Bondurant et al., 2015; Handyside and Suresh, 2010). Medically fragile infants are defenseless compared with physiologically more mature newborns, leaving little margin for error. Infants receiving care in the NICU have been shown to experience wide variation in clinical care and outcomes (Murthy et al., 2014). Although some errors occur at the point of care (e.g., a nurse administering the wrong medication), most errors occur as a result of flaws within the health care system or facility design (e.g., excessive noise levels or lapse in human vigilance in the face of long work hours) (Agency for Healthcare Research and Quality [AHRQ], 2017a). Nurses are the last layer of protection between the patient and any system failure. Therefore, the NICU is an ideal environment to apply high reliability organization (HRO) principles to accelerate quality and safety (Bondurant et al., 2015). These principles are described as: (a) *preoccupation with failure* (e.g., staff aware of signs of deteriorating patients or processes that are not reliable/sustainable with transparent measurement); (b) *reluctance to simplify interpretation* (e.g., digging deeper into adverse events for root causes); (c) *sensitivity to operations* (e.g., understanding systems and how one system change may negatively affect another); (d) *commitment to resilience* (e.g., a just culture of psychological safety in which staff can share concerns about adverse events and what can be done to prevent them in the future); and (e) *deference to expertise* (e.g., empowering those who are closest to the patient to make informed decisions, which requires effective teamwork and communication) (Weick and Sutcliffe, 2007). There is no single formula for applying HRO principles in health care, but the IHI has taken these HRO principles and applied them to health care to develop a *Framework for Safe, Reliable, and Effective Care* (Frankel et al., 2017) (see later).

This chapter offers an introduction of basic patient safety principles and includes selected improvement strategies

Box 18.1

Selected Nontechnological Improvement Strategies Definitions

1. Five rights: rules traditionally thought to safeguard against errors. The five rights of medication administration (right patient, right drug, right dose, right route, and right frequency) are the basis of most education on drug administration and considered the "safe" way to administer medications. The five rights do not safeguard against major sources of error and may limit critical thinking.
2. Forcing functions: interventions that prevent error by "forcing" a safe action, such as removing concentrated potassium from the medication carts. Forcing functions are the strongest of interventions against human failure. A common example of a forcing function is designing oral syringes such that they cannot be connected to an intravenous port.
3. Medication reconciliation: the process of avoiding such inadvertent inconsistencies across transitions in care by reviewing the patient's complete medication regimen at the time of admission/transfer/discharge and comparing it with the regimen being considered for the new setting of care.
4. Read-backs: includes the listener repeating the key information so that the transmitter can confirm its correctness.
5. TALLman lettering: highlights the dissimilar letters in two names to aid in distinguishing between the two. For example, the name pair epinephrine and ephedrine would be written epINEPHrine and epHEDrine.
6. "Time-outs": planned periods of quiet and/or interdisciplinary discussion focused on ensuring that key procedural details have been addressed. For example, the identification of a patient, for a surgical procedure, site, and other key aspects, often stating them aloud for double-checking by other team members.
7. Executive walk rounds: used for the sole purpose of discussing safety with frontline staff.
8. Storytelling: a tool used to share events in the form of a story. It helps listeners remember facts and details that otherwise might be forgotten.
9. Safety briefings: an efficient tool used to share information and to increase safety awareness among frontline staff and foster a culture of safety into the daily routine, 24 hours a day 7 days a week.

Adapted from Agency for Healthcare Research and Quality. (n.d.). *AHRQ's glossary*. Retrieved from https://psnet.ahrq.gov/glossary

and resources for neonatal nurses to build a patient safety toolkit. Selected neonatal errors and improvement strategies are included and are by no means an exhaustive list. Box 18.1 includes definitions of selected improvement strategies. Neonatal nurses need to equip themselves with the best possible safety resources and knowledge to provide a safe and caring environment.

A. Framework for Safe, Reliable, and Effective Care.

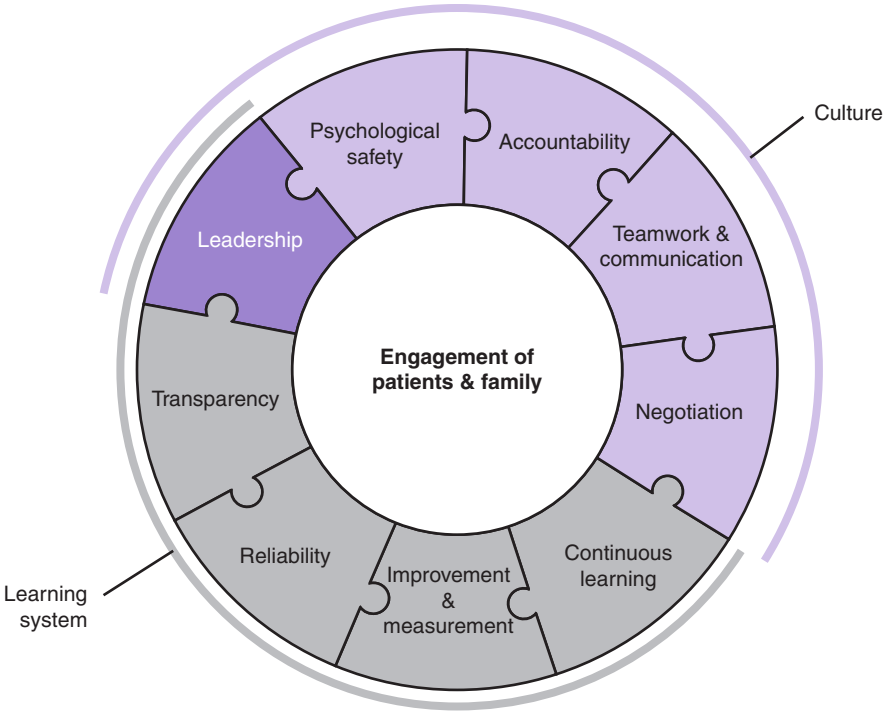
Hospital leaders are the foundation of an effective patient safety program and require an intentional, systematic, and supportive approach to creating a culture of safety. In 2017, the IHI merged with the NPSF to combine knowledge and resources to reset and focus the patient safety agenda to build safer systems across the care continuum (Frankel et al., 2017). The IHI and Safe & Reliable Healthcare (SRH) (Frankel et al., 2017) have developed the *Framework for Safe, Reliable, and Effective Care*, which is composed of two foundational domains: culture and learning system. Within these domains are nine interrelated components (leadership, psychological safety, accountability, teamwork and communication, negotiation, transparency, reliability, improvement and measurement, and continuous learning), with patient and family engagement at the core (Fig. 18.1). The *Framework for Safe, Reliable, and Effective Care* (Frankel et al., 2017) and the *Joint Commission's Patient Safety Systems Chapter* (Joint Commission, 2018) can be used as roadmaps to achieve a safe, reliable, and effective environment.

Definition, description, and application of these two domains to the NICU are provided.

Domain One—Culture

Culture is the product of individual and group values, attitudes, competencies, and behaviors that form a strong foundation on which to build a learning system (Frankel et al., 2017; Table 18.6). The AHRQ (2017a) defines a culture of safety as one in which health care professionals are held accountable for unprofessional conduct but are not punished for human mistakes, errors are identified and mitigated before harm occurs, and systems are robust to enable all members of the care team and staff to learn from errors and near-misses and prevent recurrence. The components of this domain are leadership, psychological safety, accountability, teamwork and communication, and negotiation.

a. Leadership (essential part of both culture and the learning system). The primary role is to influence others—to develop behaviors, habits, processes, and technologies that result in outstanding and ever-improving performance.



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Source: Frankel A, Haraden C, Federico F, Lenoci-Edwards J.*A Framework for Safe, Reliable, and Effective Care.* White Paper Cambridge, MA: Institute for Healthcare Improvement and Safe & Reliable Healthcare; 2017. (Available on ihi.org)

Fig. 18.1 The framework for safe, reliable, and effective care. *(From the Institute for Healthcare Improvement and Safe & Reliable Healthcare.)*

Leaders exist at all levels—not by rank. Leaders need to create a compelling vision in which patient and workforce safety is the core value and is a nonnegotiable goal. Safety needs to be a priority for boards of health care organizations and decisions made so that patient and workforce safety culture is sustainable. The culture of the board needs to encourage total engagement and involvement of patients and families (Frankel et al., 2017). There are **four leader responsibilities**:

1) Guard the learning system: Fully engage in the work of self-reflection that leads to transparency; understand, apply, and inspire the work of improvement science, reliability science, and continuous learning. *Application: Leaders actively participate in unit improvement teams, such as the Golden Hour or central line–associated bloodstream infection (CLABSI) reduction, and use improvement/reliability science methods/tools.*
2) Create psychological safety: Ensure an environment where anyone in the organization, including patients and families, can comfortably speak up and bring forth concerns, suggestions, and ideas for change. *Application: NICU and senior leaders routinely round with purpose with families to create a culture that is inclusive, open, and safe to speak up in.*
3) Foster trust: Create an environment of nonnegotiable respect and inclusion, ensuring that people feel their opinions are valued and any negative or abusive behavior is swiftly addressed. *Application: A senior leader dealing swiftly with lateral and/or hierarchical violence, regardless of the individual's rank or power.*
4) Ensure value alignment: Apply organizational values to every decision made, whether in service of safety, effectiveness, patient-centeredness, timeliness, efficiency, or equity. *Application: Leaders use learning/visual display boards to provide transparency and communication about the work being done both in the NICU and within the organization as a whole.*
5) Both senior and midlevel leaders need to articulate clear, actionable aims that align with the organization's goals. Application: If the organization's quality/safety goal is to reduce preventable harm, then the NICU's metrics should also include and support this goal—for example, reductions in unplanned extubations or CLABSI. It is imperative for

leaders at all levels to go to where the work is being done and listen to frontline staff, identify barriers, and then respond in a timely manner to staff concerns. This may be done on executive walk rounds, safety briefings, or team huddles that promote a shared mental model. Leaders should go with a sense of purpose and have a standard work and cadence for interacting with staff. Listening and not acting is insufficient. Leaders must take action to engage staff.

b. Psychological safety. Not only refers to a culture in which it is safe to speak up but also an environment that fosters: *curiosity* (individuals can ask questions without looking stupid), *request feedback* (without looking incompetent), *offer respectful critical feedback* (without appearing negative), and *suggest innovative ideas* (without appearing disruptive).
   1) Achieving psychological safety requires a flattened hierarchy and an environment that promotes people feeling comfortable to ask questions, seek feedback, and innovate. *Application: Families are encouraged and supported to stop the line and ask health care providers to wash their hands before touching their child.*
   2) Psychological safety in the NICU is imperative, especially with interdisciplinary decision making. Members of the health care team, including families, must be able to freely express themselves in a safe and nonjudgmental environment. *Application: Managing an infant's pain requires input from the entire interdisciplinary care team. Families and all members should be able to bring forth their concerns and potential treatment options from all different perspectives.*

c. Accountability.
   1) Holding people accountable for their behaviors (e.g., human error, at-risk behavior, reckless behavior) but not for flaws in processes or systems.
   2) A just culture encourages open and transparent communication, the reporting of errors, lapses, near-misses, and adverse events and an environment in which staff members accept responsibility for their own actions but know the organization will treat them fairly and not blame them for something related to human error (Marx, 2001) (Table 18.1). *Application: Retrieving a medication from an automatic dispensing unit during an emergency, a nurse relies on the standard location of the medication and the size/color of the syringe. After giving the medication, the nurse realizes that it was the wrong medication. After investigating the error, it was found that the pharacist had placed the medication in the wrong location. The event was related to human error and system design. Recommendation to create more reliable systems and console/support the staff involved in the event.*

d. Teamwork and communication.
   1) Effective groups develop conduct norms that lead to shared understanding, anticipate

Table 18.1

2019 Hospital National Patient Safety Goals

The purpose of the National Patient Safety Goals is to improve patient safety. The goals focus on problems in health care safety and how to solve them.

Identify Patients Correctly	
NPSG.01.01.01	Use at least two ways to identify patients. For example, use the patient's name *and* date of birth. This is done to make sure that each patient gets the correct medicine and treatment.
NPSG.01.03.01	Make sure that the correct patient gets the correct blood when they get a blood transfusion.
Improve Staff Communication	
NPSG.02.03.01	Get important test results to the right staff person on time.
Use Medicines Safely	
NPSG.03.04.01	Before a procedure, label medicines that are not labeled. For example, medicines in syringes, cups, and basins. Do this in the area where medicines and supplies are set up.
NPSG.03.05.01	Take extra care with patients who take medicines to thin their blood.
NPSG 03.06.01	Record and pass along correct information about a patient's medicines. Find out what medicines the patient is taking. Compare those medicines to new medicines given to the patient. Make sure the patient knows which medicines to take when they are at home. Tell the patient it is important to bring their up-to-date list of medicines every time they visit a doctor.
Use Alarms Safely	
NPSG 06.01.01	Make improvements to ensure that alarms on medical equipment are heard and responded to on time.

Table 18.1

2019 Hospital National Patient Safety Goals—cont'd

Prevent Infection	
NPSG.07.01.01	Use the hand cleaning guidelines from the Centers for Disease Control and Prevention or the World Health Organization. Set goals for improving hand cleaning. Use the goals to improve hand cleaning.
NPSG.07.03.01	Use proven guidelines to prevent infections that are difficult to treat.
NPSG.07.04.01	Use proven guidelines to prevent infection of the blood from central lines.
NPSG.07.05.01	Use proven guidelines to prevent infection after surgery.
NPSG 07.06.01	Use proven guidelines to prevent infections of the urinary tract that are caused by catheters.
Identify Patient Safety Risks	
NPSG.15.01.01	Find out which patients are at risk for suicide.
Prevent Mistakes in Surgery	
UP.01.01.01	Make sure that the correct surgery is done on the correct patient and at the correct place on the patient's body.
UP.01.02.01	Mark the correct place on the patient's body where the surgery is to be done.
UP.01.03.01	Pause before the surgery to make sure that a mistake is not being made.

From The Joint Commission: 2018 hospital national patient safety goals. Retrieved on 3/24/2018 from https://www.jointcommission.org/assets/1/6/2018_HAP_NPSG_goals_final.pdf

needs and problems, and use agreed-upon methods to manage situations, including conflict.

2) Characteristics of a strong team.
   a) Mutual trust and respect.
   b) Robust communication, including structured communication—Situation, Background, Assessment, Recommendation [SBAR] and read back/call back (Leape et al., 2012; Joint Commission, 2018).
   c) Working together to plan forward—discuss and outline next steps and agree on a plan to reduce risk and improve safety.
   d) Reflect back (e.g., team debriefing to reflect on what went well and what didn't and areas for improvement opportunities).
   e) Knowledge/information exchange that develops mutual understanding and shared knowledge, resulting in a shared mental model (Reason, 2000; Joint Commission, 2018).
   f) Team members explicitly give permission to hold each other accountable across a flat hierarchy.
   g) Effective interdisciplinary teamwork has a direct impact on patient and worker safety (AHRQ, 2008; Joint Commission, 2018). *Application: Using a structured hand-off process (nurse-to-nurse, provider-to-provider) such as I-PASS to standardize inpatient transitions in care* (Starmer et al., 2014; Starmer et al., 2017).

Structured Effective Methods of Communication

Critical information can fall through the cracks at hand-offs, especially within a chaotic and stressful environment, and communication can also be misunderstood. For example, a potential for error can occur with verbal orders for medication when it is written down by someone other than the order giver and transcribed onto an order form by a third person. Used extensively in medicine, and originating from the nuclear submarine service, SBAR is a communication tool to standardize discussion and information sharing among caregivers to ensure that patient information is consistently and accurately being delivered, especially during critical events, shift hand-offs, and patient transfers. As part of the National Patient Safety Goals, The Joint Commission (TJC) (2018) requires organizations to implement a standardized approach to hand-off communications. SBAR provides a shared mental model for all clinicians to use during hand-offs or transfers (IHI, 2017a).

Situation: What is happening at the present time?

Background: What are the circumstances leading up to this situation?

Assessment: What do I think the problem is?

Recommendation: What should we do to correct the problem?

I-PASS is a structured hand-off tool that uses a mnemonic to standardize oral and written hand-offs. In addition to the tool itself, clinical teams receive additional TeamSTEPPS (AHRQ, 2017b) training to improve communication and teamwork. The easy-to-remember mnemonic ensures key information is imparted in each hand-off (*I– Illness severity; P – Patient summary; A – Action list for the next team;*

S – Situation awareness and contingency plans; S – Synthesis and "read-back" of the information). This evidence-based pediatric hand-off tool has resulted in improved communication, decreased harm, and improved patient safety across numerous pediatric hospitals and disciplines (Fryman et al., 2017; Starmer et al., 2014; Starmer et al., 2017).

Negotiation and conflict management. Given the complexity of health care, as well as the diversity, passion, and knowledge of its members, leaders must foster a culture that successfully manages conflict and negotiation to gain agreement on important matters. The hallmarks of collaborative negotiation are appreciative inquiry and self-reflection, which allow negotiators to tease out the underlying reasons behind participants' positions. Self-reflection occurs when each member of the team works to understand the desires they bring to the table. *Application: Appreciative inquiry can be used in the NICU when trying to understand what works well (when there is good teamwork and communication during high levels of stress and acuity) to focus on safe care rather than only focusing on unsafe care or what went wrong.*

Due to the increasing complexity and specialization of care, teamwork in health care delivery is more vital than ever. Leaders must demonstrate transparency, accountability, and mutual respect and trust to create and sustain a culture of safety (Joint Commission, 2018 TJC, 2008). Rude and intimidating behaviors undermine a culture of safety and are not to be tolerated.

Domain Two—Learning System

A learning system is characterized by its ability to self-reflect and identify strengths and defects, both in real time and in periodic review intervals. In addition, learning systems are ones in which science, informatics, incentives, and culture are aligned to continuous improvement and innovation, with best practices seamlessly embedded in the care process, patients and families are fully engaged and active participants, and new knowledge is captured of care experience (Roundtable on Value & Science-Driven Health Care, Institute of Medicine, 2013). Learning systems in health care require leaders to lay the groundwork for psychological safety; organizations need to clearly convey to all staff and leaders that it is an expectation. Everyone must create and support psychological safety as part of their job. Frontline staff may not realize they should expect this, and thus do not watch for these supportive behaviors in their leaders and colleagues. The components of the learning system are leadership, transparency, reliability, improvement and measurement, and continuous learning.

A. Leadership (see "Domain One—Culture").

B. Transparency (Frankel et al., 2017). Transparency is a core tenet of HROs and helps drive improvement. Full transparency of all patient and workforce safety events and metrics should be acknowledged, displayed, tracked, and shared with leaders, staff, patients/families, and the community to create an environment of continuous improvement. Application: Senior/NICU leaders telling patient and worker safety stories, which can be powerful. These safety stories reinforce a persistent focus and relentless pursuit of eliminating harm and providing a safe work environment. These stories can be integrated into daily house-wide and NICU-based huddles with visual displays of data (aka learning boards) both within and across units to identify real-time (current) problems that can be solved at the local level or can be quickly escalated and solved with support from senior leaders. For instance, if the unit is working to reduce the frequency of unplanned extubations, highlighting and talking about specific process and balancing measures during huddles and linking process measure compliance to outcomes will help engage and provide a shared mental model to foster robust learning and improvement.

C. Reliability. Health care reliability is the ability of a system to successfully and repeatedly produce safe, efficient, person-centered care. The challenge for health care to achieve reliability is due to the complexity of the processes due to the dependence on humans and the risk for error. Therefore, health care organizations need to design safe systems that leverage people's intrinsic strengths and support their inherent weaknesses to increase the likelihood of reliable performance.

Four foundational principles for making systems and processes more reliable (Association for the Advancement of Medical Instrumentation, 2013; Frankel et al., 2017) include:

1. Standardize. To reduce nonpatient variation, design processes so people do the same thing the same way every time. *Application: Standardize central line catheter care and train staff on the process so that it becomes apparent when the process fails and where it fails, enabling the organization to better target improvements.*
2. Simplify. Avoid complex or multistepped (e.g., time-consuming) processes so people will follow the proposed steps and there will be fewer opportunities for failures and defects. Use simple and straightforward processes to make the right thing to do the easy thing to do. *Application: Use of prepackaged central line kits to minimize steps of locating supplies within a process.*
3. Reduce autonomy. Limit individual decision-making based on personal preference or belief, which can result in care variation and less consistent outcomes. Instead, to achieve greater reliability, follow evidence-based best practices, unless contraindicated for specific patients. *Application: Use of the golden hour protocol to maintain thermoregulation and stabilization in very low birth weight infants.*
4. Highlight deviation from practice. Departure from standardized processes in clinical decision making. This appropriate departure should be encouraged in order for clinicians to apply their expertise intelligently and deviate from protocols when necessary, but also relentlessly capture the deviations for

analysis. Once analyzed, the new insights can lead to educating clinicians or altering the protocol. Both result in greater reliability. *Application: A ventilator-associated pneumonia (VAP) bundle element includes head of bed to be elevated between 30 and 45 degrees; this is appropriate for most patients, but there are times when this is not appropriate based on individual patient medical variation. In this case, it's okay to depart from the best practice, document the rationale, and monitor it over time.*

5. Reliability needs to be intentional, planned, encouraged, and nurtured; it does not happen by accident. Leaders need to provide training and support in order for staff to apply improvement methods and tools to build reliable processes. Organizations need to embed operational excellence into everyday work and operations to continuously learn and make significant improvement.

D. Improvement and measurement.
This component of the framework deals with enhancing work processes and patient outcomes using standard improvement tools and measurement over time, leveraging improvement science. The Model for Improvement (Langley et al., 2009) systematically enables teams with subject-matter expertise to redesign processes and achieve outcomes that benefit patients, families, and staff. The model is made up of three questions, providing simplicity and clarity. Once frontline staff and leaders understand how to run small tests of change (with the use of Plan–Do–Study–Act [PDSA] cycles), track, interpret, and display data (e.g., run charts and control charts), they will be able to make data-informed decisions and reflect a deeper understanding of improvement (Fig. 18.2).

E. Continuous learning. A continuous learning system includes proactive and real-time identification and prevention of defects and harm with an obsession for searching for better ways to improve the lives of patients, families, and staff. An enormous amount of data is continuously generated from health care organizations; however, the data are often not translated in a timely or useful format for frontline clinicians to understand and make real change and improvement at the point of care. Through the use of continuous feedback loops and transparency of meaningful data, frontline clinicians have the ability to generate and apply evidence-based practices to improve quality, safety, and value in health care. Displaying and discussing meaningful data routinely during interdisciplinary team huddles, executive walk rounds, and safety briefings and acting on the data will foster a spirit of continuous learning and improvement. Learning organizations need to spend more time on proactive rather than reactive learning and continue to search for better ways to improve and disseminate these safer systems throughout the organization.

A proactive risk assessment increases understanding within the organization about the complexities of process design and management—and what could happen if the process fails. Use a failure modes and effects analysis (FMEA) for conducting a systematic, proactive risk analysis of a process in which harm may occur. The FMEA tool prompts teams to review, evaluate, and record steps in the process of what could go wrong (failure mode), why the failure would happen (failure causes), and what the consequence is for each failure (failure effect) (IHI, 2017b; QI Essentials Toolkit: Failure Modes and Effects Analysis). *Application: Use of a FMEA tool to understand potential points of failure before implementation of new technology for a stat code paging process.*

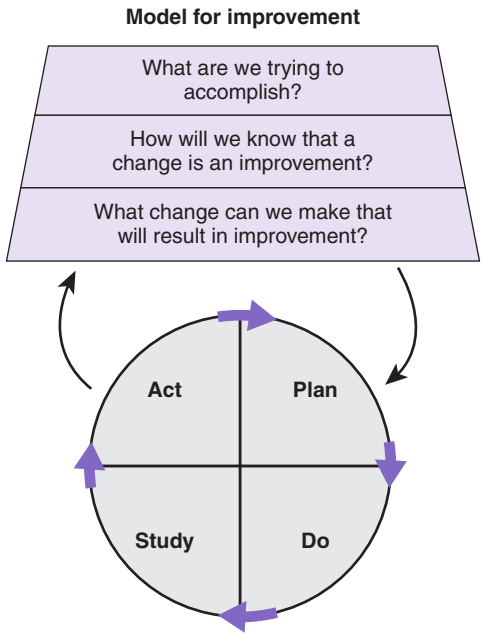

Fig. 18.2 Model for improvement. (From: The model for improvement was developed by Associates in Process Improvement. *[Langley, G. L., Moen, R., Nolan, K. M., Nolan, T. W., Norman, C. L., & Provost, L. P. (2009).* The improvement guide: A practical approach to enhancing organizational performance *(2nd ed.). San Francisco, CA: Jossey-Bass Publishers.] Retrieved from http://www.ihi.org/resources/Pages/HowtoImprove/default.aspx)*

Core Value of the Framework: Parent/Family Engagement

Patient-centered care is pivotal in the prevention of medical errors. Families are at the core of delivering patient-centered care in the NICU and family-centered care (FCC) is vital to promoting patient safety. Improving quality and safety by bringing families into the planning, delivery, and evaluation of health care is the foundation of FCC (Institute for Patient- and Family-Centered Care, 2016). Studies have shown that when health care providers and administrators partner with patients and families, the quality and safety of health care rise, the costs decrease, and provider and patient satisfaction increase (Institute for Patient- and Family-Centered Care, 2016).

Health care organizations can promote FCC by inviting families to participate in hospital and unit committees and patient and family advisory councils; creating an environment that is welcoming and inviting to families and one that provides privacy, comfort, and the ability to access information; including families in education and training programs as well as research; and developing human resources policies to promote a family-friendly environment. Specific steps to assist health care organizations in developing an FCC environment are available (Institute for Patient- and Family-Centered Care, 2016).

Families are encouraged to report concerns and to be actively involved in their infant's care as part of a patient safety strategy. National initiatives outlining strategies to encourage family participation in error prevention are available. Some of these initiatives include the TJC's (2018) "Speak-Up" initiatives, the NPSF's (2003) "Agenda for Action," and the AHRQ's (2017b) "20 Tips."

Engagement of patients and families is at the core of the framework, signifying the importance of their role in the continuum of care. All efforts in executing the framework should be based on engaging patients and families, because the framework has direct and significant implications for them. Health care systems continue to increase in complexity, and every point in the care process contains inherent risk—patients and families are the only people who are present throughout the full continuum of care. The voice of the patient/family and a true collaborative partnership are essential to achieve system changes and improve patient safety. *Application: Ways to engage and empower NICU families can include but not be limited to their active participation in family-centered rounds and all interdisciplinary committees to encourage their voice to be heard and to participate in clinical decision making.*

A. Human factor engineering and the environment. Humans are not perfect—they have known limitations, are prone to error, and become more prone to error when their physical environment impedes work efforts (e.g., poor lighting, noise, poorly designed equipment, etc.). Human factors are the leading root cause of sentinel events (Joint Commission, 2015). Human factors engineering (HFE), also known as *human factor analysis*, is a human-centered science that studies the interactions between workers and their work system to determine if the workplace design meets the needs of the people working in it (Joint Commission, 2015). The complexity of the NICU work environment puts clinicians at a high risk for errors to occur (Doerhoff and Garrison, 2015).

Selected human factors within the NICU:

1. **NICU environment.** Human factors that have contributed to errors include fatigue, communication failure, poor hand-offs, problems with cross-coverage, workload, and staffing patterns. Addressing these factors can aid in reducing medical errors. The NICU environment is a complex adaptive system conducive to human error. Frequently, the NICU is chaotic and prone to many unanticipated interruptions and life-threatening events, leaving care providers with very little time to make thoughtful and sound decisions. Patients in the NICU often require complex multidisciplinary care; each layer of this complex system presents additional opportunities for error (Doerhoff and Garrison, 2015).
2. **Fatigue.** The effects of fatigue as a result of long work hours, working at night, and insufficient sleep are often underestimated. Fatigue has been linked with slowed reaction time, lapses of attention, errors of omission, decreased ability to problem-solve, and reduced motivation and energy, all of which contribute to the potential for errors to occur (American Nurses Association [ANA], 2014). Nurses who have good sleep habits, minimize their shift rotations and excessive work hours, and use strategic naps can reduce the adverse effects of fatigue that could potentially put patients at risk. Other strategies to reduce fatigue include rest breaks, exercise, and bright lights (Baulk et al., 2009; Doerhoff and Garrison, 2015). Although limited research has been conducted in the area of fatigue specifically related to neonatal nurses and neonatal nurse practitioners (NNPs), the National Association of Neonatal Nurses (2015) and the National Association of Neonatal Nurse Practitioners (2015) have developed position statements recommending all health care employers implement guidelines to minimize staff fatigue. These recommendations encourage close collaboration between staff and their employers to develop and implement risk-reduction strategies to reduce the risk of fatigue-related incidents.
3. **The physical environment.** The NICU directly affects not only the highly vulnerable and sensitive preterm infant but also the caregiver within the environment. Overcrowded and poorly designed workspaces and workflow areas, excessive noise, inadequate lighting, poor ventilation and air flow filtration systems, and insufficient family space can all affect patient, family, and staff health and safety. Additional distractions/interruptions include multiple alarming devices, phone calls, computer alerts, changes in acuity, multiple admissions, and crying infants, all of which can heighten caregiver stress and cognitive workload and lead to increased risk for error (Doerhoff and Garrison, 2015; Johnson et al., 2017). Providing caregivers with a physical environment that lowers stress and improves job performance, safety, and satisfaction is the key for health care organizations. Many NICUs are designing or redesigning their units; efforts should focus on the individual needs of babies, families, and caregivers. Human engineers should be included in the design process to promote a safe environment for patients, families, and caregivers (White et al., 2013).

4. **Cognition**. Human factors experts classify errors in three categories: (1) Knowledge-based cognition (errors made due to lack of knowledge or experience, such as failure to recognize a change in clinical status); (2) rule-based (misinterpretation or misuse of relevant data or applying the wrong rule, such as violation of double-checking human milk); and (3) skill-based (attention and memory failures, such as omitting tasks and incorrectly reading a rule-based checklist) (Doerhoff and Garrison, 2015; Reason, 2000). Reducing stress and supporting teams within the NICU will help decrease cognitive error. Creating a setting that helps clinicians move from knowledge-based processing to skill- or rule-based processing, where the chance of error is greatly reduced, is recommended. Simulation is a strategy to reduce the chance for cognitive error by allowing clinicians a chance to repetitively practice in a safe learning environment that promotes teamwork and enhanced communication (Doerhoff and Garrison, 2015).
5. **Staffing**. Nurses are vital in providing patients with high-quality and safe care. Lower nurse-to-patient ratios are significantly associated with lower mortality, shorter length of patient stay, reduced adverse events, and preventable harm events (e.g., falls and infections), which results in safer care (ANA, 2015). However, staffing levels can be extremely complex based on minute-by-minute, hour-by-hour changes and the lack of a consistent way to measure acuity (Society of Pediatric Nursing [SPN], 2017). The American Nurses Association White Paper (2015) and the National Association of Neonatal Nurses Position Paper (2014a) on nurse staffing advocate for flexible staffing models that are able to respond to changes in patient volume and acuity. Staffing levels vary greatly across facilities, and methods for promoting safer staffing are needed. Skill mix and acuity are two additional factors that contribute to nurse staffing and its relationship to patient outcomes. A validated neonatal acuity tool is needed to determine appropriate nurse-to-patient ratios followed by a large, neonatal, multicentered, rigorous trial to conclude whether a relationship exists between increased nurse staffing (including skill mix and acuity) and improved patient outcomes.

B. Processes designed to decrease errors: Leveraging with others, evidence-based practice (EBP), and health information technology (HIT).
   1. Leveraging with others to create a safer environment. Patient safety organizations (PSOs) were created as part of the Patient Safety and Quality Improvement Act of 2005 (Patient Safety Act) and encourage clinicians and health care organizations to voluntarily report to and share quality and patient safety information with PSOs confidentially and without fear of legal discovery. Through this process, PSOs can help health care professionals learn from quality and safety events to prevent them from happening in the future (AHRQ, 2016). In addition, nationally structured neonatal/pediatric collaboratives/networks aimed at decreasing hospital-acquired harm include:
      a. Children's Hospitals' Solutions for Patient Safety (SPS)—A network of 130+ pediatric hospitals with a shared vision that no child will ever experience serious harm while they are trying to help them. Member hospitals believe that putting aside competition and sharing safety successes and failures will achieve improvement and safety goals faster. Hospitals focus on eliminating harm by implementing bundles; using error prevention tools, such as the STAR technique [Stop, Think, Act, Review] to develop strong self-checking habits; using safety coaches; and sharing, teaching, and learning from one another (http://www.solutionsforpatientsafety.org/).
      b. Children's Hospital Association (CHA) and Patient Safety—A network of 220+ pediatric hospitals with a focus on improving patient safety and achieving best outcomes through sponsorship of collaboratives and initiatives around top patient safety issues (https://www.childrenshospitals.org/Quality-and-Performance/Patient-Safety).
      c. Children's Hospitals Neonatal Consortium (CHNC)—A network of level IV NICU health care professionals and leaders committed to improving the quality and outcomes of a unique population of medically complex neonates and infants (http://thechnc.org/home-page/about-chnc/).
      d. Vermont Oxford Network (VON)—A nonprofit voluntary collaboration of health care professionals working together as an interdisciplinary community to change the landscape of neonatal care (https://public.vtoxford.org/about-us/).
   2. Evidence-based interventions.
      The use of evidence-based clinical practice guidelines (CPGs), checklists, standard work documents, protocols, and other items have been shown to reduce patient harm through improved standardization and communication (American College of Obstetricians and Gynecologists [ACOG], 2017; Gawande, 2009; Kirkpatrick and Burkman, 2010). It is possible to significantly reduce preventable harm and adverse events, and neonatal nurses are on the forefront of providing safe and efficient quality care. As neonatal nurses recognize and understand the causes of errors and rely on strict adherence to evidence-based interventions and improvement strategies, dramatic reductions of errors are possible. Knowledge and

skills associated with safety must become routine nursing practice. Improving patient safety requires assimilation of knowledge from other disciplines and industries and application of safety knowledge to health care. Since 2002, National Patient Safety Goals have been formulated by TJC to improve patient safety. These goals are drawn from recommendations by the Sentinel Event Advisory Group to spotlight problems in health care and focus on how to solve them. All TJC-accredited health care organizations are surveyed for implementation of the goals, which are revised annually (Table 18.2).

3. HIT.
   In its 2001 report, *Crossing the Quality Chasm*, the IOM identified HIT as one of the most significant interventions to improve the efficiency, cost-effectiveness, quality, and safety of health care quality in the United States. Many national agencies support the use of HIT because of its promising improvement in the efficiency, cost-effectiveness, quality, and safety of medical care and delivery in the nation's health care system. Implementation of HIT has been accelerated by the Health Information Technology for Economic and Clinical Health (HITECH) Act, enacted in 2009, which stated that health care providers must demonstrate meaningful use of electronic health records (EHRs) by 2015, or else incur penalties for failing to do so (Ranji et al., 2014). Technology eliminates duplicate work and illegible handwriting. HIT may improve care providers' decision making by integrating relevant automated decision making and knowledge acquisition tools along with evidence-based CPGs. Communication among caregivers, accessibility and availability of patient information, medication prescribing and use, and adherence to CPGs can all be improved through the use of HIT. Some of the technologies that improve medication delivery and provide decision support for medication therapy include computerized provider order entry (CPOE) with clinical decision support systems (CDSS), bar coding, handheld computers,

Table 18.2

Glossary of Patient Safety Terms

Adverse Event	Any injury caused by medical care. An undesirable clinical outcome that has resulted from some aspect of diagnosis or therapy, not an underlying disease process. Preventable adverse events are the subset that are caused by error.
Disclosure	Communication directed from health care personnel to the affected patient and/or family about an adverse event. A description of what is known and does not include speculation about causation or individuals' motivations or assumptions about judgment or fault (AAP and the Committee on Hospital Care and Institute for Patient- and Family-Centered Care, 2016).
Error	An act of commission (doing something wrong) or omission (failing to do the right thing) that leads to an undesirable outcome or significant potential for such an outcome.
Harm	An impairment of structure or function of the body and/or any deleterious effect arising therefrom, including disease, injury, suffering, disability, and death. Harm may be physical, social, or psychological, and either temporary or permanent.
Just Culture	A culture that recognizes that individual practitioners should not be held accountable for system failings over which they have no control. A just culture also recognizes that many individual or "active" errors represent predictable interactions between human operators and the systems in which they work. However, in contrast to a culture that touts "no blame" as its governing principle, a just culture does not tolerate blameworthy behavior such as conscious disregard of clear risks to patients or gross misconduct (e.g., falsifying a record, performing professional duties while intoxicated).
Patient Safety	Patient safety refers to freedom from accidental or preventable injuries produced by medical care. Thus, practices or interventions that improve patient safety are those that reduce the occurrence of preventable adverse events.
Safety Culture/ Culture of Safety	The safety culture of an organization is the product of individual and group values, attitudes, perceptions, competencies, and patterns of behavior that determine the characteristics of the organization's health and safety management. Organizations with a positive safety culture are characterized by communications based on mutual trust, by shared perceptions of the importance of safety, and by confidence in the efficacy of preventive measures.
Workforce Safety	Health care workforce safety refers to freedom from both physical and psychological harm for all those who work with patients, as well as those who oversee or provide nonclinical support for those who work with patients.

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and first-generation smart pumps and automated dispensing machines (ADMs) (Table 18.3).

Technology alone does not eliminate medication errors, and there are also concerns about the potential introduction of new errors or unintended consequences (Tolley et al., 2017). The cost of implementing HIT is a significant barrier for many health care organizations. Besides cost, there is also an element of human interface between good technology and user-friendly equipment. Health care professionals who adopt workaround strategies to override an inflexible system to achieve the desired task defeat the software-designed safeguards. Although HIT has grown exponentially, it may contribute to system complexity and additional opportunities for errors. Further research is needed to evaluate the efficacy of HIT and its impact on neonatal patient safety outcomes.

A. Future directions forecasted for HIT (Gardner, 2016; Jenders, 2017; Staggers et al., 2018).
   a. Precision medicine that uses large datasets to forecast treatment responses and to tailor treatment to individual patients.
   b. Expansion of CDSS to more settings, such as emergency units and outpatient health care.
   c. Expansion of the diagnostic capabilities of CDSS.
   d. Evidence-based, personalized CDSS that uses a uniform vocabulary.
   e. Integration of information between the EHR and point-of-care devices, such as smart pumps, monitors, and bar coding.

B. When an error occurs.

Identifying and eliminating sources of patient harm are critical in delivering safe patient care. Mitigating harm is achieved by a line management approach,

Table 18.3

Health Information Technology (HIT) Strategies

Clinical Decision Support System (CDSS)	Computerized Provider Order Entry (CPOE)	Smart Pumps	Automated Drug Dispensing Units ADU) and Machines (ADM)	Barcode Medication Administration Technology (BCMA) or Barcode Scanning Medication Administration (BSMA)
Definition: Information systems that assist health care providers and patients in making clinical decisions by providing the right evidence-based practice (EBP) in a timely manner and in a format that can be used.	**Definition:** An electronic application for writing orders that provides clinical guidance during the ordering process and intercepts potential errors at the point of order origination.	**Definition:** Programmable infusion pumps that are used to control and administer intravenous drugs and limit medication administration errors.	**Definition:** Computerized cabinets containing stock medications and supplies located on the patient unit. They are used to automate access, distribution, management, and control of medications, fluids, and supplies.	**Definition:** Technology used to prevent medication errors by placing a unique identifier (bar code) that is machine readable by an optical scanner on each medication.
Benefits: • Provides alerts and reminders, clinical guidelines, order sets, templates to help standardize documentation • Provides references to assist with diagnostic and treatment support • Provides relevant patient data reports • Associated with decreased human error	**Benefits:** • Improves legibility • Use of standard names, catalogs, and dictionaries • Automated calculations • Can monitor for adherence to best practice • Can screen for populations at risk • An evidence-based methodology for evaluating hospital-based CPOE systems has been developed by the Leapfrog Group	**Benefits:** • Decreases the chance of error by using a drug formulary that is individualized for a specific patient population • Programmed usual concentrations, dosing units (e.g., mcg/kg/min, units/hour), and dosing limits are specific to that population • Smart pumps can store data variables, such as alerts, medications administered, overrides	**Benefits:** • Allows quick access to medications • Ability to track medications from the point-of-care entry to removal from the cabinet; use of ADUs and ADMs can help eliminate errors during the dispensing of medications • Guidelines for safe use have been developed by the American Society of Health-Care Pharmacists and by the Institute for Safe Medicine Practices	**Benefits:** • BCMA matches the right medication with the right patient at the right time • Technology has also been used for mother's expressed breast milk identification

Continued

Table 18.3

Health Information Technology (HIT) Strategies—cont'd

Clinical Decision Support System (CDSS)	Computerized Provider Order Entry (CPOE)	Smart Pumps	Automated Drug Dispensing Units ADU) and Machines (ADM)	Barcode Medication Administration Technology (BCMA) or Barcode Scanning Medication Administration (BSMA)
Unintended consequences: • Elimination or shifting of human roles in decision making • Difficulty in keeping content current • Inappropriate content • Rigidity of the system • Alert fatigue	**Unintended consequences:** • Limited pediatric and neonatal-specific systems • New work demands and workflow patterns • Overdependence on technology to catch all errors • Can limit ability to obtain medications in an emergency • Alert fatigue • Workarounds to avoid perceived or actual problems • Delays in adding new orders/order sets	**Unintended consequences:** • Relies heavily on human factors and depends on error-free programming • Extensive training is required for proper implementation • Keypads allow double-value entry and are sometimes difficult to read from a distance • Overriding the soft alerts can also bypass the "smart" functionality	**Unintended consequences:** • Workaround and override concerns. Clearly stated policies should be developed detailing when system overrides are acceptable (e.g., in emergency situations) • Overrides can allow access to medications before orders have been reviewed and approved by a pharmacist • Drug dose errors related to stocking errors are also a concern	**Unintended consequences:** • Use of workarounds Causes for workarounds include hardware issues such as malfunctioning scanners and failing batteries, unreadable bar codes or patient identification wristbands, medications not kept at point-of-care, and user training
References: Ash et al., 2009 Jenders, 2017 Institute of Medicine, 2007	References: Jenders, 2017 Lehmann & Kim, 2006 Palma, Sharek, Classen, & Longhurst, 2011 Miller, Robinson, Lubomski, Rinke, & Pronovost, 2007 Morriss, 2008 Ranji, 2014 Tolley et al., 2017 Leapfrog Group, 2018	References: Bergon-Sendin et al., 2015 Lemoine & Hurst, 2012 Scanlon, 2012	References: Helmons, Dalton, & Daniels, 2012 Miller et al., 2007. American Society of Health-Care Pharmacists, 2010 Institute for Safe Medicine Practices, 2019	References: Fleischman, 2013 Koppel, Wetterneck, Telles, & Karsh, 2008 Nguyen, Mosel, & Grzeskowiak, 2018 Strudwick et al., 2018

which means that everyone in the organization is responsible for the safety of the patient. **To keep patients safe, all risk of hazards must be identified proactively by use of local resources (e.g., incident and near-miss reports) and external sources (e.g., TJC Sentinel Events, networks like the VON, and the literature). Once hazards are identified, it is important for the institution to commit resources to eliminating them (Handyside and Suresh, 2010).**

1. **Reporting methods to support learning and foster a culture of patient safety.**
   A number of reporting methods exist and have been used to identify medical errors and adverse events, including chart review (both focused/trigger-based and nonfocused), direct observation, voluntary reporting by health care providers, and review of medical malpractice claims. Multiple methods may be necessary to effectively measure harm associated with hospital-based health care.
   a. **Voluntary reporting** systems are used by many health care organizations and rely on frontline personnel directly involved in the event to report, rather than management or patient safety professionals. Voluntary reporting is a passive form of surveillance for near-misses or unsafe conditions, different from active methods of surveillance, such as direct observation of providers or chart review using trigger tools (AHRQ, 2017d). When a patient harm event occurs, rapid and timely reporting, comprehensive documentation of the event details, and a supportive and nonpunitive process are imperative (AHRQ, 2017e). The majority of event reporting systems in the NICU use a voluntary, anonymous, nonpunitive approach. An effective error reporting system requires

NICUs and organizations to have a supportive environment for event reporting that protects the privacy of staff who report occurrences, encourages a broad range of personnel to report, summarizes reported events and disseminates information back to frontline personnel in a timely fashion, and provides a structured mechanism for reviewing report and developing action plans (AHRQ, 2017d). Providing immediate and ongoing feedback to those who report events helps staff feel part of the process and solution. It is important to include near-misses and great catches when reporting to learn how to prevent errors. Automated reporting systems that allow quick and easy access are necessary for busy clinicians. Although voluntary reporting only provides a glimpse into a complex cause of error, system factors responsible for many errors can be identified in a voluntary reporting system. Once errors are identified, improvement strategies are implemented, and future errors are prevented, health care providers will recognize the benefit of reporting.

b. **Patient triggers.** Measuring the overall level of harm within a health care organization has been performed through the identification of "triggers," or clues, of adverse events during manual chart review. A trigger is defined as an "occurrence, prompt, or flag" found on review of the medical chart that "triggers" a further investigation to determine the presence or absence of an adverse event. Historically, efforts to identify adverse events have relied on voluntary reporting and tracking of errors. This method is often limited and may be unreliable because of a small percentage of errors ever being reported. Trigger methodology provides a more focused and efficient review of charts that may lead to identifying more adverse events (Sharek, 2012). An example of a neonatal trigger would be the patient use of naloxone, prompting a focused chart review for opioid-induced respiratory depression. The NICU trigger tool method is superior to identifying adverse events compared with nontrigger methods, and the NICU trigger tool can potentially be automated, allowing identification of adverse events in real time, as well as the ability to track event rates (Sharek et al., 2006). This kind of proactive search for problems is more effective than responding to reports of injuries and accidents after they occur.

c. **Additional methods of identifying errors.** Traditional chart reviews or health care provider interviews are additional methods of identifying errors. Often these methods are labor intensive, costly, inefficient, and variable. Direct observation using real-time audits during team rounds or routine nursing care can provide immediate feedback to frontline staff, which is key to behavior change for focused improvements in patient safety (Ursprung and Gray, 2010). Checklists with real-time surveillance methods identify care processes especially prone to error that are important safety areas, including mislabeled medications (tubing or syringes), absence of wristbands for patient identification, failure to follow hand hygiene practices, and inappropriate pulse oximeter settings (Ursprung and Gray, 2010). Morbidity and mortality forums and peer review also provide opportunities in which frontline providers can participate in identifying patient safety events to learn from and contribute to system improvement. A culture of safety involves promoting practices that are evidence based and safe and should be part of any NICU's quality improvement efforts. Families are also encouraged to participate in the process of identifying errors to provide a different perspective from most health care providers and to enhance the opportunity to learn about error prevention.

2. **Full disclosure** (American Academy of Pediatrics [AAP], 2016a; Harper and Smith, 2018; Massachusetts Coalition for the Prevention of Medical Error [MCPME], 2006). Transparency is a process in which errors are fully disclosed to patients and families. It is a process that can be very challenging for health care providers. Disclosure refers to providing information to a patient and/or family about a patient safety event. Data suggest that most patients and families wish to be informed of adverse events; however, nurses and physicians may find it difficult to acknowledge their mistakes, whether due to fear of litigation or just an intense shame or guilt. Health care professionals hold themselves to very high standards and as a result may find it difficult to deal with failure. Because of the emotional effects of these events on both the patients and families and the caregiver, communication failures are often the reason patients and families file malpractice suits. Support to both families and caregivers is essential in disclosing errors. Error disclosure training has become part of the curricula at many medical schools and residency training programs (Stroud et al., 2013). It has also been incorporated into interprofessional training programs (McDonough et al., 2017). When an error is discovered, it is critical that the individuals involved, or those knowledgeable about the event, briefly huddle as soon as possible to discuss what happened and determine who will lead the disclosure discussion (Harper and Smith, 2018).
   a. Strategies to support families after an adverse event through disclosure by care providers.

1) Prompt (within 24 hours after the event is discovered) and in private, compassionate, and honest communication with families after an incident telling them what happened.
2) Take responsibility and openly acknowledge the incident, be sensitive, and provide good and skillful communication. The reactions of families to incidents are influenced both by the incident itself and the manner in which the incident is handled.
3) The initial communication should be by, or at least in the presence of, a caregiver with a prior relation of trust with the patients. This may be the attending physician or primary nurse.
4) Apologize when there has been an error. The attending physician responsible for the patient's care is the person most suitable to make the apology along with the clinician responsible for carrying out the incident. However, in some situations, other health care professionals or administrators may be more appropriate for disclosing the error and apologizing. The apology helps restore the family's dignity and begin the healing process.
5) Open communication by individual clinicians should be strongly supported by institutional leaders and strongly supported by the health care team as a whole. It is difficult for the clinician to be open and honest about problems that have occurred if he or she does not feel supported by management and leadership.
6) Initial communication should focus on what happened and how it will affect the patient, including immediate effects and prognosis.
7) Commit to finding out why the event occurred, how recurrences will be prevented from happening to others, and to conducting an ongoing investigation.
8) Follow-up care should also be provided for the families after the initial incident with continued ongoing communication and support.

b. Strategies to support caregivers after an adverse event. Similar to patients and families, caregivers are also affected—emotionally and functionally—following an adverse event and are frequently unrecognized as the "second victim" (Wu, 2000). Studies have shown that neonatal nurses are at increased risk for secondary trauma related to caring for fragile patients potentially harmed through errors (Beck et al., 2017). Caregivers should be provided with institutional support that enables them to recover. Adverse medical events are a time of charged emotions and hectic activity involving a variety of clinical services. A clearly defined process is required to assess, activate, and oversee an effective support response for clinicians in these situations. A trained group of individuals to provide emotional support to the caregivers who were involved in the adverse events is recommended. Organizations need to offer caregivers professional help to manage the stress of the adverse event so healing can occur and they can comfortably return to work and take better care of their patients. Caregivers should have structured assistance in debriefing the adverse event as a team and should be given instruction on documenting the event. Coaching in communicating with the family during the emotionally intense period immediately after an incident can be critical for maintaining the relationship of compassion and trust. Training programs, including simulation training, need to be developed to teach nurses, physicians, and other clinicians, as well as department chairs and managers, how to communicate adverse events and how to provide support after experiencing an adverse event.

3. **Comprehensive investigation and analysis** (also known as a root cause analysis [RCA]) (Bagian et al., 2002; NPSF, 2016), as well as event investigation and analysis (AHRQ, 2017e).
Comprehensive analysis is a systematic process to analyze adverse events (Joint Commission, 2018). The purpose of these analyses is to identify system vulnerabilities so they can be eliminated or mitigated to prevent recurrence. It does not include focusing on individual performance as to the primary cause of the adverse event, but rather the underlying systems-level causations (NPSF, 2016). A systems approach recognizes that adverse events have multiple contributing factors outside an individual's control and that human error cannot be eliminated; therefore, the system must be altered to be safe (AHRQ, 2017a). Although these comprehensive investigations and analyses are frequently conducted, there is much variation in their application. Following are event investigation process steps for general awareness of how a systematic comprehensive analysis is performed. However, most hospitals have dedicated teams and detailed processes for conducting their own investigation analysis after a serious patient safety event. Step 1 occurs immediately, steps 2 to 7 may be done simultaneously during the first 72 hours after the event, and steps 8 to 15 are typically completed within 30 to 45 days of the event.
Step 1. Immediate action is taken to care for the patient; make the situation safe for others; and sequester equipment, products, or materials.
Step 2. Event disclosure. Disclose the event to the family (see disclosure section) and establish ongoing family contact for follow-up communication with the family.

Step 3. Family and staff support. Provide support to family and staff involved in the event. This demonstrates an ongoing commitment to and continued support to families. It also demonstrates concern about the impact on staff, supports them, and identifies those who need further support and intervention.

Step 4. Notify NICU and hospital leadership. It is important to garner support and remove barriers.

Step 5. Event reporting and risk management notification. Enter the event in the internal reporting system and notify the hospital's risk management/patient safety personnel/department (see event reporting section).

Step 6. Risk-based prioritization. Determine the severity of the event and the likelihood of recurrence.

Step 7. Conduct an immediate investigation to determine what should have happened, what did happen, and identify any gaps or direct causes and inappropriate acts. This can be initiated by the NICU leaders who are present when the event occurred. It's important to seek facts—not fault—avoid hindsight bias, and show respect and support.

Step 8. Conduct an in-depth investigation and analysis. This may include debriefs with those directly involved in the event and a chronological flow diagram or timeline, interviews, chart review, review of equipment or devices and manufacturer's recommendations/manuals, review of policies/procedures, and a review of the literature to determine best practices.

Step 9. Complete a comprehensive systematic analysis for identifying causal and contributory factors. Include a timeline of events and lessons learned.

Step 10. Finalize event classification and level of harm. Determine if there was a deviation from generally accepted performance standards and, if a clinical event, determine if the event was a known complication and if the providers did everything possible to prevent a negative outcome (Healthcare Performance Improvement [HPI], 2009).

Step 11. Identify solutions and corrective actions/mitigation strategies.

Step 12. Create an implementation timeline. Develop a timeline for the implementation of action items and mitigation strategies with assigned individual owners to carry out the action implementation.

Step 13. Measurement. Each action should have a process and outcome measure with an expected compliance threshold. A strong data management team that can assist with data analysis and provide a meaningful run and statistical control chart to frontline staff/personnel and leaders to drive improvement is imperative. An individual should also be responsible for measuring and reporting on the effectiveness of the action (NPSF, 2016).

Step 14. Feedback. Provide feedback to the CEO/board, service/department, staff involved, patient and/or patient's family, and the organization. A just culture (Marx, 2001) supports disclosure and learning from errors and encourages viewing every event as an opportunity to learn how to improve system performance. This will aid in creating a positive culture of safety.

Step 15. Complete external reporting if relevant. Report to TJC, Food and Drug Administration (FDA) if device/drug reports, and/or the PSO.

Investigating events to better understand system flaws when things go wrong is part of the Safety-I approach to preventing harm. Although it is critical to learn about such events, relying on identification of deficiencies in hindsight is inherently flawed. To achieve transformational improvement in patient safety, an additional approach is needed. Safety-II is an approach to look at normal work to understand how people compensate for flawed systems both in everyday and extraordinary circumstances. This provides a better understanding of systems and people when things go right. In today's complex NICU and health care setting, a comprehensive approach to learning why things go right and wrong is needed (Hollnagel et al., 2015).

D. **Selected types of health care errors in the NICU.**
Many selected improvement strategies are identified throughout the next section. This is not an exhaustive list, and many of the same strategies can be used for each identified error. It is important to remember that the safety and efficacy of a new practice, protocol, or piece of equipment should be examined carefully before implementation.

1. **Patient misidentification.**
Misidentification is a specific area of concern for NICU patients. Most methods used to visually differentiate individuals (age, size, gender, and hair color) are not clearly observable in the neonatal population. Relying on name alone can be risky. First names often have not yet been chosen, and relying on temporary first names such as Babyboy or Babygirl has been shown to lead to misidentification (Adelman et al., 2015). Also, it is not uncommon for units to admit more than one infant with the same last name, either due to multiple births or common surnames. Wristbands are another tool used to verify patient identification in the NICU. However, wristbands are often inaccurate, incomplete, missing, or are affixed to the patient's bedside because of concern for the preterm infant's fragile

skin that can lead to lacerations or abrasions. Use of CPOE has eliminated many errors, but one of the unintended consequences is the error of ordering services on the wrong patient (Ash et al., 2009).

Because accurate patient identification is necessary for providing safe and effective services specifically related to medication and blood product administration, laboratory specimen collection, performance of diagnostic procedures, and administration of treatments, accurate identification is of major importance.

a. Improvement strategies to reduce misidentification include:
   1) Use of a distinct naming convention for newborn infants, using the mother's first name, followed by the letter *s*, and then the gender of the infant. For multiple births, a number is added to the first name (e.g., Wendysgirl1) (Adelman et al., 2015).
   2) Use of two patient identifiers (e.g., name and medical record number).
   3) Patient verification at the beginning of each CPOE ordering session, requiring providers to confirm the infant's identity (Green et al., 2015).
   4) "Time out" immediately before starting the intervention.
   5) Use of bar codes.

2. **Wrong administration of expressed breast milk (EBM) and blood products.**
Multiple steps are involved in the process of administering EBM and blood products. Both EBM and blood products are body fluids and can carry infectious agents. Because of the risk associated with potentially administering the wrong breast milk or blood products, methods need to be identified to reduce wrong administration. Six Sigma is a process improvement strategy and has been used to reduce the incidence of incorrectly administering EBM (Drenckpohl et al., 2007). The Six Sigma approach reduces variability within a process, ultimately reducing opportunities for failures and errors. The steps are to define, measure, analyze, improve (DMAI), and control a problem (Kubiak and Benbow, 2009). Administration of human milk is complex and involves many people handling, transporting, storing, preparing, and administering the milk, resulting in the potential for error. The primary goal of Six Sigma is to eliminate the variability in a complex process. This same method can be used as an effective strategy for improving other processes related to errors within an organization.
   a. Selected strategies to avoid wrong administration of human milk.
      1) Manual versus automated identification systems. Many units have initiated bar coding for expressed human milk to help eliminate human factor errors and to provide a means for timely and accurate documentation of breast milk feedings. Barriers to initiating bar coding include cost of hardware and software, time and expertise needed for training, and space requirements for the bar-coding hardware. Both manual and automated methods must ensure that the five patient rights are enforced: right patient, right feeding, right volume, right route, and right time. In addition, attention must be paid to the expiration date for breast milk (Fleischman, 2013; Oza-Frank et al., 2017). Both methods must provide for safe, standardized methods of labeling, receiving, storing, preparing, and distributing EBM.
      2) Consider centralizing breast milk handling to improve standardization of processes and potentially reduce the incidence of microbial contamination (Steele and Bixby, 2014; Steele and Short, 2008).
      3) Develop an institution-specific policy outlining the steps to take if there is an error in breast milk administration.
   b. Selected strategies to avoid wrong administration of blood products.
      1) Standardize training and implement guidelines for transfusion, including blood typing, cross-matching, processing and delivering the blood product, and patient identification processes.
      2) To help eliminate unnecessary transfusions, develop institutional transfusion recommendations based on best evidence to help guide when transfusion of blood products should occur (Gabriella et al., 2015).
      3) Follow the most recent neonatal recommendations for the use of leukodepleted blood products, cytomegalovirus (CMV)–negative blood products, and irradiated blood products (Gabriella et al., 2015).

3. **Medication errors.** Neonates are particularly vulnerable to medication errors due to the use of very small doses, often requiring dilution; the widespread use of off-label and unlicensed drugs; the lack of evidence on pharmacotherapeutic interventions in neonates; and the lack of neonate-specific formulations. Neonates may be at additional risk of harm due to immature renal and hepatic drug clearance (Chedoe et al., 2007; Santesteban et al., 2015). Human factors that can contribute to medication errors include lack of knowledge of the medication, diagnosis, or specific patient; lack of training or experience; inadequate hand-off; fatigue; complacency; heavy

workloads; overreliance on technology; and distraction (Rostas, 2017).

Medication errors can occur throughout any stage of drug delivery (Table 18.4) and include preventable and nonpreventable adverse drug events (ADEs). In an effort to reduce the rate of pediatric medication errors, the AAP has developed recommendations uniquely pertinent to children and/or neonates (Stucky, 2003; reaffirmed 2007; retired 2011).

a. High-alert medications. The Institute for Safe Medicine Practices (ISMP, 2014) created a list of high-alert medications that bear a heightened risk of causing significant patient harm. The list provides health care professionals with specific medications that require special safeguards to reduce the risk of errors. Selected specific high-risk medications in the NICU (not an exhaustive list) are found in Box 18.2. The most commonly reported products associated with an error in the pediatric population are total parental nutrition and lipids, electrolytes, opioid analgesics (e.g., morphine and fentanyl), antimicrobial agents (gentamicin, vancomycin, and ceftriaxone), and antidiabetic agents (insulin) (Stavroudis et al., 2010).

b. Off-label medications (Kimland and Odlind, 2012). Licensing procedures are performed to ensure the safety, effectiveness, and quality of medications. However, many medications intended to treat neonates are either prescribed outside the terms of the product license (off-label) or are not licensed for this age group. Approximately 50% of medications prescribed in the NICU are used off-label. Reference standards for doses of off-label and unlicensed medications are lacking, and clinicians are faced with different published reference standards for a single medication. As a result of the limited

Table 18.4

Medication Errors at Specific Stages of Drug Delivery

Prescribing	Transcribing	Dispensing	Administration	Monitoring
Definition: Errors that occur during the decision process and in ordering a medication for a patient	**Definition:** Errors that occur with transfer of information from order or prescription to medication list or medical record	**Definition:** Errors that occur during interpretation, preparation, and delivery of medications by pharmacy staff	**Definition:** Errors that occur during medication administration to a patient	**Definition:** Errors associated with the monitoring of clinical and/or laboratory data related to response to the drug therapy
Includes: Dose errors, wrong drug, wrong regimen, inappropriate drug	**Includes:** Incorrect drug name, formulation, route, dose, dosing regimen; also includes omission of information	**Includes:** Incorrect pharmacy computer order entry; drug selection, preparation and labeling; wrong dose, route, or formulation; and failure to note allergies or contraindications.	**Includes:** Wrong patient, drug, dose, time and/or route omissions	**Includes:** Error in test interpretation, errors in pharmacokinetic calculations and incorrect dose or drug suggestions
Percent of medication errors: 14% to 74%	**Percent of medication errors:** 12% to 18.4%	**Percent of medication errors:** 11.9% to 25%	**Percent of medication errors:** 31% to 63%	**Percent of medication errors:** 1.4%
Most common errors: Dosing, including tenfold overdoses	**Most common errors:** Incorrect medication, incorrect units; use of ambiguous abbreviations can lead to transcription errors	**Most common errors:** Labeling, dilutions during delivery of medication to the wrong location or late delivery; automated dispensing systems with out-of-stock, wrong, or expired medications	**Most common errors:** Incorrect administration time, patient misidentification Errors also include administration of expired drugs	**Most common errors:** Incorrect interpretation of laboratory results

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Krzyzaniak, N., & Bajorek, B. (2016). Medication safety in neonatal care: A review of medication errors among neonates. *Therapeutic Advances in Drug Safety, 7*(3), 102–119.

Rostas, S. E. (2017). Medication safety in the neonatal intensive care unit. *Journal of Perinatal & Neonatal Nursing. 31*(1), 15–19.

Box 18.2

High-Alert Medications

- Antithrombotic agents (e.g., heparin, low-molecular-weight heparin, alteplase)
- Adrenergic agonists, intravenous (IV) (e.g., epinephrine, phenylephrine, norepinephrine)
- Adrenergic antagonists, IV (e.g., propranolol, metoprolol, labetalol)
- Anesthetic agents, general, inhaled, and IV (e.g., ketamine and propofol)
- Antiarrhythmics, IV (e.g., lidocaine and amiodarone)
- Chemotherapeutic agents
- Dextrose, hypertonic, 20% or greater
- Hypertonic sodium chloride for injection (greater than 0.9% concentration)
- Inotropic medications, IV (e.g., digoxin and milrinone)
- Insulin (subcutaneous and IV)
- Liposomal forms of drugs (e.g., liposomal amphotericin B)
- Moderate sedation agents, IV (e.g., midazolam, dexmedetomidine)
- Moderate oral sedation agents, for children (e.g., chloral hydrate)
- Narcotics/opiates, IV, transdermal, and oral (e.g., fentanyl and morphine)
- Neuromuscular blocking agents (e.g., vecuronium, succinylcholine, rocuronium)
- Concentrated potassium chloride injections
- Sodium chloride for injection, greater than 0.9% concentration
- Total parenteral nutrition solutions

Adapted from Institute for Safe Medication Practices. (2018). *ISMP List of high-alert medications in acute care settings.* Retrieved July 16, 2019 from www.ismp.org/recommendations/high-alert-medications-acute-list.

range of licensed medications in appropriate dosage forms and the need for weight-based dosing in neonates, more calculations and dilutions are involved before administration compared with those required in adults, leading to an increased number of opportunities for errors (Chedoe et al., 2007; National Association of Neonatal Nurses, 2014b).

c. Selected medication improvement strategies.
   1) Education.
      a) Instruct staff and practice mathematical calculations specific to neonates both during orientation and as part of continuing education.
      b) Independently check calculations.
      c) Follow the five rights of medication safety.
   2) Ensure medication reconciliation.
   3) Collaboration between those who prescribe, transcribe, dispense, and administer medications.
      a) Have a clinical pharmacist on the unit who is involved in multidisciplinary patient care rounds.
      b) Require double-checking by a second professional at each step of the medication process.
   4) Clear communication—written and verbal.
      a) Avoid or eliminate dangerous abbreviations, spell out dosage units, and use TALLman lettering (Table 18.5).
      b) Eliminate or restrict verbal orders.
      c) Use an incident reporting system to document medication errors and near-misses with a structured follow-up system to identify and implement strategies to eliminate sources of error.
      d) Use a zero left of a dose less than 1 (e.g., use 0.1 rather than .1) and avoid a trailing zero (e.g., use 1 rather than 1.0).
      e) Institute labeling precautions—labels on each medication dose should be specific to that single dose and contain all appropriate information. At a minimum, the label should include the patient name, room number, identification number, the medication's generic and trade names when applicable, dosage, route, frequency, and any alerts relating to the medication.
      f) Report medication errors and near-misses confidentially with a structured method of nonpunitive follow-up procedures (National Association of Neonatal Nurses, 2014b).
   5) Technology.
      a) Provide access to drug information specific to neonates through web-based drug reference materials. Ensure that the medication reference manual includes multiple dilutions of the same drug.
      b) Implement a CPOE/CDSS with "forcing functions" (functions that limit routes and frequencies of drugs that are ordered and are specific to neonates, such as weight in kilograms and age in days of life).
      c) Use bar-code medication administration (BCMA) and automated drug-dispensing units (ADUs).
      d) Use "neonatal" intravenous (IV) pumps.

Table 18.5

"Do Not Use" Abbreviations

Do Not Use	Potential Problem	Use Instead
U, u (unit)	Mistaken for "0" (zero), the number "4" (four) or "cc"	Write "unit"
IU (International Unit)	Mistaken for IV (intravenous) or the number 10 (ten)	Write "International Unit"
Q.D., QD, q.d., qd (daily)	Mistaken for each other	Write "daily"
Q.O.D., QOD, q.o.d, qod (every other day)	Period after the Q mistaken for "I" and the "O" mistaken for "I"	Write "every other day"
Trailing zero (X.0 mg)*	Decimal point is missed	Write X mg
Lack of leading zero (.X mg)		Write 0.X mg
MS	Can mean morphine sulfate or magnesium sulfate	Write "morphine sulfate"
MSO_4 and $MgSO_4$	Confused for one another	Write "magnesium sulfate"

[1] Applies to all orders and all medication-related documentation that are handwritten (including free-text computer entry) or on preprinted forms.

***Exception:** A "trailing zero" may be used only where required to demonstrate the level of precision of the value being reported, such as for laboratory results, imaging studies that report size of lesions, or catheter/tube sizes. It may not be used in medication orders or other medication-related documentation.

From The Joint Commission. (2017). Facts about the official "Do Not Use" list of abbreviations. Retrieved from https://www.jointcommission.org/facts_about_do_not_use_list

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e) Automate patient medication labels with patient identification and medication information.
f) Use an electronic medication administration record (eMAR).
g) Use automatic dispensing systems (ADS) to store unit-dosed medications.

6) Standard work.
a) Standardize all medication infusions.
b) Standardize order sets or preprinted orders.
c) Use drug standardization—all drugs should have a standardized order.
d) Use standardized abbreviations.
e) Use standardized formulary.
f) Use standard concentrations, admixtures, and diluents for each medication (Rostas, 2017).
g) Implement selected safety measures to prevent high-alert medication errors.
h) Limit access to the high-alert medications.
i) Use special labeling of syringes and pumps infusing high-alert medications (e.g., color-coded).
j) Standardize ordering, storage, preparation, and administration of products.
k) Implement double-checking/redundancies mechanisms (automated or independent double-checks).
l) Utilize smart pump technology.
m) Institute system alerts.

Remove certain high-alert drugs from "ward stock," and require dispensing only by pharmacy. Require:

n) Hand-off verification checks from one caregiver to the next for a patient receiving a high-alert drug infusion.
7) Packaging and storing medications.
8) Separate drugs that look or sound alike and reduce or eliminate the availability of multiple drug strengths.
a) Limit the number of floor-stock IV solutions. Remove all concentrated electrolytes from floor stock and never dispense them from the pharmacy.
b) Store neonatal doses away from adult doses.
c) Increase the availability of dilute forms of drugs used in neonatal areas.

4. **Health care–associated infections** (HAIs). (For detailed infectious disease information, see Chapter 32.)

With the concerted efforts of the Centers for Disease Control and Prevention (CDC) and infectious disease professionals, rates of all HAI have decreased since 2006 (CDC, 2014). However, HAIs remain a source of morbidity, mortality, and cost for both adults and neonates. For neonates, prematurity is the most important risk factor for HAI (Ramasethu, 2017).

Reducing the number of HAIs is a TJC National Patient Safety Goal (2018) (see Table 18.2). Treatment of these infections has become more complex because of an alarming rise in antibiotic resistance. Multidrug-resistant organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and certain gram-negative bacilli (GNB), are associated with increased mortality, and their incidence has risen over the past decade.

a. **CLABSIs.** CLABSIs are primary bloodstream infections typically associated with the presence of a central line or an umbilical catheter in neonates at the time of or before the onset of the infection, resulting in an increased length of

hospital stay, cost, and risk of mortality. Preterm infants are especially prone to infection, and the presence of a central line increases the odds of an infection; the longer the catheter is in place, the higher the odds of an infection (CDC, 2017.). The most common organism associated with catheter-related sepsis is coagulase-negative *Staphylococcus*. Neonatal nurses can prevent CLABSI through proper central line management. Specific techniques are addressed in the CDC's *Guidelines for the Prevention of Intravascular Cather-Related Infections* (2011), and the CDC's National Healthcare Safety Network annually publishes the incidence rate of CLABSI in preterm infants (Dudeck et al., 2016).

b. **VAP.** VAP is a serious and common complication among intubated infants in the NICU, especially very low birth weight infants, and is associated with increased length of days in the NICU and death. Neonatal nurses can help eliminate VAPs by following the CDC's *Guideline for Prevention of Nosocomial Infections* (2003; Klompas et al., 2014). The CDC's National Healthcare Safety Network annually publishes the incidence rate of VAP in preterm infants (Dudeck et al., 2016).

c. **Surgical site infections (SSIs).** Advances have been made, including improved operating room ventilation, sterilization methods, barriers, surgical technique, and availability of antimicrobial prophylaxis. SSIs still are a substantial cause of morbidity, prolonged hospitalization, and death (National Healthcare Safety Network [NHSN], 2018). Compounding the problem of SSIs are the increased acuity of in-hospital surgical patients and the increasing numbers of patients with MRSA and VRE, leading to a greater morbidity, mortality, and cost (Barnett, 2007). The CDC's guidelines for the prevention of SSIs were published two decades ago (Mangram et al., 1999), with a recent update in 2017 (Berrios-Torres et al., 2017). A recent update regarding antimicrobial prophylaxis during surgery has been developed jointly by the American Society of Health-System Pharmacists, The Infectious Diseases Society of America, The Surgical Infection Society, and The Society for Healthcare Epidemiology (Bratzler et al., 2013).

d. Antibiotic stewardship. According to data collected by the CDC, 20% to 50% of antibiotics prescribed in acute care hospitals are either unnecessary or inappropriate. A study of 127 NICUs in California showed overall antibiotic use varied 40-fold across institutions, with an average of antibiotic use of 24.5% of patient days. This use was independent of proven infection, necrotizing enterocolitis (NEC), surgical volume, or mortality (Schulman et al., 2015). Antibiotic misuse affects patient safety in three ways:

1) Antibiotics are associated with a variety of adverse drug reactions, such as allergic reactions and kidney damage.
2) Use of antibiotics alters the infant's normal bacteria, or microbiome, allowing overgrowth of other bacteria. The most common HAI is *Clostridium difficile*. Infections with this organism are estimated to cost as much as $4.8 billion for acute care facilities alone (ANA, 2017).
3) When bacteria are exposed to antibiotics over time, they can develop resistance and become difficult to treat. MRSA, VRE, and carbapenem-resistant Enterobacteriaceae (CRE) are examples of resistant bacteria.

Improvement of antibiotic management is a patient safety issue and has led to the development of the National Action Plan for Combating Antibiotic-Resistant Bacteria. Part of this plan is the development of Antibiotic Stewardship Plans. A consensus statement from the Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Diseases Society defines antibiotic stewardship as "coordinated interventions designed to improve and measure the appropriate use of [antibiotic] agents by promoting the selection of the optimal [antibiotic] drug regimen, including dosing, duration of therapy, and route of administration" (Fishman, 2012, p. 323). TJC published Antimicrobial Stewardship Standards in 2016, which were effective January 2017 (Joint Commission, 2016).

e. **Selected recommended improvement strategies reduce the risk of HAI.** There are specific, EBP recommendations to **reduce the risk of each HAI. The CDC has published recommendations, and the** Children's Hospitals SPS Network (2018) has published recommendations specifically for pediatric patients (Table 18.6).

1) Educate health care workers about multidrug-resistant organisms, CLABSI, VAPs, and SSIs and the necessity of prevention.
2) Educate families about basic infectious disease prevention, including the importance of adhering to hand hygiene practices and mode of transmission.
3) Maintain strict adherence to hand hygiene practices and use of contact precautions.
4) Implement a surveillance program to identify and track patients with HAI.
5) Aim for aggressive detection of carriers. Measure infection rates, monitor compliance

with best practices, and evaluate the effectiveness of prevention efforts.
6) Share information with hospital senior leadership, physicians, nursing staff, and other clinicians.
7) Employ NICU-based infectious disease personnel.
8) Ensure rigorous isolation of colonized patients.
9) Ensure that the environment and personal equipment are thoroughly disinfected.

5. **Unplanned extubations** (UEs).
UE is defined as the unexpected or untended removal of the endotracheal tube (ETT) by the patient (self-UE) or by health care team members during nursing and medical care (accidental extubation) (Silva et al., 2013). Unplanned endotracheal extubations requiring reintubation was in the top five neonatal adverse events reported using the NICU trigger methodology (Sharek, 2012). Adverse effects associated with unplanned extubation

Table 18.6

August 2019 SPS Prevention Bundles for CAUTI, CLABSI, SSI and VAP

CAUTI	CLABSI	SSI	VAP
Insertion—SPS Standard Elements	**Insertion—SPS Standard Elements**	**SPS Standard Elements**	**SPS Standard Elements**
Use aseptic technique for insertion	Hand hygiene	Preoperative bath	N/A
Avoid unnecessary catheterization	CHG scrub	No razor	**SPS Recommended Elements**
Maintenance—SPS Standard Elements	No iodine ointment	Appropriate antibiotic timing	Readiness to extubate
Maintain a closed drainage system	Prepackaged or filled insertion cart, tray or box	**SPS Recommended Elements**	Head of bed elevation
Maintain hygiene	Insertion checklist with staff empowerment to stop nonemergent procedure	Appropriate skin antisepsis: Use of alcohol containing agent if no contraindication	Minimize disruption of the circuit
Keep bag below level of bladder	Full sterile barrier for providers and patients	Appropriate antibiotic redosing	Oral hygiene
Maintain unobstructed flow	Insertion training for all providers		
Remove catheter when no longer needed	**Maintenance—SPS Standard Elements**		
Maintenance—SPS Recommended Elements	Daily discussion of line necessity, functionality, and utilization including bedside and medical care team members		
Secure catheter	Regular assessment of dressing to assure clean/dry/occlusive		
	Standardized access procedure		
	Standardized dressing, cap, and tubing change procedures/timing		
	Daily CHG treatments for all patients >2 months adjusted age with central venous catheters (SPS strongly recommends the use of 2% CHG wipes). Note: Those patients <2 months adjusted age* should be cared for based on institutional protocol.		
	Maintenance—SPS Recommended Elements		
	An in-depth review of all identified CLABSI with multidisciplinary involvement AND the intent to change the process if needed.		
	Daily linen changes		

CAUTI, **; *CHG*, **; *CLABSI*, central line–associated bloodstream infection; *SPS*, **; *SSI*, **surgical site infection**; *VAP*, ventilator-associated pneumonia.

*Adjusted age is <48 weeks for premature infants or <2 months of age for full-term infants. For example, if a patient is born at 28 weeks, they would receive their first CHG treatment at 20 weeks' chronological age (48 weeks adjusted).

· Standard Element: Strong evidence suggests that implementation of this element is associated with significant decrease in patient harm; all SPS hospitals should implement and measure reliability of this element.
· Recommended Element: Preliminary data and clinical expert opinion support the implementation of this element; SPS hospitals should strongly consider implementing this element.

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From Children's Hospitals' Solutions for Patient Safety: August 2019 SPS Prevention Bundles for CAUTI, CLABSI, SSI and VAP.

include cardiopulmonary deterioration, VAP, hypoxemia, hypercarbia, and trauma to the airway (Powell et al., 2016). Cardiopulmonary resuscitation (CPR) was required by 5% to 13% of infants experiencing UE (Silva et al., 2013). Limited data are available on the outcomes of unplanned ETT extubations in the NICU. Insufficient fixation of the ETT is reported as the primary rationale for unexplained ETT extubations, followed by vigorous movement in the crib or incubator. However, limited evidence suggests that a significant number of infants who experience unplanned ETT extubations do not require reintubation, signifying that many infants are remaining intubated who are ready for extubation. Additional research is needed to examine the relationship between unplanned ETT extubation and infant outcomes and potential strategies to reduce the incidence of unplanned ETT extubations.

a. Improvement strategies for unplanned extubations (Merkel et al., 2014; Powell et al., 2016; Silva et al., 2013).
   1) Standardized ETT securement procedures.
   2) Constant vigilance of tube securement.
   3) Collaboration between nursing and respiratory care staff.
      a) Determination and agreement of ETT position.
      b) Partnering in manipulation of ETT and repositioning or transferring infant.
   4) Use of two licensed professional health care team members when transferring infant.
   5) Use two licensed professional health care team members when retaping or repositioning the ETT.
   6) Identify infants who are at high risk for UE, based on unit-specific data. Possible high-risk infants include:
      a) Weight <1000 grams.
      b) Difficult airway related to facial or airway anomalies.
      c) History of previous UE.
   7) Implement weaning and extubation readiness guidelines to facilitate identifying infants who are ready for extubation.

6. Pressure injury.

Pressure injury is defined as localized damage to the skin and/or underlying soft tissue, usually over a bony prominence or related to a medical or other device (National Pressure Ulcer Advisory Panel [NPUAP] 2016).

The incidence rate of pressure injuries among neonates is high, with reports of up to 43% of infants in NICUs experiencing pressure injury. Gestational age, birth weight, and medical devices are strongly associated with injury (August et al., 2017). Risk assessment has been recognized as an intervention that can decrease the incidence of pressure injury (NPUAP, 2016). However, most current risk assessment tools were developed using combined data from adults, older children, and infants (Vance et al., 2015). Compared with adult and pediatric populations, neonatal skin is more fragile, thinner, and forms weaker connections between the epidermal–dermal junction (Grosvenor and Dowling, 2018). Valid, reliable tools specifically designed for evaluating neonates need to be developed.

a. Improvement strategies for prevention of pressure injuries. A practice bundle designed to reduce pressure injuries in children was designed by Children's Hospitals' Solutions for Patient Safety (SPS) network (Children's Hospitals' Solutions for Patient Safety, 2017). Data obtained from the SPS network and additional external evidence in the medical literature were used to identify highly reliable strategies to reduce harm to hospitalized children. The strategies include the following:
   1) Assess skin at least every shift and more often in infants with compromised circulation and in the operating room.
   2) Assess skin in contact with medical devices each shift or more frequently with other care.
   3) Turn all immobile patients at least every 2 hours or timed with care in the NICU.
   4) Appropriate bed surface: evaluate the need for a specialty mattress based on skin risk assessment. Use gel pads, pillows, and/or pressure reduction devices to cushion bony prominences.
   5) Moisture management: apply barrier cream to create a moisture barrier for all diapered patients; keep skin clean and dry.
   6) Consider forming an interdisciplinary skin care team with the goal of performing routine rounds to identify and track all skin injuries, standardize assessment and documentation of injuries, and educate the health care team (Nist et al., 2016).

E. Discharge safety instructions.

Proactively implementing a comprehensive formalized discharge process is recognized as one of the 30 safe practices outlined by the National Quality Forum (NQF) to reduce readmissions, promote more satisfied and informed patients/families, and promote better use of primary care services in the community after a hospital stay (NQF, 2010). Transitioning NICU families and their infants from hospital to home can be complex and challenging. Families need to be instructed on how to provide a safe environment at home (Boykova and Kenner, 2012; Jeffries et al., 2014). In addition to providing families with CPR instruction, immunization scheduling information, and developmental follow-up care, families need to be aware of environmental and home safety precautions. Determining infant and family readiness for discharge and complete discharge instructions are provided in

Chapter 19. Selected safety discharge topics include the following:

a. Medication reconciliation. Medication reconciliation is the process of creating an accurate list of all medications a patient is taking, with the goal of providing correct medications to a patient at all transition points (admission, transfer, and discharge). It involves continuing, discontinuing, holding, or modifying all medications at admission, discharge, and any other transition point (IHI, 2011). According to TJC's National Patient Safety Goals (2018) (see Table 18.1), patients and families should be given a complete list of medications on discharge. The infant's primary care provider should also have a complete list of medications. Careful consideration should be given to which medications will be needed after discharge and which medications can be safely discontinued. Also, the care provider can determine whether additional medications may be needed at home.
b. Environmental checklist. Checklists are used to assess patient and family safe home environment (water, electricity, heat, smoke detectors, phone, heat/air source, fire evacuation plan, etc.).
c. Car seat testing. In 1990, the AAP recommended car seat challenges for infants <37 weeks' gestation. Due to relative hypotonia and risk of airway obstruction, preterm infants are at risk for desaturation events, apnea, or bradycardia when placed in car seats. The AAP recommendations were last updated in 2009 (Bull and Engle, 2009) and include:
   1) Hospital protocols should be developed for infants <37 weeks' gestation, but may also include more mature infants with poor tone.
   2) The period of observation should last for 90 to 120 minutes or the duration of travel to home, whichever is longer.
   3) The period of observation should be conducted by trained personnel.
   4) If infant has documented desaturation and/or apnea and bradycardia events that are deemed significant, interventions to reduce the frequency of these events should be implemented before discharge and the infant should be retested.
   5) Specific information regarding positioning in a car seat is included in recommendations, including the use of positioning devices and the angle of recline.
   6) Hospitals should provide teaching for families on positioning their infant in a car seat.
   7) Time spent in a car seat should be minimized. Car seats should only be used for travel.
   8) To improve observation of infants, whenever possible, an adult should sit in the rear seat adjacent to the car seat.
   9) Car seat testing should also include inspection of the car seat to ensure that it meets current safety recommendations.

   Many hospitals also extend testing to include full-term infants with low birth weight (<2500 grams) and infants with hypotonia, congenital heart disease, and airway anomalies, such as micrognathia (Davis, 2015).
d. Abusive head trauma (shaken baby syndrome). Infants who have required a NICU stay have been found to be at a higher risk of abuse than infants born at term. The National Center for Shaken Baby Syndrome (NCSBS) has developed a program adopted by many NICUs to educate parents about normal infant crying and the dangers of shaking an infant. The Period of PURPLE Crying Program focuses on helping the parent to understand that crying is normal and to develop a coping strategy when their infant is inconsolable. PURPLE is a mnemonic for Peak Pattern (age when crying usually occurs), Unpredictable, Resistant to soothing, Pain-like look on face, Long bouts of crying, and Evening crying (NCSBS, retrieved 2018).
e. Sleep-related death reduction strategies. Studies have shown that there is an increased risk of sudden infant death syndrome (SIDS) among infants born preterm (AAP, 2016b). Information and strategies designed to prevent sleep-related death need to be included as part of every NICU family's discharge teaching. Although many neonatal nurses provide specific back-to-sleep instructions at the time of discharge, they frequently do not model safe sleep practices while infants are hospitalized (Gelfer et al., 2013). Neonatal nurses are in influential positions and need to both instruct parents and model sleep-related death reduction strategies. Specific strategies include:
   1) Neonatal nurses need to model behavior practices before discharge, placing the bed in a flat position; positioning infants on their backs; and removing toys, blankets, and extra bedding (Gelfer et al., 2013; Voos et al., 2015).
   2) Instruct parents to place the baby on the back on a firm sleeping surface with a tightly fitted sheet. No soft bedding, including crib bumpers, sheepskin, pillows, stuffed animals, and other soft products, should be in the crib.
   3) Breastfeeding is also recommended as adding protection against SIDS.
   4) Avoid overheating; babies should be clothed for sleep with a bedroom temperature that is comfortable for an adult with a light layer of clothing.
   5) Do not use commercial home monitors or positioning devices marketed to reduce the risk of SIDS.
   6) Infants should receive all recommended vaccinations.
   7) Supervised, awake tummy time is recommended daily to facilitate development.

8) Encourage a smoke-free environment.
9) To decrease the risk of SIDS, the AAP recommends room sharing, but not bed sharing, until 1 year of age optimally.
10) Instruct parents to inspect the crib to be used at home to ensure that it meets current safety requirements. The Consumer Product Safety Commission (CPSC) issues the safety standards for both full-size and non–full-size baby cribs. The most recent rules at the time of publication of this text went into effect in 2011. All cribs manufactured and sold in the United States must meet these standards. Standards relate to slat width, spacing, and strength; mattress size and composition; crib construction and hardware; and surface coatings used on the crib (CPSC, n.d.).
11) Sleepwear. Sleepwear is also regulated by the CPSC. Infant sleepwear should not be loose-fitting and should be flame resistant.
    a. Home safety topics. Topics should include, but are not limited to, bathing, medication storage, preparation, and administration (both for the neonate going home and for any other children at home), general baby care (including oral feeding), and emergency phone numbers (e.g., pediatrician, 911, or the Poison Control Center).

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CHAPTER 19

Discharge Planning and Transition to Home

Pat Hummel and Margaret M. Naber

OBJECTIVES

1. Describe current trends in the discharge of a high-risk infant.
2. Identify individualized clinical criteria for discharge.
3. Discuss the role of the family in discharge of a high-risk infant.
4. Describe discharge planning and the transition-to-home process for a high-risk neonate.
5. Identify discharge teaching needs for parents of a high-risk infant.
6. Identify key components of infant and family care post-discharge.

Introduction

Discharge planning for a high-risk neonate begins on admission to the neonatal intensive care unit (NICU). Timely discharge decreases medical costs, decreases the risks of hospital-acquired morbidity, and shortens separation of the infant and family. The discharge process can be straightforward for the infant requiring normal newborn care, or it can be very complicated when preparing a family to care for an infant with special needs. A successful discharge consists of a stable infant, a family that is well prepared to care for the infant, and a plan for follow-up care. Goals include optimal growth and development in the home setting, parents who can care for the infant alone or with assistance, and prevention of rehospitalization.

General Principles

A. **Coordinated, comprehensive discharge planning with a safe transition to home is critical for the health and well-being of high-risk infants and their families.**
B. **Infants are discharged with special needs on the premise that the home environment, as opposed to the hospital environment, is beneficial for the child and the family and that health care costs will be decreased.**
C. **Discharge planning begins on NICU admission and continues throughout the hospitalization.**
D. **An interdisciplinary team of skilled professionals ensures successful discharge (Box 19.1).**
E. **Parent–infant relationships and family dynamics are altered by emotional and financial stressors.**
F. **Parents and primary caregivers must be educated to provide complex care for their infant and be empowered to advocate for their infant, facilitating a successful transition to home.**
G. **The medical home model for delivering primary care is particularly important for children with special health care needs.**
H. **The NICU graduate may have special needs at discharge, requiring vigilant follow-up, optimizing health and development.**

Health Care Trends

A. **Medical costs are rising rapidly.**
   1. The newborn period is a major source of uncompensated care and accounts for a high proportion of catastrophic cost cases, which is becoming more prevalent with the increased incidence and survival of premature infants (Grosse et al., 2017).
   2. Economic pressures, including equitable reimbursement for services, and the utilization of costly medical resources continue to challenge health care systems when caring for the infant with complex needs in the hospital and home settings.
B. **Infants are discharged from the NICU requiring care of varying complexity, including tube feedings, multiple medications, monitors, oxygen, ventilators, dialysis, and parenteral nutrition.**
C. **Discharge of the infant with special needs can be accomplished in a safe and positive manner, benefiting the infant and family.**
   1. The infant must be physiologically stable before discharge.

Box 19.1

Members of Interdisciplinary Discharge Planning/Transition-to-Home Team

Parents
Neonatologist/neonatal nurse practitioner (NNP)/resident/primary and/or bedside nurse
Primary pediatrician
Subspecialty physicians and advanced practice nurses, as applicable
Social worker
Discharge planning coordinator/case manager
Developmental assessment and early intervention (EI)/follow-up team member
Home care nurse
Infant-specific support services as needed: therapies, including occupational, physical, and speech; registered dietitian; lactation support; respiratory therapist; pharmacist
Durable medical equipment representative

2. The parents must be able and willing to care for their infant in the home.
3. Parental education must be complete before discharge, with parents demonstrating competency in all aspects of infant care.
4. Skilled home nursing care contributes to the successful discharge of the high-risk infant.

D. **Discharge planning includes the case manager, whose role includes utilization review; insurance verification of reimbursement; and coordination of the discharge process.**

E. **Clinical pathways and care maps are effective tools for discharge planning and tracking outcomes.**

F. **The medical home model for delivering primary care is recognized as optimal in the care of the NICU graduate. The American Academy of Pediatrics (AAP) developed the medical home model for delivering primary care that is accessible, continuous, comprehensive, family centered, coordinated, compassionate, and culturally effective for all children and youth, including those with special health care needs** (AAP, 2018)**.**

G. **NICU design is moving toward private rooms, which enhances family interaction and caregiving and facilitates discharge preparation.**

H. **Electronic medical records are increasingly used, allowing improved documentation, retrieval, and interdisciplinary communication.**

I. **Evidence-based care is provided in the NICU and home care setting.**
1. Resources include the Cochrane Neonatal Reviews, the Vermont Oxford Network (VON), and the Eunice Kennedy Shriver National Institute of Child Health and Development (NICHD) Neonatal Research Group.
2. Additional organizations that publish guidelines for transition to home for the high-risk infant include the AAP, the National Association of Neonatal Nurses, the Association of Women's Health, Obstetric and Neonatal Nurses, the March of Dimes, and the National Guideline Clearinghouse.

J. **Childhood disability is increasing, and emotional, behavioral, and neurologic disabilities are now more prevalent than physical impairments.**
1. Children and youth with special health care needs are defined by the Maternal and Child Health Bureau (MCHB) of the Department of Health and Human Services, Health Resources and Services Administration as "those who have or are at increased risk for a chronic physical, development, behavioral, or emotional condition and who also require health and related services of a type or amount beyond that required by children generally." This definition is broad and inclusive, and it emphasizes the characteristics held in common by children with a wide range of diagnoses (Health Resources & Services Administration Maternal & Child Health, 2018).
2. Approximately 20% of U.S. children under 18 years of age have a special health care need, based on the MCHB definition.
3. One in five U.S. families has a child with a special health care need.

K. **Increased collaboration between neonatal providers to improve outcomes and neonatal care.** A primary example of this is the VON. VON maintains a database tracking the care and outcomes of high-risk newborn infants from over 1000 centers around the globe (Pai et al., 2018).

Individualized Discharge Criteria for the Infant and Family

A. **Careful discharge planning, ensuring medical stability of the infant before discharge, is essential to successful NICU discharge and the home experience.**

B. **The required period of stability before discharge has not been studied or standardized.**
1. Controversy and wide variations in practice exist regarding the length of time an infant is free of apnea or bradycardia alarms before discharge. There are no data to suggest that a diagnosis of apnea of prematurity is associated with an increased risk of sudden infant death syndrome (SIDS) or that home monitoring can prevent SIDS in former preterm infants. Routine home monitoring for preterm infants with resolved apnea of prematurity is not recommended except for an unusually prolonged

Box 19.2

Infant Readiness for Hospital Discharge

The AAP provides guidelines to help healthcare providers determine when discharge of the high-risk neonate is appropriate.

- Consistent pattern of weight gain.
- Able to maintain a normal body temperature.
- Able to breast or bottle feed without becoming apneic, bradycardic, or hypoxemic.
- Has reached physiologic maturity and demonstrates a pattern of stable vital signs.
- Has received recommended immunizations, as appropriate.
- Metabolic screening performed.
- Hematologic status assessed and therapy instituted if indicated.
- Nutritional assessment completed and dietary and pharmacologic therapy instituted if indicated.
- Hearing and funduscopic evaluation complete.
- Neurodevelopmental and neurobehavioral status assessed and demonstrated to parents.
- Car seat evaluation complete.
- Review of hospital course complete, unresolved medical problems identified, plans for follow-up monitoring and treatment instituted.
- Screening for critical congenital heart disease.
- Multi-disciplinary home care plan developed.

Data from The American Academy of Pediatrics, Committee on Fetus and Newborn. (2008). Hospital discharge of the high-risk neonate. *Pediatrics, 122*(5), 1119–1126.

course of recurrent apnea (Committee on Fetus and Newborn and American Academy of Pediatrics., 2003). The AAP reaffirmed this statement in 2007. The apnea monitor can usually be safely stopped after 43 weeks adjusted age.

2. Practice surrounding discharge decisions for the alarm-free period for infants with apnea of prematurity varies widely. Common practice is to discharge the infant after 5 to 7 alarm-free days (Eichenwald et al., 2016). Longer periods of monitoring may be suitable for infants born at less than 26 weeks' gestation. Infants born preterm may develop apnea with other stressors, such as general anesthesia or viral illness, and require extended monitoring.
3. The period of time to monitor an infant after discontinuing caffeine is also controversial. One study that measured caffeine levels showed that caffeine may not reach subtherapeutic levels until 11 to 12 days (Doyle et al., 2016). Other research found that caffeine can be discontinued at 33 to 35 weeks corrected age with a failure rate of 10% (Haddad et al., 2015). Bronchopulmonary dysplasia (BPD) diagnosis and Hispanic ethnicity were found to be predictive of failure. The authors state that it is generally safe to discharge infants 7 days after the caffeine was discontinued if no significant monitor events occur during that time.
4. Discharge of a technology-dependent infant should be anticipated and planned, with the interdisciplinary team and family agreeing on an end point and a stability point for discharge. Support should then be maintained and the infant prepared for discharge without changes. Because response to changes in care may not be apparent immediately in an infant with a chronic illness, weaning and other major changes must not occur close to discharge.

C. **Assessment of the home and parental capabilities guides a safe discharge.** A multitude of factors contribute to the ability of a family to care for their medically complex infant in the home. Parent health, siblings, family support, financial obligations, home facilities, proximity to health care, transportation options, child care or day care considerations, and other issues may prohibit discharge to the parent's home. Infant and parent needs must be balanced to achieve a safe discharge.

D. **General criteria for infant readiness for hospital discharge are given in** Box 19.2. The points in Box 19.2 are modified from the AAP criteria to include screening for critical congenital heart disease. See Chapter 28 for specific information regarding screening for heart disease.

Parenting in the NICU and After Discharge

A. **Parents need emotional support as they struggle to cope with the ups and downs and uncertainties that accompany parenting an ill newborn** (Purdy et al., 2015).
   1. Research with mothers and fathers in the NICU suggests that posttraumatic stress symptoms and acute stress disorders are common in parents of very low birth weight (VLBW) infants (Helle et al., 2018).
   2. Discharge of the infant is a joyful but stressful time for parents, particularly when the infant has complex needs (Bowles et al., 2016; Boykova, 2016a, 2016b).
   3. Fathers' emotional experiences with their preterm infants in the NICU vary, requiring individualized

support (Stefana et al., 2018). Some fathers are eager to touch their infant without fear, whereas others prefer not to touch their baby at first, with fears of breaking or infecting their infant. Fathers of infants of lower gestational age are less likely to touch and interact with their infant.

4. Social work, pastoral care, and NICU parent-to-parent support groups can be beneficial and optimally tailored to meet the family's needs (Hall et al., 2015). March of Dimes and other organizations provide parent support online; local chapters may also provide support groups. Online and social media support groups are available as well.

B. **Parenting an infant after NICU discharge may present many challenges, including multiple physician appointments, complex infant care, and the uncertainties of the infant's future.**
   1. The impact of preterm birth on parents and families was explored 2 years after NICU discharge (Lakshmanan et al., 2017). Lower family functioning was associated with parents taking more unpaid hours off from work, increased debt, financial worry, unsafe home environment, and social isolation. Emotions affecting the parent were also associated with social isolation and unpaid time off from work. Parental time limitations were associated with social isolation, unpaid time off from work, financial worry, and an unsafe home environment.
   2. Enrollment in early intervention (EI) and Medicaid were found to be helpful to parents.

C. **Postpartum depression is common and exacerbated by parenting a high-risk infant.**
   1. NICU staff and home care nurses must remain vigilant, referring mothers for further care when depression is recognized (Hynan et al., 2015).
   2. Research with parents of very preterm infants found that mothers and fathers have elevated rates of depression and anxiety symptoms that declined over time, although remaining above expected levels throughout the newborn period and at 6 months (Pace et al., 2016).
   3. A systematic review and meta-analysis of NICU-based interventions to reduce maternal depressive or anxiety symptoms was conducted (Mendelson et al., 2017). The evidence is strongest for the impact of cognitive-behavioral therapy interventions on maternal depressive symptoms, but was not found to reduce anxiety symptoms.
   4. Mothers with mental health disorders require more support to be ready for discharge (McGowan et al., 2017). Research revealed that mothers with a mental health disorder perceived less NICU support, less emotional readiness for discharge, and lower family cohesion compared with mothers without mental health disorders.

D. **Cultural differences should be considered, as some families may expect the infant to stay in the hospital until the special needs are resolved.**

E. **The family is the constant in the infant's life and needs to be an active participant in care, starting at NICU admission.**
   1. Continuing parental education involves assessment of knowledge and readiness to learn. Most parents desire an understanding of their infant's disease process and status. Caregivers assist parents in learning their infant's behaviors and providing individualized care. Parents learn from observing NICU care and actively participating in their infant's care. Parent participation in daily rounding, care conferences, and discharge planning supports the family in their roles as decision makers and in advocating for their infant. Fathers, as well as mothers, identify NICU environmental factors as potential barriers or facilitators to parent involvement (Feeley et al., 2013).
   2. Parents of children with medically complex care were interviewed to examine the discharge process (Leyenaar et al., 2017). Important aspects discovered were effective engagement with health care providers, respect for families' discharge readiness, care coordination, timely and efficient discharge processes, pain and symptom control, self-efficacy to support recovery and ongoing child development, and normalization and routine. These same factors also emerged in interviews with health care providers, with minor differences.

F. **Assessment of parental knowledge base and previous infant care experience contributes to an individualized teaching plan.**
   1. Family educational, social, emotional, and financial needs must be assessed, and discharge plans should be individualized according to these needs.
   2. Barriers to parental learning and participation in care need to be assessed and resources identified to alleviate the barriers. Recognizing parental needs and addressing each area in the discharge plan will ease the transition to home. Current caregiver knowledge level is assessed before teaching sessions, and each session is individualized according to the needs of the infant and family. Health care providers' perceptions of barriers include obstacles to parent visitation, communication/language barriers, difficulties in establishing breastfeeding, insufficient human resources, and poor links between hospital and community-based resources (Raffray et al., 2014).
   3. Learning experiences can be offered through hands-on care, demonstration of specific care practices, and verbal reinforcement. Information can be obtained from a variety of sources, including individual demonstration, group teaching sessions with

other parents, published teaching tools, videos, simulation, written materials, and Internet resources (Raines, 2017).

4. The teach-back method of patient education is a way of checking understanding by asking the parent to state in their own words what they need to know or do about their infant's health (Agency for Healthcare Research and Quality, 2015). This includes the show-me method to confirm that parents can perform care that has been instructed.

Discharge Preparation and Process for All NICU Infants

A. **Discharge planning begins at admission.**
   1. A long-term view of the infant's hospitalization is essential to discharge planning.
   2. A care map may assist in this process by cueing the team at specific intervals to plan for discharge.

B. **Discharge teaching should begin well before the projected discharge date.**
   1. Planning should include a timeline to complete parent education and all steps necessary for home transition.
   2. Written information regarding the infant's care must be provided. Consider simulation to help parents feel more prepared (Raines, 2017).

C. **Feeding management.**
   1. Encourage breastfeeding and provide lactation support. Facilitate acquisition of a high-quality breast pump early in hospitalization.
   2. Significant factors affecting duration of breastfeeding include exposure to kangaroo care, maternal education, and volume of breast milk expressed during the first week after discharge (Briere et al., 2014).
   3. Optimal nutrition is essential for improving developmental outcomes in preterm infants. Changes in nutritional care have been abundant, and most NICUs have achieved improvements in preterm infant growth. A large retrospective study in California found that growth to discharge progressively improved from 1997 to 2012, but growth parameters remained lower than normal in infants (Wells et al., 2017). Research in infants with birth weights under 1500 grams found an association between lower body weight at corrected age of 6, 12, and 24 months and poor neurodevelopmental development (Hsu et al., 2018). Close nutritional follow-up and special formulas providing increased caloric and nutrient density are frequently necessary (Japakasetr et al., 2016).
   4. Provide prescriptions as needed for formula well before discharge. Specialized formulas may be difficult to find and may need to be ordered.
   5. The Women, Infant, and Children (WIC) nutritional program may not provide special formulas or may not provide enough formula for the infant's needs; identification of this obstacle must be ascertained well before discharge.
   6. Assess parental ability to buy formula, especially expensive elemental formulas, and help as needed. Letters of necessity may assist in obtaining coverage.

D. **Medication management.**
   1. Most infants are discharged with vitamin and iron supplementation.
   2. Optimize dosing of medication and provide prescriptions and instructions for parents.
   3. Encourage parents to bring prescribed medications to the NICU to verify the correct medication and to facilitate teaching of appropriate dosage.

E. **Health care appointments after discharge.**
   1. A primary care provider (PCP) is selected and an appointment is scheduled within 1 week of NICU discharge. The discharge team may be able to recommend a PCP who is willing and able to care for the infant's needs. Parental requests and third-party payor restraints should be equally considered in this process. Ideally, parents may meet with the PCP before discharge.
   2. Subspecialty appointments are scheduled as appropriate, such as ophthalmology, urology, neurology, and developmental follow-up.
   3. The family may require transportation assistance to attend appointments.
   4. Ongoing assessment and assistance with family financial needs should be addressed before discharge, with referrals to the appropriate agencies (i.e., WIC, Social Security, state governmental assistance, private charities). Families should be aware of community resources available to them, such as EI services, case management services, counseling, and transportation assistance. Volunteer agencies, local and national parent support groups, and Internet resources may be recommended, as appropriate.

F. **A comprehensive discharge summary, including resolved and ongoing problems, is given to the family on discharge and sent to postdischarge caregivers.** See Box 19.3 for a list of information to be given to parents. An electronic summary and information can be provided on a disc or flash drive for computerized use.

G. **Key teaching points.**
   1. Basic infant care practices such as bathing and diapering.
   2. Circumcision care.
   3. Back to sleep/safe sleep practices (Box 19.4).
   4. Car seat use (Box 19.5).
   5. Shaken baby syndrome prevention (Box 19.6).

Box 19.3

Pertinent Information for Parents and Care Providers at Time of Discharge

Comprehensive discharge summary, including resolved and ongoing problems
List of follow-up appointments with timing, location, and phone numbers specified
Immunizations given
Respiratory syncytial virus (RSV) prophylaxis given
Written plan of care, particularly for complex discharge (could be electronic)
Medication schedule
Nutrition plan and formula recipe
Testing/imaging results: head ultrasound, renal ultrasound; computed tomography (CT), electroencephalogram (EEG), electrocardiogram (ECG); echocardiogram, magnetic resonance imaging (MRI), other pertinent testing
Additional test results such as pneumograms/sleep studies, eye examination findings, hearing screen results, newborn metabolic/state screen results
Pertinent laboratory values: recent complete blood count with hematocrit, hemoglobin, and reticulocyte count; bone health; medication levels

Box 19.4

Safe Sleep Guidelines

- Do not fall asleep with your baby in your bed. If you breastfeed, be sure to place baby back in the crib before dosing off.
- Do not allow the baby to sleep with other children. Babies should never bed-share with children or adults.
- Use a bare crib with a firm mattress. Put nothing in the bed but the baby and the clothes needed to stay warm but not too warm. Don't use pillows, positioning devices, blankets, or other coverings. Remove bumper pads from baby's crib. Make sure nothing can ever get close to the face. There is evidence that rebreathing (inhaling the air that was breathed out) can affect the infant's arousal.
- Keep your baby's crib in the parents' room until he or she is at least 6 months of age and has learned to easily roll both ways on his or her own.
- Babies should be safely put in a bare crib on their backs even when they are fretful, have a cold, or are otherwise needing extra comfort. Just keep the crib close to you and you will both be comforted. Babies with colds are at higher risk for sudden infant death.
- Do not allow anyone to smoke around the baby. Do not have your baby in a room or car where people have recently been smoking.
- Offer your baby a pacifier. For breastfeeding mothers, introduce the pacifier after the baby has learned to feed. Do not attach the pacifier to the baby or crib because it can cause a choking hazard. Several studies have found a lower risk of sleep-related death when babies use a pacifier.
- Breast-feed your baby. This can lead to an overall healthy baby and may help soothe a fretful baby.
- Some mothers learn that putting babies on their stomachs may make them cry less. And although that is true for many, if not most, babies, it is dangerous and puts babies at higher risk for sleep-related deaths.
- Give your baby plenty of interactive tummy playtime. This should never be in a bed. A good place for this is on a play mat on the floor. Never leave the baby on their stomach unattended. Play with them as they do baby push-ups.
- When you travel with your baby, be sure to plan a safe place for him to sleep. Call ahead to the hotel to make sure they have safe cribs available, or take your own portable crib.
- Do not put too many clothes on the baby or keep him or her in a room that is too hot. If the baby is sweating, remove some of the clothing.
- If your baby has periods of not breathing, going limp, or turning blue, tell your pediatrician at once. And if your baby stops breathing or gags excessively after spitting up, discuss this with your pediatrician immediately.
- Thoroughly discuss each of these points with all caregivers.
- If you take your baby to daycare or leave him with a sitter, provide a copy of this list to them. Make sure they follow all recommendations.

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Box 19.5

Car Seat Guidelines and Testing

Discharge policies for newborns should include the following:

1. Determination of the most appropriate car safety seat for each newborn according to maturity and medical condition by a designated hospital employee.
2. Provision of information and training for parents and guardians should be presented before discharge on the generic issues related to correct use of car safety seats. Hands-on teaching including "return demonstration" should be a part of this instruction. The installation of a specific car seat in a specific car must be the parent's responsibility. Resources to address these issues are available from the American Academy of Pediatrics (AAP).
3. Infants born at less than 37 weeks' who demonstrate apnea, bradycardia, or oxygen desaturations while sitting in car safety seats should have a car seat test before hospital discharge. The car seat test should be performed preferably with the infant's own car safety seat and the period of observation should be at least 90 to 120 minutes or the duration of travel, whichever is longer. The car seat test should be performed with the infant optimally restrained and with the safety seat placed at an angle that is approved for use in the vehicle. Hospitals should develop protocols for car safety seat observation before discharge for infants at high risk including those born at less than 37 weeks of gestation and older at-risk infants such as those with hypotonia, micrognathia (Pierre Robin sequence), and infants who have undergone congenital heart surgery. Additional information is available at the AAP website.

From Bull, M.J., Engle, W.A., Committee on Injury, Violence, and Poison Prevention and Committee on Fetus and Newborn, American Academy of Pediatrics. (2009). Safe transportation of preterm and low birth weight infants at hospital discharge. *Pediatrics*, *123*(5),1424–1429.

Box 19.6

Shaken Baby Syndrome/Abusive Trauma

Shaken baby syndrome/abusive head trauma (SBS/AHT) is a term used to describe the constellation of signs and symptoms resulting from violent shaking or shaking and impacting of the head of an infant or small child. The American Academy of Pediatrics (AAP) describes SBS as a subset of AHT, with injuries having the potential to result in death or permanent neurologic disability.

Why is Shaking a Baby Dangerous?

Violent shaking for just a few seconds has the potential to cause severe injuries. Although shaking may cause injury to children of any age, children are most susceptible to being injured during their first year of life. Factors that contribute to a baby's vulnerability include:

- Babies' heads are heavy and large in proportion to their body size.
- Babies have weak neck muscles.
- Babies have fragile, undeveloped brains.
- There is a large size and strength difference between the victim and the perpetrator.

Possible Signs and Symptoms of SBS/AHT

- Lethargy/decreased muscle tone
- Extreme irritability
- Decreased appetite, poor feeding, or vomiting for no apparent reason
- Grab-type bruises on arms or chest
- No smiling or vocalization
- Poor sucking or swallowing
- Rigidity or posturing
- Difficulty breathing
- Decreased level of consciousness
- Seizures
- Head or forehead appears larger than usual
- Soft spot on head appears to be bulging
- Inability to lift head
- Inability of eyes to focus or track movement
- Unequal size of pupils

Consequences of SBS/AHT

- Learning disabilities
- Physical disabilities
- Visual disabilities or blindness
- Hearing impairment
- Speech disabilities
- Cerebral palsy
- Seizures
- Behavior disorders
- Cognitive impairment
- Death

The Period of PURPLE Crying program is an evidence-based SBS/AHT prevention program available since 2007. The program has two aims:

- To support parents and caregivers in their understanding of early increased infant crying
- To reduce the incidence of SBS/AHT

The letters in PURPLE crying stand for

P: Peak of crying: Your baby may cry more each week, the most in month 2, then less in months 3 to 5

Continued

Box 19.6—cont'd

Shaken Baby Syndrome/Abusive Trauma—cont'd

U: Unexpected: Crying can come and go and you don't know why
R: Resists soothing: Your baby may not stop crying no matter what you try
P: Pain-like face: A crying baby may look like they are in pain, even when they are not
L: Long lasting: Crying can last as much as 5 hours a day or more
E:. Evening: Your baby may cry more in the late afternoon and evening

For more information on PURPLE Crying see https://dontshake.org/purple-crying

From https://dontshake.org

6. Infant cardiopulmonary resuscitation (CPR) training.
   a. Encourage parents and other caregivers to attend an infant CPR class. These are frequently taught by a CPR nurse instructor, individually or in groups, before discharge (Murray and Joseph, 2016).
   b. The AAP, in coordination with the American Heart Association and using the technology of Laerdal Medical, developed *Infant CPR Anytime*, which contains everything needed for a lay individual to learn infant CPR and relief of choking. This is a self-directed learning product that allows those caring for infants to learn the core skills of infant CPR and relief of choking in about 20 minutes. For more information see http://cpr.heart.org/AHAECC/CPRAndECC/Training/CPRAnytime/InfantCPRAnytime/UCM_473170_Infant-CPR-Anytime-Training-Kits.jsp.
7. Anticipatory guidance, educating parents regarding expectations postdischarge, and tips on adapting to home (Box 19.7).

Box 19.7

Tips for Parents

Home Readiness for Special-Needs Infant

Place for infant to sleep safely
Car seat
Heat, electricity, telephone, running water
Normal baby supplies: diapers, clothing, bottles
Formula, measuring cups and spoons, blender, pitcher
Medications and syringes
Equipment—monitor, oxygen, etc.
Emergency phone numbers and plan
Flashlight with extra batteries
Thermometer and bulb syringe (provided on discharge)
Pediatrician appointment arranged within 1 week
Other appointments made before discharge

Take Care of Yourself

Ask for help from family, friends, and health care providers.
Depression is common, get treatment—you want to be the best parent you can be.
Enjoy your infant.

Infant Adjusting to the Home

Realize that your baby will notice a difference in surroundings.
Try to get into a routine.
Your baby may sleep better initially if there is a constant background noise (fan, soft music). Try to gradually lower the volume until your baby can sleep without noise.
Put your baby in bed when awake, when possible; this allows learning how to get to sleep independently rather than depending on you. This will help with sleeping through the night.
Some babies cry more in the evening because they have received too much stimulation during the day—try decreasing the noise and activity throughout the day.

Helping Your Infant Grow and Develop

Hold your baby and respond to cries. Try not to hold your baby constantly. Short periods of crying are fine if not due to hunger or need for other attention. This helps your baby learn that you are there, but helps learn self-calming.
Talk to your baby often.
Read books to your baby.
Turn off the television and videos—these hurt your baby's ability to pay attention for longer periods and decrease their ability to calm themselves. Children should not watch TV until they are 2 years old.
Get therapies for your baby as the NICU or care provider recommends. Many infants need extra help for development. Therapies help your baby to develop the best he or she can, and therapy keeps your baby from developing or keeping abnormal developmental skills.
Avoid walkers, exersaucers, and jumpers. These place a baby upright before they are ready and keep the baby from developing normally.

Box 19.7

Tips for Parents—cont'd

Babies need as much time as possible on their tummy, on a firm surface (playpen, floor), when they are awake and you are with them.
Make feeding time pleasant. Do not force-feed your baby. Ask for help if you have problems feeding your baby.

Websites and Social Media for Parents

http://www.preemies.org. Support and resources for parents of preemies
www.prematurity.org. Support preemie parents by providing information on prematurity and preemie care
www.preemiecare.org. Helping families and NICU support groups not only grow but blossom
www.support4NICUparents.org. Provides useful resources for both parents and professionals
www.synagis.com. Gives information on Synagis for RSV (respiratory syncytial virus) protection
www.facebook.com. Search for groups for support groups and information

Box 19.8

Infection Prevention After Discharge

Routine infant immunizations
Respiratory syncytial virus (RSV) protection: monthly injections November through March for certain preterm infants
Influenza injections: for infants more than 6 months old, given in the fall in two doses 1 month apart
Influenza injections: for all caregivers, all people in the home
Handwashing—the best method to prevent infection
Disinfectant hand gels used by caregivers
Avoid contact with ill people, especially children

8. Infection prevention (Box 19.8).
9. Infant temperament, developmental tasks, and milestones reviewed, including sleep patterns, feeding patterns, and infant state regulation.
10. Review care issues such as vaccinations, traveling, and visitors.

Additional Considerations for Discharge of Infants With Complex Medical Needs (Table 19.1)

A. **Many infants are discharged from the NICU with chronic conditions requiring ongoing medical care and increasing societal burden.** Major morbidities tend to be highest in the smallest survivors (<1000 g at birth) and can include significant lifelong conditions such as cerebral palsy, cognitive delays, and visual or hearing loss (Johnson and Marlow, 2017; Johnson et al., 2016). Some infants outgrow their special discharge needs; others do not.

B. **Efficient discharge for medically complex patients requires support of an interdisciplinary team to proactively address discharge needs, ensuring patients are ready for discharge when medical goals are met** (Statile et al., 2016).

C. **Intermittent care conferences with the family throughout hospitalization ensure open communication, facilitating a smooth transition to home.** These can be formalized and include all team members or simplified to include the parents and a few key team members.

D. **For complex discharges, a comprehensive care conference must be completed well before discharge.**
   1. Parents are encouraged to bring a list of questions and needs to the conference.
   2. All community providers can be invited to participate in the discharge care conference. Direct contact with the PCP confirms willingness to care for the infant and enables communication and discussion of ongoing health issues and needs.
   3. Criteria for discharge are discussed, and the teaching plan is reviewed. The anticipated course of recovery and ongoing problems are outlined, and the home care/durable medical equipment needs are discussed.
   4. Strategies to prevent rehospitalization are discussed. Nurses can help minimize rehospitalization of infants by parental education, telephonic counseling, frequent observation, and home care support (Aykanat Girgin and Cimete, 2017). Parents should know how and when to contact health care providers with questions and when to contact 911.

E. **Infant care specifics to be completed before complex discharge.**
   1. Perform parent and home evaluation, which may include a home visit if the infant has extensive needs.
   2. Establish a realistic plan for care at home, including feeding schedules, medication schedules, and treatments.

Table 19.1

Planning for Discharge With Technology

Potential Technology	Stability Criteria	Diagnosis/ Problem	Teaching Required	Home Nursing Needs	Supplemental Services
Oxygen Apnea monitor Pulse oximeter	Stable oxygen flow without changes for a defined number of days before discharge (varies from 5 to 10 days, per unit discretion)	BPD Other CLD	Signs or symptoms of respiratory distress DME CPR demonstration Medication administration	Intermittent skilled nursing visits	Occupational and physical therapy Speech therapy Nutrition
Nasogastric or gastrostomy tube feedings	Stable pattern of weight gain (15 to 30 g/day)	FTT Severe GERD Oral aversion Feeding dysfunction	Nasogastric tube placement Gastrostomy tube care Tube feedings High-caloric formula preparation Bolus (gravity feedings) Pump feedings	Intermittent skilled nursing visits	Speech therapy Nutrition
Apnea monitor	Free of apnea/bradycardia events requiring intervention, for a defined number of days before discharge (varies from 2 to 7 days, per unit discretion)	Apnea of prematurity GERD	DME CPR demonstration Medication administration Positioning	Intermittent skilled nursing visits	
Tracheostomy	Stable oxygen requirement	Various disorders affecting airway competence or need for ventilation	Signs or symptoms of respiratory distress DME CPR demonstration Medication administration Suction equipment Tracheostomy care	Private duty nursing (approximately 8 hours/day) or intermittent skilled nursing, depending on family preference and needs	Speech therapy Occupational or physical therapy Respiratory therapy (usually by DME provider)
Ventilator	Stable respiratory condition without changes in ventilator support or medication for an agreed-upon period before discharge (varies from 2 to 4 weeks, per unit discretion) Generally need to be stable on Fio_2 40% or less	BPD Central hypoventilation Various disorders affecting ventilation	Signs or symptoms of respiratory distress DME CPR demonstration Medication administration Power needs in the home Ventilator problem solving Ventilator setting adjustments	Private duty nursing (approximately 12 to 24 hours/day)	Occupational or physical therapy Speech therapy Respiratory therapy (usually by DME provider) Apply for handicapped parking permit
TPN	Steady growth on parenteral nutrition	Inability to grow on enteral feedings	IV pump setup and troubleshooting TPN bags and tubing setup. Signs of bloodstream infection Central line dressing change	Intermittent skilled nursing, daily with hanging new bag and tubing until parent comfortable	DME provider for pump Team/professional to order IV fluids and monitor TPN pharmacy Plan for blood draws/laboratory testing

BPD, Bronchopulmonary dysplasia; *CLD*, chronic lung disease; *CPR*, cardiopulmonary resuscitation; *DME*, durable medical equipment; *FTT*, failure to thrive; *GERD*, gastroesophageal reflux disease; *IV*, intravenous; *TPN*, total parenteral nutrition.

F. **Complex medication management.**
   1. Optimize dosing and do not change close to discharge. Round home medication doses to the nearest 1/10 (0.1) mL (except in extraordinary circumstances) to reduce the chance for error.
   2. Provide prescriptions several days before discharge for parents to fill and bring to the hospital for verification and teaching. Some medications need to be compounded by the pharmacy and may not be immediately available.
   3. Verify that the medication is covered by insurance. In absence of coverage, determine if the parent is able to afford the medication.
   4. Ensure that the medication is ordered and filled with the correct concentration, as several formulations may be available.
   5. Problems occur when the generic name is used on the bottle and the trade name is on the medication list. Verify that names match, or provide both names.
   6. Complete a medication sheet for home use, providing the dose and time of each medication. Avoid medication administration more than three times daily, and avoid nighttime dosing. Schedule medications carefully, as some medications cannot be mixed together or given concurrently.
   7. Have the caregiver bring the medication to the bedside. Verify that the container is properly labeled and instructions are documented in milliliters to be given, not with milligrams only.
   8. Observe the parent drawing up the medication.

G. **Formula/feeding teaching for specialized formulas and nonoral feeding.**
   1. Teach the parent how to mix the formula. Verify that the parent has the correct measuring cups/spoons, blender, and pitcher, as these may need to be provided.
   2. Written recipes for mixing formulas must be provided.
   3. Observe the parent feeding the infant, either orally or by nasogastric (NG) or gastrostomy tube.
   4. Gastroesophageal reflux symptoms are common in many infants. The use of medications to suppress or block stomach acid is controversial (D'Agostino et al., 2016). Parents must be taught how to manage reflux symptoms.

H. **Home oxygen care is taught by hospital staff and durable medical equipment (DME) provider personnel.**
   1. Clarify hospital flow rate and verify in the home. Hospital flow is usually in decimals (0.25 L/min); home flowmeters are often in fractions (¼ L/min). Round up oxygen flow in the hospital to increase the oxygen, and avoid decreased oxygen flow in the home.
   2. Increased flow may be needed in the home because of the long tubing or when using an oxygen concentrator because the output is of slightly lower concentration than that from the tank.
   3. Clarify that the parent knows how to appropriately adjust oxygen flow in case of an emergency. A parent may think that they are increasing the oxygen when they are turning the flow ½ to ¼ L/min, because the denominator number is larger.
   4. Establish an outpatient plan for weaning the oxygen before discharge. One study of infants with BPD discharged on oxygen found that the median age of weaning off supplemental oxygen was about 10 months after NICU discharge (Yeh et al., 2016). This study also found that unsupervised weaning of supplemental oxygen occurred in about one third of subjects with BPD.

I. **Apnea monitor teaching.**
   1. This teaching is generally completed by the DME provider personnel.
   2. Review monitor use and troubleshooting.
   3. Teach alarm response and CPR.
   4. Parents may remove the monitor when they are directly attending to the infant.

J. **Specialized teaching topics such as tracheostomy care, suctioning, ventilator, ostomy care, central line care, feeding alternatives, and any special equipment** (see Table 19.1).
   1. NG feedings can help improve short-term growth after hospital discharge in children with chronic illness. Research with a population of infants and children discharged with NG feedings revealed that the average time to discontinuation of NG feeds was 4.8 months, with about 50% attaining full oral feedings, 10% having a gastrostomy tube placed, and 9% remaining on NG feedings (Rosen et al., 2016).
   2. Helpful website for tracheostomy teaching is at www.tracheostomy.com with a mission "[t]o help assure the highest quality home care for children with tracheostomies."
   3. A helpful website for tube feeding and IV nutrition is at www.oley.org. Their mission is "[s]triving to enrich the lives of those living with home intravenous nutrition and tube feeding through education, advocacy, and networking."
   4. DME is ordered and teaching sessions arranged.
   5. Overnight stay in the transition room if possible.
   6. Respite care is explored, including strategies to deal with stress.

K. **Selection of a home nursing agency and DME provider that will meet the needs of the infant and the family.**
   1. Identify home nursing needs—intermittent or private duty.
   2. Arrange home nursing care after verification of third-party payor requirements and restraints.

3. Home care personnel should be familiar with the infant's medical issues, with skilled, experienced personnel available for home visitation.
4. Criteria for selecting a DME provider.
   a. Third-party payor restraints.
   b. Availability of appropriate supplies.
   c. Ability to respond to emergencies.
   d. Availability of backup equipment.
   e. Experience of care providers.
   f. Location of the agency.

L. **Discharge to a location other than the parent's home may be necessary because of medical necessity, family proximity to facilitate teaching, or family dynamics.** The NICU team and parents may determine that transfer to an interim facility that routinely transitions children with special needs into the home or a facility geographically closer to the parent would facilitate transition to the parent's home.
   1. Most infants are discharged to the parent's home; transfer to a transitional care facility is infrequent, even for children with multiple chronic conditions (Berry et al., 2016). This varies significantly by race/ethnicity and across states. Further investigation is needed to assess reasons for this variation and to determine for which children home health care and transitional facilities are most effective.
   2. Alternatives vary but can include specialized foster care, pediatric rehabilitation hospitals, pediatric nursing homes, transitional care/respite facilities, or inpatient hospice care.
   3. Verify that the facility is able to provide care that meets the infant's needs and that the costs are covered by third-party payors or through state Medicaid waivers.
   4. Parental visitation of the facility before transfer will facilitate selection and help the parent feel confident that the facility will provide appropriate, safe, and competent care for their child.

Family and Infant Care Postdischarge (Box 19.9)

A. **A successful discharge plan and transition to home facilitate collaborative care postdischarge.**
   1. Routine follow-up phone calls after discharge from the NICU can help with the transition and

Box 19.9

Prematurity-Related Problems That Present or Continue After Discharge

Respiratory
Ongoing oxygen dependency
Apnea
Reactive airway disease
Infections

Cardiac
Right ventricular hypertrophy
Cor pulmonale/pulmonary hypertension
Uncorrected congenital heart disease with cyanosis and/or congestive heart failure

Gastrointestinal
Emesis
Gastroesophageal reflux
Constipation
Strictures and bowel obstruction
Hernias (umbilical and inguinal)

Nutritional
Slow growth
Weight less than the 10th percentile on preterm growth curve
Feeding fatigue
Oral aversion
Need for nutritional supplements or hypercaloric formula
Need for adjunct feeding devices (e.g., tube feeding or gastrostomy)

Hematologic
Anemia

Dentition
Delayed tooth eruption
Altered oral and dental structures with arched palate secondary to dolichocephaly, exacerbated by prolonged oral intubation
Enamel defects

Sensory
Visual deficits secondary to retinopathy of prematurity (ROP): myopia, hyperopia, blindness
Strabismus and amblyopia
Cortical blindness
Hearing deficits
Speech and language delays
Hydrocephalus, ongoing shunt problems, such as infection and blockage

Central Nervous System and Neurodevelopmental Differences
Difficult temperament and behavior
Sensory integration dysfunction
Tone and movement abnormalities
Cerebral palsy
Intellectual and developmental disabilities
Learning disabilities
Attention deficits
School problems

improve the discharge process as unidentified problems are addressed (Aykanat Girgin and Cimete, 2017).

2. The effects of a transition home program on 90-day rehospitalization rates of preterm infants were evaluated in a state in the eastern portion of the United States (Vohr et al., 2017). The transition home team worked closely with the NICU, follow-up clinic, and PCP. Team members educated parents; connected parents to community resources; and assisted parents in obtaining transportation, housing, and supplies. Higher-risk families received a predischarge home visit. Postdischarge components included a phone call within 24 hours, a neonatal nurse practitioner home visit within the first week, referral to EI, and around-the-clock phone availability of study physicians. Study findings found that Medicaid insurance (compared with private), non–English-speaking, multiple pregnancies, and BPD were associated with increased risk of hospitalization. The major cause of rehospitalization was respiratory illness. The authors concluded that strategies must be directed at both social/environmental and medical risk factors to decrease the risk of rehospitalization.

B. **Home care nursing may include intermittent home visits or in-home care for infants requiring complex, around-the-clock care.**

1. Transition from a high-tech hospital setting to the home environment may be facilitated by home care nursing. In a survey of parents receiving home nursing visits after NICU discharge, mothers with fewer children and mothers of preterm infants found home nursing visits most helpful (Awindaogo et al., 2016).
2. Infants with complex care are a vulnerable population. Home care and health care utilization errors were investigated in a prospective observational cohort study (Patel et al., 2017). In this research, a total of 363 errors were identified in 241 infants during 635 home visits. The authors concluded that home visits can provide an opportunity to identify, intervene, and resolve homecare and health care utilization errors.
3. Telemedicine was implemented and evaluated in Sweden after NICU discharge, where families were randomized to either routine home care or to home care nurses with telemedicine support, including web pages and video calls (Robinson et al., 2016). The use of the web page and video calls decreased the number of emergency visits to the hospital, and parents felt they did not need as many scheduled follow-up appointments. Parents and nurses were favorable to using telemedicine, but organizational restrictions prevented its optimal use.
4. A Swedish early discharge program for infants at least 34 weeks corrected age with NG tubes and/or oxygen is described where experienced neonatal nurses work in collaboration with neonatologists (Lundberg et al., 2016). Nurses visit the home on a daily to weekly basis, depending on the need. Parents provide the infant's care with guidance. The nurses consult with the neonatologists as needed. Readmission rates were low at 5.2%. The program was evaluated as safe and effective at reducing readmissions.
5. The home care nurse ideally meets with the parents and infant before hospital discharge.
6. The home care nurse reinforces the teaching and clarifies discharge instructions as needed.
7. Intermittent home care is appropriate for infants who are medically stable, with parents able to provide care 24 hours a day without in-home direct nursing care. The home nurse assesses the infant, educates the parent, monitors medications and feedings, and communicates with the medical provider and the payor. Status updates are provided to the medical provider, and a plan of care is formed in conjunction with the multidisciplinary team. The nurse assesses responses to changes in care on subsequent visits. Intermittent nursing visits conclude when the parent is independent with care and the infant is medically and nutritionally stable, is not home-bound, and does not require frequent monitoring.
8. Continuous in-home nursing care is another form of home care reserved for infants with such complex needs that the parents cannot provide care 24 hours a day. Continuous nursing care is usually required for infants with a tracheostomy or home ventilation or for infants requiring constant monitoring or care due to special medical or nursing needs. Continuous nursing care may be provided 24 hours a day or in shorter segments as needed. Twenty-four-hour-a-day nursing care is rarely possible because of financial and staffing constraints.
9. The primary long-term goal of home care nursing is to foster independence. This is achieved by educating the parent and by facilitating resource use and support services.

C. **Links to community agencies and resources facilitate coping with the changing needs of the child.**

1. These links can start before discharge and are facilitated by the home care nurse and the primary provider.
2. A review of articles about parenting a child with a tracheostomy revealed three main themes: (1) parents' experiences of caregiving, (2) parents' social experiences, and (3) experiences of service delivery of having a child with a tracheostomy (Flynn et al., 2013). Although parents encountered emotional

and social challenges, some positive responses to these challenges were reported.

D. **Problems related to prematurity often continue after discharge from the NICU.** Hospital readmissions are common. Parents need education to recognize risk factors leading to readmission to the hospital and for the potential for ongoing problems (see Box 19.9)

E. **Neurologic, developmental, neurosensory, and functional morbidities increase with decreasing birth weight.** Risk factors significantly associated with increased neurodevelopmental morbidity include a complicated NICU course, intracranial hemorrhage or cysts, and ongoing chronic illnesses such as BPD. Preterm infants have a higher incidence of cerebral palsy, intellectual disabilities and disorders of cortical function, language disorders, visual perception problems, attention deficits, and learning disabilities (Griffin et al., 2015; Odd et al., 2016; Upadhyay et al., 2015). In addition, many infants less than 1000 g at birth have weights at less than the 10th percentile at 36 weeks of postmenstrual age (Cleminson et al., 2016; Jadcherla et al., 2017). Particular attention needs to be focused on postnatal growth and developmental assessment postdischarge.

F. **Referrals to a developmental follow-up clinic and to the state EI program are essential components of follow-up care.**
   1. EI programs for preterm infants have a positive influence on cognitive and motor outcomes during infancy, with cognitive benefits persisting into preschool age (Spittle et al., 2015). Follow-up clinics often have criteria that qualify the infant for inclusion, such as gestational age, birth weight, neurologic abnormalities, or other risk factors. The goals of the follow-up clinic include early identification of developmental disability, parent counseling (anticipatory guidance), and identification and treatment of medical complications, along with providing outcome data for the NICU. Clinics are usually staffed by a multidisciplinary team of professionals, including physician, nurse practitioner, occupational therapist, physical therapist, audiologist, psychologist, ophthalmologist, speech and language specialist, respiratory therapist, nutritionist, neurologist, and subspecialists. The first visit usually occurs 1 to 4 months after discharge; follow-up continues for months to years. The goals of a follow-up program may include the following:
      a. Developmental assessment, screening and/or diagnostic, is essential for the infant's well-being and for evaluation of NICU outcomes.
      b. Management of sequelae.
      c. Consultant follow-up assessment.
      d. Parent support.

G. **Many infants discharged from the NICU will meet criteria for EI.**
   1. EI services: A federal mandate requires that each state provide services up to the age of 3 years. The goal of EI is to enhance the development of infants and toddlers with disabilities and to minimize their potential for developmental delay. Each state establishes criteria for eligibility within parameters set by the federal government.
   2. Refer qualifying infants before discharge. Optimally, EI personnel meet with the family before discharge, informing them of services planned and provided.
   3. EI provisions may include screening and assessment; family training; counseling; home therapies (speech therapy, physical therapy, occupational therapy); and services such as psychological, audiology, vision, social work, and transportation.
   4. Therapy utilization after discharge from the NICU was tracked in 57 infants born ≤30 weeks' gestation (Nwabara et al., 2017). Referral for therapy at NICU discharge was accomplished in 91% of the infants, but only 77% received at least one type of therapy during the first 2 years of life. About half of the children who did not receive any therapy in the first 2 years had a developmental delay at an age of 2 years.

H. **Palliative and hospice care.**
   1. Infants with life-limiting conditions without hope for a cure or recovery require a shift of the focus of treatment toward maximizing quality of life. End-of-life care, or hospice care—one aspect of palliative care—supports a peaceful, dignified death for the infant and the provision of loving support to the family and health care providers (National Association of Neonatal Nurses, 2015).
   2. Palliative care should be instituted well before discharge. The infant can be transitioned to the home setting or a palliative care/hospice setting. Referral to an agency or facility that is prepared to care for the infant and family should occur well before discharge. NICU personnel work closely with the agency caregivers and planners to ensure a seamless transition to the postdischarge setting.
   3. The End-of-Life Nursing Education Consortium (ELNEC) project is a national education initiative to provide palliative care training for nurses. Neonatal/pediatric options are available (American Association of Colleges of Nursing, 2018).

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CHAPTER 20

Genetics: From Bench to Bedside

Julieanne Heidi Schiefelbein

OBJECTIVES

1. Define birth defects and possible causes.
2. Become familiar with genetic terminology.
3. Identify the number of chromosomes in a normal human cell.
4. Describe the characteristics and causes of structural and numeric chromosomal abnormalities, modes of inheritance of single-gene disorders, and multifactorial inheritance.
5. Describe what prenatal diagnostic tests are available and which anomalies they detect.
6. Describe the components and benefits of genetic counseling.
7. Identify three patient care management issues in genetic counseling.
8. Verbalize the systematic process used to evaluate the malformed infant.
9. List common congenital malformations and possible mechanisms of cause.

The neonate born with a genetic defect or fetal anomaly presents a challenge to the neonatal intensive care unit (NICU) team. A definitive diagnosis is essential for management and care of the neonate and the neonate's family.

Congenital malformations commonly have multiple causes. This chapter includes information on basic genetics, characteristics, and causes of some common fetal anomalies and a systematic process for the evaluation of the malformed infant. Commonalities of patient care management issues are addressed, with the understanding that every family requires individualized care.

Basic Genetics

TERMINOLOGY

A. **Allele:** one of a series of alternative forms of a gene at the same locus on a chromosome (Jones et al., 2013; Jorde et al., 2016).
B. **Autosome:** one of 22 chromosomes that do not determine the sex of the individual.
C. **Birth defect:** an abnormality of structure, function, or metabolism, whether genetically determined or a result of environmental interference during embryonic or fetal life. A congenital defect may cause disease from the time of conception through birth or later in life (March of Dimes Foundation, 2008).
D. **Chromosome:** structural elements in a cell nucleus that carry the genes and convey genetic information.
   1. Each cell (except erythrocytes) in the body contains all the chromosomes received from both parents within its nucleus.
   2. There are 23 pairs of chromosomes, for a total of 46 chromosomes, with one maternal and one paternal chromosome creating each pair.
E. **Diploid:** containing a set of maternal and a set of paternal chromosomes, for a total of 46 chromosomes.
F. **Gamete:** one of two cells, containing 23 chromosomes (haploid number), with the union of a male gamete and a female gamete required during sexual production to create a new individual (with the diploid number of chromosomes).
G. **Gene:** the smallest unit of inheritance of a single characteristic, responsible for a physical, biochemical, or physiologic trait and located with other genes in linear sequence along the chromosome.
H. **Genotype:** hereditary composition of an individual.
I. **Haploid:** having half the number of chromosomes found in the person's cells; characteristic of the gametes.
J. **Locus:** the position that the gene occupies on a chromosome.
K. **Karyotype:** pictorial representation of the chromosomal characteristics of an individual or species.
L. **Penetrance:** The degree to which an inherited trait is manifested in the person who carries the affected gene (Nussbaum et al., 2016).

M. **Sex chromosomes:** the X and Y chromosomes, which are responsible for gender determination—XX for female and XY for male.

DOMINANCE AND RECESSIVENESS

A. **Phenotype:** observable characteristics of an individual.
B. **Heterogeneous chromosomes:** differing pair of chromosomes, one from each parent, arraying differing genes for specific traits. When there are unlike genes on a locus, one gene dominates.
C. **Homologous chromosomes:** a matched pair of chromosomes, one from each parent, carrying the genes for the same traits.
D. **Dominant gene:** a gene that is expressed in the heterozygous state. In a dominant disorder, the mutant gene overshadows the normal gene. A dose of this gene is needed for expression.
E. **Recessive gene:** a gene whose effect is masked or hidden unless both genes of a set of homologous chromosomes at a given locus are abnormal, thus showing the disease. In a heterozygote (carrier), the normal gene overshadows the mutant gene.
F. **Possible combinations of chromosomes.**
   1. Both genes can be dominant—AA (homozygous).
   2. Both genes can be recessive—aa (homozygous).
   3. One gene can be dominant and one can be recessive—Aa (heterozygous).

AUTOSOMAL DISORDERS

A. **Autosomal-dominant disorders**.
   1. Characteristics of autosomal-dominant disorders.
      a. Males and females are both affected equally; either parent can pass the gene on to sons or daughters.
      b. An affected offspring has an affected parent if the mutation is not new.
      c. Half the sons and half the daughters of an affected parent can be anticipated to have the disorder. There is a 50% chance with each pregnancy.
      d. Unaffected offspring of an affected parent will have all normal offspring if the mate is an unaffected person (assuming complete penetrance).
      e. If two affected people mate, three-fourths of their offspring will be affected. A double dose of the mutant gene in any of the offspring will result in a lethal anomaly (except in the case of Huntington's disease).
      f. Family history of an anomaly indicates a vertical route of transmission through successive generations on one side of the family (if not a new mutation).
   2. Examples of autosomal-dominant disorders: myotonic dystrophy, neurofibromatosis, and coronary artery disease (Cassidy and Allanson, 2010; Jones et al., 2013).
B. **Autosomal-recessive disorders.**
   1. Characteristics of autosomal-recessive disorders.
      a. Both males and females are affected equally.
      b. Parents of affected offspring are rarely affected and are usually heterozygous carriers.
      c. After the birth of an affected offspring, there is a 25% chance with each pregnancy of having another affected offspring and a 50% chance that the offspring will be a carrier.
      d. There may be a distant relative with the disorder.
      e. Affected people who mate with unaffected people will have offspring who will be heterozygous carriers.
      f. If two affected people mate, all offspring will be affected.
      g. No family history indicates a horizontal route of transmission in the same generation.
      h. There can be a difference in expression of the disorder: very mild in one member and extremely severe in another.
   2. Examples of autosomal-recessive disorders: cystic fibrosis, sickle cell anemia, Tay–Sachs disease, thalassemia major (Jones et al., 2013).

X-LINKED DISORDERS

A. **X-linked dominant disorders**.
   1. Characteristics of X-linked dominant disorders.
      a. Both sexes can be affected; because females have a double chance of receiving the mutant X chromosome, they have twice the risk of being affected.
      b. Affected males will have all affected daughters and no affected sons.
      c. Affected females will transmit the disorders in the same manner as with autosomal-dominant patterns.
      d. Two-thirds of the time, affected females have an affected mother; one-third of the time, they have an affected father.
      e. Family history shows no father-to-son transmissions.
   2. Example: vitamin D–resistant rickets.
B. **X-linked recessive disorders.**
   1. Characteristics of X-linked recessive disorders.
      a. Only male offspring are affected, with rare exceptions. A female offspring will be affected if she has both a carrier mother and an affected father.
      b. Carrier females transmit the disorder.
      c. All sons of affected males will be normal.
      d. All daughters of affected males will be carriers (with each pregnancy).
      e. Heterozygous females transmit the gene to half their sons, who will be affected, and to half their daughters, who will be carriers.
      f. Transmission is horizontal among males in the same generation; in addition, a generation will be skipped, and second-generation males will be affected.

2. Examples: Duchenne's muscular dystrophy, hemophilia, color blindness, and glucose-6-phosphate dehydrogenase deficiency (Kingston, 2002).

MITOCHONDRIAL DISORDERS

A. **The great majority of genetic diseases are caused by defects in the nuclear genome. However, a small but significant number of diseases are the result of mitochondrial mutations.**
B. **Because of the unique properties of mitochondria, these diseases display characteristic modes of inheritance and a large degree of phenotypic variability** (Jorde et al., 2016).
C. **The mitochondria, which produce adenosine triphosphate (ATP), have their own unique deoxyribonucleic acid (DNA). Mitochondrial DNA (mtDNA) is maternally inherited and has a high mutation rate. A number of diseases are known to be caused by mutations in mtDNA.**
D. **Organ systems with large ATP requirements and high thresholds tend to be the ones most seriously affected by mitochondrial diseases; for example, the central nervous system (CNS) consumes 20% of the ATP the body produces and is often affected by mtDNA mutations.**
E. **Mitochondrial mutations are also involved in some common human diseases, for example, a form of deafness** (Jorde et al., 2016).

Chromosomal Defects

ABNORMAL NUMBER

A. **Polyploidy:** more than two sets of homologous chromosomes, showing multiples of the haploid number.
B. **Nonmultiples** are designated by the suffix "-somy"; monosomy is one less than the diploid number (45), and trisomy is one more than the diploid (47).
C. **Causes.**
   1. Nondisjunction: failure of paired chromosomes to separate during cell division.
   2. Chromosome lag: failure of a chromosome to travel to the appropriate daughter cell.
   3. Anaphase lag: chromosome lag during the third state of division of a cell nucleus in meiosis and mitosis.
   4. Mosaicism: nondisjunction of an anaphase lag that occurs during mitosis after fertilization, resulting in two different cell lines in the same person (Jones et al., 2013).

ABNORMAL STRUCTURE

A. **Deletion:** loss of a chromosomal segment.
B. **Duplication:** any duplication of a region of DNA that contains a gene. It is a process that can result in a new mutation.
C. **Translocation:** occurrence of a chromosomal segment at an abnormal site, either on another chromosome or in the wrong position on the same chromosome (i.e., an inversion).
D. **Inversion:** occurs when a segment of the chromosome breaks off and reattaches in the reverse direction.
E. **Nonreciprocal translocation:** a one-way transfer of a chromosomal segment to another chromosome.
F. **Polygenic defects:** type of inheritance in which a trait is dependent on many different gene pairs with cumulative effects.
G. **Environmental influences:** inadequate nutritional intake, certain drugs, irradiation, and viruses are examples that could alter the genetic makeup of an offspring while in vitro. Multifactorial: genes plus environment.
H. **Basic generalizations.**
   1. Loss of an entire autosome is usually incompatible with life.
   2. One X chromosome is necessary for life and development.
   3. If the male-determining Y chromosome is missing, life and development may continue but will follow female pathways.
   4. Extra entire chromosomes, the translocation of extra chromatin material, and the insertion of extra chromatin material are often compatible with life and development.
   5. Multiple congenital structural defects are present when gross aberrations are present (Blackburn, 2018).
I. Incidence.
   1. Autosomal aberrations: 5 in 1000 births.
   2. Sex chromosome aberrations: 2 in 1000 births.
   3. Spontaneous abortions: 60% are associated with chromosomal aberration (Jorde et al., 2016) (see Table 20.1).

Prenatal Diagnosis

Recent technological advances and marked progress in the understanding of the etiology and pathogenesis of many common disorders have allowed many families a prenatal diagnosis.

INDICATIONS AND ADVANTAGES OF PRENATAL DIAGNOSIS

A. **Indications.**
   1. Advanced maternal age.
   2. Prior child with a chromosomal disorder.
   3. Family history of neural tube defects.
   4. Previous child with multiple malformations.
   5. Carriers of X-linked diseases.
   6. Carriers of chromosome translocation.
   7. Couples at risk of having a child with a specific inborn error of metabolism (previous child or by carrier testing).

Table 20.1

Chromosome Anomalies

Autosomal	**Trisomies**: Down syndrome 21, Edwards syndrome 18, Patau syndrome 13 trisomy 9, Warkany syndrome 28, cat eye syndrome/trisomy 22, trisomy 16 **Monosomies/deletions:** 1q21.1 deletion syndrome/1q21.1 duplication syndrome/TAR syndrome 1, Wolf–Hirschhorn syndrome 4, cri du chat/chromosome 5q deletion syndrome 5 Williams syndrome 7, Jacobsen syndrome 11, Miller–Dieker syndrome/Smith–Magenis syndrome 17 DiGeorge syndrome 22, 22q11.2 distal deletion syndrome 22, Angelman syndrome/Prader–Willi syndrome 15 distal 18q-/proximal 18q-
X/Y linked	**Monosomy**: Turner syndrome (45,X) **Trisomy/tetrasomy, other karyotypes/mosaics:** Klinefelter syndrome (47,XXY),XXYY syndrome (48,XXYY), XXXY syndrome (48,XXXY), 49,XXXYY, 49,XXXXY Triple X syndrome (47,XXX), tetrasomy X (48,XXXX). 49,XXXXX, Jacobs syndrome (47,XYY), 48,XYYY, 49,XYYYY, 45,X/46,XY
Trans/locations	**Other**: fragile X syndrome, uniparental disomy, XX male syndrome/46,XX testicular disorders of sex development, marker chromosome, ring chromosome, 6; 9; 14; 15; 18; 20; 21, 22 **Leukemia/lymphoma: lymphoid and myeloid**

Part 2

8. Ultrasonographic identification of major malformation, polyhydramnios, and/or intrauterine growth restriction (Jorde et al., 2016).

B. **Advantages**.
1. Knowledge that the fetus is unaffected.
2. Time to explore options and prepare for an affected newborn infant.
3. Opportunity electively to choose either to avoid starting a pregnancy or to abort an affected fetus.
4. Opportunity for the physician to plan delivery, management, and care of the infant when the disease is diagnosed in the fetus (Jorde et al., 2016).

PRENATAL TESTS

Triple and Quad Screen Tests

A. **Screening test.** Performed at 15 to 20 weeks of gestation. The triple screen is a group of three tests that are used to screen pregnant woman in the second trimester of pregnancy. The quad screen adds a fourth test to the group. The test helps evaluate the risk that a fetus has certain abnormalities, including trisomy 21, and neural tube defects. Each test performed measures a different substance found in the blood: α-fetoprotein (AFP); human chorionic gonadotropin (hCG), unconjugated estriol (uE_3); and with the quad test, inhibin A. The newest marker, inhibin A, increases both the sensitivity and specificity of the screen. These tests have been established as a triple or quad screen because the power lies in their use together. A mathematical calculation involving the levels of these three or four substances and considerations of maternal age, weight, race, and diabetic status are used to determine a numeric risk for trisomy 21 and other selected chromosomal anomalies (i.e., trisomy 18). This risk is compared with an established cutoff. If the risk is higher than the cutoff value, it is considered positive or increased.
1. **α-Fetoprotein** is a protein produced by fetal tissue. During development, AFP levels in fetal blood and amniotic fluid rise until about 12 weeks, then levels gradually fall until birth. Some AFP crosses the placenta and appears in the maternal blood.
2. **Human chorionic gonadotropin** is a hormone produced by the placenta. Levels rise in maternal blood for the first trimester of pregnancy and then fall to less than 10% by the end of pregnancy.
3. **Unconjugated estriol** is a form of estrogen that is produced by the fetus through metabolism. This process involves the liver, the adrenals, and the placenta. Some of the uE_3 crosses the placenta and can be measured in the mother's blood. Levels rise around the eighth week and continue to increase until shortly before delivery.
4. **Inhibin A** is a hormone also produced by the placenta. Inhibin is a dimer (has two parts) and is sometimes referred to as DIA, or dimeric inhibin A. Levels in maternal blood decrease slightly from 14 to 17 weeks of gestation and then rise again.

B. **Screening test, not a diagnostic test.** An abnormal result does not indicate an abnormality but will indicate the possible need for a diagnostic test to rule out abnormalities.
1. **Trisomy 21:** the levels of AFP and uE_3 tend to be low and hCG and inhibin A levels high.
2. **Trisomy 18:** the levels of uE_3 and hCG levels are low and AFP levels are variable.
3. **Open neural tube defects:** where there is an opening in the infant's spine, head, or abdominal wall that allows higher-than-usual amounts of AFP to pass to the mother's blood.

C. **Shortfalls of this test.**
1. The test result is highly dependent on the accurate determination of the gestational age of the fetus. If

the gestational age of the fetus has not been accurately determined, the results may be falsely high or low.
2. In multiple-gestation pregnancies, calculation of the risk of trisomy 21 or trisomy 18 is difficult. For twin pregnancies, a "pseudo-risk" can be calculated comparing results to normal results in other twin pregnancies. For higher gestation pregnancies, risk cannot be calculated from these tests.
3. Evaluation of the risk of open neural tube defects in twin pregnancies can be determined, although it is not as effective as in singleton pregnancies.

D. **Results and further testing:** A multiple marker test or triple screen is used to determine if a fetus is at an increased risk of having certain congenital abnormalities. The test has a high rate of false positives; as few as 10% of women with abnormal results go on to have babies with congenital defects. The purpose of the test is to determine whether further testing (such as ultrasound or amniocentesis) is warranted.

ULTRASONOGRAPHY

A. **Procedure.** Transducer coated with ultrasonic gel is placed on the mother's abdomen, with high-frequency sound waves used to display sectional planes of the uterine contents on a monitor. Ultrasonography cannot detect all anomalies and cannot guarantee fetal outcome.
B. **Initial assessment** recommended by 16 to 20 weeks of gestation for the verification and evaluation of gestational age.
C. **Ultrasonography:** to detect abnormalities of fetus, placenta, amniotic fluid, and uterus; to monitor changes in anatomy and growth with serial ultrasonography.
D. **Diagnostic capability:** only as good as the person's training—not just contingent on the equipment.
E. **No known harmful effects.**
F. **Critical to safety of amniocentesis:** chorionic villus sampling and percutaneous blood sampling.
G. **Anatomic landmarks commonly observed:** fetal spine, kidneys, bladder, stomach, three-vessel cord, cord insertion, four-chambered heart, face, upper lip, biparietal diameter, head circumference, abdominal circumference, femur length, transcerebellar diameter, placenta, amount of amniotic fluid, uterus, and adnexa.
H. **Detectable anomalies:** many, including those indicative of various syndromes. Examples: anencephaly, atrial septal defect, cardiac anomalies, choroid plexus cyst, cleft lip, craniosynostosis, cystic hygroma, cystic kidneys, encephalocele, gastroschisis, hydrocephalus, microcephaly, myelomeningocele, omphalocele, and skeletal dysplasia (Jorde et al., 2016).

AMNIOCENTESIS ("AMNIO")

A. **Removal of 10 to 30 mL of amniotic fluid** through a needle placed into the woman's abdomen for the purpose of chromosomal analysis and other biochemical tests as indicated.
B. **Procedure.** Normal results of amniocentesis do not guarantee a good fetal outcome. Obtain mother's blood type before procedure. If she is Rh negative, obtain father's blood type.
C. **Usual timing of procedure:** 16 to 18 gestational weeks, but amniocentesis can be performed later in gestation and as early as 14 weeks.
D. **Indications.**
1. Woman of advanced maternal age (>35 years at the time of expected delivery).
2. Previous fetus with Down syndrome.
3. Previous fetus with neural tube defect.
4. Both parents known as heterozygous carriers of autosomal-recessive chromosome.
5. Both parents known as carriers of sex-linked recessive disorder.
6. Client or partner with balanced chromosomal translocation of his or her chromosomes.
7. A woman with an abnormal triple or quad screen.

E. **Fluid analysis:** requires 2 to 3 weeks for cells to grow adequately for accurate analysis.
F. **Risks:** Overall risk to mother or fetus is 1%.
1. Spontaneous abortion: approximately 0.5% of cases.
2. Hemorrhage.
3. Infection.
4. Premature labor.
5. Rh sensitization from fetal bleeding into maternal circulation.
6. Trauma to fetus or placenta.

G. **Analysis**.
1. Fetal sex: determined through special staining techniques, karyotype, or amniotic fluid testosterone levels, providing risk information for X-linked disorder.
2. α_1-Fetoprotein: abnormally high or low levels raise concern (see earlier section on triple and quad screening, under "Prenatal Tests").
3. Biochemical: metabolism disorders, including Tay–Sachs disease (a lipid disorder) and amino acid, carbohydrate, and mucopolysaccharide metabolism disorders, can be discovered by 20 weeks of gestation.
4. Chromosomes: abnormalities, including Down syndrome, other trisomies, and other chromosomal abnormalities, can be detected at 16 weeks of gestation by karyotyping.

H. **Postamniocentesis care**.
1. It is important that the mother receive immune globulin (RhoGAM) if she is Rh negative and if father of fetus is either Rh positive or of unknown blood type. Do not give RhoGAM if Rh sensitization has occurred (Jenkins and Wapner, 2018).

CHORIONIC VILLUS SAMPLING

A. **Transvaginal or transabdominal sampling** of the chorionic villi. Obtain fetal cells for the purpose of chromosomal analysis and other biochemical tests. Chorionic villus sampling (CVS) cannot identify neural tube defects.
B. **Preparation:** Review risks and benefits of the procedure, discuss options, and arrange to obtain CVS results. Obtain written consent for this procedure.
C. **Timing of procedure:** usually 8 to 10 weeks of gestation.
D. **Indications.**
   1. Mother prefers to make decisions regarding pregnancy in the first trimester.
   2. Severe oligohydramnios.
E. **Contraindications**.
   1. Multiple gestation.
   2. Uterine bleeding during this pregnancy.
   3. Active genital herpes infection or other cervical infection.
   4. Uterine fibroids.
F. **Fetal cell analysis:** requires 24 to 48 hours for initial results.
G. **Risks:** overall, 2% to 3%.
   1. Infection.
   2. Bleeding.
   3. Cervical lacerations.
   4. Miscarriage: 1% to 5%.
H. **Techniques of CVS.**
   1. Vaginal CVS: catheter is inserted through the vagina and cervix into the chorion outer tissue of the embryonic sac, and a tiny amount of the chorionic villi is aspirated by suction or cut with forceps.
   2. Abdominal CVS: needle is inserted through the abdomen into the chorion to obtain a sample of the chorionic villi.
I. **Post-CVS care.**
   1. Same recommendations as for postamniocentesis care.

PERCUTANEOUS UMBILICAL BLOOD SAMPLING

A. **Sampling:** removal of fetal blood through a needle placed into the woman's abdomen and into the umbilical vein.
B. **Preparation:** same as that recommended for CVS.
C. **Timing:** 18 weeks to term.
D. **Indications.**
   1. Mother wants fast results to support her decision making regarding pregnancy.
   2. Abnormality is identified by ultrasonography late in pregnancy.
   3. Mother has been exposed to infectious disease that could affect development of fetus.
   4. Blood incompatibility (Rh disease).
   5. Drug or chemical level in fetal blood needs to be assessed.
E. **Risks**.
   1. Same as amniocentesis: infection, bleeding, isoimmunization, miscarriage, trauma to the fetus—overall 1% to 5% risk factor.
   2. Perforation of uterine arteries, clotting in fetal cord.
   3. Premature delivery.
F. **Results:** fetal blood analysis takes 3 days.
G. **Postsampling care:** same as postamniocentesis care (Drugan et al., 2015).

Postnatal Testing

A. **Chromosome analysis/karyotype:** an ordered display of an individual's chromosomes. This can be done on amniotic fluid prenatally. Chromosomes are analyzed by staining techniques that result in visibility of dark and light bands that are designated in a standardized way from the centromere. If there is concern regarding chromosomal anomalies, start with a karyotype with reflex to microarray testing.
B. **High-resolution banding/prometaphase banding:** Some disorders cannot be seen reliably on standard chromosome analysis and require special handling during processing. Prometaphase banding is used because the cell growth during culturing is adjusted to maximize the number of cells in prometaphase, where the chromosomes are much less condensed and therefore longer, rather than in metaphase, where the cell growth is stopped in standard chromosome studies. High-resolution banding can have from 550 to 800 bands and allows a much more detailed analysis.
C. **Fluorescence in-situ hybridization (FISH)** is a molecular cytogenetics technique that combines chromosome analysis with the use of fluorescence-tagged molecular markers (probes) that are applied after the chromosome preparation is produced. This method relies on the phenomenon of hybridization of complementary pieces of DNA. FISH is a powerful tool useful not only in diagnosing relatively common microdeletion or microduplication disorders but also for identifying the origin of extra chromosome material (Drugan et al., 2015). FISH can only detect deletions or duplications of regions specifically targeted by the probe used and that are larger than the probe used. It is possible that rare, very small deletions may not be detected.
D. **Polymerase chain reaction (PCR)** is a powerful technique in amplifying many copies of a segment of DNA so that it can be analyzed. PCR is useful in disorders with recurring mutation, for example, achondroplasia.
E. **Comparative genomic hybridization** (CGH) microarray testing: this testing is an advancement in cytogenetic technology that is used for the detection of cytogenetic imbalances that are smaller than what can be detected through routine chromosome analysis. Testing will detect the loss (deletion) or gain (duplication) of

chromosomal regions. Array CGH cannot identify balanced structural changes in the chromosomes and may not detect mosaicism. For these reasons, positive CGH microarray findings are usually followed up by FISH analysis. FISH can confirm if an array result is clinically significant and can also detect carriers of balanced chromosome abnormalities. FISH testing may need to be extended to the patient's parents to refine the clinical interpretation of the microarray.

Human Genome Project

A. **What is the Human Genome Project?**
   1. The Human Genome Project was an international 13-year effort formally begun in October 1990 to discover all the estimated 30,000 to 35,000 human genes and make them accessible for further biologic study.
   2. The project started in the mid-1980s and is the single most important coordinated medical research initiative in the history of biomedical research. It culminated in the completion of the full human genome sequence in April 2000 (www.genome.gov).
   3. The goals of the project were to map genes on chromosomes and to determine the sequence of the nucleotides that make up human DNA, which is the basic genetic material. One of the top priorities was to generate complete sets of full-length chromosomal DNA (cDNA) clones and sequences for both human and model organism genes. It is expected that genome research will produce a ream of new information about the genes involved in inherited disorders, birth defects, and common conditions influenced by genetic factors.
   4. One insight already obvious is that even on a molecular level, we are more than the sum of our 35,000 or so genes. However, surprisingly, this new estimated number of genes is only one third of what was previously thought, although the numbers may be revised as more analyses are performed. This suggests to scientists that the genetic key to human complexity lies not in the number of genes but in how gene parts are used to build different products in a process called *alternative splicing*.
   5. In December 1999, the first human chromosome, chromosome 22, was sequenced. This is the location of defects that can cause DiGeorge syndrome, chronic myeloid leukemia, and neurofibromatosis. It is also the final autosome in the human sequence as outlined by the National Institutes of Health Human Genome Report in 2003 (Collins et al., 2003).
   6. Though the outcome of the Human Genome Project itself is not ethically problematic, the use of the data generated presents major ethical questions that must be addressed. The future, then, presents the challenges of addressing the project's implications (Blackburn, 2018; Larsson, 2001).

B. **Ethical, legal, and social issues program**.
   1. Study is now under way on the ethical, legal, and social issues related to increasingly rapid progress in the field of human genetics. Four areas were identified for initial emphasis: privacy of genetic information, safe and effective introduction of genetic information in the clinical setting, fairness in the use of genetic information, and professional and public education.
   2. The program also emphasizes the importance of understanding the cultural, ethnic, social, and psychological influences that must inform policy development and service delivery issues.
   3. With time, these issues must be addressed to ensure that the maximal benefit is gained from the project (Blackburn, 2018; Larsson, 2001).

Genetic Counseling

A. **Definition:** Genetic counseling is a nondirective communication process that deals with the human problems associated with the occurrence, or the risk of occurrence, of a genetic disorder in a family. This process involves collaboration of people from multiple disciplines (physician, sonographer, nurse, genetic counselor, social worker, neonatologist, and pediatric specialist, as indicated) and family support.

B. **Principles of genetic counseling.**
   1. Based on correct diagnosis and pattern of inheritance.
   2. Nondirective.
   3. Reinforcement of information previously presented.
   4. Emphasis on communication with the primary care physician.

C. **Goal of genetic counseling** is to assist the family in comprehending the following:
   1. Diagnosis.
   2. Role of heredity.
   3. Recurrence risks and options.
   4. Possible courses of action.
   5. Methods of ongoing adjustment.

D. Indications (Blackburn, 2018; Drugan et al., 2015).
   1. Previously affected child, parent, or grandparent.
      a. Congenital malformation.
      b. Sensory defect.
      c. Metabolic disorder.
      d. Intellectual disability.
      e. Known or suspected chromosome abnormality.
      f. Neuromuscular disorder.
      g. Degenerative CNS disease.

2. Previously affected cousins.
   a. Muscular dystrophy.
   b. Hemophilia.
   c. Hydrocephalus.
3. Consanguinity.
4. Hazards of ionizing radiation.
5. Recurrent miscarriages.
6. Concern for teratogenic effect.
7. Advanced maternal age.
8. High or low maternal serum AFP.

E. **Methods of obtaining information needed.**
1. Questionnaire.
2. Pedigree.
3. Medical records.
4. Physical examination.
5. Laboratory tests.
6. Carrier detection.

F. **Provision of medical facts.**
1. Differential diagnosis.
2. Risks to fetus and mother.
3. Probable course of disorder.
4. Recommended management for prenatal course.
5. Type and timing of delivery.
6. Neonatal, pediatric, and long-term care requirements.

G. **Explanation of hereditary factors that contribute to the disorder.**

H. **Discussion with parents regarding all alternatives.**
1. Home care of newborn infant.
2. Institutionalization.
3. Adoption.
4. Appropriate method of termination for gestational age.
5. Objective information regarding fetal and neonatal status. Provide statistical risk factors as they relate to this individual fetus.
6. Identification of the normal characteristics that can exist in the affected fetus. Point these out in pictures to promote awareness of the total condition of the fetus.
7. Assistance to parents: understanding of causes, risks of recurrence, and limits of current treatments.
8. Discussion of options available for dealing with risk of recurrence.
9. Written information for parents and information regarding support groups.
10. Explanation of recommended obstetric care, mode and timing of delivery, and neonatal care (Jones et al., 2013).

Newborn Care

DIAGNOSIS

A. **Complete diagnosis:** important in planning care. Consideration for the infant's overall problems, in addition to the defect, is essential.

B. **Evaluation of infant with a birth defect.** A birth defect is a structural or functional abnormality of the body that is present from birth. The effects of a birth defect may be either immediate or delayed until later in life.

C. **Syndrome.**
1. Definition: a constellation of anomalies that cannot be explained otherwise and that result in similar patterns of expression.
2. Examples: fetal alcohol syndrome, trisomy 21.

D. **Sequence**.
1. Definition: a primary event or anomaly that sets a pattern of other events (anomalies). Designates a series of anomalies resulting from a cascade of events initiated from a single malformation.
2. Example: Pierre Robin sequence. Lannelongue and Menard first described Pierre Robin syndrome in 1891 in a report on two patients with micrognathia, cleft palate, and retroglossoptosis. In 1926, Pierre Robin published the case of an infant with the complete syndrome. Until 1974, the triad was known as *Pierre Robin syndrome*; however, the term *syndrome* is now reserved for those errors of morphogenesis with simultaneous presence of multiple anomalies caused by a single etiology. The term *sequence* has been introduced to include any condition that includes a series of anomalies caused by a cascade of events initiated by a single malformation. The initial event, mandibular hypoplasia, occurs between the 7th and 11th week of gestation. This keeps the tongue high in the oral cavity, causing a cleft in the palate by preventing the closure of the palatal shelves. This explains the classic inverted U-shaped cleft and the absence of an associated cleft lip. Oligohydramnios could play a role in the etiology, because the lack of amniotic fluid could cause deformation of the chin and subsequent impaction of the tongue between the palatal shelves.

E. **Association**.
1. Is a nonrandom occurrence in two or more individuals of multiple anomalies not known to represent a sequence or syndrome.
2. Example: *c*oloboma, *h*eart defect, *a*tresia choanae, *r*estricted growth and/or development, *g*enital anomalies, and *e*ar anomalies (CHARGE) association.

F. **Malformation**.
1. Definition: an abnormality of morphogenesis due to intrinsic problems within the developing structures.
2. Examples: neural tube defects, cleft lip and palate.

G. **Deformation**.
1. Definition: an abnormality of morphogenesis due to intrinsic problems within the developing structures.

Part 2

2. Examples: Pierre Robin sequence, uterine position defects, and oligohydramnios sequence.

H. **Disruption**.
1. Definition: an abnormality of morphogenesis due to disruptive forces acting on the developing structure. Can be due to pressure on developing structures.
2. Examples: amniotic bands, vascular accidents, and infections.

I. **Genetic heterogeneity.**
1. Definition: different causes may produce similar characteristics.
2. Examples: hydrocephalus, cleft lip and palate.

HISTORY

A. **Family history.**
1. History of three generations.
2. Defects in the family history related to the problem in the child.
3. Medical records and/or photos of similarly affected relatives.
4. History of consanguinity.
5. Reproductive history, such as frequent spontaneous abortions.
6. Pattern of inheritance of the problems.

B. **Prenatal history**.
1. Length of gestation.
2. Fetal activity level.
3. Maternal exposures: infections, illness, high fevers, medications, x-ray examinations, known teratogens, alcohol, smoking, and use of street and prescription drugs.
4. Obstetric factors: uterine malformations, complications of labor, and presenting fetal part.
5. Neonatal factors: birth weight, length, head circumference, and Apgar scores.

EXAMINATION AND CARE

A. **Physical examination.**
1. General: asymmetry, problems of relationship, and inappropriate size and strength.
2. Face: configuration; centered features with normal spacing; round, triangular, flat, birdlike, elfin, coarse, or expressionless characteristics.
3. Head: size of anterior fontanelle, prominence of frontal bone, flattened or prominent occiput, abnormalities in shape (proportionally large or small).
4. Skin: intact, or presence of skin tags, open sinuses, tracts.
5. Hair: texture, hairline, presence of whorls.
6. Eyes: structure and color of iris, presence of colobomas, centering and spacing of epicanthal folds (hypotelorism or hypertelorism), ptosis, slanting, eyelash length.
7. Ears: protruding or prominent shape, location, low-set, unilateral or bilateral defect, presence and/or degree of rotation.
8. Nose: beaked, bulbous, pinched, upturned, misshapen, number of nares, flattened bridge, patency, centered on face.
9. Oral: intact palate, presence of smooth philtrum, natal teeth; shape and size of tongue, mouth, jaw (micrognathia).
10. Neck: short and/or webbed, redundant folds.
11. Chest: symmetrical; presence of accessory nipples.
12. Abdomen: number of cord vessels, presence of abdominal wall defects and abdominal musculature, prune belly.
13. Genitourinary system (male): hypospadias—four degrees, dependent on placement of meatus; chordee; ambiguous genitalia; testes descended.
14. Anus: position, patency.
15. Spine: intact, scoliosis, lordosis, kyphosis.
16. Extremities: length, shape, absence of bones.
17. Hands and feet: broad, square, or spadelike shape; polydactyly, clinodactyly, syndactyly, abnormal creases in the palm of the hand (simian or Sydney creases), contractures, abnormally large or small size, overriding fingers, proximally placed thumb, rocker-bottom feet.

B. **Causation of defect.**
1. Identify the primary abnormality.
2. Recognize etiologic heterogeneity (a defect having more than one cause).
3. Determine category of congenital malformation, according to etiology.
   a. Malformation.
   b. Deformation.
   c. Disruption.
   d. Syndrome.
   e. Association
   f. Sequence.
   g. Genetic heterogeneity.

C. **Family care management for all genetic syndromes or disorders.**
1. Provide grief counseling. Acknowledge short- and long-term grief; promote awareness that each of the parents may be in a different stage of the grief process, creating additional stress. Recommend that parents communicate their needs to each other and ask for support when needed.
2. Encourage genetic counseling.
3. Facilitate family use of support systems: social services; Aid to Families with Dependent Children; Women, Infants, and Children (WIC) program; March of Dimes; clergy; mental health services; support groups; Internet information.
4. Provide unconditional emotional support. Allow parents and siblings to verbalize feelings.
5. Present obvious defects at delivery. Be honest and open about your findings and their possible implications.

6. Identify normal aspects of the neonate that can coexist with the syndrome or disorder.
7. Promote parent involvement in care; offer choices in care and interventions.
8. Discuss treatment options and their risks and benefits.
9. Provide literature.
10. Obtain legal and ethical counsel when parents prefer not to pursue medical interventions (Nelson, 2018).

EXAMPLES OF SPECIFIC DISORDERS

(FOR MORE SPECIFIC DISORDERS, SEE CHAPTER 35)

VATER Association

VATER is an acronym for *v*ertebral anomalies, *a*nal atresia, *t*racheo*e*sophageal fistula, and *r*adial and *r*enal dysplasia.

A. Etiology and precipitating factors: unknown.
B. Incidence: 1.6 in 10,000.
C. Clinical presentation: three or more of the following defects are present:
   1. Vertebral anomalies.
   2. Anal atresia with or without fistula.
   3. Tracheoesophageal fistula with esophageal atresia.
   4. Radial dysplasia, including thumb or radial hypoplasia, polydactyly, and syndactyly.
   5. Renal anomaly.
   6. Single umbilical artery.
D. **Complications and outcome.**
   1. Failure to thrive.
   2. Possibility of normal life after slow mental development during infancy.
E. **Care management.**
   1. Supportive: prognosis and management depend on the extent and severity of the anomalies.
   2. Surgery: surgical correction of anomalies.

VACTERL ASSOCIATION

VACTERL is an acronym for an association characterized by the sporadic, nonrandom association of specific abnormalities: *v*ertebral abnormalities, *a*nal atresia, *c*ardiac abnormalities, *t*racheoesophageal fistula and/or *e*sophageal atresia, *r*enal agenesis and dysplasia, and *l*imb defects.

A. **Etiology and precipitating factors.**
   1. Unknown.
   2. Injury between 4 and 6 weeks to a specific mesodermal area may produce simultaneous anomalies of the hindgut, lower vertebral column, lower urinary tract, and developing kidney.
   3. Abnormalities: average of seven or eight per patient.
B. **Incidence:** rare (about 250 reported cases worldwide).
C. **Clinical presentation (Hockenberry and Wilson, 2019; Jones et al., 2013).**
   1. Vertebral anomalies.
   2. Anal atresia with or without fistula.
   3. Cardiac anomalies: commonly ventricular septal defects.
   4. Tracheoesophageal fistula with or without esophageal atresia.
   5. Radial dysplasia, including thumb or radial hypoplasia, polydactyly, and syndactyly.
   6. Renal anomaly.
   7. Single umbilical artery.
D. **Complications and outcome.**
   1. Failure to thrive.
   2. Normal life: minimal CNS anomalies with only occasional intellectual disability.
E. **Care management** (Hockenberry and Wilson, 2019).
   1. Supportive: prognosis and management depend on the extent and severity of the anomalies.
   2. Surgery: surgical correction of anomalies.

COMMON TRISOMIES

Trisomy 21 (Down Syndrome) (Table 20.2)

A. **Incidence and etiology.**
   1. Incidence by maternal age is as follows:
      a. 15 to 29 years: 1 in 1500.
      b. 30 to 34 years: 1 in 800.
      c. 35 to 39 years: 1 in 270.
      d. 40 to 44 years: 1 in 100.
      e. 45 years or older: 1 in 50.
   2. Accounts for 15% to 20% of cases of severe intellectual disability.
   3. Risk increases with maternal age.
   4. 25% of Down syndrome infants receive an extra chromosome from their father.
   5. Person has 47 chromosomes (3 of chromosome 21).
   6. Extra chromosome fits into group G21,22. Extra chromosome results from nondisjunction during meiosis. May occur unrelated to maternal risk factors and appear as follows:
      a. Chromosomes: 46.
      b. Translocation of chromosome 21.
      c. Familial transmission autosomal dominant.
      d. No abnormalities if chromosomes are balanced. There is one no. 21 and one no. 14 chromosome.
      e. Production of unbalanced gametes by balanced carriers: should consider prenatal diagnosis.
   7. Some infants have mosaicism for trisomy 21 or translocation 14/21 or 21/22.
      a. Some have all the defects.
      b. Some have only a few.
      c. Some of this group may have normal intellectual ability.
B. **Clinical presentation** (Jones et al., 2013).
   1. Size: small; 20% are premature.
   2. Skull: short and round with a flat occiput.
   3. Eyes: slant upward and outward.

Table 20.2

Clinical Features of Common Trisomies

Clinical Features	Trisomy 21	Trisomy 18	Trisomy 13
General	Hypotonia—mouth open Relatively small stature	Feeble fetal activity Weak cry Altered gestational timing (preterm or post-term birth)	Often SGA
Neurologic	Hypotonia/noted mid-face	Hypertonicity (beyond neonatal period)	Holoprosencephaly type defect with varying degrees of incomplete development of forebrain
Craniofacial	Flat facies Brachycephaly Mild microcephaly	Prominent occiput, wide fontanelles Cleft lip and palate	Moderate Microcephaly Wide fontanelles and sagittal suture
Eyes	Slanted palpebral fissures Epicanthal folds Brushfield's spots/iris	Short palpebral fissures Inner epicanthal folds	Microphthalmia colobomas of iris
Ears	Small ears/hearing loss 60%, malformed auricles	Low-set, malformed auricles	Abnormal helices with/without low-set ears
Mouth	Protruding tongue	Micrognathia, small oral opening Narrow palatal arch	Cleft lip/palate or both
Abdomen	Diastasis recti	Inguinal or umbilical hernia	Inguinal or umbilical hernia
GI/Renal	Duodenal atresia	Malpositioned anus Omphalocele	Omphalocele
Thorax		Short sternum	
Neck	Neck short redundant tissue		
Hands/feet	Wide spaced gaps between first and second toe Dysplasia of mid-phalanx of fifth finger Simian crease	Clenched hands Overlapping fingers Hypoplastic nails	Polydactyly Simian crease Flexion of fingers
Cardiac	Cardiac anomaly 40%	VSD ASD	
Other skeletal			Thin posterior ribs/missing ribs
Pelvis	Dysplasia of pelvis	Small pelvis Limited hip abduction	
Joints	Hyperflexibility of joints		
Genitalia	Small penis ↓ Testicular volume	Male cryptorchidism	Male cryptorchidism
Skin	Cutis marmorata	Cutis marmorata	Cutis aplasia Capillary hemangioma
Other	Single umbilical artery	Single umbilical artery Polyhydramnios	Single umbilical artery

ASD, Atrial septal defect; *SGA*, small for gestational age; *VSD*, ventricular septal defect.

4. Prominent epicanthal fold.
5. Flat face.
6. Brushfield's spots: iris may be speckled with a ring of round, grayish spots or flecks of gold in light-colored eyes.
7. Cheeks: red.
8. Palate: narrow and short.
9. Nose: short with a flat nasal bridge.
10. Tongue: protrudes; can become dry and wrinkled.
11. Skin loose around lateral and dorsal aspects of the neck.
12. Hands.
    a. Fingers: short.
    b. Hands: square.
    c. Single simian creases.
13. Feet.
    a. Wide space between great toe and second toe.
    b. Deep crease that starts between the great toe and the second toe and curves.
14. Muscular hypotonia.
15. Narrow acetabular angle.
16. Narrow iliac index.

17. Broadened iliac bones.
18. Delayed psychomotor development.
19. Cardiac ventricular septal defects or other congenital heart defects found in 50% of infants.
20. Duodenal atresia.

C. **Complications and outcome.**
1. Congestive heart failure due to congenital heart disease.
2. Upper respiratory tract infections.
3. Delayed development: IQ ranges from 25 to 70.

TRISOMY 18

A. **Etiology and precipitating factors.**
1. Nondisjunction most frequent; also possible partial trisomy, translocation, or mosaicism.
2. Advanced parental age.

B. **Incidence:** 1 in 3500 births.

C. **Clinical presentation.**

D. The following characteristics appear in most cases:
1. Weight: low birth weight in term infant.
2. Ears: low set and/or abnormal shape.
3. Micrognathia and microstomia.
4. Intellectual disability.
5. Hands.
   a. Clenched hand with flexed fingers.
   b. Flexion contraction of the two middle digits.
   c. Unfolded thumb.
6. Cardiac: usually ventricular septal defect with patent ductal arteriosus.
7. Feet: rocker bottom.

E. The following characteristics may also appear:
1. Eyes: ptosis of one or both eyelids.
2. Syndactyly.
3. Head: abnormally prominent occiput.
4. Genitourinary defects.
5. Hernias, especially umbilical.
6. Simian crease appears in 25%.
7. Arches on seven or more fingers in 80% of cases.

F. **Complications and outcome.**
1. Mortality rate: 30% die within 2 months of birth, usually of heart failure.
2. Survival: 10% survive past the first year with severe developmental delay.

G. **Care management.**
1. No treatment beyond supportive care.
2. Gavage/gastric tube feedings as needed for poor feeding.
3. Oxygen as needed for respiratory distress.
4. Parental support.

TRISOMY 13

A. **Etiology:** unknown; may be related to older maternal age.

B. **Incidence:** 1 in 15,000 births.

C. **Clinical presentation.**
1. Psychomotor delay.
2. Ears: malformed.
3. Hands: flexion deformities of hand, fingers, and wrist (postaxial polydactyly).
4. Cardiac: usually ventricular septal defect, patent ductus arteriosus, or rotational anomalies such as dextroposition.
5. Feet: rocker bottom.
6. Eyes: microphthalmos, colobomas of iris, cataracts.
7. Nose: broad and flattened, cleft lip and palate (not always).
8. Umbilicus: hernia, omphalocele.
9. Genitalia.
   a. Female: bicornuate or septate uterus.
   b. Male: cryptorchidism, small scrotum and anterior placement.
10. Kidneys: polycystic.
11. Skin: cutaneous hemangiomas, cutis aplasia.
12. Brain: gross defects, grand mal seizures, myoclonic jerks.
13. Hematologic abnormalities, such as increased frequency of nuclear projections in neutrophils and/or persistence of embryonic and/or fetal type of hemoglobin.

D. **Complications and outcome.**
1. Mortality rate: 44% die within the first month.
2. Survival: 18% survive the first year.
3. Severe intellectual disability.

E. **Care management.**
1. No treatment beyond supportive care.
2. Parental support.

Part 2

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CHAPTER 21

Intrafacility and Interfacility Neonatal Transport

Webra Price-Douglas and Tammy Rush

OBJECTIVES

1. Discuss planning for an intrafacility transport of a critically ill neonate.
2. Identify important considerations in the selection of transport vehicles.
3. Discuss the important factors to be considered in selecting team composition.
4. Describe the process of neonatal transport from the referring call, to transport of the patient, to arrival at the receiving hospital.
5. List four methods to increase safety in the transport environment.
6. Discuss legal and ethical considerations relating to neonatal transport.

In the late 1950s and early 1960s, intensive care for newborns first became available. As the scope of care for critically ill infants expanded, so did the number of hospitals offering this service. Unfortunately, because of the uneven distribution of these services, many areas remained without available resources. In the early 1970s, the need to regionalize perinatal care was recognized by health care providers. In 1976, the National Foundation – March of Dimes released the report "Toward Improving the Outcome of Pregnancy" that described regionalized care and identified criteria for level I, II, and III hospitals (Committee on Perinatal Health, 1976). The report also recommended the establishment of formal relationships between hospitals delivering different levels of care within a region so that every infant could receive appropriate care. The concept of regionalization led naturally to the need for the development of neonatal transport.

The U.S. Department of Health and Human Services reported almost 4 million live births in the United States in 2010, with 8.1% of low birth weight (less than 2500 grams) (Martin et al., 2012). Advances in neonatology and technology have led to increased survival rates of these low birth weight infants. These infants may be born outside a regional center and require transport to a neonatal intensive care unit. Infants with congenital anomalies or multisystem problems may also require transport to a regional neonatal intensive care center. The neonatal period is defined as the first 4 weeks of life and is the period of greatest mortality in childhood, with the highest risk occurring during the first 24 hours of life (March of Dimes, 2005).

Intrafacility and interfacility transport of the critically ill neonate presents unique challenges. Transport of neonates occurs over 20,000 times annually in the United States (Shah et al., 2008). The transport environment does not provide optimal conditions. The goal is to transport these critically ill neonates in the most stable condition possible and to minimize adverse effects. The neonatal transport team must be knowledgeable about neonatal physiology and clinical requirements to provide optimal care and outcome. This chapter discusses various aspects of intrafacility and interfacility neonatal transport.

Historical Aspects

A. **1899:** When most infants were born at home, the first ambulance incubator was developed to transport premature infants from home to Chicago's Lying-In Hospital (Butterfield, 1993; Cone, 1985).
B. **1935:** The Chicago Board of Health operated a special ambulance with incubator, oxygen, and humidity and was staffed with public health nurses (Chou and MacDonald, 1989).
C. **1948:** The New York City Department of Health, Maternity and Newborn Division established a well-organized transport service staffed with ambulance drivers, nurses, a pediatrician, and a transport clerk (Losty et al., 1950; Wallace et al., 1952).
D. **1966:** Dr. Sydney Segal published guidelines for neonatal transport (Segal, 1966) that were expanded in 1972 into a comprehensive transport manual (Segal, 1972).
E. **1970s:** The number of organized transport programs increased as a result of regionalization of perinatal care (Wood and Bose, 2005).

F. **1990s:** Regionalization was further emphasized to provide care to families with an emphasis on risk identification and access to appropriate services that ensure compliance, continuity, and comprehensiveness (Committee on Perinatal Health/March of Dimes, 1993).
G. **2010:** Regionalization was further emphasized to provide care to families with an emphasis on quality and safety (Committee on Perinatal Health/March of Dimes, 2010).
H. **2016:** Most neonatal and pediatric transport programs are affiliated with nonprofit tertiary care centers; however, there are a growing number of for-profit stand-alone aeromedical transport services with variable neonatal and pediatric expertise (American Academy of Pediatrics [AAP], 2016).
I. **2017:** A comprehensive, integrated perinatal delivery system with efficient resource utilization providing care to all women and children is ideal; this has not been accomplished due to financial incentives, competition, and duplication of services (AAP and the American College of Obstetricians and Gynecologists [ACOG], 2017).

Philosophy of Neonatal Transport

A. **The neonatal transport team is an extension of the neonatal intensive care unit** (Ohning et al., 2012).
   1. Interfacility neonatal transport is inherently different from typical emergency medical services (EMS) transport. Stabilization during interfacility transport is accomplished in the controlled setting of a medical facility, such as a hospital or medical clinic, in comparison with stabilization performed at the scene of an accident with limited support services. During interfacility transport, the patient is moved from a controlled setting (i.e., referring hospital) to the transport environment before arriving in the controlled setting of the receiving center. Scene-response systems move a patient from an uncontrolled setting to the controlled setting of a medical facility. The focus of EMS is on immediate short-term stabilization to sustain the patient until arrival at the medical facility. Interfacility transport systems focus on providing intensive care services from the referral facility and throughout the transport; thus, more time is spent in stabilization at the point of origin. The exception is when immediate access to specialty services not available at the referral hospital is indicated—for example, neurology or surgery or a complex diagnostic procedure. Transport is a particularly vulnerable time for the patient.
   2. The level of care should either remain the same or be increased during neonatal interfacility transport (AAP, 2016).

B. **Crew and patient safety must be the highest priority of a transport program** (AAP, 2016).
   1. Crew and patient safety must be the highest priority for both ground and air neonatal transport programs. The focus of a transport safety program is reducing preventable adverse events and accident prevention. However, when an accident does occur, a systematic approach should be used to minimize the impact. Every team member is responsible for a safe program. Crew members' attitudes, participation, education, and judgment are variables that influence the safety program. Unsafe behaviors or practices are unacceptable in the transport environment.
C. **The neonate is a member of a family unit.**
   1. The transport team plays a role in the initiation or continuation of family-centered care. There still exists some controversy about family presence in certain situations, including transport. Although it may be preferable to include a parent on transport, team safety must be considered. If a parent is unable to travel with the neonate, the parents must be given detailed information about the child's destination (AAP, 2016).
   2. Transport team members may be the first point of contact and may serve families with diverse health beliefs, customs, and practices. Thorough documentation of parental requests must be communicated to the accepting team. Strategies for addressing cultural and language barriers must be available to all transport team members (AAP, 2016).
   3. Parents and families of a critically ill neonate experience a mixture of emotions. Reactions of the parents may vary based on the condition of their infant and on their perception of the situation, past experiences, support systems, and coping mechanisms. The transport team plays a pivotal role assisting the family to cope with the crisis.
D. **Intrafacility and interfacility neonatal transport** should be planned and organized with appropriate transport staff and adequate equipment.
E. **Intrafacility and interfacility preparation, stabilization, and transport** should be performed as efficiently as possible using skilled staff and appropriate equipment. The continuum of care should not be interrupted during the transport process.

Intrafacility Neonatal Transport (AAP, 2007, 2016; Demmons and James, 2008; National Association of Neonatal Nurses, 2010a)

A. **Preparation**.
   1. Neonates may require intrafacility transport for diagnostic and invasive procedures. The same

concepts used for interfacility transport apply to intrafacility transport to avoid adverse outcomes.
2. Level of care must be maintained or increased.

B. **Staffing**.
1. Staff must be knowledgeable in neonatal physiology and pathophysiology and have excellent assessment and clinical skills. They must have the combined expertise and skills to provide safe transport.
2. The type and number of personnel required are determined by patient acuity level and equipment.
3. It is essential to have the bedside registered nurse (RN) as part of the transport staff because of patient knowledge. Patient assignments must be adjusted to provide appropriate care for infants being transported out of the intensive care unit. Transport is a particularly vulnerable time for the neonate (AAP, 2016).

C. **Effective communication** between staff of the neonatal intensive care unit, intrafacility transport team, and procedure department is critical. Transitions should be seamless (AAP, 2016). A formal hand-off process should be performed.

D. **Equipment.**
1. Type of equipment selected is based on patient acuity level.
2. Anticipate potential complications.
3. Maintenance of a neutral thermal environment during the procedure presents challenges. The neonate may be transported to the procedure in a transport incubator or radiant warmer, depending on the patient's clinical condition and potential problems with hypothermia. Prevention of hypothermia during the procedure may require additional supplies.
   a. Radiant warming lights, with safety features to monitor heat output.
   b. Warm blankets.
   c. Hat.
   d. Chemical heat packs or thermal pad especially designed for neonates (do not place against fragile skin).
   e. Polyethylene wrap or bag.
4. Monitoring devices should be compatible with the type of procedure performed.
5. Equipment should have battery backup capabilities. Plug in equipment to an electrical outlet to maintain the battery charge.

E. **Safety**.
1. Use the most expeditious route between the unit and the procedure department.
2. Anticipate and plan for potential problems (e.g., elevator not functioning).
3. Supplies and equipment should be packaged for safe transport.
4. Staff remaining with patient during the procedure should be provided with protective clothing and monitoring devices depending on the type of procedure.
5. The neonate and monitoring equipment should be positioned for optimal visualization.
6. Staff may be required to stay with the neonate during the procedure, given that other health care providers may not have the expertise to manage a neonate.
7. The neonate should be assessed frequently during the procedure.
8. Documentation must, at a minimum, be the same as the inpatient unit as monitoring devices will allow.
9. Intrafacility transport of neonates must be a part of an ongoing performance/quality improvement process to evaluate and document the care and safety of neonates being transported within the facility. The process must be transparent and include team members, unit managers, and hospital administrators or representatives from other departments.

Interfacility Neonatal Transport

TYPES OF TRANSPORTS
(AAP, 2007, 2016)

A. **One-way transport.**
1. One-way transport uses services of personnel, equipment, and vehicles dispatched by the referral hospital to the receiving center.
2. Advantages of one-way transport.
   a. Saves time in patient arrival to the receiving center.
   b. Knowledge of the patient by referring staff.
3. Disadvantages of one-way transport.
   a. The expense of maintaining experienced staff and equipment due to low volume of transports.
   b. May deplete the resources of local EMS or the referring hospital for the duration of the transport.
   c. Referring hospital and local EMS staff may not have appropriate equipment or training for transport of neonates. Studies have shown that there is an increased morbidity and mortality when neonates are transported by an untrained versus a trained neonatal team.

B. **Two-way transport.**
1. Two-way transport uses the services of personnel, equipment, and vehicles dispatched by the receiving center. This is the most common for neonatal and pediatric transports.
2. Advantages.
   a. More cost-effective use of expensive equipment.
   b. More experienced transport staff trained specifically in neonatal transport.
   c. Improved neonatal stabilization techniques.
   d. Provide equipment specifically for neonatal transport.
   e. Continuity of care.

3. Disadvantages.
   a. Time delay in moving patient from referring facility.
   b. Expense of maintaining transport program.

C. Three-way transport.
1. The neonate is transported from the referring facility to the receiving facility by a transport team from a third facility or air medical company.
   a. A vetting process is essential to determine advantages and disadvantages.
   b. Skill set and expertise of staff may vary.
   c. Access to age-appropriate supplies and equipment must be ensured.
   d. Cost may vary.
   e. Most often operate with an established transport agreement.

D. Back/return transport (National Association of Neonatal Nurses [NANN], 2010a).
1. Neonates are transferred back to the local or birth hospital when they no longer require the resources of the regional neonatal intensive care center. The family should be involved in the decision of transferring the infant.
   a. Parents should visit the local or birth hospital/unit before the transfer.
2. Advantages.
   a. More efficient use of beds at regional center.
   b. Improved relations between community hospitals and tertiary care center.
   c. Greater opportunity for parental involvement.
   d. Familiarity of primary physician with infant before discharge home.
   e. Potential decreased cost during convalescence.
3. Disadvantages.
   a. Financial analysis of cost to keep infant at the regional facility versus cost of transport. Transfer of neonate back to referring hospital may depend on managed care or insurance contract.
   b. Potential need for transport back to higher-care facility if patient's condition deteriorates at community hospital.
   c. Parental anxiety and loss of continuity of care.

E. Transfers out.
1. Neonates are transferred for a specialized procedure or treatment not available at the current facility (i.e., extracorporeal membrane oxygenation, surgical procedure).
2. The neonate may be transported by a team from the receiving hospital, the referring hospital, or a third facility or company. The level of care during transport must remain the same or be increased.
3. The receiving facility should consider back-transport after completion of the treatment or procedure.

SELECTION OF TRANSPORT VEHICLES

A. General considerations (AAP, 2007, 2016; Ohning et al., 2012).
1. The ideal transport vehicle should be safe, reliable, quiet, fast, comfortable, and equipped to take care of one to two patients, in separate incubators, with two to four transport team members. The vehicle should be easy to load and allow access to the patient, with the transport team secured with restraining devices. The selection of mode of transport should always be based on safety.
2. Vehicle purchasing and leasing decisions or transport agreements, including vehicle selection, should be made with input from people who are knowledgeable about the transport environment and members of the transport team who are directly and routinely involved in transport decisions. Vehicles must best fit the goals of the program and the population they serve.
3. Appropriate vehicle selection may be dictated by diagnosis, clinical condition of the patient, available resources at the referring hospital, location of referring hospital, distance and duration of transport, geographic characteristics (road conditions, traffic conditions, construction detours), size of team, vehicle availability, weather, cost of the transport, and reimbursement.
4. Vehicles must be appropriately equipped, including power supplies, inverter, oxygen and air supply, suction, lighting, altitude pressurization where appropriate, means for securing incubators and all equipment, and room for adequate personnel.
5. An integrated system using multiple modes of transportation allows maximum flexibility to meet patient needs in a cost-effective manner.
6. Decisions regarding the appropriate vehicle for individual transport should be made by the medical control physician at the tertiary hospital, the transport team, and the referring physician in consideration of the impact on patient care and outcome, advantages and disadvantages of each vehicle, and cost.
7. Vehicle design and equipment placement must allow for continuation of patient care throughout the transport.
8. The vehicle must be equipped with appropriate locking devices and storage to secure the incubator and equipment.
9. Vehicle selection and mode of transport must be monitored as part of an ongoing performance/quality improvement process and must include team members, vendors, hospital administration, and regulatory agencies when appropriate. The process must be transparent.

10. Vehicles and modes of transports used infrequently, less than 10% of total volume of transports, must have regularly scheduled training, reorientation, simulation to maintain familiarity, and ensure state of readiness in an emergency.

B. Specific vehicle considerations.
   1. Ambulance (AAP, 2007; Ohning et al., 2012).
      a. Advantages.
         1) Lower transport costs.
         2) Operates in weather conditions that restrict air transport.
         3) Does not require a landing zone or runway.
         4) Ability to carry equipment and personnel for two incubators in specially equipped ambulances.
         5) Increased space and patient more accessible.
         6) Ability to stop vehicle or divert to the closest hospital in an emergency.
      b. Disadvantages.
         1) Long response times due to speed limitations, road conditions, traffic congestion, and geographic location.
         2) Delay of admission to tertiary care center because of long-distance ground transport.
   2. Helicopters (AAP, 2007; Ohning et al., 2012).
      a. Advantages.
         1) Speed in response to calls and in returning patient to the receiving center for distances up to 150 miles.
         2) Decreased response time to the referring facility.
         3) Use of one-way helicopter transport to increase team's response time to referring hospital.
         4) Avoid traffic delays and ground obstacles.
      b. Disadvantages.
         1) Need for landing zone.
         2) Increased noise and vibration levels.
         3) Difficult to identify problems when they occur because of noise and vibration (e.g., pneumothorax, extubation).
         4) High operational costs.
         5) Space and weight limitations, including restricted patient access during flight.
         6) Increased downtime because of weather.
         7) May require ground transportation depending on landing zone location.
         8) Securing the same incubator in a helicopter and an ambulance may not be possible because of different mounts and stretcher configurations. This must be evaluated before the transport.
   3. Fixed-wing aircraft (AAP, 2007; Ohning et al., 2012).
      a. Advantages.
         1) Primarily beneficial for long-distance transports, usually longer than 150 miles.
         2) Although fixed-wing transportation is expensive, favorable cost comparison possible over long distances when staff time is taken into consideration.
      b. Disadvantages.
         1) If no contractual agreements with aircraft vendors, possible inadequate equipment and unfamiliarity of team with the aircraft or with general vendor operation.
         2) Requires coordination of ground transportation on both ends of the flight.
         3) Space limitations, and patient access may be limited.
         4) Securing the same incubator in a fixed-wing aircraft and an ambulance may not be possible because of different mounts and stretcher configurations. This must be evaluated before the transport.
         5) Requires an airport for landing and takeoff.
         6) Multiple patient movements from aircraft and ambulances.
   4. Before each transport, careful evaluation of risks and benefits of various available modes/vehicles for transport must be completed before transport with distance, time, logistics, and resources considered. This is a requirement of the referring physician under the Emergency Medical Treatment & Labor Act (EMTALA). Safety must be a priority and the responsibility of everyone involved in the transport. The selection of an appropriate, safe, and reliable vehicle is as important as the training, experience of the pilots, emergency vehicle operators, and mechanics responsible for their operation. Only partners/vendors (air or ground) with demonstrated commitment to safety should be considered (AAP, 2016).

TRANSPORT PERSONNEL

A. **Composition of a neonatal transport team** varies with federal, state, and local regulations, as well as budget, availability, professional standards, patient population, mission, referral area, expectations and available resources at referral hospital, skill and educational level of team, acuity, and volume of transports. The team must possess the combined expertise to assess, plan, implement, and evaluate actual and potential complications during transport of a critically ill neonate (AAP, 2016; Commission on Accreditation of Medical Transport Systems [CAMTS], 2018; NANN, 2010a). The team may be staffed by using various combinations of personnel, as appropriate to the specialty, with a minimum of two patient care providers trained in the management of critically ill neonates. These patient care providers are in addition to the ambulance drivers or pilots. At least one of the patient care providers must be a physician, RN with neonatal experience/expertise, or neonatal nurse practitioner (NNP). Team

composition may remain constant or vary according to patient acuity (AAP, 2016). Karlsen found over 26 different team configurations in a national survey of over 200 neonatal transport programs. The most common neonatal transport configuration is an RN and a respiratory therapist (Karlsen et al., 2011).

When transporting two neonates in the same vehicle in separate incubators, specific patient care providers should be assigned to each infant. Cross-training staff within scope of practice and licensure increases the efficiency of the team. Transport teams may be configured using a combination of the following personnel:

1. Physicians and neonatologists.
2. Fellows and residents.
3. RNs.
4. NNPs.
5. Respiratory therapists (RTs).
6. Emergency medical technicians or paramedics.

B. **Roles for transport personnel**, including functions, responsibilities, qualifications, and competencies, must be clearly outlined in job descriptions.
   1. Transport personnel should function as a team.
   2. Cross-training personnel within scope of practice and licensure.
   3. The program should have a written policy specific to job performance for physical requirements and disqualifying mental conditions of team members.
      a. Weight and height requirements, especially in air transport.
      b. General physical condition.
      c. Notification to transport administration of use of prescription and over-the-counter medications (certain medications may delay mental function and reflexes).
   4. Staff should participate in neonatal transport with sufficient frequency to maintain expertise.

C. **Team composition considerations** (AAP, 2007, 2016; CAMTS, 2018).
   1. Physicians.
      a. Neonatologists should be utilized when their additional expertise is required.
      b. May limit resources in a busy neonatal practice.
      c. Residents provide less consistency as a result of rotations and lack of educational experience in neonatal intensive care.
      d. Fellows provide more consistency and increasing levels of expertise as they advance through their fellowship. Fellows may be involved in the transport in medical control under the supervision of an attending physician. Limited research has demonstrated that well-trained nurse practitioners/nurses and respiratory therapists function safely and independently in the transport environment without a physician (Leslie and Stephenson, 2003).
   2. NNPs.
      a. Licensed in most states to perform diagnostic and therapeutic procedures.
      b. Highly skilled, in addition to their advanced knowledge of neonatal intensive care therapies.
      c. Increased cost in comparison to an RN; however, this may eliminate the need for resident/fellow/neonatologist presence.
   3. RNs.
      a. Requires advanced knowledge and experience in neonatal intensive care. Ideally, 2 to 5 years of experience caring for critically ill neonates.
      b. May be the team leader.
   4. RTs.
      a. Frequent team members because the majority of neonates transported have a respiratory problem.
      b. Require advanced knowledge in neonatal intensive care. Ideally, 2 to 5 years of experience caring for critically ill neonates.
      c. May assist with nursing functions as licensed by the state.
      d. Responsible for respiratory equipment, airway maintenance, and maintaining adequate oxygenation and ventilation during transport.
   5. Emergency medical technicians and paramedics.
      a. Role varies, depending on experience and education in neonatal care.
      b. Functions may include nursing or respiratory therapy responsibilities.

D. **Educational requirements for ALL team members** may include in-service programs, formal team training and simulation, and national certifications, including the Basic Life Support Course, the AAP/American Heart Association (AHA) Neonatal Resuscitation Program, the AAP/AHA Pediatric Advanced Life Support Course, the S.T.A.B.L.E. (Sugar and Safe Care, Temperature, Airway, Blood Pressure, Lab Work, Emotional Support) Program, the S.T.A.B.L.E. Program Cardiac Module, the S.T.A.B.L.E. Program Physical and Gestational Age Assessment Program, Certified Neonatal and Pediatric Transport (C-NPT), Certified Transport Registered Nurse (CTRN; for NNPs and RNs), and Neonatal Pediatric Specialty (NPS; for RTs). Providing education in a team setting provides additional opportunities for team building and sharing various knowledge and skills, building on each team member's strengths (Karlsen, 2016).
   1. Each program must have orientation programs for team members and specific competencies and skills that must be completed before independent practice and provide ongoing evaluation.
      a. Expertise required within the transport team (AAP, 2016; NANN, 2010a).
         1) History taking.
         2) Physical examination and gestational age assessment.
         3) Interpretation of laboratory and radiologic findings.

4) Knowledge of neonatal physiology and pathophysiology.
5) Excellent communication and public relations skills.
6) Technical and clinical competence.
7) Leadership skills.
8) Ability to work as a team/team member.
9) Physical examination and fitness criteria (physical agility and stamina).
10) Knowledge of aviation physiology, if transporting by air.
11) Transport safety.
12) Knowledge of transport environment and vehicles.
13) Independence and flexibility.
14) Procedures.
a) Bag-and-mask ventilation.
b) Endotracheal intubation.
c) Laryngeal mask airway insertion.
d) Arterial access (umbilical artery catheters, percutaneous artery catheters, arterial sampling).
e) Needle thoracostomy.
f) Thoracostomy tube insertion.
g) Venous access (umbilical venous catheters, peripheral intravenous [IV] lines).
h) Intraosseous insertion.
i) Mobile extracorporeal membrane oxygenation, as applicable.
j) Administration of surfactant, vasoactive agents, or any medication administered in the neonatal intensive care setting.

E. **Considerations for a dedicated neonatal team.**
1. Essential neonatal knowledge and skill to provide care comparable to the neonatal intensive care unit.
2. Staffing: dedicated, unit based, on call.
3. Use of personnel when there are no transports.
4. Volume of transports.
5. Review of other systems that could transport neonates. These systems should demonstrate appropriate clinical expertise and possess equipment to transport a critically ill neonate. They should also possess ongoing clinical practice and expertise in a neonatal intensive care unit and demonstrate periodic competency in neonatal care.
6. Cost and reimbursement.

F. **Medical director** (AAP, 2007, 2016). The role of the neonatal transport team medical director, including qualifications and responsibilities, must be clearly outlined in a job description.
1. A board-certified or board-eligible neonatologist.
2. License to practice medicine in the transport program's state.
3. Additional formal training, experience, and knowledge in transport medicine.
4. Oversees medical aspects of the transport program, including annual review and update of protocols, policies, and guidelines to ensure the practice of evidence-based care in the transport environment.
5. Involved in the quality management program.
6. Involved in administrative aspects: selection of team members, orientation, education, program operation, policies, public relations, and outreach education.

G. **Transport manager/coordinator.**
1. In a unit-based team, the nurse manager may also be the manager of the transport team.
2. Must be a health care provider and meet the requirements noted earlier for team members.
3. Advocate for patients, families, and transport team members.
4. Responsible for ongoing education, safety, quality, performance improvement programs related to transport, and interfaces with referral and receiving hospitals.

Transport Equipment (Gershanik, 2006; Orlando et al., 2007)

A. **Transport equipment and supplies must be checked regularly** to ensure that they are adequately stocked, functioning properly, and ready for immediate transport. Equipment should be scheduled for preventive maintenance regularly. A formal checklist may be used before each transport to ensure that correct equipment and correct number of supplies are secured for the transport. Demonstrated safety of all equipment used in transport is mandatory. Techniques for securing team members, patients, equipment (stretchers, ventilators), and supplies (including medications) must be reviewed regularly and rigorously. Attention to how the transport environment may affect supplies and equipment and medications must be addressed, including but not limited to changes in temperature, humidity, light, vibration, barometric pressure, altitude, and electromagnetic interference. Proper storage, dispensing, and documentation of medications must comply with manufacturer, institutional recommendations, and state and federal regulations (AAP, 2016).

B. **Recommended equipment must be operable on battery power. Battery or backup supply must reflect the distances traveled by the transport program.**
1. Transport incubator for patients less than 5 kg; age-appropriate, federally approved restraining devices for larger infants.
2. Cardiorespiratory monitor with pressure tracing and recorder.
3. Pulse oximeter.
4. Infant ventilator.
5. Air–oxygen blender.

6. End-tidal carbon dioxide monitor or adaptors.
7. Airway humidification system.
8. Invasive and noninvasive blood pressure monitors.
9. IV infusion safety pumps.
10. Transilluminator.
11. Point-of-care testing, including portable blood gas analyzer and glucometer (state regulations vary regarding use and quality control checks in mobile intensive care environments).
12. Defibrillator/pacer (minimum capacity, 2 watt-seconds).
13. Liquid oxygen, oxygen tank in vehicle, or portable oxygen cylinders.
14. Air tank in vehicle, portable air cylinders, or air compressor.
15. Inverter in vehicle. Equipment should have battery backup.
16. Specialized equipment: nitric oxide, extracorporeal membrane oxygenation, and high-frequency ventilation during neonatal transport.

C. **Supplies for neonatal transport** (Box 21.1) (AAP, 2016).

Box 21.1

Supplies for Neonatal Transport

Respiratory Equipment

Laryngoscope handle with blades, sizes Miller 00, 0, and 1
Spare laryngoscope bulbs and batteries
ET tube stylet (fits into the endotracheal tubes)
Anesthesia bag (not to exceed 750 mL) or self-inflating bag with oxygen reservoir
Manometer
Face mask (micropremie, premature, and term)
ET tubes, sizes 2.0, 2.5, 3.0, 3.5, and 4.0
Oral airways (sizes 000, 00, and 0)
Suction catheter and glove sets, sizes 5F, 6F, 8F, and 10F
Portable suction
Meconium aspirator
Blood gas kit
CPAP neonatal prongs (extra small to large neonate)
Nasal cannula (premature, infant)
Ventilator circuit, nitric oxide circuit
Roll of waterproof tape or endotracheal tube securing device
Thoracentesis setups:
- Syringe, 60 mL
- Three-way stopcock
- IV catheters, 20 and 22 gauge
- Tubing T-connector
- Antiseptic solution
- Heimlich valves/closed drainage system
- Chest tubes, sizes 8F, 10F, and 12F
- Oxygen hood
- Laryngeal mask airway (size 1 with 5-mL syringe)
- Bulb syringe
- End-tidal carbon dioxide monitor/carbon dioxide adapters

IV Therapy Equipment

Bags of D_5W, $D_{10}W$, 0.9% saline, 0.45% saline
IV pump tubing
IV filters
Platelet and blood infusion sets
Umbilical catheters, sizes 3.5F and 5F (single, double, triple lumen)
IV extension tubing
T-connectors, multiport connectors
Sterile drapes
Syringes, sizes 1 to 60 mL
Needleless connecting system
Three-way stopcock and stopcock plugs
Antiseptic wipes
Scalp vein needles, 23 and 25 gauge
IV catheters, 22, 24, and 26 gauge
Skin barrier
Safety razor
Medication additive labels
Tape measure
Armboards, sizes premature and infant
Intraosseous needles (intraosseous device)
Assorted tape
Umbilical tape
Antiseptic solution
Sizes 3-0 and 4-0 silk suture with curved needle
Umbilical catheter and thoracotomy set, including:
- Two sterile drapes
- Iris forceps
- Needle holders
- Scissors
- Curved forceps
- Tongue tissue forceps
- Sterile gauze pads, 2 × 2
- Scalpel and blade
- Blunt-end adapters, 17, 18, and 20 gauge

Thermoregulation and Monitoring Equipment

Hat
Polyethylene wrap or bag
Chemical heat packs or thermal pad especially designed for neonates

Box 21.1

Supplies for Neonatal Transport—cont'd

Space blankets
Thermometer
Neonatal electrocardiogram electrodes
Lead wires for heart monitor (premie and term newborn styles)
Capillary tubes
Point-of-care testing equipment (glucose and blood gas analyzers)
Lancets
Arterial transducer tubing

Miscellaneous

Camera
Parent information
Blood culture collection equipment
Scissors and hemostat
Flashlight
Gauze pads, 2 × 2
Limb restraints
Tourniquet
Pacifiers (various sizes)
Christmas tree adapters
Feeding tubes, sizes 5F and 8F
Salem sump tubes, sizes 10F and 12F
Dual-flow gastric tubes, sizes 10F and 12F
Sterile glove packs (assorted sizes)
Sphygmomanometer with blood pressure cuffs, sizes premature, neonate, and infant
Neonatal stethoscope
Trash bag; needle disposal system
Personal protective equipment (goggles, gowns, masks, gloves)
Visceral pack: normal saline solution, sterile gauze, sterile operating room drape, or sterile plastic bag

Medications

Epinephrine, 1:10,000
Sodium bicarbonate, 4.2%
Calcium gluconate, 10%
Dopamine
Dobutamine
Prostaglandin E_1 (Alprostadil)
Phenobarbital
Fosphenytoin
Diazepam (Valium)
Neuromuscular blocking agents
Analgesics
Lidocaine (Xylocaine), 1%
Heparin (1000 units/mL)
Normal saline diluent, 0.9%
Sterile water diluent
Flush solution
Broad-spectrum antibiotics
Albumin, 5%, and/or normal saline solution
$D_{50}W$ (for making higher-glucose-concentrated IV fluid)
Adenosine
Digoxin (Lanoxin)
Surfactant replacement therapy
Ophthalmic ointment
Vitamin K
Lorazepam (Ativan)
Sedative(s)
Milrinone
Reversals:
- Neostigmine (reverses neuromuscular blocking agents)
- Flumazenil (reverses benzodiazepine)
- Naloxone (reverses narcotic-induced respiratory depression)

CPAP, Continuous positive airway pressure; *D_5W*, *$D_{10}W$*, and *$D_{50}W$*, 5%, 10%, and 50% dextrose in water; *ET*, endotracheal; *IV*, intravenous.

D. **Fixed-wing transports.**
   1. Ensure incubator fits through door of aircraft before transport.
   2. Ensure electrical and compressed gas support is sufficient.

E. **Evaluate type and grounding of electrical outlets in vehicles** before transport. Voltage and amperage differences may affect equipment.

Neonatal Transport Process (AAP, 2007, 2016; NANN, 2010a)

A. **Referral call.** The initial transport request call may be taken by a dispatch center, transport team, neonatologist, or neonatal intensive care staff. Ideally, all communication is recorded and the intake process is part of a comprehensive safety, quality, or performance improvement plan for the entire transport process. The referring physician is responsible for selection of an appropriate receiving facility and contacting the receiving physician to request patient transfer. During the initial call, information should be obtained to activate the appropriate team, select the mode of transport, and anticipate any special supplies or equipment that may be required during the transport. A neonatologist may provide consultation to the referring hospital as needed until the transport team arrives. Management given via phone must be accurately documented and preferably

recorded. Transport computer electronic medical record systems are available.

1. Information to be obtained during the initial referral call includes the following:
   a. Time and date of referral call.
   b. Patient name and gender.
   c. Date and time of birth.
   d. Gestational age, birth weight, and current weight.
   e. Parent's name and demographic information (admissions may require this for admitting patient to the hospital).
   f. Referring physician.
   g. Referring institution, including city, state, and phone number.
   h. Reason for transfer request/preliminary diagnosis.
   i. Current management (vital signs, respiratory support, fluid management [to prevent aspiration, the infant should receive nothing by mouth before transport], medications, significant findings of physical examination, pertinent laboratory and radiographic data).
   j. Additional information may be obtained.
      1) Maternal prenatal, labor, and delivery history.
      2) Other pertinent patient findings or medical management.
      3) Infection control issues.

B. **Selection and notification of team members.**

C. **Selection and dispatch of appropriate vehicle.**

D. **Selection of appropriate equipment and supplies.**

E. **Planning en-route to referring hospital.**
   1. Team members will discuss provisional and differential diagnoses, proposed plan of care, and division of responsibilities.
   2. Referring hospital should be notified of time of team's dispatch, mode of transport, and estimated time of arrival to referring hospital.
   3. Emergency and anticipated medication dosages and IV fluid amounts are calculated on the basis of weight.
   4. Potential complications are anticipated, and a plan of action formulated.
   5. History and diagnostic study results to be obtained at referring hospital are identified.

F. **Stabilization at referral hospital.**
   1. Introduce transport team members to referring physicians, staff, and family members. Check identification band on infant. All patients should be transported with identification band on. Parents' religious, cultural, and ethnic preferences should be incorporated into care if the care or safety of the neonate and/or crew are not compromised.
   2. Maintain latex-safe environment.
   3. Perform initial assessment of neonate to determine need for immediate interventions.
   4. Obtain further details of history and current management.
   5. Review previous diagnostic test results, including radiographic images.
   6. Obtain vital signs, including pain assessment and glucose screening results. Determine blood gas values if clinical situation warrants.
   7. Perform complete physical examination, as tolerated by infant.
   8. Complete pain assessment using a validated pain-scoring tool as part of the initial assessment, and reassess during the transport (Blackburn, 2018).
      a. Low birth weight and extremely low birth weight neonates display less organized and less vigorous response to pain.
      b. Transport team should observe for cues that the neonate is experiencing pain.
      c. The transport team should anticipate painful procedures to the neonate.
      d. The transport team should utilize nonpharmacologic techniques and/or administer pain medication or sedation as ordered or by protocol.
      e. The neonate should be reassessed for effectiveness of therapy after treatment of pain as reflected by ongoing documentation using a pain scoring tool.
   9. Initiate monitoring systems as appropriate, including but not limited to cardiorespiratory, peripheral blood pressure, arterial blood pressure monitoring, end-tidal carbon dioxide, and pulse oximetry.
   10. Consult with a neonatologist or designee regarding management plan and anticipated complications en-route, including transport protocols.
   11. Attempt to achieve homeostasis as reflected by normal or optimal blood gas values, blood pressure, temperature, perfusion, serum glucose level, and acid–base balance according to the plan of care.
   12. Transition to transport equipment, including ventilator and IV pumps, carefully monitoring changes in patient status.
   13. Notify receiving unit of estimated time of arrival; current patient status; family's status; and supplies, equipment, and additional personnel needs on admission.
   14. The transport team plays a pivotal role in recognizing the family in crisis, anticipating further crisis, intervening, and assisting the family through the transport process and admission to the receiving hospital.
      a. Identify members of the family unit, that is, parenting dynamics and extended family members.
      b. If possible, encourage and at least provide the option of allowing the parents to remain in the room as their newborn is prepared for the transport. When the mother is requiring ongoing inpatient care, include maternal care providers in

communication to facilitate reinforcement of education and reassurance.
c. Update current patient status; discuss anticipated complications during transport and treatment plans. The parents should be involved in the plan of care.
d. Assess the parents' understanding of the infant's condition, plans for traveling to the receiving center, and their needs for physical and emotional support.
e. Provide information about the receiving center, including location, phone numbers, directions, attending physician, primary/admitting nurse, and visiting policy.
f. Obtain written transport consents.
g. Take a picture of the infant or provide a set of handprints or footprints of the infant to leave with the parents. Initiate the process for bedside video/webcam if available at the receiving hospital.
h. The family may request that special objects, such as toys, pictures, or religious and cultural objects, be transported with their infant. The team should attempt to support the request if it does not interfere with safe transport and it is within the hospital policy.
i. Leave a bonding agent (i.e., cloth) with a parent to keep against the skin that will be given to the infant during visitation.
j. Discuss feeding options. Encourage breastfeeding and pumping while the infant is critically ill; provide evidence of the benefits. If the mother is planning to breastfeed, discuss storage and transport of milk to receiving hospital.
k. Allow the parents to touch the infant before departure. This is helpful in bonding and in making the birth seem more real.
l. Depending on the team's policy and mode of transport, one parent may be allowed to accompany the infant. Policy may include team, patient, and parent safety topics, including but not limited to motion sickness, vehicle limitations of space, securing in the vehicle, and explanations for the family when it is unsafe or problematic for them to accompany the neonate.

15. Obtain copies of prenatal, maternal, and neonatal medical records. The records should be secured during the transport in accordance with the Health Insurance Portability and Accountability Act (HIPAA).
16. Distribute transport evaluation form(s) to referring hospital staff and/or parents.

G. **Planning en-route to receiving hospital.**
1. Infant should be secured in incubator with a restraint device. Loose equipment must never be placed inside the incubator.
2. Continuously monitor temperature, pulse, respirations, blood pressure, oxygenation/ventilation, and pain status as indicated.
3. Documentation at regular intervals, as indicated by infant's condition.
a. Vital signs, blood pressure, color, pain level.
b. Readings of oxygenation and ventilation monitors and of respiratory support settings (including altitude if appropriate).
c. Serum glucose screening or other point-of-care testing as available.
d. Transport timeline, including arrival at referring hospital, departure from referring hospital, and time of transfer of care to receiving hospital staff.

H. **Arrival to receiving facility.**
1. Transport team should notify the parents/family.
2. Transport team provides report to hospital staff.
3. Follow-up may be provided to referring staff and physicians during the infant's hospitalization at the receiving center, maintaining patient confidentiality and following HIPAA regulations.

I. **Neonates should be transported using individualized developmental care techniques**.
1. The sick premature infant experiences significant physiologic stress when incoming stimuli resulting from high noise levels and increased vibration, lighting, and handling exceed the immature nervous system's ability to respond. The infant responds with autonomic instability, hypoxia, and increased oxygen requirements. Incorporating developmental care techniques may decrease these maladaptive responses.
2. Shield the neonate's eyes from light or glare by placing an eye shield on the infant or covering the incubator with a flame-retardant incubator cover. The infant's eyes should be covered before using lights in the vehicle. Limit use of overhead fluorescent lighting. Install and use dimmer switches in the vehicle. Indirect lighting should be directed away from the neonate to facilitate staff needs.
3. The neonate should be positioned in the incubator to support posture and movement and promote a calm, regulated behavioral state. Nesting or boundaries support the infant's position and conserve energy by containing movement. Positioning aids may be purchased, or blanket rolls may be used.
4. Incubator portholes and doors should be closed with care. Objects should not strike the incubator.
5. A gel mattress may be used to decrease vibration and aid in positioning.
6. Decrease noise levels inside the vehicle by reducing speech levels, excluding radio or television use, and responding promptly to monitor alarms. An intercom system may be used for staff communication.
7. On ground transport, request that the ambulance driver avoid rough areas in road.

J. **Special transport stabilization considerations.**
1. Very low birth weight (VLBW) infant (AAP & AHA, 2016; Thigpen, 2002).
   a. Ventilation.
      1) Susceptibility to barotrauma with high peak inspiratory pressures.
      2) Administration of surfactant replacement therapy by the transport team may be considered for infants meeting specific clinical criteria or for long-distance transports. Ventilatory status must be closely monitored to prevent pulmonary air leaks because of changes in lung compliance after administration. Transport from the referring hospital may be delayed to stabilize the infant and monitor lung compliance changes before departure in the vehicle.
      3) The VLBW infant may experience increased incidence of hypoxia and oxygen requirements because of the stresses of transport. Developmental care techniques should be incorporated into care. Sedation before transport may be required.
      4) Continuous pulse oximetry and an air–oxygen blender should be used to monitor oxygen saturations and adjust oxygen concentrations to prevent hyperoxia.
   b. Hypothermia.
      1) May require supplemental warming devices in addition to the prewarmed transport incubator: chemical heat packs or mattresses, especially designed for neonates; hats; polyethylene wrap or bags especially designed for infants less than 28 weeks (often used for infants >28 weeks in the transport environment). Increase environmental temperature, warm objects before placing in contact with neonate.
      2) Because of the fragility of the skin, extreme care must be taken to not place warming devices in direct contact with skin.
      3) Transport incubator door and portholes should be kept closed as much as possible.
      4) Cover the outside of the incubator with a flame-retardant incubator cover.
      5) In cold weather, preheat the vehicle before loading the incubator.
   c. Skin fragility.
      1) Minimal to gentle handling.
      2) Use monitoring devices designed for the VLBW infant.
      3) Minimize invasive procedures and placement of monitoring devices on skin.
      4) Maintain appropriate level of hydration. IV fluid administration is calculated on increased insensible water loss with decreased gestational age. Glucose should be closely monitored. Avoid rapid infusions of IV fluid.
      5) Application of a semipermeable polyethylene membrane or specific products designed for the VLBW infant may be placed on the skin to maintain integrity and decrease insensible water loss.
2. Spinal immobilization (Gomella, 2009).
   a. Traumatic injuries to the neonatal spinal cord are extremely rare.
   b. Injuries may occur because of a congenital defect, birth injury, fall, or nonaccidental trauma. Most spinal cord injuries are caused by lateral or longitudinal stretching force of the neck or torsion of the neck.
   c. The spinal column in the neonate is more susceptible to hyperextension injury as a result of increased elasticity.
   d. Spinal motion restriction may be required. Immobilization device and/or blanket roll support should fit into the incubator.
   e. Anticipate respiratory problems with higher spinal cord injuries.
3. Inhaled nitric oxide (iNO).
   a. iNO may be initiated at the referring hospital or by the transport team. If initiated during transport, the treatment should continue for the duration of the transport.
   b. Requires continuous monitoring of all iNO delivery equipment.
   c. Follow Federal Aviation Administration regulations for rotor-wing and fixed-wing transports. The pilot should be informed when iNO is taken on board the aircraft and when started.
   d. Ensure that a hand ventilation system is available.
   e. Staff education, including the appropriate use of iNO, is essential. Staff should have access to Material Safety Data Sheet (MSDS) documentation, as well as a policy to address occupational exposure of iNO.
4. Ventilation and airway assist devices.
   a. Conventional ventilator.
   b. High-frequency ventilation (jet or oscillator).
   d. Heated humidified high-flow nasal cannula.
   e. Noninvasive positive pressure ventilation.
   f. Continuous positive airway pressure.
   g. Oxygen mask, nasal cannula.
5. Transporting multiple births.
   a. If possible, transport at same time.
   b. Each neonate should have minimum of one transport staff responsible for direct patient care (depending on the diagnosis and clinical condition). Additional transport staff should be available to assist in patient care as needed.
   c. Each neonate should have a separate incubator, a set of transport equipment, and supplies, including cardiorespiratory monitoring and airway equipment.

d. Each neonate should have his or her own documentation records, including consent forms.

6. Therapeutic-induced hypothermia (Fairchild et al., 2010; Jacobs et al., 2011; Karlsen, 2013).
   a. Infants ≥35 weeks, greater than 1800 grams with hypoxic–ischemic encephalopathy.
   b. Time-sensitive transport, cooling must begin before 6 hours of age.
   c. Active cooling—use of servo control device.
   d. Passive cooling may begin in the referral hospital—incubator temperature turned off.
   e. Continuous core temperature (esophageal temperature) monitoring.
   f. Monitor for and document adverse effects of hypothermia.
   g. In addition to the documentation of clinical status and the core temperature, record the servo-controlled cooling mattress temperature and ambient temperature.
   h. Sedation for comfort per protocol.

Documentation

A. **Necessity of documentation.** Patient status and the care provided must be documented throughout the transport.

B. **Logistical documentation.**
   1. Time of transport call.
   2. Time of departure en-route to referring hospital.
   3. Time of arrival at referring hospital.
      a. Monitor stabilization time as a quality indicator.
      b. Develop a plan to address prolonged stabilization and provision for additional resources as indicated.
   4. Time of departure from referring hospital.
   5. Time of arrival at receiving hospital.
   6. Transport delays.
   7. Names of transport staff.
   8. Mode of transport.
   9. Names of referring facility and physician.
   10. Other indicators such as temperature of transport vehicle, additional data related to therapeutic devices or interventions (end-tidal CO_2, core temperature, and temperature of servo-controlled devices).
   11. Logistics of transport must be included in a comprehensive safety, quality/performance improvement plan for ongoing evaluation. For example, for prolonged stabilization time, are there provisions for providing additional resources, or was the mode of transport or team composition appropriate, etc.?

C. **Patient care documentation.**
   1. Significant maternal history, including medical history before pregnancy, prenatal, labor, and delivery history.
   2. Date and time of birth.
   3. Gestational age.
   4. Birth weight.
   5. Delivery room resuscitation, including Apgar scores.
   6. Care provided before the team's arrival at the referring hospital, including laboratory and radiographic findings and medications administered.
   7. Patient status on arrival of the transport team to the referring hospital, including physical assessment, vital signs, and current patient management.
   8. Problem list, including current and resolved problems.
   9. Ongoing documentation of patient assessment, management, and consultations with designated transport physician.
   10. Patient status on arrival of the transport team to the receiving hospital, including assessment, vital signs, and monitor readings.

Safety (AAP, 2016; CAMTS, 2018; Levick, 2010)

A. **Safety must be the highest priority in any transport program.**
   1. The transport program should develop a comprehensive safety program for team members and patients. Safety plans may include but are not limited to operations, vehicle performance, environmental factors, training, teamwork, shift work/circadian disruptions, and physical demand of transport. A defined process for responses to accidents and incidents must be available and reviewed regularly by all team members.
   2. Training should consist of orientation to the vehicle, emergency and evacuation procedures, survival training, crew resource management, and quality management.
   3. The number and names of all persons on board the transport vehicle must be documented and provided to dispatch before departing.
   4. Any passenger(s), including parent(s) riding in a vehicle, should receive a safety briefing before the transport. The name(s) of any passengers must be provided to dispatch. Passenger(s) must meet all weight and/or height restrictions and must be able to be secured.
   5. During each transport, the team should review evacuation procedures for the crew, the passenger(s), and the neonate.
   6. Debriefing should be performed between crew members after each transport.
   7. Critical incident stress management should be available for each crew member.
   8. Resiliency training and self-care strategies must be available for each crew member.

B. **Uniforms**.
   1. Team members should be appropriately attired to the environmental conditions when on transport.
      a. Appropriate outer garments may be worn to protect against environmental conditions.
      b. Reflective material or striping on uniforms for night operation, garments such as jackets, gloves, socks, and underclothing made from heat resistant, fire-retardant, or natural fibers for rotor- and fixed-wing transports.
      c. Boots or sturdy footwear.
      d. Identification badge.
      e. Helmets should be worn during helicopter transports. Visors should be available to protect the eyes and face from projectile objects. Helmets may also be worn during fixed-wing and ground transport. Helmets must have annual inspection and maintenance as indicated (CAMTS, 2018).
      f. Hearing protection should be worn by all crew who assist with patient loading and unloading while rotor blades are activated on the helicopter.

C. **Flotation vests should be available to all crew members who fly over water.**

D. **Survival and first-aid kits should be located on each vehicle.**

E. **All equipment and articles in the ambulance or aircraft must be secured.**
   1. The incubator may be mounted on a cart or stretcher.
   2. The cart or stretcher must be locked into the vehicle.
   3. Majority of vehicles use longitudinal placement of the incubator rather than horizontal placement.

F. **Restraint of all passengers, including the neonate, during transport.**
   1. The neonate should be secured in the transport incubator with a restraint device. Due to different gestational ages, the restraint device must adjust to fit various sizes and weights. The restraint must not constrict the thoracic cavity. A cushioned head pad should be placed in the incubator to provide protection to the neonate's head.
   2. All staff and/or passengers should have seat belts/shoulder harnesses fastened.

G. **Establish a written policy on the use of emergency warning devices (EWDs: lights and sirens).**
   1. Follow state and local regulations.
   2. Use only for life-threatening emergencies.
   3. Monitor indications and use of EWD as part of a safety, quality, and performance improvement program.

H. **Communication equipment.**
   1. Communication devices are used between team members, dispatch and team, hospital and team, and team and medical control. All communication equipment must be maintained in full operating condition and in good repair.
   2. Types of communication devices may include:
      a. Head sets.
      b. Pagers.
      c. Cell phone.
      d. Satellite phone.
      e. Global system for mobile communication (GSM).
      f. Radio.

I. **Preaccident planning and procedures.**
   1. Every transport program must have a well-defined procedure outlining actions to be taken in the event of an accident involving the vehicle, staff, and patient. This procedure must be readily available and articulated by all team members.
      a. Notification of transport and hospital administration, risk management, public relations.
      b. Provision for staff to receive care.
      c. Provision for patient care and completion of the transport. The patient may return to the referring hospital for evaluation and treatment from the accident or go on to the receiving hospital, whichever is most appropriate.
      d. Notification of transport team's emergency contact.
      e. Notification of the neonate's family.
      f. If appropriate, notification of other team members of the incident.
      g. If appropriate, lock-down of dispatch or transport office to limit the amount of personnel in the area.
      h. Assistance may be required to staff phones. Consider providing a separate phone number other than the team number to provide incident information and updates. A website may also be used to disseminate information.
   2. Staff must complete an emergency contact form that is updated annually or when there is a change of information. The contact information may include the following based on the employer:
      a. Name of employee.
      b. Home address.
      c. Name, address, and phone, cell, and pager numbers of emergency contact.
      d. Alternative emergency contact information.
      e. Information on children.
      f. General directions to crew member's home.
      g. Current photograph in uniform.
      h. Fingerprints, if required by institution or state or regulatory agencies.
      i. Name, address, and phone number to obtain dental records.
   3. Contact hospital employee assistance department or local or state agencies for critical incident stress debriefing for the team. Immediate and long-term debriefing may be required.

4. Staff should be aware of the benefits and services available before an incident. Benefits and services include but are not limited to workers compensation, accident insurance, life insurance, and insurance coverage by vehicle vendor and organization. Staff should be knowledgeable if life insurance policy covers an accident while flying.

J. **Infection control.** Infection control and adherence to universal precautions should be planned because of the confined space of the transport vehicle.

Disaster Preparation (AAP, 2016; Gershanik, 2006; Orlando et al., 2007)

The neonatal transport team may have to assist in evacuating a neonatal intensive care unit.

A. Nontraditional transport equipment may be required because of the time limitation of having one infant in a transport incubator; size and weight of transport incubator may be prohibitive in certain aircraft.
B. Establish system of family notification of where the infant is being transported.
C. Establish system of patient tracking, patient identification, and medical record transfer.
D. Coordination with local, state, and federal agencies is essential. This may affect transport reimbursement.
E. Neonatal transport program may be asked to assist local state and federal agencies during hospital or external disasters or situations of mass causality, including but not limited to, biological or chemical agents, weapons of mass destruction, and natural disasters.
   1. Hospital and EMS may become overwhelmed, and all transport personnel may be mobilized in a crisis.
   2. Transport team members must avail themselves of any opportunities regarding operational awareness and knowledge in disaster situations.
   3. The AAP provides resources on various types of disasters: https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Children-and-Disasters/Pages/default.aspx

Air Transport Considerations

A. **Altitude**.
   1. Anticipate increased oxygen requirement or ventilatory support at higher altitudes.
   2. Provide supplemental oxygen for staff above 10,000 feet if in a nonpressurized aircraft.
   3. Neonates are at increased risk of developing hypoxia as the partial pressure of alveolar oxygen decreases during ascent.
   4. Slow ascent and descent are recommended to prevent rapid re-expansion of gas, which increases the risk for pneumothorax and air embolism in the neonate.

B. **Dysbarism**.
   1. Increased atmospheric pressure results in expansion of gases.
   2. Anticipate expansion of "trapped" gases in body spaces (pulmonary air leaks, necrotizing enterocolitis, bowel obstruction).
      a. Gastrointestinal tract: insert orogastric tube and empty stomach of air.
      b. Pulmonary air leaks: consider needle thoracentesis or tube thoracotomy for decompression before the transport.
      c. Equalization of pressures in the eustachian tubes may be restricted in the neonate or in staff with upper respiratory or sinus problems. Providing a pacifier to the infant during descent, if appropriate, can maintain patency of the eustachian tubes.

C. **Effects of motion.**
   1. Staff should recognize and understand the stresses of transport and flight.
   2. Anticipate patient instability on ascent and descent or during any increase/decrease in movement.
   3. Staff should be able to differentiate monitor artifact from actual recordings.

D. **Noise and vibration.**
   1. Provide ear protection for staff and for the neonate (especially in rotor-wing aircraft).
   2. Provide routine hearing screens for staff.
   3. Minimize noise levels in patient compartment of vehicle.
   4. Anticipate patient instability.
   5. Use mattress and padding to minimize vibration in incubator.
   6. Consider the impact of vibration on equipment and monitoring devices.

E. **Evaluation for extubation and pulmonary air leaks:** possibly difficult during transport, especially in rotor-wing aircraft. Anticipate problems during transport on the basis of diagnosis and clinical presentation.

F. **Out-of-state and international transport.**
   1. **Before departing on international transports, the destination country should be investigated to ensure safety of the transport team.** Updated information on every country, including travel alerts and warnings, are available from the U.S. State Department's website at http://travel.state.gov.
   2. **The team should be knowledgeable regarding out-of-state and international transport regulations and issues.**
      a. Language barriers.
      b. Time change issues.
      c. Landing permits and fees.
      d. Airport hours of operation.
      e. Fueling.

f. Ground ambulance: availability, type, fees.
g. Customs/immigration.
h. Determine if there are any restrictions to transporting specific medications (i.e., narcotics) into a country. Some medications may be required to stay aboard the aircraft or are restricted in certain countries.
i. Communication with regional neonatal intensive care center.
j. Electrical systems vary in different countries and may not be able to accommodate equipment.
k. Some countries require that a physician be present for the patient to be released from the country.

G. **Plan for crew hydration and nutrition on long-distance transports.**
H. **Plan for crew rest periods and overnight stays on long-distance transports.**
I. **Transport configuration and on-loading/off-loading procedures should be predetermined, documented, and practiced before an actual patient transport. Discuss securing of incubator and equipment in receiving state's/country's ambulance or mode of transportation before arrival.**

Legal and Ethical Considerations

A. **Legal issues** (AAP, 2016; NANN, 2010a).
1. Determination of the level of responsibility of the receiving and referring staffs and institutions during the transport process has not been clearly defined and is open to legal interpretations.
a. Referring institution's level of responsibility gradually decreases as the receiving physician and transport team assume increasing responsibility for the management and care of the infant.
b. Transport team should be aware of national and state regulations regarding transport and professional standards: Federal Aviation Administration; National Health, Transportation and Safety Administration; Department of Transportation; Federal Communications Commission; Health Care Financing Administration; The Joint Commission; the Clinical Laboratories Improvement Act; HIPAA; and the Consolidated Omnibus Budget Reconciliation Act.
c. Receiving institution acquires increasing responsibility from the time of the transport call and the initial consultation until the time of admission to the receiving hospital.
2. Parents or legal guardian must receive information regarding the infant's status, treatment options, the risks and benefits of transport, and the risk of not transferring.
a. The transport program should have a policy on transporting a neonate in an emergency situation when the parent(s) are not able to provide consent.
3. Responsibilities of transport team members should be clearly outlined in their job functions and should be compatible with practice acts.
4. The transport nurse should be aware of federal and state regulations governing the transport and administration of controlled substances.
5. The transport program may not be able to perform neonatal transport for a specific period due to external and internal factors.
a. The program may not be able to perform transports due to weather (i.e., hurricanes, tornadoes, and snowstorms), transport accident, and neonatal intensive care bed status.
b. Develop a plan on how to communicate this information to referral centers.
c. If the team is operational, develop a plan for performing three-point transports. Team and facility will maintain relationship with the referring hospital.
d. If the team is not operational, develop a plan for contacting another neonatal transport service.

B. **Ethical issues.** Dilemmas regarding the transport of neonates should be addressed by administrative, medical, and transport staff and should include information on the following (NANN, 2010b):
1. Infants with expected poor outcomes, including those with genetic disorders, severely asphyxiated infants, extremely low birth weight infants, and those with lethal anomalies.
2. Debriefing of the team should be provided.

Quality Management (CAMTS, 2018; NANN, 2010a, GAMUT, 2019)

Total quality management is a philosophy for continuously improving the quality of services and processes. The transport program should develop a quality management program to monitor, evaluate, and improve patient outcome and service. All members of the transport team and vendors should be involved in quality improvement planning and process, including regularly scheduled meetings. Written quality management plan with action plan and thresholds and documentation of meetings are transparent, and are a portion of a larger institution/hospital quality program. There is now the ability to track, report, and compare transport data with similar programs internationally. The Ground Air Medical qUality Transport Quality Improvement Collaborative uses the GAMUT Database as a free resource for transport teams to track, report, and analyze their performance on transport-specific quality metrics by comparing it to other programs (2019). Additional information can be found at gamutqi.org/.

A. **Quality indicators may include but are not limited to:**
   1. Transport statistics (number of completed transports, referral hospitals, referral physicians).
   2. Equipment malfunction, failure, or supply.
   3. Transport delays.
   4. Stabilization times.
   5. Crew and patient safety issues.
   6. Number of transports per team member.
   7. Procedures performed by crew on transport.
   8. Documentation of patient care and medications.
   9. Vehicle availability and out-of-service time.
   10. Patient outcome (performance of cardiopulmonary resuscitation, death during transport, death within 24 hours of transport, intubation and/or extubation during transport, transport without vascular access due to inability to obtain).
   11. Hypothermia, hyperthermia, hypotension, hypoxemia/hypoxia, hypoglycemia during transport.
   12. Appropriateness and timeliness of interventions and patient's response.
   13. Family and referring hospital customer satisfaction.
   14. Staff education and skills.
   15. Number of aborted and canceled transports.
   16. Review of transport policies and procedures a minimum of every 2 to 3 years, as defined by hospital/institution.
   17. Staff injuries.
   18. Ground transports with red lights and sirens.
   19. Trending of occurrences or near-miss occurrences.

B. **Quality improvement may be attained through a number of mechanisms. A combination of these mechanisms is probably most effective.**
   1. Case review by the team, medical director, and transport director.
   2. Use of peer review.
   3. Regular staff meetings.
   4. Case review with team members, which can be effectively accomplished by review of selected cases, including:
      a. Initial referral call.
      b. Transport logistics.
      c. Stabilization of the infant by the referring hospital as well as the transport team.
      d. Care provided during transport.
      e. Patient outcome.

C. **Peer review may be used to provide feedback to individuals.**
   1. Appropriateness of care provided.
   2. Clarity of treatment plan.
   3. Treatment plan rationale and outcome.
   4. Documentation.

D. **Issues identified through any of these mechanisms should be addressed with recommendations and plans for follow-up.**

E. **Outreach education.** Transport team members should be available to discuss transport stabilization, issues, and concerns with the health care providers from the referring hospitals.

F. **Policy manual.** Reflects evidence-based care and is either electronic or hard copy and is accessible to all personnel.

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CHAPTER 22

Care of the Extremely Low Birth Weight Infant

Sharron Forest

OBJECTIVES

1. Discuss the mortality and morbidity associated with extreme prematurity.
2. Identify principles of nursing care specific to the extremely low birth weight (ELBW) infant population and their families.

Overview

Care of premature infants with birth weights between 1000 and 1500 g has become almost routine in most neonatal intensive care units (NICUs) in the United States. The most recent challenge in neonatology is the care of extremely low birth weight (ELBW) infants (birth weight <1000 g). Although they represent a small percentage of overall births and NICU admissions, ELBW infants are often the most critically ill and are at the highest risk for mortality and long-term morbidity of any NICU patient. They remain hospitalized for long periods, suffer the most acute and long-term complications of neonatal intensive care, and consume a disproportionate number of hospital days. The purpose of this chapter is to provide an overview of topics related to care of the ELBW infant. Detailed information on resuscitation, thermoregulation, ventilation, and fluids and electrolytes can be found in those specific chapters.

Epidemiology (Centers for Disease Control and Prevention [CDC], 2017; March of Dimes, 2018)

A. **Nearly 400,000 babies per year (1 of every 10 infants) are born preterm in the United States.**
B. **Preterm-related causes of death grouped together accounted for 36.3% of all U.S. infant deaths in 2013, more than any other single cause.**
C. **Prematurity and low birth weight account for 26% of all neonatal deaths** (March of Dimes, 2016).
D. **Risk factors for preterm birth include a history of preterm birth, uterine or cervical problems, multifetal pregnancy, smoking, maternal age under 20 or over 40, obesity, birth spacing less than 18 months, and socioeconomic status.**
E. **The preterm birth rate varies by race and ethnicity. In 2016, the percentage of non-Hispanic African American infants born preterm was 13.3%, American Indian/Alaska Native was 10.5%, Hispanic was 9.1%, non-Hispanic white was 8.9%, and Asian/Pacific Islander was 8.5%.**
F. **Births at the threshold of viability, early preterm birth, or birth of an ELBW infant—especially those weighing less than 750 g or less than 26 weeks of gestation—pose a variety of complex medical, social, and ethical considerations.** The effect of such births on the infants, their families, the health care system, and society is profound. Preterm birth is a leading cause of long-term neurologic disabilities in children.
G. **Preterm birth costs the U.S. health care system more than $26 billion each year.**

Mortality and Morbidity (Eichenwald, 2018; Revenis, 2016; Stoll et al., 2015)

A. **Survival increased between 2009 and 2012 for infants born at 23 weeks' gestation (27% to 33%) and 24 weeks (63% to 65%), with smaller relative increases for infants at 25 and 27 weeks' gestation. No change was observed for infants at 22 or 26 weeks.**
B. **Although survival without major morbidity increased for infants born at 25 to 28 weeks' gestation, there has been no change for infants at 22 to 24 weeks' gestation.**

TABLE 22.1

Comparison of Survival and Select Morbidities for 22 to 28 Weeks' Gestational Age (401 g to 1500 g)

	SURVIVAL (%)			
	1993–1997	1998–2002	2003–2007	2008–2012
Survival to discharge without major morbidity	18	24	25	29
Necrotizing enterocolitis	9	9	11	10
Bronchopulmonary dysplasia	36	43	42	45
Severe intraventricular hemorrhage	13	17	14	15
Severe retinopathy of prematurity	14	17	16	12
Late-onset sepsis	35	35	36	24

From Eichenwald, E.C. (2018). Care of the extremely low-birthweight infant. In C. A. Gleason & S. E. Juul (Eds.), *Avery's diseases of the newborn* (10th ed., pp. 390–404). Philadelphia, PA: Elsevier.

C. **There has been a 65% increase in the number of multiple-gestation births over the past four decades, largely due to artificial reproductive technology (ART) and fertility-inducing drugs. Approximately 3% of all pregnancies in the United States are twin, triplet, and higher-order gestations.**
D. **Multiple gestations account for 10% to 12% of perinatal deaths and constitute a disproportionate number of admissions to the NICU compared with singletons. The risk of preterm birth is higher among multifetal gestations, and these babies are at risk for prematurity-related complications.**
E. **ART accounts for 3.5% of low birth weight and 4.3% of very low birth weight infants in the United States.**
F. **Some studies have shown that in addition to low birth weight and complications of preterm birth, multiples may be at increased risk for congenital anomalies, cerebral palsy, infection, and sudden infant death syndrome** (Revenis, 2016).

Table 22.1 details the rates for mortality and morbidity for 22 weeks to 28 weeks gestational age between 1993 and 2012.

Perinatal Management (American Academy of Pediatrics [AAP] and American College of Obstetricians and Gynecologists [ACOG], 2017)

A. **Neonates born to women transported during the antepartum period have better survival rates and decreased risks of long-term sequelae than those transferred after birth.**
B. **Because ELBW and/or very preterm infants are at increased risk of predischarge mortality, they should be delivered at a level III/IV facility unless precluded by the mother's medical condition or geographic constraints.**
C. **Antepartum transport avoids separation of mother and infant in the immediate postpartum period, allows mothers to communicate directly with NICU health care providers, and supports the goal of family-centered health care.**

Perinatal Consultation (Cummings and Committee on Fetus and Newborn, 2015)

A. **Decision making regarding delivery room management should be individualized and family-centered, considering known fetal and maternal conditions/risk factors and parental beliefs about the infant's best interests.**
B. **In general, parents of extremely preterm fetuses can be counseled that infants delivered between 22 and 24 weeks' gestation are less likely to survive, and those who do survive are likely to have neurodevelopmental disabilities in early childhood, which may extend to school age and even adulthood.**
C. **Whenever possible, data specific to the age, weight, and gender of the fetus should be used to aid management decisions made by obstetricians and parents of fetuses at risk of preterm delivery.** This information may be developed by each institution and should indicate the population used in determining estimates of survivability.
D. **The Eunice Kennedy Shriver National Institute for Child Health and Development (NICHD) Neonatal Research Network's Extremely Preterm Birth Outcome Data website (NICHD, n.d.) provides a calculator to estimate infant outcomes based on birth weight, gestational age, gender, and antenatal corticosteroid administration**. The calculator is available at http://www.nichd.nih.gov/about/org/der/branches/ppb/programs/epbo/pages/epbo_case.aspx.

E. **If the physicians involved believe that there is no chance of survival, resuscitation is not indicated and should not be initiated. If the physicians consider a good outcome to be very unlikely, then parents should be given the choice of whether resuscitation should be initiated, and physicians should respect their preference.**
F. **When the physicians' judgment is that a good outcome is reasonably likely, physicians should initiate resuscitation and, together with the parents, continually evaluate whether intensive care should be continued.**

Antenatal Steroids

Enhancement of fetal pulmonary function with the use of antenatal steroids lessens the prevalence and severity of neonatal respiratory distress syndrome. Current recommendations in the *Guidelines for Perinatal Care* (AAP and ACOG, 2017) include:

A. **A single course of corticosteroids (betamethasone or dexamethasone) is recommended for pregnant women between $24^{0/7}$ weeks and $33^{6/7}$ weeks of gestation who are at risk of preterm delivery within 7 days, including those with ruptured membranes and multiple gestations, and may be considered starting at 23 weeks of gestation if there is risk of preterm delivery within 7 days, irrespective of membrane status.**
B. **Administration of betamethasone may be considered in pregnant women between $34^{0/7}$ weeks and $36^{6/7}$ weeks of gestation who are at risk of preterm birth with 7 days and have not received a previous course of antenatal corticosteroids.**
C. **A single repeat course of antenatal corticosteroids should be considered in women who are less than $34^{0/7}$ weeks of gestation with an imminent risk of preterm delivery within 7 days and whose prior course of antenatal corticosteroids was administered more than 14 days previously.**
D. **Rescue-course corticosteroids could be provided as early as 7 days from the prior dose if indicated by the clinical scenario**.

Timing of Umbilical Cord Clamping After Birth (ACOG, 2017; AAP, 2017; AAP and American Heart Association [AHA], 2016)

A. **Evidence supports delayed umbilical cord clamping in preterm infants**. As with term infants, clamping should be delayed for 30 to 60 seconds after birth with the infant at a level below the placenta.
B. Delayed cord clamping for preterm infants is associated with decreased mortality, improved hemodynamics, decreased need for blood transfusions, decreased incidence of intracranial hemorrhage, and lower risk of necrotizing enterocolitis.
C. Timing of umbilical cord clamping should not be altered for the purpose of collecting umbilical cord blood for banking and should not interfere with the active management of the third stage of labor.
D. To prevent hypothermia during delayed cord clamping, infants may be wrapped in polyethylene plastic.

Delivery Room Care Specific to ELBW Infants

A. Careful adherence to details in the delivery room and during the first few hours after birth is essential to help avoid immediate and long-term complications in the ELBW infant. NICUs should have a consistent approach to the initial care of the ELBW infant in the delivery room and upon admission to the NICU (Table 22.2).
B. All neonatal resuscitations and delivery room management should follow the guidelines found in the *Textbook of Neonatal Resuscitation, 7th edition* (AAP and AHA, 2016). Also please see Chapter 5.

Table 22.2

Treatment Guidelines for Initial Management of ELBW Infants

Delivery Room and NICU Admission	
Delivery room	Immediately place into polyethylene wrap or food-grade plastic bag up to the neck Ensure good thermoregulation "Gentle" ventilation as required Avoid hyperventilation and hyperoxia Administer surfactant (if prophylaxis approach) Initiate NCPAP (if early CPAP approach)

Continued

Table 22.2

Treatment Guidelines for Initial Management of ELBW Infants—cont'd

NICU admission	Obtain weight measurement Administer surfactant within first hour (if rescue approach) Establish vascular access Peripheral intravenous catheter Umbilical arterial catheter Umbilical venous catheter (central, double-lumen) Start intravenous fluids as soon as possible with dextrose and amino acid solution Limit evaporative water losses (humidified incubator) Minimize stimulation Avoid hyperventilation and hyperoxia Maintain target oxygen saturations Obtain specimens for complete blood count with differential, blood culture, blood glucose measurement Give antibiotics as indicated Give parents information about their child
First 24 to 48 Hours	
Cardiovascular	Monitor blood pressure, give vasopressors as required Maintain vigilance for presence of patent ductus arteriosus Obtain echocardiogram as indicated
Respiratory	Give additional surfactant doses as indicated Maintain low tidal volume ventilation Avoid hyperventilation and hyperoxia Extubate infant and start on CPAP when possible
Fluid management	Obtain weight every 12 to 24 hours Monitor serum electrolyte, blood glucose, and calcium concentrations every 4 to 12 hours Use of humidity Limit evaporative water losses Administer skin care
Hematologic	Obtain second blood count Administer transfusion support as indicated Monitor bilirubin, begin phototherapy as indicated
Infection	Consider discontinuing antibiotics if blood culture results are negative at 48 hours
Nutrition	Start parenteral nutrition Discuss trophic feedings
Neurologic	Minimize stimulation Perform screening head ultrasonography
Social	Provide daily updates to the family Arrange to meet with family

CPAP, Continuous positive airway pressure; *NCPAP*, nasal continuous positive airway pressure; *NICU*, neonatal intensive care unit.

From Eichenwald, E.C. (2018). Extremely low-birthweight infants. In C. A. Gleason & S. U. Devaskar (Eds.), *Avery's diseases of the newborn* (10th ed., pp. 390–404). Philadelphia, PA: Elsevier Saunders.

Thermoregulation (see Chapter 6) (AAP and ACOG, 2017; Eichenwald, 2018)

A. Very low birth weight (<1500 g) preterm babies are likely to become hypothermic despite the use of traditional techniques for decreasing heat loss. Because infants younger than 28 weeks of gestation may become hypothermic while being dried, they should be immediately covered up to their necks in polyethylene wrap or a food-grade plastic bag and placed under a radiant warmer.
B. The infant's temperature must be monitored closely, because overheating has been described when plastic wrap is used in combination with an exothermic mattress. The goal should be an axillary temperature of approximately 97.7° F (36.5° C).

Ventilatory Practices in the Delivery Room (AAP and AHA, 2016)

A. **Administration of supplemental oxygen in the delivery room.**
   1. Current practice recommends that supplemental oxygen administration be based on objective monitoring of oxygenation. It is recommended that

pulse oximetry be used when resuscitation can be anticipated, supplemental oxygen is administered, positive pressure is administered for more than a few breaths, or cyanosis appears to persist. Supplemental oxygen is indicated when the pulse oximeter remains below the minute-specific target saturation range.

2. Because many babies born at less than 32 weeks of gestation will not reach target saturations when resuscitated with air, blended oxygen may be used. If blended oxygen is not available, resuscitation should be initiated with air.
3. Hyperoxygenation may result in the formation of free radicals and cause lung damage. For infants less than 35 weeks' gestation, the blender should initially be set to deliver 21% to 30% FiO_2. The oxygen concentration should be adjusted to keep the preductal saturation within the target values specific for the infant's age in minutes.

B. **Assisted ventilation in the delivery room.**

1. If positive pressure ventilation is required, it should be provided with low inspiratory pressure to prevent overdistention of the lungs, which can result in air leak and other lung injury. Adequate positive end-expiratory pressure (PEEP) will help to maintain lung volume and remove fluid. In very preterm infants, visual assessment of chest movement may not be reliable, increasing the risk of overinflation. Adequate ventilation may be achieved without apparent chest movement. The provider should carefully monitor for other signs of adequate ventilation, including rising heart rate, audible breath sounds, and risk of oxygen saturation. Several large trials demonstrate the effectiveness of nasal continuous positive airway pressure (NCPAP) for resuscitation and early management in the delivery room (Diblasi and Courtney, 2017).

C. **Surfactant administration in the delivery room.**

1. Studies have compared prophylactic surfactant followed by a period of mechanical ventilation (MV); intubation, surfactant administration, and extubation to continuous positive airway pressure (CPAP) (referred to as the INSURE technique); and NCPAP without surfactant. Results suggest that spontaneously breathing preterm infants who show early signs of respiratory distress syndrome (RDS) should be given surfactant at a low threshold (FiO_2 <0.45), after which they can be quickly extubated and placed on NCPAP to reduce ventilator-induced lung injury (Isayama et al., 2015; Suresh et al., 2017).
2. No matter the timing of the surfactant administration, it is only given after endotracheal tube position is confirmed (AAP and ACOG, 2017).
3. Minimally invasive methods of surfactant administration that allow for spontaneous breathing without intubation are currently being studied. Methods include the use of a thin catheter to administer surfactant, nasopharyngeal administration, aerosolization, and laryngeal mask and pharyngeal administration. With the thin catheter method of surfactant administration, CPAP is delivered by a nasopharyngeal tube after delivery, and a thin catheter (1.3 mm diameter) is inserted into the trachea 20 to 30 minutes after birth, through which surfactant is administered over 2 to 5 minutes. Studies have found increased survival without major complications such as pneumothorax and intraventricular hemorrhage, less need for intubation, and fewer days on MV with this method (Suresh et al., 2017).

Admission to the Neonatal Intensive Care Unit

A. **General care.**

1. All infants should be weighed upon admission; frequent determination of subsequent weights is a valuable tool in managing fluid and electrolyte balance. In many centers, ELBW infants are initially placed under a radiant warmer for easier access (i.e., for surfactant administration and catheter placement) (Eichenwald, 2018).
2. Because of the high transepidermal fluid losses in these infants, intravenous (IV) fluids containing 5% to 10% dextrose should be started as quickly as possible after admission, and efforts should be made to reduce evaporative water losses by increasing the relative humidity surrounding the infant (Eichenwald, 2018).

B. **Ambient humidity.**

1. **High humidity decreases transepidermal water loss (TEWL) and heat loss.** Humidity also decreases fluid requirements and electrolyte imbalances.
2. Seventy percent or higher humidity in the first week of life is needed to affect a difference in TEWL.

C. **Oxygen saturation range.**

1. The optimal range for oxygen saturation continues to be controversial.
2. A systematic review and meta-analysis compared the effects of restricted (Spo_2, 85% to 89%) versus liberal (Spo_2, 91% to 95%) oxygen exposure for extremely preterm infants and concluded that the risk of death before hospital discharge and necrotizing enterocolitis was increased for neonates in the restricted oxygen group compared with those who were cared for with a more liberal oxygen-saturation target. Rates of bronchopulmonary dysplasia (BPD), neurodevelopmental outcomes,

hearing loss, and retinopathy of prematurity (ROP) were similar between the two groups (Manja et al., 2015).

3. In general, oxygen is given for saturations less than 85% and weaned for saturations greater than 95%.

Vascular Access (see Chapter 15)

A. **Umbilical catheters.**
   1. **Umbilical arterial catheter** (**UAC**). Close monitoring of blood pressure, arterial blood gases, and serum chemistries during the first few days after birth is necessary for high-risk ELBW infants. Insertion of a UAC allows for reliable arterial access in critically ill infants. For infants greater than 1200 g, a 5F catheter should be used. Infants less than 1200 g require a 3.5F catheter (Said and Rais-Bahrami, 2013).
   2. **Umbilical venous catheter** (**UVC**). Placement of a UVC at the same time the UAC is placed also provides the clinician with reliable venous access for infusion of fluids, medications, and blood products. Use of a double-lumen UVC allows administration of inotropes or medications. For infants weighing less than 1.2 kg, a 3.5F catheter should be used (Said and Rais-Bahrami, 2013).
   3. Umbilical lines are generally discontinued after 7 to 10 days to reduce the risk of catheter-related infection and vascular complications, although practices vary by hospital (Eichenwald, 2018).

B. **Percutaneous central venous catheter.**
   1. Before the UVC is removed, it is advisable to insert a peripherally inserted central catheter (PICC) for infusion of parenteral nutrition and medications. PICC line sizes include 1.2F, 1.9F (single or double lumen), 2F, and 3F. The size PICC to be inserted should be determined by the size of the vein being used for cannulation (Said and Rais-Bahrami, 2013).

Skin Care (see Chapter 36)

A. **Gestational age is strongly linked to epidermal barrier function**. Maturity of the epidermis is present at birth only for infants born after 32 weeks' gestation. Poor epidermal barrier function predisposes the extremely preterm infant to percutaneous absorption of toxic agents, and high TEWL may lead to heat loss, dehydration, and electrolyte disturbances. The skin barrier of premature infants is injured easily and can serve as a portal of entry for infectious organisms (Papageorgiou et al., 2016).

B. **Preservation of skin integrity should be incorporated into the care of the extremely preterm infant**.
   1. Adhesive use should be limited in the ELBW infant.
   2. Avoid alcohol for cleansing and bonding agents (e.g., benzoin).
   3. Use a hydrocolloid as a protective layer.
   4. Avoid using adhesive on areas of skin breakdown.
   5. Extreme care should be used for adhesive removal: avoid removers/solvents, and facilitate removal with mineral oil, petrolatum, and emollients.

C. **Frequent repositioning of the infant to avoid pressure points of the skin and use of soft bedding or a water mattress are the minimum requirements** (Eichenwald, 2018).

D. **Assessment of the overall skin condition involves evaluating all skin surfaces, head-to-toe, daily or more frequently.** Risk factors for skin injury include less than 32 weeks of gestation, edema, and adhesives applied to the skin to secure tubes, lines, and medical (e.g., NCPAP) and monitoring equipment.

E. Turning the infant a minimum of every 4 hours is necessary, along with careful inspection of skin surfaces. Even when turning side-to-side is not feasible, lifting the head, shoulders, and hips and supporting these areas with pressure-reducing surfaces is helpful. It is important to note that maintaining the infant's head in a midline position is associated with a decrease in intracranial pressure (Fraser, 2017).

Assisted Ventilation (see Chapter 26)

A. **Noninvasive respiratory support (NRS).**
   1. NRS, primarily CPAP and noninvasive positive-pressure ventilation (NIPPV), is becoming increasingly popular as a method of respiratory support in sick newborn infants.
   2. A variety of continuous distending pressure (CDP) devices available today allow breaths to be delivered above the baseline CPAP pressure and to be synchronized or nonsynchronized to the infant's own breaths. The goal of such devices is to enhance CO_2 removal and stimulate breathing. Various CDP devices provide an adjunct to weaning infants off MV after they have been extubated and also help manage apnea of prematurity (Diblasi and Courtney, 2017).
   3. Marked bowel distention ("CPAP belly") is frequently seen. The air from the CPAP easily passes into the esophagus and is swallowed. Increased abdominal girth and visibly dilated intestinal loops may be seen. An increased risk

of gastric perforation has been reported. An orogastric tube should always be placed whenever CPAP is used (Diblasi and Courtney, 2017).

B. **Mechanical ventilation**.
   1. MV is indicated when gas exchange is insufficient or the ELBW infant is acidotic, apneic, or bradycardic. In the first few days of life, surfactant administration is commonly needed.
   2. A variety of devices are now available for use: synchronized intermittent mandatory ventilation (SIMV), assist–control ventilation, volume-controlled ventilation, high-frequency jet ventilation (HFJV), and high-frequency oscillatory ventilation (HFOV).

C. **Methylxanthines**.
   1. Caffeine has been found to decrease the frequency of apnea of prematurity, as well as decrease the need for MV.
   2. Caffeine has been shown to reduce the need for respiratory support and supplemental oxygen requirements and the incidence of BPD, cerebral palsy, and death or disability at 18 months (Kandasamy and Carlo, 2017).
   3. Short- and long-term effects of caffeine at 18 to 21 months in very low birth weight infants include a decreased rate of BPD, decreased death, less cerebral palsy, and decreased incidence of severe ROP (Eichenwald, 2018).

Nutritional Management (Dell, 2019; Poindexter and Martin, 2019) (see Chapters 8 and 10)

A. **ELBW infants are born with limited nutrient reserves, immature pathways for nutrient absorption and metabolism, and higher nutrient demands.** Medical conditions associated with extreme prematurity may complicate the adequate delivery of nutrients.

B. **All infants have a physiologic weight loss that is a reduction in extracellular water.** In very premature infants, the loss of extracellular fluid within the first few days of life can be as high as 15%.

C. **ELBW infants have high insensible water losses, primarily via the skin and respiratory tract.**

D. **Fluid requirements.**
   1. Initial fluid therapy should be aimed at allowing a normal physiologic weight loss while preventing dehydration and electrolyte imbalances.
   2. Maintenance fluids required during the first week of life are displayed in Table 22.3. Fluids should be adjusted based upon the infant's clinical condition and any factors that may alter the fluid requirements.

E. **Parenteral nutrition.**
   1. ELBW infants are initially almost entirely dependent on parenteral nutrition. The extremely premature neonate is born with minimal glucose stores and can lose 1% of body protein per day when provided with IV glucose alone. Initiating fluids quickly is paramount in ELBW infants.

F. **Glucose**.
   1. Glucose is the primary energy substrate for the brain. The normal glucose requirement is 8 to 9 mg/kg/min in extremely preterm infants. A reasonable approach is to start at a rate of 6 mg/kg/min and advance to 10 to 12 mg/kg/min as long as hyperglycemia does not develop. Infants who weigh greater than 1000 g usually tolerate a 10% glucose solution initially, whereas infants weighing less than 1000 g should start on a 5% glucose solution.
   2. ELBW infants are susceptible to hyperglycemia. Careful monitoring to avoid both hypoglycemia (plasma glucose level <40 mg/dL) and hyperglycemia (plasma level >150 mg/dL) is necessary, with adjustment of dextrose as necessary. Generally, plasma glucose levels less than 200 mg/dL do not require treatment.

G. **Amino acids.**
   1. Failure to provide adequate protein can significantly affect the long-term outcome of extremely premature infants.

TABLE 22.3

Maintenance Fluid Requirements During the First Week of Life

Birth Weight (g)	Insensible Water Loss (mL/kg/day)	Day 1 to 2 (mL/kg/day)	Day 3 to 7 (mL/kg/day)
<750	100+	100 to 200	120 to 200
750 to 1000	60 to 70	80 to 150	100 to 150
1001 to 1500	30 to 65	60 to 100	80 to 150
>1500	15 to 30	60 to 80	100 to 150

Adapted from Dell, K. M. (2019). Fluid, electrolytes, and acid-base homeostasis. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh (Eds.), *Fanaroff and Martin's neonatal-perinatal medicine: Diseases of the fetus and newborn* (11th ed., pp. 1854–1870). St. Louis, MO: Elsevier Mosby.

2. Provision of IV amino acids, even when total caloric intake is low, can help limit catabolism, improve protein balance, and preserve endogenous protein stores. Extremely premature infants may lose approximately 1.2 g/kg of protein per day, equivalent to a daily loss of 1% to 2% of total endogenous body protein stores, if IV amino acids are not administered.
3. Generally, protein requirements for infants weighing less than 1200 g is estimated at 4.0 g/kg/day; some experts recommend 4.0 to 4.5 g/kg/day to duplicate fetal growth for infants weighing up to 1000 g.
4. Serum blood urea nitrogen (BUN) and pH should be monitored because azotemia, hyperammonemia, and metabolic acidosis may be evidence of protein intolerance.
5. The appropriate balance of glucose and lipids in parenteral nutrition is critical. Nutrient and protein retention is maximal if the balance between carbohydrates and lipids is approximately 60:40.

H. **Lipids**.
1. IV lipids are important not only to prevent essential fatty acid deficiency but also as a significant source of nonprotein energy. Fat provides the major source of energy for growing preterm infants.
2. Essential fatty acid deficiency can develop in preterm infants within 72 hours. This deficiency can be avoided with a minimum of 0.5 to 1 g/kg/day of IV lipids.
3. IV lipids are available as 10%, 20%, and 30% emulsions. The 20% solutions are preferred because they have lower phospholipid-to-triglyceride ratios and liposomal content than the 10% solutions, resulting in lower plasma triglyceride, cholesterol, and phospholipid concentrations.
4. Lipid infusion rates in excess of 0.25 g/kg/hr can be associated with decreases in oxygenation.
5. IV lipids, infused over 24 hours, can be started at 3 g/kg/day with the first day of full parenteral nutrition without the need to slowly increase in a stepwise fashion. Lipids should not exceed 3 to 4 g/kg/day.
6. Triglyceride concentrations are most often used as an indication of lipid tolerance and should be maintained below 150 to 200 mg/dL.

I. **Complications of parenteral nutrition.**
1. The primary complications of parenteral nutrition are cholestasis (parenteral nutrition–associated liver disease) and complications related to the IV line. The exact cause of cholestasis remains unknown.
2. The most frequently identified risk factors in cholestasis are duration of parenteral nutrition, degree of immaturity, and delayed enteral feeding.

J. **Enteral nutrition.**
1. Providing consistent enteral nutrition to ELBW infants is challenging. Issues of immature gut motility and function, as well as the fear of necrotizing enterocolitis, are prevalent.
2. Human milk is the optimal food for infants because it provides immunologic and antibacterial factors, hormones, and enzymes not present in other infant food sources. The benefits of human milk for gastrointestinal function, host defense, and possibly neurodevelopmental outcome have been well documented.
3. Early initiation (within the first few days after birth) of low-volume feedings (10 to 20 mL/kg/day) are not meant to give the infant significant nutrition, but only to promote continued functional maturation of the gastrointestinal tract. Studies support physiologic and clinical benefits of early minimal enteral feeding with no increased risk of necrotizing enterocolitis (Poindexter and Martin, 2019).
4. Small aliquots of human milk or premature formula may be provided (<25 mL/kg/day). Evidence suggests that these small trophic feedings may reduce or prevent intestinal atrophy in this high-risk population (Poindexter and Martin, 2019).
5. One common approach is to advance feedings by 20 to 30 mL/kg/day for very low birth weight infants and by 15 to 25 mL/kg/day for ELBW infants as long as the infant tolerated the previous 24 hours of feeding; this typically results in full enteral feeding (150 mL/kg/day) in 7 to 10 days. A Cochrane review concluded that slow feeding does not appear to provide benefits (Oddie et al., 2017).
6. As enteral feeds approach full volumes, usually 150 to 160 mL/kg/day, consideration should be given to increasing caloric density.
7. Oral care with human milk can provide benefits to the infant and family and should be done after the mother pumps around the clock until the infant can receive human milk by mouth (National Association of Neonatal Nurses (NANN), 2015).
8. Although measuring gastric residuals is common practice in some NICUs, there is no evidence to support discontinuing enteral feeds based on gastric residuals in the absence of other symptoms (Poindexter and Martin, 2019).

K. **Prebiotics and probiotics**: Several clinical trials of probiotics have been performed in neonates and have suggested that administration of probiotics may prevent necrotizing enterocolitis. There is currently no Food and Drug Administration (FDA)–approved product for use in infants.

Management and Prevention of Infection (Esper, 2019) (see Chapter 32)

Bacterial and fungal infections are an important cause of illness and death among ELBW infants.

A. **Early-onset bacterial sepsis.**
   1. The incidence of neonatal sepsis for infants with birth weights less than 1500 g is 10.96 per 1000 live births, and mortality rates for early preterm infants are as high as 30% to 54%.
   2. Early-onset sepsis (EOS) is generally acquired vertically from bacteria colonizing the mother's lower genital tract or from infected amniotic fluid. The exception is transplacental transmission of *Treponema pallidum* and *Listeria monocytogenes*.
   3. Risk factors for EOS.
      a. Maternal factors.
         1) Intrapartum fever (>37.5° C).
         2) Chorioamnionitis.
         3) Prolonged rupture of membranes, greater than 18 hours.
         4) Maternal colonization with group B streptococcus.
         5) Colonization with genital mycoplasmas.
      b. Neonatal factors.
         1) Less than 37 weeks of gestation.
         2) Birth weight less than 2500 g.
         3) The incidence is 10 times higher in infants with a birth weight less than 1000 g.

B. **Predominant organisms.**
   1. *Escherichia coli* is the most common cause of EOS in very low birth weight infants (Table 22.4).

C. **Clinical manifestations of sepsis and antimicrobial therapy (see** Chapter 32**).**

TABLE 22.4

Organisms Associated With Early-Onset Sepsis in VLBW Infants

Escherichia coli = 44%
Haemophilis influenzae = 8.3%
Citrobacter = 2.4%
Other gram-negative = 6%
CoNS = 10.7%
GBS = 10.7%
Viridans streptococci = 3.6%
Listeria monocytogenes = 2.4%
Other streptococci = 4.8%
Other = 4.8%
Candida albicans = 2.4%

CoNS, Coagulase-negative staphylococcus; *GBS*, group B streptococcus; *VLBW*, very low birth weight.

Data from Eichenwald, E. C. (2018). Care of the extremely low-birthweight infant. In C. A. Gleason & S. E. Juul (Eds.), *Avery's diseases of the newborn* (10th ed., pp. 390–404). Philadelphia, PA: Elsevier.

Neurosensory Complications (Papageorgiou et al., 2016)

A. **The major neurosensory complications associated with extreme premature birth are intraventricular hemorrhage (IVH), periventricular white matter injury, and ROP.**
   1. Although the incidence of severe IVH has fallen with improvements in management and increased antenatal steroid use, it remains a major cause of brain injury with consequent abnormal neurodevelopment.
   2. The incidence of ROP, a vascular proliferative disorder that affects the incompletely vascularized retina of preterm infants, has increased as survival rates for ELBW infants has increased. Approximately 7% of surviving ELBW infants will develop severe retinopathy (unilateral or bilateral stage 4 or 5 disease or disease requiring laser or bevacizumab in at least one eye).

B. **NICUs should have a routine protocol of screening for neurosensory complications. Screening guidelines for common complications are shown in** Table 22.5**.**

C. **The initial follow-up visit should occur shortly after discharge from the NICU. The frequency of subsequent follow-up visits is determined by the severity of specific active medical and neurodevelopmental issues for the individual child** (Wilson-Costello and Payne, 2019).

Developmental Interventions (Eichenwald, 2018) (see Chapter 11)

A. **Infants born preterm are at increased risk of developing cognitive and motor impairments compared with infants born at term**. Early developmental interventions have been used in the clinical setting, with the aim of improving the overall functional outcome for these infants.

B. Modification of the NICU environment to limit exposure of ELBW infants to negative stimuli by lowering ambient light and reducing noise, clustering caregiving periods and procedures to allow periods of uninterrupted sleep, and using positioning aids to promote containment is an intuitive part of their care.

C. Newer NICU designs, transitioning from open common rooms to private room settings, may also facilitate a better environment for vulnerable infants and enhance parental involvement.

D. Skin-to-skin holding. Skin-to-skin holding, or kangaroo care, offers significant benefits for the neonate and family, including the following: stabilizing heart rate,

Table 22.5

Screening Guidelines for Common Complications

Recommended Screening for Common Complications of ELBW Infants Complication	Screening
IVH (initial screening)	HUS on days 1 to 3; repeat on days 7 to 10
Germinal matrix hemorrhage	Repeat HUS at 30 days
IVH	Repeat HUS every 3 to 7 days until stable or resolved
IVH with ventricular dilatation or intraparenchymal bleeding	Repeat HUS every 3 to 7 days until stable or resolved Consider measurement of resistive indices for progressive ventricular dilatation
Periventricular white matter disease	HUS at day 30; repeat at 36 weeks' postmenstrual age or at discharge Consider magnetic resonance imaging if HUS findings are equivocal
ROP	Perform ophthalmologic examination at 4 to 6 weeks' postnatal age Repeat every 2 weeks if no ROP Repeat weekly if ROP present Repeat twice weekly for prethreshold disease or rapidly progressive ROP
Audiology screening	Hearing screen no earlier than 34 weeks' postmenstrual age, but before discharge home

ELBW, Extremely low birth weight; *HUS*, head ultrasonography; *IVH*, intraventricular hemorrhage; *ROP*, retinopathy of prematurity.

From Eichenwald, E.C. (2018). Extremely low-birthweight infants. In C. A. Gleason & S. U. Devaskar (Eds.), *Avery's diseases of the newborn* (9th ed., pp. 390–404). Philadelphia, PA: Elsevier Saunders.

oxygen saturation, and breathing patterns; improving sleep–wake cycles; increasing growth rate; decreasing pain; improving breastfeeding; and improving parental attachment. Kangaroo care can be done with ventilated infants (Conde-Agudelo and Díaz-Rossello, 2016; Fraser, 2017).

End-of-Life Care (AAP and ACOG, 2017)

A. **Noninitiation or withdrawal of intensive care for high-risk infants.**
   1. Parents should be active participants in the decision-making process concerning the treatment of severely ill infants. This approach requires honest and open communication.
   2. Ongoing evaluation of the condition and prognosis of the high-risk infant is essential. The health care provider must convey this information accurately and openly to the parents of the infant.
   3. It is inappropriate for life-prolonging treatment to be continued when the condition is incompatible with life or when the treatment is judged to be harmful, of no benefit, or futile.
   4. Whenever nonresuscitation is considered an option, a qualified individual should be involved and present in the delivery room to manage this complex situation.
   5. The decision to initiate or continue intensive care should be based only on the judgment that the infant will benefit from the intensive care.

B. **Compassionate and comfort care.**
   1. Comfort care should be provided to all infants for whom resuscitation is not initiated or is not successful.
   2. Compassionate care to ensure comfort must be provided to all infants, including those for whom intensive care is not being provided.
   3. When the extremely preterm newborn does not survive, support should be provided to the family by physicians, nurses, and other staff after the infant's death.

Future Directions

A. **The medical care of the ELBW infant is complex, and wide variability in approaches to the care of these infants exists among practitioners and NICUs, as does variability in outcomes.** NICUs involved in treating ELBW infants should develop a coherent approach to the medical and ethical aspects of their care.

B. **Web-based tools may help with the development of individual "outcome trajectories" that may help with prediction of death or neurodevelopmental impairment in extremely premature infants.** The effects of various complications on long-term outcomes in ELBW infants would be useful to clinicians and parents in determining plans of care (Ge et al., 2013).

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CHAPTER 23

Care of the Late Preterm Infant

M. Terese Verklan

OBJECTIVES

1. Recognize that the late preterm infant (LPI) is at high risk for complications from birth to hospital discharge.
2. Identify the physiologic challenges that place the LPI at increased risk for complications.
3. Explain the importance of validating the gestational age of the LPI.
4. Discuss why frequent assessment of the respiratory system is essential in the LPI.
5. Examine the need for timely assessments for symptoms of hypothermia, sepsis, hyperbilirubinemia, and feeding challenges in the LPI.
6. Identify short- and long-term outcome concerns for LPIs.

The neonate born between $34^{0/7}$ weeks and $36^{6/7}$ weeks of gestation is classified as a late preterm infant (LPI). Birth rates of LPIs in the United States declined to 6% between 2006 and 2014, largely due to fewer clinician-initiated obstetrical interventions (Petrou, 2019). Mortality and morbidity risks are increased in LPIs due to physiologic and metabolic immaturity. Complications of LPIs constitute approximately one third of all neonatal intensive care unit (NICU) admissions (Mohan and Jain, 2018). Medical vulnerabilities include respiratory difficulties, thermoregulation issues, hypoglycemia, sepsis, hyperbilirubinemia, and feeding challenges. An evidence-based standard of care for LPIs has been developed by the Association for Women's Health, Obstetric and Neonatal Nurses (Holditch-Davis et al., 2017). If the LPI is not ill enough to justify care in the NICU, the infant is often cared for in the normal newborn nursery or rooming in with the mother, where policies and care models are focused toward the needs of the full-term infant. Thorough assessment of risk and health status, interventions, and parent education for these neonates is critical and should be individualized (Holditch-Davis et al., 2017). These infants will have a size, weight, and overall appearance similar to that of a full-term infant, and because of this, parents and professional caregivers may tend to treat them similarly to full-term infants. However, these LPIs may present with factors that increase their risk for morbidity over the first days of life (Mohan and Jain, 2011) (Box 23.1).

Communication among staff members is essential to provide optimal, high-quality care for the LPI. A number of complications can arise after birth while in the hospital and/or after discharge that require close observation (Medoff-Cooper et al., 2012) (Box 23.2).

Gestational Age Assessment (see Chapter 7) (Holditch-Davis et al., 2017; Trotter, 2019)

A. Because the LPI can resemble the term neonate, accurate determination of gestational age is essential to help identify risk factors associated with morbidity.
B. Use the date of the last menstrual period and/or an ultrasound performed in the first trimester.
C. Use the New Ballard Score or other recognized tools to determine gestational age. The assessment should be done within 12 hours of birth for optimal accuracy.
D. After obtaining height, weight, and head circumference, use the growth curves to determine if the LPI is small, appropriate, or large for gestational age. Small for gestational age neonates have higher rates of mortality and morbidity.

Respiratory (see Chapters 24 and 25) (Holditch-Davis et al., 2017; Mohan and Jain, 2018; Williams and Pugh, 2018)

A. LPIs are born during the stages of lung development when remodeling of the alveoli and bronchioles occurs. Surfactant synthesis and secretion are also affected, predisposing LPIs to respiratory distress syndrome (RDS).
B. Difficulties absorbing fetal lung fluid decreases gas exchange and promotes transient tachypnea of the newborn (TTN).

Box 23.1

Late Preterm Infant Risk Factors for Increased Morbidity

Younger than expected gestational age	Maternal diabetes
Small for gestational age	Maternal pulmonary, renal, or cardiac disorders
Multiple gestation	Maternal medications, illicit drug use
No antenatal corticosteroid administration	Apgar score of less than 7 at 5 minutes
Emergency or elective cesarean birth	Male gender
Complicated vaginal birth	Racial or ethnic minority
Antepartum hemorrhage	Maternal smoking
Gestational or chronic hypertension	Public insurance

From Mohan, S. S., & Jain, L. (2011). Later preterm birth: Preventable prematurity? *Clinics in Perinatology*, *38*, 547–555.

Box 23.2

Potential Complications of the Late Preterm Infant

Hypothermia	Hypoglycemia
Respiratory distress	Feeding difficulties and associated dehydration
Sepsis	Apnea
Hyperbilirubinemia	Developmental, learning, and behavioral challenges

From Medoff-Cooper, B., Holditch-Davis, D., Verklan, M. T., Fraser-Askin, D., Lamp, J., Santa-Donato, A.,...Bingham, D. (2012). Newborn clinical outcomes of the AWHONN late preterm infant research-based practice project. *Journal of Obstetric, Gynecologic, & Neonatal Nursing*, *41*(6), 774–785.

C. Cesarean delivery without labor and maternal/fetal complications increases risk of RDS, TTN, persistent pulmonary hypertension (PPHN), and apnea.
D. Antenatal administration of betamethasone decreases the need for respiratory support in the first 72 hours of life, decreases respiratory complications, and reduces length of stay in the NICU.
E. Increased risk of PPHN is due to increased amount of smooth muscle in the walls of the pulmonary blood vessels.
F. Increased incidence of obstructive, central, and mixed apnea because of:
   1. Immature neurologic system.
   2. Physiologic immaturity of respiratory system.
   3. Decreased ventilatory response to increasing carbon dioxide levels.
   4. Biphasic ventilatory response to hypoxia.
   5. Very compliant chest wall and upper airway.
   6. Lack of coordination between sucking, swallowing, and breathing during feedings.
G. Perform a detailed respiratory examination immediately after birth and as frequently as clinical condition warrants.
H. Observe for increased work of breathing and tachypnea, especially during transition.
I. Pulse oximetry ranges should be 90% to 95%.
J. Ventilatory therapies may be necessary, such as supplemental oxygen, nasal cannula, mechanical ventilation, inhaled nitric oxide, or extracorporeal membrane oxygenation.
K. Monitor for hypothermia and hypoglycemia.

Thermoregulation Issues (see Chapter 6) (Holditch-Davis et al., 2017; Mohan and Jain, 2018; Williams and Pugh, 2018)

A. Temperature may decrease as much as 2° to 3° C in the first 30 minutes of life; risk for temperature instability continues beyond first day of life.
B. High risk for thermal instability because of:
   1. Decreased brown adipose tissue (BAT) and subcutaneous fat.
   2. Nonkeratinized, thin skin.
   3. Immature response to temperature receptors.
   4. Increased surface area–to–body mass ratio.
   5. Decreased glycogen stores and ability to convert stored glycogen.
   6. Neuromuscular immaturity reduces ability to flex extremities and decrease surface area.
C. Cold stress stimulates release of norepinephrine.
   1. Increases metabolic rate, consumption of oxygen, and use of glucose.
   2. Increased oxygen consumption may lead to hypoxemia and hypoxia.

3. Exacerbates respiratory distress/complications.

D. Minimize/prevent thermoregulatory instability.
   1. Assess axillary temperature within 30 minutes of life and then every 30 minutes until the neonate's condition has remained stable for 2 hours. Axillary temperatures should be 97.7° to 99.5° F (36.5° to 37.5° C). After stabilization, assess axillary temperature every 4 hours for first 24 hours and then as condition warrants.
   2. If stable, place the LPI skin-to-skin with mother's naked chest and cover with a warmed blanket and hat.
   3. If unstable, place on a prewarmed radiant warmer using servo-control, and monitor axillary and skin temperatures as needed.
   4. Delay the first bath until there is thermal, respiratory, and cardiovascular stability.
   5. Maintain a neutral thermal environment by preventing heat loss through radiation, conduction, evaporation, and convection.
   6. Monitor for signs of cold stress and hypothermia: tachypnea, apnea, color change (pallor, mottling, cyanosis), poor feeding, and lethargy due to peripheral vasoconstriction and metabolic acidosis.

Hypoglycemia (see Chapter 9) (Blackburn, 2018; Holditch-Davis et al., 2017; Mohan and Jain, 2018; Williams and Pugh, 2018)

A. May not be detected if LPI is rooming in with mother or is in well-baby nursery.
B. Is three-fold greater than that in full-term neonates.
C. Requires glucose infusion rate of 6 to 8 mg/kg/min, which may need to be increased if complications such as respiratory distress, cold stress, and sepsis are present.
D. Has inadequate glycogen stores, decreased glucose production, and increased glucose utilization.
E. Feeding difficulties are common.
F. Immature/decreased hepatic enzymes for glycogenolysis, gluconeogenesis and hormonal dysregulation of catecholamine, glucagon, and corticosteroids.
G. Immature pancreatic beta cells have difficulty regulating insulin production.
H. Risk for hypoglycemia increases if:
   1. Maternal conditions include obesity, gestational/diabetes mellitus, pregnancy-induced hypertension, use of tocolytics, intrapartum administration of glucose, difficult delivery, and category II or III fetal heart rate pattern.
   2. Neonatal conditions include 5-minute Apgar less than 7, perinatal distress, intrauterine growth restriction, multiple gestation, respiratory complications, sepsis, and temperature instability.
I. Perform a screening test using heel or venous sampling within first 2 hours of life and before each feeding for the first 24 hours. Monitor blood glucose levels per unit/hospital protocols or the American Academy of Pediatrics (AAP) guidelines for postnatal glucose homeostasis (Adamkin and AAP Committee on Fetus and Newborn, 2011).
J. If glucose is less than 40 to 45 mg/dL, provide intravenous glucose per protocol/provider orders. Oral dextrose gel may be used to increase blood glucose levels.
K. Monitor for adequate oral intake. Feedings should be on demand every 2 to 3 hours.
L. Evaluate for symptoms of hypoglycemia: change in feeding pattern, hypotonia, lethargy, abnormal cry, irritability, jitteriness, apnea, tachypnea, change in color, hypothermia, change in level of consciousness.

Sepsis (see Chapter 32) (Blackburn, 2018; Holditch-Davis et al., 2017; Mohan and Jain, 2018)

A. Immature immune system despite normal cell counts.
B. Decreased transference of maternal antibodies.
C. Impaired skin integrity.
D. Increased exposure to microorganisms due to prolonged hospitalization and invasive tests and procedures.
E. Maternal risk factors.
   1. Group β-hemolytic streptococcus (GBS) status positive or unknown.
   2. Herpes simplex virus (HSV).
   3. Human immunodeficiency virus (HIV).
   4. Previous delivery of a baby with GBS infection.
   5. Prolonged rupture of membranes greater than 18 hours.
   6. Inadequate antenatal antibiotic prophylaxis.
   7. Maternal temperature greater than 100.4° F and/or diagnosed chorioamnionitis.
F. Neonatal risk factors.
   1. Male gender.
   2. African American race.
   3. Difficult delivery, including Apgar score less than 7 at 5 minutes.
   4. Congenital anomalies.
G. Evaluate at birth and every 4 hours for signs/symptoms of infection in the first 24 hours and then once per shift until discharge.
   1. Change in feeding behaviors, poor feeding.
   2. Lethargy, hypotonia, irritability, jitteriness.
   3. Temperature instability.
   4. Respiratory distress.
   5. Apnea and bradycardia.
   6. Hypotension, poor perfusion.
   7. Vomiting, diarrhea, gastric distention.
   8. Hypoglycemia.

9. Hyperbilirubinemia/jaundice.
10. Rashes, pustules, or other skin lesions.

H. If signs of infection are observed, obtain cultures and treat with antibiotics.
1. Complete blood count.
2. Chest radiograph if respiratory distress is noted.
3. Lumbar puncture if sepsis truly suspected.

Hyperbilirubinemia (see Chapter 29) (Blackburn, 2018; Holditch-Davis et al., 2017; Mohan and Jain, 2018; Williams and Pugh, 2018)

A. Most common reason for hospital readmission.
B. Compared with full-term neonates, LPIs are much more likely to develop hyperbilirubinemia; in addition, it lasts longer and is more pronounced.
C. Total serum bilirubin (TSB) levels peak on day of life five at 10 to 12 mg/dL.
D. Decreased ability to conjugate indirect bilirubin to direct bilirubin (water soluble).
E. Feeding difficulties and immature gastrointestinal function contribute to increased enterohepatic circulation.
F. Risk factors for severe hyperbilirubinemia and kernicterus.
1. Jaundice appearing in first 24 hours.
2. Cephalohematoma or significant bruising.
3. History of sibling who required phototherapy.
4. Blood group incompatibility/hemolytic disease.
5. TSB or total cutaneous bilirubin (TcB) in high-risk zone as plotted on the bilirubin nomogram at time of discharge (see Chapter 29, Fig. 29.8).

G. Assessment and intervention includes evaluating:
1. For the presence of risk factors.
2. The quality/adequacy of feeding, especially if exclusively breastfed.
3. Presence of jaundice within first 24 hours and begin screening for hyperbilirubinemia using TSB or TcB.
4. Bilirubin levels before discharge and plotting the values on the bilirubin nomogram.
5. Initiation of appropriate phototherapy when the bilirubin level reaches threshold for treatment per AAP guidelines (AAP, 2004) (Fig 23.1).
6. Perform exchange transfusion as indicated per AAP guidelines.

Feeding Difficulties (see Chapter 10) (Evans et al., 2019; Holditch-Davis et al., 2017; Mohan and Jain, 2018; Williams and Pugh, 2018)

A. Primary reason for prolonged hospitalization.
B. Neuronal immaturity, decreased oromotor tone, and inadequate generation of intraoral pressures contribute to the poor coordination of suck, swallow, and breathe.
C. Decreased oral muscle strength results in difficulties with latch, suck, and swallow.

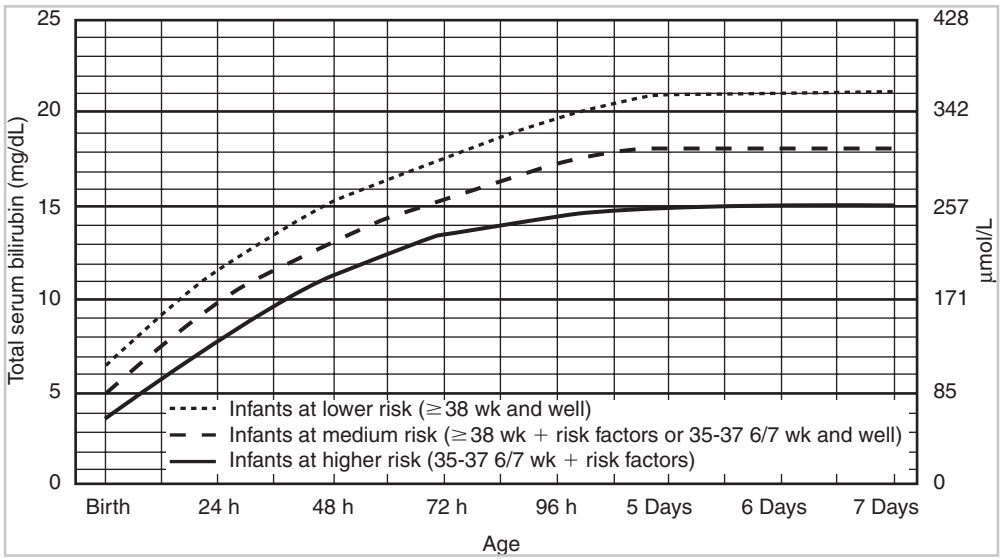

Fig. 23.1 Guidelines for phototherapy in hospitalized infants of 35 or more weeks of gestation. *(From American Academy of Pediatrics. [2004]. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation.* Pediatrics, *114[1], 297–316.)*

Part 2

D. Have fewer awake–alert periods and tend to be sleepy.
E. Less likely to initiate breastfeeding compared with term neonate.
F. Delayed lactogenesis may also compound breastfeeding difficulties.
G. Decreased nutritional intake may lead to poor weight gain, weight loss, and/or dehydration.
H. Gastrointestinal immaturity contributes to relaxation of the lower esophageal sphincter and gastroesophageal reflux, which may contribute to dehydration and hypernatremia.
I. Assessment and intervention.
   1. Ensure feeding readiness before oral feedings.
      a. Evaluate suck, swallow and breath, and strength of suck.
      b. No evidence of respiratory distress.
      c. Demonstrating cues for feeding readiness.
   2. Evaluate physiologic stability before, during, and after feeding.
   3. If breastfeeding, evaluate mother's position and feeding technique, including milk transfer. Obtain lactation consultation, breast pump, and nipple shields, as needed.
   4. Monitor for hypoglycemia, dehydration, weight loss, and hypernatremia.

Neurologic Development
(see Chapter 34) (Mohan and Jain, 2018; Williams and Pugh, 2018; Woythaler, 2019)

A. Brain (and lungs) are among the last organs to mature.
B. Oligodendroglia, neuronal arborization and connectivity, neurotransmitter systems, and brain growth are still maturing, resulting in a 30% increase in overall brain growth in the last weeks of gestation.
C. LPI brain size approximates 66% of the full-term brain.
D. Gyri and sulci not fully formed and cerebral cortex is smooth.
E. Myelination and interneuronal connectivity incomplete and may result in altered brain development.
F. Greater risk for speech and language delays.
G. White/gray matter injury, especially in the thalamus and periventricular white matter, can result in developmental delays.
H. State system stability emerging as demonstrated by limited awake time, lack of smooth transition from sleep to awake, and rapid movement between sleep and awake states.
I. Limited ability to focus on visual stimuli.
J. Brain continues to grow until 2 years of life, when it approximates 80% of adult brain volume.
K. Risk factors.
   1. Any factors that decrease stability of subsystems with illness and interfere with transition to extrauterine life.
   2. Apnea of prematurity, especially with bradycardia.
   3. Immature suck, swallow, and breathe coordination.
   4. Increased sleep requirements with need to awaken frequently for feedings.
   5. Decreased muscle tone leading to need for supportive positioning and care of airway during feeds.
L. Assessment and intervention.
   1. Provide developmentally supportive care practices (i.e., observe limited noise and light levels, developmental positioning techniques/tools, facilitated tucking, skin-to-skin care).
   2. Promote physiologic stability, use of oxygenation at "safe" levels, and avoid metabolic acidosis.
   3. Offer cue-based, individualized care; teach parents cues and supportive measures.
   4. Offer voice or face stimulation separately, observing cues for tolerance before adding more stimulation.
   5. Transition to increased lighting; promote dimmed light when alert, quiet.
   6. Support day–night cycling of light and stimulation.
   7. Consider cranial ultrasound or other neuroimaging study, as warranted.

Parent Education and Support
(see Chapters 17 and 19) (Holditz-Davis et al., 2017; Williams and Pugh, 2018)

A. Support parents in their new role.
   1. Encourage rooming-in and use of skin-to-skin (kangaroo care), when feasible.
   2. Help parents understand/recognize the LPI's periods of alertness, hunger, and satiety cues.
B. Educate when and how often to see primary health care provider (i.e., respiratory distress, jaundice, feeding, weight checks).
C. Ensure temperature assessment and maintenance at home; avoid overdressing and underdressing.
D. Use of hand hygiene/infection control principles. Avoid contact with ill family members, and limit contacts with visitors/avoid public places. Avoid people with upper respiratory tract infections or viral infections.
E. Avoid exposure to secondhand smoke.
F. Develop feeding plan to include adequate intake (nutritional and fluid) for appropriate growth and development.
G. Monitor for jaundice and dehydration (number of stools and wet diapers).
H. Provide instruction in:
   1. Infant cardiopulmonary resuscitation.

2. Sudden infant death syndrome (SIDS) prevention, "Back to Sleep," and safe sleeping environment.
3. Respiratory syncytial virus exposure, prophylaxis, and preventing its spread.
4. Behavior expectations—amount of sleep–awake time to expect, cues.

I. Arrange for developmental follow-up program and early intervention services to promote surveillance of developmental outcomes.

Discharge Criteria (Mohan and Jain, 2018; Williams and Pugh, 2018)

A. Have an established feeding pattern that promotes growth.
B. Maintain body temperature without excessive clothing.
C. Have a documented period free from apnea of prematurity.
D. Serum total bilirubin or transcutaneous bilirubin measured and plotted on bilirubin nomogram. Appropriate follow-up based on results.
E. Schedule the first appointment with an identified provider within 24 to 48 hours of discharge.
F. Metabolic screenings completed.
G. The first hepatitis B vaccine given.

Long-Term Outcome (Woythaler, 2019)

A. Three times more likely than full-term infant to need intervention for developmental issues (21% to 30% of LPI compared with 12% of full-term infants).
B. Less proficient in reading and mathematic skills, often requiring standardized education plans and special education classes. Language abilities at age 2 in LPIs and full-term infants were similar.
C. Lower levels of cognitive performance and higher rates of behavioral problems (overall decreased intelligent quotient [IQ] scores).
D. Increased incidence of cerebral palsy.
E. Increased communication impairments at 18 and 36 months.

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PART 3
Pathophysiology: Management and Treatment of Common Disorders

CHAPTER 24
Respiratory Distress

Debbie Fraser

OBJECTIVES

1. Describe the anatomic and biochemical events associated with lung development.
2. Discuss the physiology of respiration.
3. Describe common respiratory disorders seen in the newborn infant.
4. Discuss common findings in respiratory distress syndrome, meconium aspiration syndrome (MAS), pneumonia, pulmonary hypertension, and bronchopulmonary dysplasia.
5. Describe nonpulmonary causes of respiratory distress.
6. Identify treatment strategies for common respiratory problems.
7. Formulate a plan of care for infants with respiratory disorders.

The most common life-threatening diseases in newborns are respiratory in origin. This is evidenced by the number of infants admitted to the neonatal intensive care unit (NICU) in respiratory distress. Respiratory distress syndrome (RDS), retained lung fluid syndromes, aspiration syndromes, air leaks, and congenital pneumonia account for approximately 90% of all respiratory distress in newborns. Pulmonary disease, however, is not the cause of all respiratory distress in newborn infants. Congenital malformations, metabolic abnormalities, central nervous system (CNS) disorders, and congenital heart disease may also present with respiratory distress. This chapter discusses common respiratory problems of the newborn infant, along with pathophysiology, clinical presentation, differential diagnosis, and management.

Lung Development

A. **Anatomic events**. Five stages of lung development have been identified and are described as follows (Blackburn, 2018):
   1. Embryonic development (weeks 1 to 5). The endoderm-derived embryonic foregut provides a single lung bud that begins to divide ventrocaudally through the mesenchyme surrounding the foregut. The pulmonary vein develops and extends to join the lung bud. The trachea develops at the end of the embryonic period. There are three divisions on the right side and two on the left side that will eventually become the lobes of the lungs.
   2. Pseudoglandular period (weeks 6 to 16). All conducting airways are formed. Cartilage appears, main bronchi are formed, demarcation of major lobes occurs, formation of new bronchi is complete, capillary bed is formed with connecting bronchial blood supply, and no connection made with terminal air sacs. The lung at this time undergoes 14 more generations of branching and the formation of the terminal bronchioles. The lung resembles an exocrine organ because of surrounding loose mesenchymal tissues, hence the name *pseudoglandular*.
   3. Canalicular period (weeks 16 to 26). Formation of gas-exchanging acinar units (i.e., respiratory units). The appearance of glycogen-rich cuboidal cells and inclusions for surface-active material storage are seen, capillaries invade terminal airway walls, and type II alveolar epithelial cells appear. The airway changes from glandular to tubular and increases in length and diameter. The vascular system proliferates, and the capillaries are now closer to the epithelium-conducting airways. Respiratory bronchioles that will participate in gas exchange can be differentiated.
   4. Terminal sac period (weeks 26 to birth). Around week 26 alveolar sacs are formed, air–blood surface area is limited for gas exchange, and type II cells are unable to release surfactant in sufficient quantity to maintain air breathing. Capillary loops increase; type II cells cluster at alveolar ducts, become numerous and mature; more budding

occurs from alveolar ducts; and lung size increases rapidly because there is an exponential increase in the surface area for gas exchange.

5. Alveolar period (week 32 to 8 to 10 years). This phase is characterized by continued alveolar proliferation and development.

B. **Biochemical events.**

1. Surface-active phospholipids line terminal air spaces and maintain alveolar stability by reducing surface tension.
2. Surfactant is a mixture of at least six phospholipids and four apoproteins.
   a. Dipalmitoylphosphatidylcholine (DPPC) is the major surface-active lipid component of surfactant. DPPC reduces the surface tension at the air–water interface in the alveolus almost to zero (Blackburn, 2018).
   b. Surfactant includes cholesterol, proteins, complex carbohydrates, and glycolipids.
   c. Phospholipids are responsible for the surface-active properties of surfactant. Surfactant proteins have recently been found to have important properties.
   d. There are two groups of surfactant proteins: the hydrophilic surfactant proteins A and D (SP-A and SP-D) and the hydrophobic surfactant proteins B and C (SP-B and SP-C). SP-B and SP-C are known to enhance the surface tension–lowering properties of surfactant and facilitate its absorption and spread.
      1) SP-A with SP-B forms the tubular myelin lattice network. SP-A probably also has a role in the recycling of surfactant. SP-A activates alveolar macrophages and thus has a role in host defenses. SP-A is the most abundant of the surfactant proteins.
      2) SP-B is important in the formation of tubular myelin, enhances the uptake of phospholipids by the type II cell, and is important in the recycling of surfactant.
      3) SP-C may have a role in surfactant dispersal and recycling, enhancing the rate of absorption and spreading of surfactant.
      4) SP-D may also have a role in host defense mechanisms and is upregulated during periods of acute lung inflammation (Gaunsbaek et al., 2013).
   e. Surfactant reduces surface-tension forces in the alveoli that are capable of producing collapse at expiration (Blackburn, 2018).
      1) Surfactant is produced in the type II pneumocyte beginning at 25 to 30 weeks of gestation and continuing to term (Diehl-Jones, 2012). Type II pneumocytes synthesize, store, secrete, and recycle surfactant (Blackburn, 2018).
      2) When the lungs are inflated, receptors in type II cells mobilize intracellular calcium, which causes the release of the contents of lamellar bodies into the air space. After secretion, surfactant may be taken back into type II cells with a turnover time of 10 hours.
3. The changing pattern of phospholipids in amniotic fluid can be used to assess surfactant production and maturation of pathways.
   a. Material from the fetal lung contributes to amniotic fluid.
   b. Concentrations of various phospholipids can be measured and will assist in determining lung maturity.
4. Sphingomyelin concentration remains stable, with a small peak at 28 to 30 weeks.
5. Lecithin and phosphatidylinositol concentrations remain low until 26 to 30 weeks, when an increase begins. A peak occurs at 36 weeks.
6. Phosphatidylglycerol (PG) appears at 30 weeks, peaks at 35 to 36 weeks, and increases as the phosphatidylinositol level falls.
   a. When PG is present, the risk that RDS will develop in the infant is less than 1%.
   b. PG is measured as absent or present.
   c. Blood and meconium do not affect test results.
7. The lecithin/sphingomyelin (L/S) ratio has been used to assess fetal lung maturity.
   a. An L/S ratio greater than 2:1 is considered to indicate fetal lung maturity.
   b. An infant of a diabetic mother may develop RDS even with a mature L/S ratio (presence of PG ensures lung maturity).
   c. Chronic fetal stress (e.g., maternal hypertension, retroplacental bleeding, maternal drug use, smoking) will tend to accelerate surfactant production, resulting in a mature L/S ratio in premature infants.
8. Fetal lung maturity.
   a. Measures ratio of surfactant to albumin.
   b. Sample should be free of blood and meconium.
   c. Less than 50 = immaturity; 50 to 70 = borderline maturity; greater than 70 = mature lungs.

C. Role of antenatal steroids (American College of Obstetrics and Gynecology [ACOG], 2017).

1. Antenatal corticosteroids and glucocorticoids (e.g., betamethasone or dexamethasone) affect lung maturation and present a strategy for preventing RDS. Betamethasone appears to significantly decrease neonatal death and morbidity (Gyamfi-Bannerman et al., 2016; Roberts et al., 2017). Steroids accelerate the normal pattern of lung growth by increasing the rate of glycogen depletion and glycerophospholipid biosynthesis. This leads to thinning of the intra-alveolar septa and increases

the size of the alveoli. The number of surfactant-producing type II pneumocytes increases, as does the number of lamellar bodies inside the cells. This leads to increased synthesis of surfactant phospholipids.

a. Treatment with steroids is recommended for the following:
   1) Maternal risk of preterm delivery between 24 and 34 weeks of gestation. More recently, the recommendation to give steroids for threatened preterm delivery has been extended to those pregnancies between 34 and $36^{6/7}$ weeks' gestation (ACOG, 2017).
   2) Treatment with corticosteroids less than 24 hours before delivery is still associated with a decrease in mortality, RDS, and intraventricular hemorrhage (IVH). It should be given unless delivery is imminent.
b. Administration of corticosteroids in premature rupture of the membranes is not associated with a higher risk of chorioamnionitis.
c. Two doses of betamethasone 12 mg should be given intramuscularly (IM) 24 hours apart, or four doses of dexamethasone 6 mg should be given IM every 12 hours in patients at risk for preterm delivery between 24 and 34 weeks of gestation. Repeated courses of glucocorticoids should not be routinely used; however, a single rescue course of steroids may be considered when birth is expected within 1 week if the previous treatment was more than 2 weeks prior and the gestational age of the fetus is less than 33 weeks.

2. Infants exposed to chronic stress in utero are usually small for gestational age and have more mature lungs (they also have small thymuses and large adrenal glands, suggesting high glucocorticoid levels in utero).

Physiology of Respiration

Refer to Chapters 4 and 26.

Respiratory Disorders

RESPIRATORY DISTRESS SYNDROME

A. **Definition**.
   1. Developmental disorder starting at or soon after birth and occurring most frequently in infants with immature lungs.
   2. Increasing respiratory difficulty in the first 3 to 6 hours, leading to hypoxia and hypoventilation.
   3. Progressive atelectasis.

B. **Incidence**.
   1. The incidence of RDS is inversely related to gestational age and birth weight, affecting 51% of all infants born weighing less than 1000 g (Jackson, 2018).

C. **Etiology**.
   1. Surfactant deficiency.
   2. Pulmonary hypoperfusion.
   3. Anatomic immaturity.
   4. Precipitating factors associated with incidence and/or severity of RDS (Jackson, 2018).
      a. Prematurity and low birth weight.
      b. Cesarean delivery without labor.
      c. Maternal diabetes, especially if infant was born at less than 38 weeks of gestation.
      d. Second twin (Blickstein and Shinwell, 2015).
         1) May be due to greater risk of asphyxia.
      e. Perinatal hypoxia–ischemia.
      f. Male/female ratio of 2:1.

D. **Pathophysiology**.
   1. Production of surfactant is inadequate, occurring when the utilization of surfactant exceeds the rate of production. This leads to diffuse alveolar atelectasis, pulmonary edema, and cell injury (Jackson, 2018). Progressive worsening of these three factors will contribute to a loss of functional residual capacity and alteration in the ventilation–perfusion ratio (Jackson, 2018).
   2. Serum proteins, which inhibit surfactant function, leak into the alveoli. The increased water content, immature mechanisms for clearance of lung liquid, lack of alveolar–capillary apposition, and decreased surface area for gas exchange, typical of the immature lung, also contribute to the disease (Jobe, 2017).
   3. Histologic findings are the presence of hyaline membranes and an eosinophilic material derived from injury to epithelial cells. The alveolar spaces are generally collapsed, with pulmonary edema, hemorrhage, and hemorrhagic edema noted (Wambach and Hamvas, 2015).

E. **Clinical presentation.**
   1. Almost exclusively in premature infants.
      a. May appear to be a normally grown, healthy premature infant with good Apgar scores at birth.
      b. Distress begins at or soon after birth.
   2. Increasing respiratory difficulty related to progressive atelectasis. Symptoms are progressive.
      a. Tachypnea (>60 breaths per minute) is usually the first sign; color may be initially maintained.
      b. Audible expiratory grunt.
         1) Heard during first few hours.
         2) Caused by forcing of air past a partially closed glottis.

3) Used to maintain positive end-expiratory pressure (PEEP) at the alveolar level in an attempt to prevent alveolar collapse.
4) More pronounced with severe disease.

c. The chest wall in an infant is very compliant. When an infant breathes spontaneously, pleural pressure decreases during inspiration. When there is parenchymal disease, the chest wall produces greater negative pressure and the more compliant chest wall caves inward with a moderate decrease in pleural pressure, which results in retractions. Retractions are seen at the sternum and subcostal and intercostal spaces of the infant's chest (Jackson, 2018).
d. Nasal flaring.
e. Cyanosis due to increasing hypoxemia.

3. Oxygen requirements increase to maintain arterial Po_2 at 50 to 70 mm Hg because of decreased lung compliance secondary to decreased surfactant. Additional physical effort is needed to keep terminal airways open, resulting in increased work of breathing.
4. Paradoxical seesaw respirations may be seen.
5. If signs and symptoms are unattended, infant becomes obtunded and flaccid.
   a. Pallor may obscure severe central cyanosis.
   b. Poor capillary filling time (>3 to 4 seconds).
   c. Progressive edema, usually seen in the face, palms, and soles.
6. Oliguria is common in the first 48 hours.
7. Breath sounds diminish and lung auscultation is usually described as "poor air entry" despite vigorous effort on the infant's part.
8. Crackles become audible as the disease progresses.
9. Cardiac murmurs are generally not heard until after 24 hours of age.
10. Tachycardia (heart rate >160 beats per minute [bpm]) is common and even more prevalent if acidosis and hypoxemia are present.

F. **Diagnosis**.
1. Signs and symptoms as previously described.
2. Hypoxemia (defined as arterial Po_2 level <50 mm Hg in room air) as a result of ventilation–perfusion mismatch and right-to-left intrapulmonary shunting, responding to supplemental inspired oxygen; respiratory failure secondary to alveolar hypoventilation (Pco_2 >50; pH ≤7.25).
3. Chest x-ray (CXR) reveals low lung volumes, hazy lung fields, and a fine reticulogranular pattern of density with air bronchograms. Occasionally the disease may appear worse in one lung than the other (Wambach and Hamvas, 2015).
4. Diagnostic studies.
   a. CXR examination.
   b. Arterial blood gas (ABG) measurements.
   c. Blood cultures, complete blood cell count if risk factors are present. Pneumonia caused by group B streptococcus (GBS) has similar radiographic features; therefore, infection must be considered.
   d. Blood glucose level. Prematurity and increased work of breathing results in increased glucose consumption.

G. **Differential diagnosis.**
1. Pneumonia. Similar signs, symptoms, and radiologic features can be found in neonates with pneumonia and those with RDS.
2. Transient tachypnea of the newborn (TTN) can present with the same signs and symptoms, but these infants usually require ≤40% Fio_2, improve more quickly, and have larger lung volumes on CXR.
3. Pulmonary edema. A primary cardiac disorder with pulmonary edema (such as a patent ductus arteriosus [PDA]) can mimic RDS.

H. **Complications**.
1. Pulmonary.
   a. Air leaks.
   b. Pulmonary edema.
   c. Bronchopulmonary dysplasia (BPD).
2. Cardiovascular.
   a. PDA.
   b. Systemic hypotension.
3. Renal.
   a. Oliguria.
      1) Most likely to follow hypoxia, hypotension, or shock ("prerenal" renal failure).
   b. Immature renal function with decreased glomerular filtration in very low birth weight infants.
   c. Natural diuresis will occur at approximately 48 to 72 hours of age, as infant's condition improves.
4. Metabolic.
   a. Acidosis. Atelectasis with increased work of breathing will lead to hypoxemia and acidemia, resulting in vasoconstriction of the pulmonary vasculature. This limits alveolar capillary blood flow, which further impedes the production of surfactant and compounds the problem.
   b. Hyponatremia or hypernatremia.
   c. Hypocalcemia.
   d. Hypoglycemia.
5. Hematologic.
   a. Anemia—may be iatrogenic due to blood loss required for diagnostic testing. Hematocrit should be corrected to near-normal levels to ensure adequate oxygen-carrying capacity.
6. Neurologic.
   a. Seizures: may result from hypoglycemia or an IVH.

b. Hypoxia, positive pressure ventilation, rapid fluid infusions, and acidosis are all factors that may precipitate an IVH (Ballabh, 2014).

7. Other.
   a. Secondary nosocomial infections.
   b. Retinopathy of prematurity (ROP).
   c. Dislodged endotracheal tubes.
   d. Thrombus formation. Complication of umbilical catheters and peripheral central catheters needed to monitor respiratory status and provide adequate nutrition.

I. **Management**. RDS is a disease that is self-limited and transient. Adequate surfactant can be produced by the premature infant within 48 to 72 hours.

1. Goal of treatment is supportive until disease resolves and to prevent further lung injury (Wambach and Hamvas, 2015).
2. Surfactant replacement therapy.
   a. Benefits include the following (Polin et al., 2014):
      1) Reduced morbidity and mortality rates.
      2) Improved compliance, thereby reducing the need for mechanical ventilation.
      3) Improved overall oxygenation of the infant.
   b. Surfactants approved by U.S. Food and Drug Administration (FDA) for treatment of RDS.
      1) Natural surfactants: beractant (Survanta), poractant alfa (Curosurf), and calfactant (Infasurf). Composed of minced bovine, porcine, or calf lung with added lipids.
      2) A synthetic form of surfactant (Surfaxin) was approved in 2012.
   c. Three treatment approaches are related to timing.
      1) Prophylaxis. Treatment within 15 minutes of birth: infants born at less than 27 to 30 weeks of gestation, especially if the mother did not receive antenatal steroids; dose given via endotracheal tube after initial resuscitation. Additional doses may be given if necessary. Early studies of prophylactic use of surfactant demonstrated a decrease in the incidence and severity of RDS and a reduced risk of air leak, BPD, and death (Bahadue and Soll, 2012). Most recent studies no longer show this benefit and, in fact, compared with infants treated with continuous positive airway pressure (CPAP), those receiving surfactant had an increased risk of BPD and death (Polin et al., 2014). Because of the risks associated with intubation, controversy exists as to which infants should be selected for prophylactic surfactant (Jackson, 2018).
      2) Early rescue. Treatment of infants within 1 to 2 hours of life with signs of RDS; multiple doses can be given. The goal of intervention is to avoid progressive alveolar atelectasis leading to respiratory failure requiring intermittent positive pressure ventilation (IPPV) (Jackson, 2018).
      3) Late rescue: treatment at 4 to 6 hours of age for infants requiring mechanical ventilation and more than 40% Fio_2. Early or prophylactic therapy has been shown to confer more benefit than late rescue treatment; however, by delaying intubation and surfactant administration, some infants who otherwise may have been intubated and treated may be successfully managed with noninvasive treatment methods such as nasal CPAP (nCPAP) (Jackson, 2018).
      4) Combining surfactant administration and CPAP: in an effort to avoid intubation and mechanical ventilation, many centers are now using an approach that combines intubation and surfactant administration with immediate extubation to nCPAP. This approach, referred to as INSURE, has been shown to reduce the need for subsequent mechanical ventilation in low birth weight (LBW) infants (Kandraju et al., 2013).
      5) Administering surfactant without intubation: In an effort to provide the benefit of early surfactant administration while avoiding the hazards of intubation, some centers are studying the administration of surfactant through small catheters inserted into the trachea (Dargaville et al., 2013) or via a laryngeal mask (Attridge et al., 2013). The development of less invasive methods of surfactant delivery is likely to result in increased utilization and potential benefit to the very LBW infant.
      6) Beractant (Survanta): dose is 4 mL/kg through the endotracheal tube above the carina. Four doses can be given during the first 48 hours of life (Gardner et al., 2016b).
      7) Poractant alfa (Curosurf): initial dose is 2.5 mL/kg given in two aliquots via the endotracheal tube. Two subsequent doses of 1.25 mL/kg can be administered at 12-hour intervals if needed (Gardner et al., 2016b).
      8) Calfactant (Infasurf): given via the endotracheal tube, dose is 3 mL/kg divided in two aliquots; subsequently the same dose can be administered every 12 hours for a total of three doses if needed (Gardner et al., 2016b).

9) Lucinactant (Surfaxin): dose is 5.8 mL/kg given via the endotracheal tube, repeated every 6 hours based on response (Gardner et al., 2016b).

3. Provide warm, humidified oxygen to maintain normal Pao_2.
4. Provide CPAP via nasal prongs or endotracheal tube if indicated.
5. Use assisted ventilation for profound hypoxemia (Pao_2 <50 mm Hg) and/or hypercapnia ($Paco_2$ >60 mm Hg).
6. Monitor oxygenation by pulse oximetry and/or transcutaneous monitoring.
7. Monitor pulmonary status with CXR examination, as clinically indicated.
8. Other measures.
   a. Stabilize temperature.
   b. Provide adequate fluid and electrolyte intake. Monitor intake and output, blood urea nitrogen, and serum creatinine.
   c. Monitor arterial/capillary blood gases, electrolytes, calcium, bilirubin, and glucose.
   d. Monitor blood pressure for hypotension. Give pharmacotherapeutic agents (e.g., dopamine, dobutamine, or hydrocortisone) as indicated.
   e. Maintain hematocrit.
   f. Administer antibiotics for associated pneumonia/rule out sepsis.
   g. Optimize nutrition with early introduction of total parenteral nutrition with protein and initiation of minimal enteral feeds as soon as the infant is medically stable.

J. Prevention of RDS.
1. Maternal glucocorticoid administration prenatally.
2. Use of L/S ratio, fetal lung maturity, and PG determination for timing labor induction or elective cesarean delivery.
3. Perinatal management to avoid situations leading to pulmonary circulation compromise in the fetus or newborn infant.
   a. Obstetric.
      1) Maternal hypotension.
      2) Oversedation.
      3) Maternal hypoxia.
      4) Fetal distress without prompt delivery.
   b. Neonatal.
      1) Delayed resuscitation.
      2) Uncorrected hypoxia or acidosis.
      3) Hypothermia, hypoglycemia, and hypovolemia.

K. **Outcome**.
1. Infants with chronic lung disease improve slowly and progressively if they can be kept infection free. May have episodes of bronchiolitis and pneumonia (especially pneumonia caused by respiratory syncytial virus [RSV]); long-term sequelae are related to specific complications (e.g., BPD, IVH, ROP).
2. Infants who weigh more than 1500 g who have mild to moderate RDS have the same developmental outcome as infants of the same gestational age without RDS.

PNEUMONIA

A. **Definition**. Infection of the fetal or newborn lung; may be intrauterine or neonatal.
1. Intrauterine infection.
   a. Passage of infecting agent by infection of fetal membranes.
   b. Transplacental transmission.
   c. Aspiration of meconium or infected amniotic fluid during delivery.
2. Neonatal infection.
   a. Acquired during nursery stay.
   b. Pathogens are generally different from those acquired in utero.
   c. Results from passage from other infants, equipment, or caregivers.

B. **Incidence**.
1. Neonatal pneumonia occurs in 1% of term infants and in 10% of LBW infants (Crowley, 2015). The incidence varies by institution and according to causative agent.
2. The incidence of ventilator-acquired pneumonia (VAP) is more difficult to determine because of the difficulty in applying diagnostic criteria to newborn infants; however, estimates place the rates of VAP at 0.6 to 1.6 per 1000 ventilator days (Patrick et al., 2014).

C. **Etiology**.
1. Risk of infection is greatest in premature infants because of immature immune system and lack of protective maternal antibodies. Pneumonia can occur by several routes: transplacental, amniotic fluid, at delivery, and nosocomially (Crowley, 2015).
2. Immature ciliary system in the tracheobronchial tree, leading to suboptimal removal of inflammatory debris, mucus, and pathogens. The number of pulmonary macrophages is insufficient for bacterial clearance.
3. Multiple organisms cause neonatal pneumonia (Box 24.1).

D. **Pathophysiology**.
1. Congenital pneumonia.
   a. Infant may be born critically ill or stillborn to a mother with a history of chorioamnionitis. At autopsy, evidence of pulmonary inflammation is found in 20% to 60% of stillborn infants and liveborn neonatal deaths (Crowley, 2015). Other factors linked to congenital pneumonia include excessive obstetric manipulation,

Box 24.1

Common Organisms Associated With Neonatal Pneumonia

Transplacental	Amniotic Fluid
Rubella	Cytomegalovirus
Cytomegalovirus	Herpes simplex virus
Herpes simplex virus	Enteroviruses
Adenovirus	Genital mycoplasma
Mumps virus	*Listeria monocytogenes*
Toxoplasma gondii	*Chlamydia trachomatis*
L. monocytogenes	*Mycobacterium tuberculosis*
M. tuberculosis	Group B streptococcus (GBS)
Treponema pallidum	*Escherichia coli*
	Haemophilus influenzae (nontypeable)
	Ureaplasma urealyticum

At Delivery	Nosocomial
GBS	*Staphylococcus aureus*
E. coli	*S. epidermidis*
S. aureus	GBS
Klebsiella spp.	*Klebsiella* spp.
Other streptococci	*Enterobacter* spp.
H. influenzae (nontypeable)	*Pseudomonas* spp.
Candida spp.	Influenza viruses
C. trachomatis	Respiratory syncytial virus
U. urealyticum	Enteroviruses

From Weisman, L. E., & Hansen, T. N. (Eds.). (2003). *Contemporary diagnosis and management of neonatal respiratory diseases* (3rd ed., p. 142). Newtown, PA: Handbooks in Health Care (division of AMM Co.).

prolonged labor with intact membranes, maternal fever, and maternal urinary tract infection (Orlando, 2012).

b. Prolonged rupture of membranes (>18 hours); ascending organisms may infect amniotic fluid. If mother is in active labor, contamination occurs more rapidly.

c. Infective organisms may cross the placenta and enter the fetal circulation, causing septicemia that may present as pneumonia.

d. Infants usually show signs of generalized illness from birth, but signs of illness may be delayed hours to days if the infective fluid is aspirated during delivery.

2. Neonatal pneumonia.

a. Infection occurs days to weeks after birth.

b. Pathogenic organism is acquired from hospital personnel, parents, or other infected infants.

c. Both bacterial and viral pathogens are associated with neonatal pneumonia. The most common bacterial organisms include GBS, *Escherichia coli*, *Klebsiella*, *Pseudomonas*, *Proteus*, *Staphylococcus epidermidis*, group A streptococci, *Listeria*, *Enterobacter*, *S. aureus*, *Mycoplasma*, and *Ureaplasma*. Viral infections such as herpes, cytomegalovirus, *Toxoplasma gondii*, varicella-zoster virus, RSV, enterovirus, adenovirus, and parainfluenza virus are also seen (Crowley, 2015).

E. **Clinical presentation.**

1. Labor longer than 24 hours.

a. Prolonged rupture of membranes (>18 hours).

b. Maternal fever/chorioamnionitis.

c. Foul-smelling or purulent amniotic fluid.

d. Fetal tachycardia.

e. Decreased fetal heart rate variability.

2. Signs and symptoms.

a. Often indistinguishable from other forms of respiratory distress and sepsis.

b. Tachypnea, grunting, retractions, cyanosis, hypoxemia, hypercapnia, and hypoglycemia.

c. With severe involvement, shock-like syndrome, usually in the first 24 hours of life, with recurrent apnea followed by cardiovascular collapse, profound hypoxemia, and persistent pulmonary hypertension. These signs represent a poor prognosis.

3. Physical examination.

a. Physical signs are variable.

b. Diminished breath sounds may be present over one or more areas.

c. In addition, localized dullness, harshness, or rales may be audible.
d. Radiologic findings can mimic those seen with RDS. In addition, pleural effusions may be seen on CXR with GBS pneumonia.

F. **Diagnostic evaluation.**
1. History of any previously mentioned contributing factors is suggestive.
2. Infant may require resuscitation in the delivery room.
3. CXR findings are variable.
a. Unilateral or bilateral alveolar infiltrates.
b. Diffuse interstitial pattern.
c. Pleural effusions.
4. Blood culture because septicemia may present as pneumonia.
5. A complete blood cell count may show neutropenia/leukopenia or may have an abnormal ratio of immature to total neutrophils.
6. Polymerase chain reaction (PCR) to detect herpes viruses.
7. ABG values should be obtained because metabolic acidosis may be severe.
8. Tracheal aspirate culture should be obtained, especially if the infant has an endotracheal tube in place.
9. Cerebrospinal fluid cultures should be obtained when infant is stable, because meningitis often accompanies pneumonia.

G. **Differential diagnosis.**
1. RDS.
2. Sepsis/meningitis.
3. TTN.
4. Meconium aspiration.
5. Lung hypoplasia.
6. Pulmonary hemorrhage.
7. Congenital heart disease.

H. **Complications**.
1. Cardiopulmonary complications similar to those of RDS.
2. Systematic inflammatory response syndrome.
3. Disseminated intravascular coagulopathy (DIC).
4. Persistent pulmonary hypertension.
5. Meningitis.

I. **Management**.
1. Antibiotic therapy (see Chapter 32).
2. Maintain normal temperature.
3. Monitor glucose levels.
4. Monitor blood pressure and treat hypotension.
5. Use oxygen with or without assisted ventilation to maintain normal ABG values.
6. Correct respiratory and metabolic acidosis.
7. Provide adequate fluid and electrolyte intake.
8. Monitor for evidence of DIC.
9. High-frequency ventilation, nitric oxide, and extracorporeal membrane oxygenation (ECMO) have been used for patients who are critically ill with pneumonia, with variable outcomes.
10. Provide support for the family.

RETAINED LUNG FLUID SYNDROMES—TRANSIENT TACHYPNEA OF THE NEWBORN

A. **Definition**. Delayed clearance of the fetal lung fluid—TTN.

B. **Incidence.**
1. TTN occurs at a rate of 5.7 per 1000 live births (Crowley, 2015).

C. **Clinical presentation.**
1. Term and near-term infants.
2. In the first few hours, tachypnea results in respiratory rates of 60 to 120 breaths per minute; grunting and retractions may also be present.
3. Hypercapnia and respiratory acidosis.
4. Duration may be 1 to 5 days.

D. **Etiology**.
1. Delay in removal of lung fluid.
2. Excessive amount of lung fluid.

E. **Pathophysiology**.
1. Fetal lung fluid has a higher chloride concentration than plasma, interstitial fluid, or amniotic fluid. During labor, a surge of fetal catecholamines occurs resulting in the cessation of active transport of chloride and reabsorption of fetal lung fluid via a protein gradient and removal by the lymphatic system. Approximately two thirds of the lung fluid is removed before birth. Infants born without labor or prematurely may not have the time to reabsorb the fetal lung fluid.
2. Infants at highest risk for retained fetal lung fluid include the following:
a. Birth near or at term.
b. Cesarean delivery without labor.
c. Breech delivery.
d. Second twin.
e. Maternal asthma.
f. Precipitous delivery.
g. Delayed cord clamping (results in a transfusion of blood, which may transiently elevate the central venous pressure).
h. Macrosomia.
i. Male sex.
j. Maternal sedation.
3. TTN may originate from reduced lung compliance because of delayed reabsorption of lung fluid at the time of birth and/or the distention of interstitial spaces by fluid, leading to decreased lung compliance (Crowley, 2015).
4. Delayed clearance of lung fluid by pulmonary lymphatic system. The retained fetal lung fluid accumulates in the peribronchiolar lymphatics and bronchovascular spaces and interferes with

forces promoting bronchiolar patency and results in bronchiolar collapse. Hypoxemia results from continued perfusion of poorly ventilated alveoli, and hypercarbia results from mechanical interference with alveolar ventilation. Decreased lung compliance results in tachypnea and increased work of breathing (Crowley, 2015).

F. **Diagnosis**.
   1. Early signs and symptoms may be difficult to distinguish from those of other respiratory problems; however, they are usually milder.
   2. CXR examination reveals diffuse haziness and streakiness in both lung fields, with clearing at the periphery. Fluid may be present in the interlobar fissures, and mild hyperinflation may be present.
   3. Diagnosis is frequently one of exclusion.

G. **Differential diagnosis.**
   1. RDS.
   2. Pneumonia/sepsis.

H. **Management**.
   1. Because diagnosis is not conclusive, other disorders should be ruled out.
   2. Supportive management.
      a. CPAP with or without supplemental oxygen.
      b. Temperature regulation.
      c. Adequate fluid intake and nutritional support.
      d. Maintain ABGs within acceptable levels.
      e. Maintain blood glucose at normal levels.
   3. If respiratory rate is greater than 60 breaths per minute, delay feedings to avoid possible aspiration.
   4. If history indicates risk of infection, broad-spectrum antibiotics (e.g., ampicillin and gentamicin) should be administered until culture results are negative.

I. **Outcome**.
   1. Self-limited.
   2. Need for respiratory support and tachypnea decreases steadily over several days. Infant may remain mildly tachypneic beyond the need for CPAP.
   3. Some infants with TTN have high pulmonary artery pressures documented by echocardiography. If hypoxemia and tachypnea persist, persistent pulmonary hypertension of the newborn (PPHN) may be present.

PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN

A. **Definition**. PPHN is caused by right-to-left shunting through the fetal shunts at the atrial and ductal levels. It is secondary to persistent elevation of pulmonary vascular resistance (PVR) and pulmonary artery pressure (Steinhorn and Abman, 2018). Seventy-seven percent of infants are diagnosed in the first 24 hours of life, 93% diagnosed by 48 hours of life, and 97% of the infants by 72 hours of life (Gardner et al., 2016b). Incidence is 0.2% in term and 2% in preterm infants (Steinhorn and Abman, 2018).

B. **Pathophysiology**.
   1. After delivery, adequate oxygenation depends on lung inflation, closure of fetal shunts, decreased PVR, and increased pulmonary blood flow.
   2. Over the first 12 to 24 hours of life, PVR normally falls dramatically, rapidly increasing pulmonary blood flow (Steinhorn and Abman, 2018).
   3. When PVR remains high, adaptation from fetal to neonatal circulation is impaired.
   4. Neonatal pulmonary vessels have greater vasoactive properties than adult pulmonary vessels and respond to hypoxia and acidosis with vasoconstriction. Numerous factors increase and decrease PVR.
   5. Development of increased vascular smooth muscle contributes to vasospasm. Development of pulmonary artery musculature occurs late in gestation, making PPHN generally a condition of the term and post-term infant.
   6. High PVR and pulmonary hypertension impede pulmonary blood flow, which promotes hypoxemia, acidemia, and lactic acidosis.
   7. Newborns with persistent elevation of PVR share several characteristics, including pulmonary vascular remodeling and increased circulating levels of endothelin, a vasoconstrictor (Steinhorn and Abman, 2018).
   8. Studies have proposed that a genetic link of the urea cycle may contribute to this process of PPHN (Kaluarachchi et al., 2018).

C. **Etiology**.
   1. Maladaptation. The pulmonary vascular bed is structurally normal, but PVR remains high. Maladaptation generally results from active vasoconstriction, which may be transient or persistent (Fuloria and Aschner, 2017).
      a. Hypoxia/asphyxia. This is the most common precipitating factor in PPHN. It is correlated with abnormal muscularization and remodeling of small pulmonary arteries. Acute asphyxia may induce persistent pulmonary vasospasm.
      b. Pulmonary parenchymal disease (RDS, meconium aspiration, pneumonia, other aspiration syndromes) can cause pulmonary vasospasm and may be associated with vascular remodeling.
      c. Bacterial sepsis. The underlying mechanism may be endotoxin-mediated myocardial depression or pulmonary vasospasm associated with high levels of thromboxanes and leukotrienes.
      d. Prenatal pulmonary hypertension.
         1) Fetal systemic hypertension.
         2) Premature closure of ductus arteriosus, associated with maternal use of aspirin,

prostaglandin inhibitors (nonsteroidal antiinflammatory drugs [NSAIDs]), phenytoin (Dilantin), lithium, or indomethacin. However, some studies have shown no increase in PPHN rates in infants exposed to NSAIDs in utero (Van Marter et al., 2013).

3) Maternal selective serotonin reuptake inhibitor use in late pregnancy has been associated with an increase in the risk of PPHN in the newborn (Steinhorn and Abman, 2018).

4) Maternal conditions, including diabetes, asthma, preeclampsia, and smoking.

e. Any condition preventing normal circulatory transition at delivery (CNS depression, delayed resuscitation, hypothermia).

f. Hypothermia and hypoglycemia contributing to acidosis, which will potentiate pulmonary vasoconstriction.

g. Hyperviscosity/polycythemia. This may lead to a functional obstruction of the pulmonary vascular bed.

2. Maldevelopment: abnormal pulmonary vessels. Musculature is hypertrophied and extends into normally nonmuscularized arteries. The excessive muscularization affects lumen size, which increases vascular resistance. Causes of maldevelopment include the following:
   a. Intrauterine asphyxia: increases systemic arterial blood pressure in the fetus and diverts more blood to the lung, resulting in pulmonary vessel development.
   b. Fetal ductal closure: forces cardiac output from the right ventricle through the lungs, resulting in maldevelopment.
   c. Congenital heart disease: abnormal pulmonary vessels resulting from various defects.
3. Underdevelopment: decreased number of pulmonary vessels. Blood is shunted because there are too few vessels for blood to flow through the lungs. There is a decreased cross-sectional area available for gas exchange. Severity depends on the timing of the interruption of lung development in utero: reduced numbers of bronchial generations if early (<16 weeks) and decreased number of alveoli if later in gestation. Contributing conditions include the following:
   a. Pulmonary hypoplasia (i.e., Potter sequence).
   b. Space-occupying lesions or lung masses (e.g., diaphragmatic hernia, cystic adenomatoid malformation) that prevent normal development of lung tissue and the capillary bed.
   c. Congenital heart disease. Pulmonary atresia or tricuspid atresia may lead to decreased blood flow and vascular underdevelopment.

D. **Clinical presentation.**
1. Near-term, term, or post-term infants.
2. History of hypoxia or asphyxia at birth.
   a. Low Apgar scores.
   b. Infant usually slow to breathe or difficult to ventilate.
   c. Meconium-stained fluid, nuchal cord, abruptio placentae or any acute blood loss, and maternal sedation.
3. Respiratory abnormalities.
   a. Symptoms seen before 12 hours of age.
   b. Tachypnea.
   c. Retractions if airway is obstructed (e.g., because of aspiration).
   d. Cyanosis out of proportion to degree of distress; cyanosis of sudden onset that often is intractable.
   e. Low Pao_2 despite high oxygen concentration administration because of right-to-left shunting. Differences are seen between preductal and postductal oxygenation.
   f. CXR may be normal unless aspiration or pneumonia present (will see infiltrates in these cases).
4. Cardiovascular abnormalities.
   a. Blood pressure is usually lower than normal.
   b. Electrocardiogram will show a right-axis deviation.
   c. Systolic murmur is frequently heard, usually from a PDA, foramen ovale, or tricuspid insufficiency. Single loud second heart sound (S_2), resulting from high pulmonary pressures, may be heard.
   d. Echocardiogram shows dilated right side of the heart and evidence of pulmonary hypertension and shunting across the foramen ovale.
   e. Congestive heart failure has been reported occasionally.
5. Metabolic abnormalities.
   a. Hypoglycemia.
   b. Hypocalcemia.
   c. Metabolic acidosis.
   d. Decreased urine output or coagulopathy caused by kidney and liver damage from asphyxia may occur.

E. **Diagnosis**.
1. PPHN will be suspected on the basis of history and clinical course.
2. Preductal and postductal arterial blood samples or oxygen saturation monitoring. Because of the right-to-left shunting at the level of the ductus arteriosus, there will be a preductal and a postductal Pao_2 difference. Difference in Pao_2 of 15 mm Hg or greater documents ductal shunting (Orlando, 2012).
3. Hyperoxia test. A right-to-left shunt is demonstrated if Po_2 does not increase in 100% oxygen.

Cause may be either PPHN or congenital heart disease.
4. An echocardiogram will rule out structural heart disease, evaluate myocardial function, measure pulmonary artery pressures, and diagnose right-to-left shunting at the level of the PDA or foramen ovale.
5. CXR may or may not be helpful, but should be taken to rule out other lung pathology.
6. Electrolytes, calcium, serum lactate, and glucose levels and complete blood cell count should be obtained.
7. An ABG measurement is done to determine degree of acidosis and hypoxemia.

F. **Differential diagnosis**.
1. Congenital heart disease.
2. Pulmonary disease.
   a. Severe disease may mimic PPHN.
   b. Disease may coexist with PPHN.

G. **Complications**.
1. Pulmonary.
   a. Air leaks. Related to high mean airway pressures used in ventilator management.
   b. BPD.
2. Cardiovascular.
   a. Systemic hypotension.
   b. Congestive heart failure.
3. Renal.
   a. Decreased urine output related to asphyxia and hypotension.
   b. Acute tubular necrosis caused by asphyxia.
   c. Hematuria, proteinuria.
4. Metabolic.
   a. Hypoglycemia, hypocalcemia.
   b. Metabolic acidosis.
5. Hematologic.
   a. Thrombocytopenia.
   b. DIC: depends on precipitating cause of PPHN.
   c. Hemorrhage (e.g., gastrointestinal, pulmonary).
6. Neurologic.
   a. CNS irritability.
   b. Neurodevelopmental delay.
7. Iatrogenic.
   a. Thrombus formation or complications of invasive monitoring equipment.
   b. Dislodged endotracheal tube.
8. Other.
   a. Edema due to "third spacing."
   b. Side effects of pharmacologic agents used for treatment.

H. **Management**.
1. Main goal is to correct hypoxia and acidosis (major contributing factors) and promote pulmonary vascular dilation, as well as support extrapulmonary systems.
2. Management will depend on the cause of PPHN.
3. Supportive care.
   a. Monitor vital signs.
   b. Temperature stabilization. Avoid exposure to cold drafts, which can trigger pulmonary vasoconstriction (diving reflex).
   c. Adequate intravenous (IV) fluid infusion.
   d. Monitor electrolytes, glucose, calcium, complete blood cell count, ABGs.
   e. Correction of metabolic abnormalities.
   f. Blood cultures and antibiotics.
4. Specialized monitoring.
   a. Umbilical catheters.
      1) Arterial: blood gas access, arterial pressure monitoring.
      2) Venous: infusion of vasopressors.
   b. Right radial arterial line: monitor preductal blood gases.
   c. Pulse oximetry. Preductal and postductal applications can be helpful.
5. Oxygen: most potent pulmonary vasodilator.
6. Ventilation.
   a. Conventional mechanical ventilation.
   b. High-frequency ventilation (HFV), high-frequency oscillatory ventilation (HFOV), or high-frequency jet ventilation (HFJV). Used when conventional mechanical ventilation fails or when excessive barotrauma is a concern. Meta-analysis has failed to demonstrate a consistent benefit of HFOV over conventional ventilation (Cools et al., 2015).
      1) Oxygenation.
         a) Goal is to keep Pao_2 at greater than 50 mm Hg.
         b) Danger of ROP is minimal because most infants are born at or near term.
      2) Adequate ventilation to keep $Paco_2$ values in normal range. Low normal CO_2 levels aid in reducing acidosis and pulmonary artery pressure caused by the vasoconstriction effects of hypercapnia. Previous practices of hyperventilation to induce hypocarbia are less commonly used because of the adverse effects (Blackburn, 2018).
   c. Inhaled nitric oxide (iNO) reduces death or the need for ECMO in infants with PPHN. Oxygenation improves in about 50% of infants receiving iNO. A similar benefit of iNO for infants with congenital diaphragmatic hernia has not been demonstrated (Barrington et al., 2017).
      1) iNO is a selective pulmonary vasodilator.
         a) Potent and short acting, with a half-life of 3 to 5 seconds.
         b) Combines with hemoglobin and becomes inactivated.

c) Inactivation results in formation of methemoglobin; levels need to be monitored during treatment.

2) A starting doses of 20 parts per million (ppm) in term newborn infants with PPHN is commonly used (Steinhorn and Abman, 2018).

3) iNO withdrawal (weaning) needs to be systematic; in some infants abrupt discontinuation may result in rebound increased PVR (Kinsella, 2017).

4) Infants with severe parenchymal lung disease/underinflation and PPHN respond better to iNO when it is combined with HFOV.

d. Surfactant replacement: especially for etiology based on significant parenchymal disease (Orlando, 2012).

e. ECMO may be used when conventional therapies are unsuccessful.

7. Minimal stimulation and handling.

a. Infants will show marked fluctuation (generally decreases) in their Pao_2 if handled or manipulated.

b. The pulmonary arteries are very reactive to changes in Pao_2; therefore, any action that causes a decrease in Pao_2 (e.g., suctioning, blood sampling, vital signs, ventilator changes) will cause further vasoconstriction.

c. Suction only as needed to maintain a patent airway.

d. Sedatives and analgesics are used for procedures and treatments.

e. The bedside nurse must be a strong advocate for these patients and keep noise and environmental stimuli to a minimum.

8. Pharmacologic support.

a. Vasopressors.

1) Goal is to keep the systemic pressure above pulmonary pressure to decrease right-to-left shunting.

2) Dopamine is an endogenous catecholamine with a short half-life and must be given by constant infusion. Dosage: 5 to 20 mcg/kg/min of continuous IV infusion (Steinhorn and Abman, 2018).

3) Dobutamine is a synthetic catecholamine with primary β_1-adrenergic receptor effects to support blood pressure in patients with shock and hypotension related to myocardial ischemia, pulmonary hypertension, and cardiomyopathy. Dobutamine may cause a fall in systemic blood pressure or an increase myocardial oxygen consumption and should be used with caution in neonates with PPHN (Mathew and Lakshminrusimha, 2017). Dosage: 2 to 15 mcg/kg/min by continuous infusion (Gardner et al., 2016b).

b. Pulmonary vasodilators.

1) iNO (previously described).

2) Sildenafil may be as effective as iNO in improving pulmonary vasodilation (Gardner et al., 2016b). It has been suggested as adjunctive therapy to facilitate weaning of iNO. A Cochrane review of this therapy suggests the need for additional research before widespread adoption (Kelly et al., 2017).

3) Milrinone has been shown to decrease pulmonary vascular resistance and improve left ventricular function in neonates with PPHN. It may act synergistically with iNO to reduce pulmonary hypertension (Lakshminrusimha et al., 2016). Dosage: 0.2 to 0.99 mcg/kg/min (McNamara et al., 2013; Steinhorn and Abman, 2018).

c. Analgesics and sedatives.

1) Fentanyl citrate. In addition to analgesic effect, fentanyl produces a sedative effect. Dosage: 0.3 to 2 mcg/kg per dose by slow IV push. Repeat as required (usually every 2 to 4 hours). Frequently used as a constant infusion at 0.3 to 5 mcg/kg/hour. Tolerance may develop rapidly, requiring weaning to prevent significant withdrawal symptoms (Gardner et al., 2016a).

2) Morphine sulfate. Dosage: 0.05 to 0.2 mg/kg per dose IV. Repeat as required, usually every 4 hours. For continuous infusion, usual dose is 10 to 15 mcg/kg/hour. Tolerance may develop with prolonged use, requiring slow weaning to prevent significant withdrawal symptoms (Gardner et al., 2016a).

I. **Outcome**.

1. PPHN survival rate is dependent on the center and the underlying disease process.
2. Residual chronic lung disease is common, although recently low-dose iNO has reduced the need for ECMO (Barrington et al., 2017).
3. Sensorineural hearing loss is higher among children treated for PPHN.

MECONIUM ASPIRATION SYNDROME

A. Definition and etiology of meconium aspiration syndrome (MAS).

1. Meconium is a mixture of epithelial cells and bile salts found in the fetal intestinal tract.
2. With intrauterine stress or asphyxia, peristalsis is stimulated and relaxation of the anal sphincter occurs, releasing meconium into the amniotic fluid. Postmature fetuses pass meconium more readily than those that are less mature.

3. Aspiration may occur whenever meconium passes into the amniotic fluid, but the risk increases when repeated episodes of severe asphyxia lead to gasping respirations in utero.

B. **Incidence**. Meconium-stained amniotic fluid is present in approximately 8% to 29% of all newborns delivered. Of these, between 3% and 12% develop MAS (Vain and Batton, 2017).

C. **Pathophysiology**.
1. Complete or partial airway obstruction can occur.
2. Atelectasis or ball–valve air trapping leads to hyperinflation.
3. A chemical pneumonitis develops (probably caused by bile salts). Inflammation develops that is mediated by neutrophils and macrophages, resulting in edema in the alveoli that interferes with surfactant production and increases surface tension (Edwards et al., 2013; Mokra and Calkovska, 2013).
4. Meconium decreases the levels of surfactant proteins SP-A and SP-B and large numbers of phospholipids (Mokra and Calkovska, 2013).
5. The hypoxia associated with meconium aspiration increases PVR.

D. Clinical presentation/diagnosis.
1. MAS is a disease of term or post-term infants. It is rarely seen in infants born at less than 36 weeks of gestation.
2. Asphyxia and the results of chronic hypoxia may predispose these infants to PPHN.
3. Vigorous resuscitation is frequently needed in the delivery room because of central depression.
4. Respiratory distress signs are nonspecific and may include tachypnea, nasal flaring, and retractions.
5. Respiratory distress may range from mild and transient to severe and prolonged.
6. If there has been prolonged placental insufficiency, infants may appear to be wasted, with hanging skinfolds (usually around knees, buttocks, and axillae).
7. Nail beds and skin may be stained a yellow-green.
8. The chest may appear to be hyperinflated or barrel shaped.
9. CXR shows hyperexpanded lucent areas mixed with areas of atelectasis throughout lung fields.
10. Expiration phase of respirations may be prolonged.
11. Coarse crackles are common on auscultation.
12. No specific laboratory data are useful for diagnosis of MAS.
13. ABGs will show the following:
    a. Respiratory and metabolic acidosis in severe cases.
    b. Low PaO_2 even with 100% oxygen administration.

E. **Complications**.
1. Pulmonary.
    a. Air leaks (pneumothorax and pneumomediastinum) due to ball–valve phenomenon leading to overinflation and air trapping and high ventilator pressures.
    b. Pneumonia.
    c. PPHN.
2. Metabolic.
    a. Acidosis.
    b. Hypoglycemia.
    c. Hypocalcemia.
3. Neurologic: will depend on degree of hypoxia, if any.

F. **Management and prevention.**
1. Delivery room management.
    a. Use a bulb syringe to clear meconium-stained secretions from the mouth and nose. If the infant is depressed with no respiratory effort and poor muscle tone and/or has a heart rate less than 100 bpm after initial care, proceed with ventilation (American Academy of Pediatrics [AAP], 2016).
2. Respiratory care.
    a. ABGs to determine degree of respiratory compromise and type of therapy needed.
    b. Assisted ventilation.
        1) May need to use a lower level of PEEP to avoid inadvertent PEEP and a higher respiratory rate to induce alkalosis and prevent PPHN.
        2) May choose HFV.
        3) iNO if PPHN develops.
    c. Surfactant replacement therapy every 6 hours for up to four doses has been shown to reduce the severity of respiratory illness, lessen the need for ECMO, and improve gas exchange (El Shahed et al., 2014). More recently, lung lavage with surfactant has been shown to improve clinical outcome in MAS. Further research in this area is needed to confirm the optimal approach to lung lavage (Hahn et al., 2013).

G. **Outcome**.
1. The prognosis for infants with mild cases of MAS is generally excellent unless complications such as PPHN or severe asphyxia occur during the course of the disease.
2. In more severe cases, neurologic sequelae are common and death may occur despite vigorous, maximal support.

BRONCHOPULMONARY DYSPLASIA

A. **Definition**.
1. In 1967, Northway et al. (1967) originally described the four stages of BPD based on the time that the change occurred (from birth to 30 days of life) and on the type of alveolar and bronchial damage and repair that occurred.
2. A more clinically useful definition now focuses on the need for oxygen or ventilatory support.

Table 24.1

Definition of Bronchopulmonary Dysplasia: Diagnostic Criteria

	GESTATIONAL AGE AT BIRTH	
	<32 Weeks	**≥32 Weeks**
Time point of assessment	36 weeks PMA or discharge to home, whichever comes first	>28 days but <56 days of postnatal age or discharge to home, whichever comes first
	Treatment with oxygen >21% for at least 28 days **plus**	
Mild BPD	Breathing room air at 36 weeks PMA or discharge, whichever comes first	Breathing room air by 56 days postnatal age or discharge, whichever comes first
Moderate BPD	Need* for <30% oxygen at 36 weeks PMA or discharge, whichever comes first	Need* for <30% oxygen at 56 days' postnatal age or discharge, whichever comes first
Severe BPD	Need* for ≥30% oxygen and/or positive pressure (PPV or nCPAP) at 36 weeks PMA or discharge, whichever comes first	Need* for ≥30% oxygen and/or positive pressure (PPV or nCPAP) at 56 days' postnatal age or discharge, whichever comes first

BPD, Bronchopulmonary dysplasia; *nCPAP*, nasal continuous positive airway pressure; *PMA*, postmenstrual age; *PPV*, positive pressure ventilation.
* A physiologic test confirming that the oxygen requirement at the assessment time point remains to be defined. This assessment may include a pulse oximetry saturation range.
Adapted from Jobe, A. H., & Bancalari, E. (2001). Bronchopulmonary dysplasia. *American Journal of Respiratory and Critical Care Medicine*, *163*(7), 1723–1729.

The subjectivity of x-ray changes or clinical symptoms has been removed from this definition (Keller and Ballard, 2018).

3. A newer definition is an infant who was treated with oxygen for longer than 28 days and requires oxygen or positive pressure at 36 weeks of postmenstrual age (Table 24.1). This definition also established criteria for mild, moderate, and severe BPD (Keller and Ballard, 2018).

B. **Incidence**.
1. Statistics vary because of the difference in diagnostic criteria and practices in individual centers.
2. The estimated incidence of BPD varies widely and is related to birth weight and gestational age. Estimates suggest that the rate of BPD or death before 36 weeks postmenstrual age (PMA) is 81% in infants less than 750 g, 49% in infants 751 to 1000 g, and 25% in infants 1001 to 1250 g at birth (Keller and Ballard, 2018).
3. Genetic variations in surfactant proteins, interleukins, and proteases are thought to contribute to BPD (Keller and Ballard, 2018).

C. **Etiology**.
1. The etiology of BPD is multifactorial, resulting from acute lung injury, arrested alveolar development, and abnormal repair processes that occur in the lung.
2. Maternal chorioamnionitis has been implicated in the development of BPD (Keller and Ballard, 2018).
   a. Before delivery, chorioamnionitis triggers an inflammatory response that may prime the preterm lung for injury (Keller and Ballard, 2018).
   b. The relationship between inflammation and BPD is difficult to interpret because of the variability of the fetal response to inflammation and the concomitant exposure to antenatal steroids (Keller and Ballard, 2018).
3. Oxygen toxicity plays a role in the development of BPD (Keller and Ballard, 2018).
   a. The preterm infant has lower levels of antioxidant mediators as well as vitamins C and E, which have antiinflammatory properties. These together make the premature pulmonary system especially vulnerable to oxygen toxicity (Keller and Ballard, 2018).
   b. High inspired oxygen concentrations cause the production of reactive oxygen species (ROS) and the release of chemotactic factors that attract neutrophils to the lung, initiating the inflammatory cycle. An ongoing inflammatory process in the lung ensues that causes and continues parenchymal damage (Keller and Ballard, 2018).
   c. The correlation between initial oxygen exposure and subsequent development of BPD is generally linear; however, LBW infants receiving oxygen later in the neonatal course are still at risk of developing BPD (Keller and Ballard, 2018).
   d. When ROS injures epithelial and endothelial cells, pulmonary edema and activation of inflammatory cells result (Bancalari and Walsh, 2015).
   e. Pulmonary edema results in a leak of proteins into the alveoli, which inactivates surfactant, exacerbating the surfactant deficiency of prematurity (Bancalari and Walsh, 2015).
4. Assisted ventilation with positive pressure results in lung damage (barotrauma and volutrauma), which contributes to BPD development.
   a. Intubation interrupts normal pulmonary function (mucociliary function is damaged; dead space is increased, leading to increased pressure needs).

b. Barotrauma is related to the intensity and amount of time exposed to elements of positive pressure ventilation (peak inspiratory pressure, inspiratory time, and PEEP). Repeated distention of distal airways during mechanical ventilation of infants with poor alveolar compliance results in ischemia. Because of the immaturity of the pulmonary system, the alveolar capillary unit is further disrupted by mechanical ventilation, leading to pulmonary edema. Many factors contribute to barotrauma, such as the structure of the tracheobronchial tree and the physiologic effects of surfactant deficiency.
c. Ventilation using volumes that are too low results in cycles of alveolar collapse (atelectrauma), which is as damaging as overventilation (Berger et al., 2013).

5. Increased shunting (left to right) via a PDA has been described as a possible cause of BPD (Bancalari and Walsh, 2015). Medical or surgical treatment of the PDA, however, has not been shown to decrease rates of BPD (Bancalari and Walsh, 2015).
6. Excessive fluid intake contributes to the development of BPD (Keller and Ballard, 2018).
7. Gestational age plays an important role in the development of BPD.
   a. Damage to the developing lung is more likely in infants weighing less than 1500 g.
   b. Damage may occur with less exposure to the previously noted factors in the infant less than 1250 g.
8. Nutritional deficits contribute to the risk for developing BPD.
   a. Adequate caloric and protein intake is required for cell growth and division.
   b. Vitamin A is essential for differentiation, integrity, and repair of respiratory epithelial cells (Keller and Ballard, 2018). Vitamin A supplementation in neonates has been shown to reduce the incidence and severity of BPD (Keller and Ballard, 2018).
   c. Poor nutrition may result in decreased alveolar number and increased vulnerability to infection (Keller and Ballard, 2018).

D. **Pathophysiology**. All levels of the tracheobronchial tree are involved.
1. Large airways.
   a. Submucosal glandular hypertrophy.
   b. Increased bronchial smooth muscle.
   c. Bronchial mucosa hyperplasia.
   d. Submucosal fibrosis.
   e. Inflammatory infiltrates.
   f. Granulation tissue.
   g. Loss of cilia.
   h. Tracheomalacia or bronchomalacia frequently develops.
2. Small airways.
   a. Bronchiolar smooth muscle hypertrophy.
   b. Focal mucosal squamous metaplasia.
   c. Chronic inflammation.
   d. Peribronchial edema.
   e. Peribronchiolar fibrosis.
   f. Necrosis with intraluminal debris.
   g. Luminal narrowing.
   h. Excessive production of mucus.
3. Alveoli.
   a. Decreased number of alveoli.
   b. Enlarged alveoli.
   c. Alveolar septal destruction, which leads to emphysematous blebs.
4. Pulmonary vascular bed.
   a. Muscular hypertrophy of the medial layer of pulmonary arterioles leads to increased pulmonary pressures.
   b. Dysgenesis resulting in fewer capillaries.
   c. Endothelial cell hyperplasia, which leads to a decreased cross-sectional area.

E. **Clinical presentation.**
1. Predisposing risk factors.
   a. Oxygen, intubation, and assisted ventilation.
   b. Gestational age less than 32 weeks.
   c. Nutritional deficiencies.
   d. Underlying lung disease.
   e. Air leaks.
   f. Infection.
   g. PDA.
2. Increase in ventilatory requirements or inability to be weaned from ventilator.
3. Hypoxia, hypercapnia, and respiratory acidosis.
4. Audible crackles and wheezing.
5. Retractions.
6. Increased secretions.
7. Bronchospasm.
8. Electrocardiogram showing right ventricular hypertrophy and right-axis deviation.
9. CXR showing hyperinflation, infiltrates, blebs, and cardiomegaly.
10. Fluid intolerance, as evidenced by increase in weight, edema, and decrease in urine output, despite no change in fluid intake.

F. **Diagnosis**.
1. Diagnosis of exclusion.
2. CXR findings (see Chapter 14).
3. Clinical signs (e.g., tachypnea, hypercapnia, hypoxia, crackles) help make diagnosis.

G. **Complications**.
1. Intermittent bronchospasm.
2. Inability to be weaned from ventilator and/or oxygen supplementation.

3. Recurrent infections.
   a. Pneumonia.
   b. Upper respiratory tract infections.
   c. Otitis media.
4. Congestive heart failure from cor pulmonale.
5. BPD "spells."
   a. Infant becomes irritable, agitated, and dusky; has increased respiratory effort, hypoxia, and hypercapnia.
   b. Cause is unknown but may be bronchospasm or increased PVR.
6. Gastroesophageal reflux.
7. Developmental delays.

H. **Prevention**.
1. Prevention of preterm birth is the first strategy to reduce the risk of BPD (Bancalari and Walsh, 2015).
2. Administration of antenatal steroids reduces the incidence of RDS and the need for mechanical ventilation; however, studies have been inconsistent with regard to the effect on the incidence of BPD (Bancalari and Walsh, 2015).
3. Prophylactic surfactant therapy has been shown to reduce the risk of BPD (Keller and Ballard, 2018).
4. Routine use of systemic steroids (e.g., dexamethasone) for prevention or treatment of chronic lung disease in preterm infants is not recommended (Keller and Ballard, 2018).
5. Gentle ventilation, permissive hypercapnia, and early extubation have all been suggested as ways to decrease BPD. Synchronized intermittent mandatory ventilation is associated with less severe BPD because the incidence of pulmonary air leaks decreases.
6. HFV has not been shown to consistently reduce BPD (Bancalari and Walsh, 2015).
7. Aggressive nutrition is needed to promote lung growth, maturation, and repair and to protect the damaged lung from infection (Bancalari and Walsh, 2015). High-calorie formulas and supplements have been shown to improve growth and overall outcome in these infants (Bancalari and Walsh, 2015).

I. **Management**.
1. Minimize length of exposure to mechanical ventilation.
2. Intubation for surfactant administration and extubation to nCPAP has been shown to reduce the rate of mechanical ventilation (Polin et al., 2014).
3. Continue respiratory support as needed.
   a. nCPAP.
      1) Some very low birth weight infants can be supported by nCPAP alone, avoiding intubation and mechanical ventilation (Polin et al., 2014).
   b. Assisted ventilation.
      1) Weaning should be attempted as quickly as the infant's condition allows.
      2) Use synchronized modes of ventilation with the minimal amount of pressure and volume needed to deliver adequate tidal volumes, but always assess each infant individually.
   c. Oxygen is administered as needed to prevent hypoxia and avoid cor pulmonale.
      1) The appropriate target for oxygen saturation (Spo_2) has not been established. Current recommendations suggest an initial target of 90% to 95% pending further research (Bancalari and Walsh, 2015).
      2) Avoid large variations in oxygen saturation, which can contribute to lung injury and long-term developmental problems (Martin et al., 2015).
      3) Weaning can usually be accomplished by use of pulse oximetry and occasional monitoring of blood gas.
4. Diuretics may be used to control fluid retention leading to pulmonary edema. Furosemide (Lasix) is used most often. Despite the benefits of diuretics in decreasing edema and interstitial water, there is no strong evidence of long-term improvements in outcome (Keller and Ballard, 2018). Decreased calcium reabsorption leads to hypercalciuria, bone demineralization, and renal calcifications (Keller and Ballard, 2018). Metabolic alkalosis may result in compensatory hypoventilation. Ototoxicity may occur in infants receiving diuretic therapy (Keller and Ballard, 2018). Follow serum electrolyte values to monitor for hyponatremia, hypokalemia, and metabolic alkalosis.
5. Caffeine.
   a. Caffeine has been shown to have both a lung-protective and brain-protective effect, perhaps in part due to the shorter duration of mechanical ventilation in infants receiving caffeine (Keller and Ballard, 2018).
6. Fluid restriction may help reduce pulmonary edema and right-sided heart failure.
7. Cardiac evaluation for complications.
   a. Cor pulmonale (right ventricular hypertrophy) due to prolonged pulmonary hypertension.
   b. Electrocardiography and echocardiography should be performed periodically to evaluate the progression/development of right ventricular hypertrophy.
8. Optimal nutrition. Adequate early caloric intake reduces the incidence and severity of BPD (Bancalari and Walsh, 2015). Provide increased calories to compensate for increased work of breathing and fluid restriction. Infant may need 150 to 180 kcal/kg/day.

9. Use of steroids.
   a. High-dose dexamethasone has not been shown to have any benefit compared with low-dose therapy and has an increased risk of adverse neurodevelopmental outcomes (Keller and Ballard, 2018).
   b. Low-dose dexamethasone (0.02 mg/kg/day) may facilitate extubation in LBW infants without the increased risk seen in high-dose therapy. Selective use of a short course of low-dose steroids may have a role in infants older than 1 or 2 weeks who cannot be weaned from the ventilator (Bancalari and Walsh, 2015).
   c. Complications include impairment of growth, possible increase in neurodevelopmental abnormalities, hypertension, myocardial hypertrophy, gastrointestinal hemorrhage and perforation, gastric ulcerations, nosocomial sepsis, hyperglycemia, and transient adrenal suppression.
   d. Has not been found to have a substantial impact on long-term outcomes such as duration of supplemental oxygen requirement, length of hospital stay, or mortality.
   e. Early treatment with inhaled corticosteroids in very low birth weight infants has no discernible benefits in the prevention and treatment of chronic lung disease and is not recommended (Keller and Ballard, 2018).
10. RSV: BPD infants are at high risk for RSV outbreaks and account for many readmissions, with 25% of BPD infants needing assisted ventilation. Treatment modalities include the following:
   a. Benefits of RSV prophylaxis.
      1) Palivizumab (Synagis): humanized monoclonal antibody against RSV. Administration of Synagis results in half the rate of hospital admissions for RSV (Committee on Infectious Diseases and Bronchiolitis Guidelines Committee, 2014).
   b. AAP recommendations include the following:
      1) Five doses of RSV prophylaxis to infants who are less than 2 years of age with chronic lung disease requiring medical therapy within 6 months before the anticipated start of the RSV season, infants born at 29 to 32 weeks of gestation (prophylaxis up to 6 months of age), and infants born at 28 weeks of gestation and younger (prophylaxis until 12 months of age). A total of five doses is completed for all infants in this risk category.
      2) Infants 32 to 35 weeks: prophylaxis in the first 3 months of life for infants at highest risk of RSV exposure. That is either those attending day care or those with one or more children less than 5 years of age living in the home. Prophylaxis for this group is only given until 3 months of age with a maximum of three doses.
      3) Infants with severe chronic lung disease may benefit from prophylaxis during a second RSV season if they continue to require medical therapy.
   c. Palivizumab dose is 15 mg/kg, IM route, given monthly during RSV season, with the first dose to be given at the start of the season (Committee on Infectious Diseases and Bronchiolitis Guidelines Committee, 2014).

J. **Outcome**.
1. Mortality rate.
   a. The prognosis for infants with BPD is dependent on the severity of the disease and the infant's overall health status.
      1) Death is uncommon and is usually caused by respiratory failure (Bancalari and Walsh, 2015).
      2) Complications such as cor pulmonale or infection may also be a cause of mortality in infants with BPD.
2. Some infants will be discharged home with oxygen supplementation.
3. Pulmonary function.
   a. Long-term follow-up of BPD infants suggests that although there is some normalization of lung mechanics, abnormalities of the alveoli and small airways persist (Bancalari and Walsh, 2015).
   b. Asthma is more prevalent in premature infants with BPD compared with those without (Islam et al., 2015).
4. Neurologic and developmental sequelae.
   a. Infants with BPD demonstrate neurodevelopmental deficits compared with term children and have higher rates of attention-deficit/hyperactivity disorder (ADHD); special education services may be required. Cerebral palsy is also more common (Bancalari and Walsh, 2015; Beaudoin et al., 2013).
   b. Sensorineural hearing loss and visual difficulties are more common in premature infants with BPD compared with those without BPD (Jensen and Schmidt, 2014).

Pulmonary Air Leaks (Pneumomediastinum, Pneumothorax, Pneumopericardium, Pulmonary Interstitial Emphysema)

A. **Definition**. Alveolar overdistention and rupture. May occur spontaneously or as a secondary cause, usually when assisted ventilation is used.

B. **Incidence**. Air leaks occur in 1% to 2% of all newborns; however, many are asymptomatic (Fraser, 2012). In infants receiving CPAP, bag-and-mask ventilation, or mechanical ventilation, the incidence ranges from 16% to 36% (Gardner et al., 2016b).

C. **Pathophysiology**.
   1. Iatrogenic, resulting from the use of excessive airway pressure during resuscitation or with assisted ventilation.
   2. Can occur spontaneously if there is uneven air distribution at birth.
      a. Some areas are expanded, whereas others remain collapsed.
      b. Infant will generate pressure to expand unopened areas, leading to greater pressure in already expanded areas, which results in the air leak.
   3. Frequently, underlying lung disease is present.
      a. Obstructive: such as ball–valve trapping of air, seen with MAS.
      b. Poor lung compliance: such as seen with RDS.
   4. Overdistention of alveoli leads to rupture, with gas moving into nonventilated tissues. Air travels via vascular sheaths to the lining of the lung. Interstitial air can dissect around blood vessels or along lymphatics, becoming pulmonary interstitial emphysema (PIE). Air can move from the lining to the mediastinum, resulting in pneumomediastinum, and through to the thoracic cavity and visceral pleura, resulting in a pneumothorax. When the air moves along the great vessels to the pericardium, a pneumopericardium results. If air dissects down from the mediastinum through the sheaths of the great vessels, pneumoperitoneum results.

D. Clinical presentation and diagnosis (see Chapter 14 for x-ray findings).
   1. Pneumothorax.
      a. Sudden deterioration if air leak is large.
      b. Decreased breath sounds on the affected side, hypotension, skin mottling, and shift of the mediastinum (detected by shift of the point of maximal cardiac impulse on auscultation) to the unaffected side.
      c. Obtain CXR.
      d. Transillumination (translucent glow when fiberoptic light is placed against the skin) of the chest wall may confirm presence of pneumothorax, without having to wait for a CXR.
      e. If the air leak is small, may be asymptomatic.
   2. Pneumomediastinum.
      a. Should be anticipated with MAS.
      b. Signs include increased anteroposterior diameter of chest and indistinct heart sounds.
      c. CXR may show "sail sign," indicating elevation of the thymus surrounded by air.
   3. Pneumopericardium.
      a. Immediate presentation with hypotension, muffled heart sound, and bradycardia from cardiac tamponade.
      b. Life-threatening.
      c. CXR will show air encircling the heart, halo appearance.
   4. PIE.
      a. Difficult to interpret.
      b. Limited to infants with poor lung compliance who are receiving CPAP or positive pressure ventilation.
      c. CXR shows microcystic areas throughout one or both lungs; may show hyperinflated lungs and flattened diaphragm.
      d. May progress to pneumomediastinum and/or pneumothorax.
      e. Hypoxia and hypercapnia commonly present.

E. **Management**.
   1. Pneumothorax.
      a. If asymptomatic, will often resolve without treatment.
      b. Symptomatic (tension) pneumothorax requires emergency removal of air. Associated with hypoxia, hypotension, and cardiopulmonary arrest.
         1) Thoracentesis (needle aspiration to remove air) may be necessary until a chest tube can be placed, if infant's condition has acutely deteriorated, or until adequate pain, pharmacologic support can be administered.
         2) Thoracostomy tube is placed in the anterior chest and connected to underwater seal drainage system, with continuous negative pressure of 10 to 15 cm H_2O, and left in place until air ceases to bubble from the chest tube for at least 24 hours and pneumothorax is resolved by CXR examination. The chest tube may be left in place for some time after the suction is discontinued.
         3) In infants with minimal symptoms, administration of supplemental oxygen may aid the absorption of the air in the pneumothorax and the pleural capillaries. Because of the toxic effects of oxygen, this treatment is not recommended for preterm infants.
   2. Pneumomediastinum.
      a. Usually not treated.
      b. If associated with pneumothorax (common occurrence), supplemental oxygen may help resolve condition, as described previously.
   3. Pneumopericardium. Emergency treatment is required by placement of a long catheter or chest tube into the pericardial sac with constant application of gentle negative pressure.

4. PIE.
   a. If unilateral and persistent, intubation of mainstem bronchus supplying opposite lung may show improvement in condition.
   b. If bilateral, supportive treatment is given (e.g., oxygen, ventilation, fluids).
   c. Minimize positive inspiratory pressure and shorten inspiratory time.
   d. HFV.
   e. Place affected side in dependent position.

F. **Outcome**.
1. Outcome depends on underlying lung pathology.
2. Mortality rate is high with pneumopericardium, bilateral pneumothoraces, and bilateral PIE.
3. In survivors of bilateral PIE, the risk of chronic lung disease is high.

Pulmonary Hypoplasia

A. **Definition**. Defective or inhibited growth of the lungs, either unilateral or bilateral. Developmental disorder that results in decreased numbers of alveoli, bronchioles, and arterioles.

B. **Pathophysiology**.
1. Conditions that compress the lungs or limit lung growth (e.g., diaphragmatic hernia, cystic adenomatoid malformation) are one etiology of pulmonary hypoplasia.
2. Conditions that result in oligohydramnios (e.g., renal disorders, amniotic fluid leakage) are associated with pulmonary hypoplasia caused by thoracic compression.
3. Associated congenital malformations, such as renal dysgenesis (Potter syndrome), phrenic nerve absence, and vertebral and chromosomal anomalies, should be considered.

C. **Diagnosis**.
1. Often very difficult to diagnose.
2. Any of the previous conditions are suggestive of pulmonary hypoplasia.
3. Usually present with severe respiratory distress.
4. Higher-than-usual pressures needed for ventilation; pneumothorax common.
5. Hypercapnia difficult or impossible to treat early in disease course.
6. CXR will usually show decreased volume of the thorax.
7. Symptoms of PPHN possible.

D. **Management**. Treatment is supportive and directed at respiratory failure.
1. Assisted ventilation/HFV.
2. Treatment of PPHN.
3. iNO.
4. ECMO.

E. **Outcome**.
1. Degree and etiology of hypoplasia determine outcome.
2. Mortality rate is high.
3. Management is difficult, but infant can function adequately if treatment and support can be continued until lung growth occurs, although this outcome is rare.

Pulmonary Hemorrhage

A. **Definition**.
1. Localized areas of bleeding into alveoli (generally found at autopsy); also known as hemorrhagic pulmonary edema.
2. Can be a massive generalized bleeding event.

B. **Etiology and pathophysiology.**
1. Usually occurs as a complication of other disorders such as prematurity, erythroblastosis, intracranial hemorrhage, asphyxia, aspiration, heart disease, sepsis, hypothermia, PDA, and surfactant replacement.
2. May be due to trauma from improper suctioning technique.
3. Usually due to large increase in pulmonary microvascular pressure; results in capillary rupture and fluid transudation from other capillaries (Fraser, 2012).

C. **Clinical presentation.**
1. May present with sudden, severe respiratory distress.
2. Bright red blood or frothy pink secretions may be suctioned from the trachea.

D. **Management**.
1. Use of assisted ventilation is necessary to maintain gas exchange and provide PEEP.
2. Transfusion of packed red blood cells if large hemorrhage with decreased hematocrit/hemoglobin.
3. Identify any clotting abnormalities and treat.
4. Assess for and treat PDA.
5. Treat other underlying diseases.

E. **Outcome**.
1. If bleeding is massive, death will occur quickly despite vigorous management.
2. If hemorrhage is small or isolated, infant will recover and outcome will be dependent on underlying disease.

Other Causes of Respiratory Distress

A. **Upper airway disorders.**
1. Choanal atresia.
   a. Incidence is 1 in 8000 births. Ninety percent of choanal atresia results from bony occlusion

while 10% of infants have a membranous occlusion (Bean et al., 2017).
b. Bone or membrane protrudes into nasal passages, causing blockage or narrowing.
c. If condition is bilateral, gasping respirations and cyanosis occur immediately after birth because neonates are obligate nose breathers. Many infants have associated anomalies (Treacher Collins syndrome, tracheoesophageal fistula, palatal abnormalities, CHARGE association [coloboma, *h*eart disease, choanal *a*tresia, *r*estricted growth and development, *g*enital hypoplasia, and *e*ar anomalies]), congenital heart disease.
d. Signs of distress are intermittent when condition is unilateral.
e. These infants usually present with pink color when crying but become blue when not crying due to the fact that the mouth is open and provides a patent airway during crying.
f. Failure to pass a catheter through the nasal passages to the posterior oropharynx will make the diagnosis.
g. Initially treat by placing infant in prone position with a large oral airway taped securely in place (an endotracheal tube can be used if placement of an oral airway is difficult).
h. Surgical correction of the problem is necessary and consists of perforation of the obstruction and serial dilation by use of obturators.

2. Micrognathia.
a. Defined as mandibular undergrowth.
b. Occurs with certain syndromes and sequences such as Pierre Robin syndrome, trisomy 18, trisomy 22, and cri-du-chat syndrome (deletion of the short arm of chromosome 5).
c. Airway distress may be alleviated by prone positioning.
d. Use of an oral airway or endotracheal tube will provide an open airway.
e. If an endotracheal tube is in place, humidification will be needed to prevent the drying of secretions.
f. Tracheostomy may be necessary in rare cases.
g. Generally mandibular growth "catches up" by 6 to 12 months of age.
h. Mandibular distraction osteogenesis is considered for infants with significant respiratory or feeding compromise (Ramieri et al., 2017).

3. Cystic hygroma.
a. Form of cystic lymphangioma, with benign water cysts occurring most frequently in the neck (80%); can also be found in the groin, axilla, and mediastinum.
b. Usually seen at birth.
c. Mass will occupy the submandibular region and may compromise the airway in 25% of cases.
d. Symptoms depend on the size and location.
e. Treatment is related to complications.
1) If infant is free of symptoms, surgical excision is performed between 4 and 12 months of age.
2) Excision must be performed at an earlier age if the airway is compromised or if infections are recurrent.
3) Multiple excisions are usually performed to prevent damage to nerves and vascular structures.

4. Obstruction of larynx or trachea.
a. Stridor is a major symptom and usually requires no specific treatment, but mechanical causes must be ruled out.
b. Direct laryngoscopy will reveal structural abnormalities such as polyps, webs, and granulomas.
c. Hemangiomas of the larynx or trachea may cause obstruction.
d. Extrinsic compression of the upper airway occurs with thyroglossal duct cyst, cervical neuroblastoma, vascular ring, and double aortic arch.
e. Laryngotracheomalacia results from collapse of the larynx and cervical trachea, which produces stridor; condition is usually self-limiting and resolves by 6 to 12 months of age, when the tracheal diameter increases and the cartilage matures.

5. Tracheoesophageal fistula (refer to Chapter 29).

B. **Congenital thoracic disorders.**
1. Cystic pulmonary airway malformation (CPAM).
a. Primary pulmonary tissue dysplasia resulting from an overgrowth of abnormal tissue. CPAMs were previously referred to as *congenital cystic adenomatoid malformations (CCAMs).*
b. Confusion exists regarding the nomenclature used to describe CPAM (Keller et al., 2018). Currently there are five types of CPAMs classified according to the location and type of tissue found in the abnormal growth.
1) Type 0 CPAMs arise from the tracheobronchial tree. The tissue is normally lobulated and contains no alveoli.
2) Type 1 CPAM is the most common, occurring in 60% to 65% of cases. It presents as a single or a few large (3- to 10-cm) cysts that communicate with the bronchi. Type 1 CPAMs are usually limited to one lobe of the lung.
3) Type 2 CPAM is found in 15% to 20% of cases. It is composed of multiple small, evenly distributed cysts that resemble

terminal bronchioles (0.5 to 2.0 cm); 50% of these infants have other anomalies, and only 56% survive. Most common associated anomalies are sirenomelia, renal agenesis, and extralobar pulmonary sequestration.

4) Type 3 CPAM is found in 5% to 10% of cases. It is a large, bulky, solid lesion composed of evenly distributed small (<0.2 cm in size) cysts. This type resembles the early canalicular stage of fetal lung development and may be the result of an insult at the time of lung bud branching.

5) Type 4 CPAM has been added to the CPAM types and describes a lesion similar to type 1 CPAM. Type 4 CPAM consists of larger cysts, usually in the periphery of one lobe. The presentation of type 4 CPAM often consists of mild respiratory distress and may be detected incidentally.

c. Respiratory distress may be seen at birth, or the malformation may cause no symptoms.
d. Prenatal hydrops is predictive of a poor outcome (Keller et al., 2018).
e. May be confused with diaphragmatic hernia or pulmonary sequestration on x-ray.
f. Type I CPAMs can develop malignant changes; therefore, long-term follow-up is necessary (Keller et al., 2018).
g. Some lesions regress and disappear spontaneously.
h. Treatment of choice is surgical excision of the involved lobe.

2. Bronchogenic cyst.
   a. Mucus-producing cyst.
   b. May cause tracheal, bronchial, or esophageal obstruction.
   c. Distress usually not severe.
   d. Treatment is surgical excision.
3. Congenital lobar emphysema.
   a. Overdistention of one or more lobes of the lung (upper lobes generally affected; 10% in right middle lobe).
   b. Inability of the lung to deflate properly, possibly because of a defect in bronchial cartilage.
   c. Possibility of severe respiratory distress within hours of birth but usually delayed for weeks or months.
   d. CXR examination is diagnostic (refer to Chapter 14).
   e. Treatment of choice: surgical resection.
4. Chondrodystrophies.
   a. Group of disorders of bone growth, resulting in short stature.
   b. Possible respiratory distress because of small thoracic cavities.
   c. Treatment: based on degree of distress.
5. Neuromuscular disorders.
   a. Conditions resulting in hypotonia, such as spinal muscular atrophy and myotonic dystrophy, result in varying degrees of respiratory distress.
   b. Management will depend on degree of distress.

C. **CNS disorders.**
   1. Seizures.
   2. Hypoxic–ischemic injury.
   3. Intracranial hemorrhages.
   4. Drugs.
   5. Meningitis.

D. **Cardiovascular and hematologic disorders.**
   1. Congenital heart disease.
   2. Anemia.
   3. Polycythemia.
   4. Shock.
   5. Sepsis.

E. **Diaphragmatic disorders (see also Chapter 14).**
   1. Diaphragmatic hernia.
   2. Diaphragmatic paralysis.
   3. Diaphragmatic eventration.

F. **Renal disorders.**
   1. Pulmonary hypoplasia results from renal agenesis or renal dysgenesis.

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CHAPTER 25
Apnea

Lindsey Churchman

OBJECTIVES

1. Define the types of apnea seen in the newborn infant.
2. Identify three causes of apnea.
3. Describe the pathogenesis of apnea in the premature infant.
4. Describe the evaluation process for the infant with apnea.
5. Discuss management techniques for controlling apnea.
6. Discuss the current status of home monitoring.

Apnea represents one of the most frequently encountered respiratory problems in the premature infant. It is not known why some infants are affected and others are not, although certain factors have a good predictive value. Apnea in the term infant is not ever a normal finding and must always be investigated. In the preterm infant, apnea that presents in the first 24 hours has historically been perceived as pathologic, whereas that occurring later has most often been attributed to immaturity. The mechanism of action is not fully understood but can be characterized as an immature respiratory system faced with demands it is ill equipped to handle. This chapter will provide a comprehensive review of apnea of the newborn infant, including causes, evaluation, treatment, and long-term home follow-up.

Definitions of Apnea (Table 25.1)

A. **Periodic breathing.**
   1. Definition: recurrent sequences of pauses in respiration lasting 5 to 10 seconds followed by 10 to 15 seconds of rapid respiration.
   2. Seen in less than 2% of healthy term infants and in 30% to 95% of healthy preterm infants more than 24 hours of age.
   3. Not accompanied by cyanosis or changes in heart rate.
   4. Episodes of periodic breathing in the preterm infant decrease significantly by 39 to 41 weeks of postmenstrual age (Gauda and Martin, 2018).
   5. Studies do not support a link between periodic breathing and significant apnea or sudden infant death syndrome (SIDS) (Gauda and Martin, 2018).

B. **Apnea**.
   1. Definition: cessation of respiration for at least 20 seconds, or less if complicated by cyanosis, pallor, hypotonia, or bradycardia.
   2. Most apnea occurs in the healthy preterm infant without organic disease. It is inversely related to gestational age and occurs in the vast majority of infants less than or equal to 28 weeks' gestation (Patrinos, 2015).

Types of Apnea

A. **Primary apnea.**
   1. Definition: initial cessation of respiratory movements after a period of rapid respiratory effort as a result of asphyxia during the delivery process.
   2. Exposure to stimulation and/or oxygen will usually induce spontaneous respiratory effort.

B. **Secondary apnea.**
   1. Definition: apnea occurring after a period of deep, gasping respirations, and fall in blood pressure and heart rate brought about by prolonged asphyxia during the delivery process. The gasping becomes slower and weaker and then ceases.
   2. Infant will not respond to stimulation and will require more vigorous resuscitation.
   3. For each minute in secondary apnea before resuscitation, there is a 2-minute delay before gasping is reestablished and another 2 minutes before the onset of regular respirations.
   4. It is not usually possible to distinguish primary from secondary apnea at birth (Kattwinkel, 2010).

Table 25.1

Apnea Types and Definitions

Types of Apnea	Definition
Central apnea	Absence of airflow and respiratory effort.
Obstructive apnea	Absence of airflow with continued respiratory effort associated with blockage of airway at the level of pharynx and/or larynx (Kattwinkel, 2010).
Mixed apnea	A combination of central and obstructive apnea; obstruction usually at the level of the pharynx.
Primary apnea	Initial cessation of respiratory movements after a period of rapid respiratory effort as a result of asphyxia during the delivery process.
Secondary apnea	Apnea occurring after a period of deep, gasping respirations and fall in blood pressure and heart rate brought about by prolonged asphyxia during the delivery process. The gasping becomes slower and weaker and then ceases.
Idiopathic, or apnea of prematurity	Diagnosis after exclusion of pathologic processes in the premature infant.

C. **Central apnea.**
   1. Definition: absence of airflow and respiratory effort.
   2. Cause of central apnea in the preterm infant is not fully understood.
   3. Contributing factors are thought to include the following:
      a. Chest wall afferent neuromuscular signals and chest wall instability.
      b. Diaphragmatic fatigue.
      c. Immature, paradoxic response of neonate to hypoxia and hypercapnia.
      d. Altered levels of local neurotransmitters in the brainstem region of the central nervous system (CNS).
   4. Fifteen percent of apnea episodes are central in origin.
   5. Closure of upper airway occurs in about half of cases of central apnea (Al-Sufayan et al., 2009).

D. **Obstructive apnea.**
   1. Definition: absence of airflow with continued respiratory effort; associated with blockage of airway at the level of the pharynx and/or larynx (Kattwinkel, 2010).
   2. Hyperextension or flexion of the neck may induce obstruction of the airway.
   3. May be caused by obstruction of airflow at the mouth or nose as a result of anatomic abnormalities such as macroglossia (Beckwith–Wiedemann syndrome, congenital hypothyroidism) or micrognathia (Pierre Robin sequence).
   4. Up to 30% of apnea episodes are obstructive in origin.

E. **Mixed apnea.**
   1. Definition: a combination of central and obstructive apnea; obstruction is usually at the level of the pharynx.
   2. Fifty percent to 60% of neonatal apnea episodes are mixed.

F. **Idiopathic apnea, or apnea of prematurity.**
   1. Diagnosis after exclusion of pathologic processes in the premature infant.
   2. Developmental disorder that reflects physiologic rather than pathologic immaturity of respiratory control (Patrinos, 2015).
   3. Not necessarily associated with the presence of periodic breathing.
   4. Recurrent apnea seen in preterm infants who show no other abnormalities.
   5. Onset within the first week of life, usually at 24 to 48 hours. If not present within the first week of life, will usually not appear unless later illness develops. If mechanically ventilated, apnea may not present until postextubation.
   6. More likely to be obstructive than central in the first 2 days of life.
   7. Episodes of apnea cease by term in 95% of infants; may persist longer in infants born at less than 28 weeks of gestational age (Gauda and Martin, 2018).

Pathogenesis of Apnea in the Premature Infant

A. **Immature central respiratory center.**
   1. Decreased afferent traffic occurs as a result of the following:
      a. Poor CNS myelinization.
      b. Decreased number of synapses.
      c. Decreased dendritic arborization.
   2. Decreased amounts of neurotransmitters have been measured in infants with apnea and may play an important role in respiratory control (Kattwinkel, 1977).
   3. Fluctuating respiratory center output has been implicated.

B. **Chemoreceptors**.
   1. Located in the medulla (central) and the carotid and aortic bodies (peripheral), chemoreceptors relay information to the respiratory center in the brain regarding pH, P_{O_2}, and P_{CO_2} via the vagus and glossopharyngeal nerves.
      a. Hypoxemia is sensed in the carotid and aortic bodies and results in an increase in alveolar ventilation. Premature infants with apnea do not respond to hypoxemia as effectively as infants who do not have apnea (MacFarlane et al., 2013).
      b. Hypercapnia is sensed centrally. The normal response to an increased arterial P_{CO_2} is an increase in minute ventilation. Neonates can increase ventilation by only 3 or 4 times the baseline values compared with the 10- to 20-fold increase that adults can obtain. Premature infants exhibit a blunted response to elevated P_{CO_2}, resulting in ongoing hypoventilation and hypercapnia. This diminished response predisposes them to apnea (MacFarlane et al., 2013).
   2. Biphasic response of the premature infant to hypoxia.
      a. During the first minute of hypoxia, a brief increase in respiratory effort occurs. It is followed in the next 2 to 3 minutes by a decrease in respiratory rate and by periodic breathing, respiratory depression, and apnea. Initial stimulation of the peripheral chemoreceptors is followed by overriding depression of the respiratory centers as a result of hypoxia (Kattwinkel, 2010).
      b. At 7 to 18 days of postnatal age, an infant can maintain the adult response to hypoxia of sustained hyperventilation.
   3. Depressed response to hypercapnia. The premature infant exhibits decreased sensitivity to increased levels of carbon dioxide, requiring higher levels of carbon dioxide to stimulate respirations (Gauda et al., 2013).

C. **Thermal afferents.**
   1. Apnea is increased in an environment that may be too warm for the infant.
   2. Thermal receptors in the trigeminal area of the face produce an apneic response to stimulation by a cold or hot gas mixture.

D. **Mechanoreceptors**.
   1. Stretch receptors alter the timing of respiration at various lung volumes.
      a. Head's paradoxic reflex: a gasp followed by apnea after abrupt lung inflation.
      b. Hering–Breuer reflex.
         1) Vagally mediated, it acts to inhibit inspiration and/or prolong expiration.
         2) Lung inflation initiates inhibitory impulses that terminate inspiration and prolong expiratory time.
         3) Mechanoreceptors are very active in the neonate but rarely seen in the adult.
   2. Pharyngeal collapse and airway obstruction are produced by negative pharyngeal pressure generated during inspiration.
   3. Intercostal phrenic inhibitory reflex, an inward movement of the rib cage during inspiration, prematurely ends inspiration (Mathew, 2011).

E. **Protective reflexes.**
   1. Stimulation of the posterior portion of the pharynx with suctioning, endotracheal or gavage tube placement, or gastroesophageal reflux can stimulate apnea.
   2. Pulmonary irritant receptors can produce an apneic response to direct bronchial stimulation.
   3. Laryngeal taste receptors can produce an apneic response to various chemical stimuli (Kattwinkel, 1977).

F. **Sleep state.**
   1. Eighty percent of the neonate's day is spent in sleep.
   2. Respiratory depression occurs predominantly in rapid eye movement (REM) or transitional sleep.
      a. May be influenced by central mechanisms at the level of the brainstem.
         1) May be due to a defect in a sleep-related feedback loop or respiratory command.
         2) Variability of respiratory rhythmicity is seen in active sleep.
      b. May be related to paradoxical respirations in which chest wall movements are out of phase, resulting in rib cage collapse with abdominal expansion during inspiration. This would lead to a decrease in lung volume and functional residual capacity.
      c. May be related to decreased skeletal muscle tone of the tongue and pharynx during sleep, which could lead to increased resistance and obstruction in the upper airway (Mathew, 2011; Zhao et al., 2011).

Causes of Apnea (Table 25.2)

A. **Prematurity**.
B. **Hypoxia**.
C. **Respiratory disorders.**
D. **Cardiovascular disorders.**
E. **Infection**.
F. **CNS disorders.**
G. **Drugs**.
   1. Maternal drugs.
      a. Narcotics.
      b. Analgesics.

Table 25.2

Causes of Apnea

Causes of Apnea	Examples
Prematurity	
Hypoxia	
Respiratory disorders	RDS, pneumonia, aspiration, acidosis, airway obstruction, pneumothorax, atelectasis, pulmonary hemorrhage, postextubation status, congenital anomalies of the upper airway
Cardiovascular disorders	Hypotension, arrhythmias, congestive heart failure, PDA
Infection	Sepsis, pneumonia, meningitis, viral infections, NEC
CNS disorders	Congenital malformations, seizures, asphyxia, intracranial hemorrhage, kernicterus, tumors
Drugs	Maternal: narcotics, analgesics, anesthesia, β-blocker antihypertensive agents, magnesium sulfate Neonatal: anticonvulsants, prostaglandin E1, narcotics/analgesics
Metabolic disorders	Hypocalcemia, hypoglycemia, hypermagnesemia, hyponatremia, acidosis, hyperammonemia
Hematopoietic disorders	Polycythemia, anemia
Reflex stimulation	Posterior pharyngeal stimulation, gastroesophageal reflux (controversial)
Environmental factors	Rapid warming, hypothermia, hyperthermia, elevated environmental temperature, feeding, stooling, painful stimuli

CNS, Central nervous system; *NEC*, Necrotizing enterocolitis; *PDA*, patent ductus arteriosus; *RDS*, respiratory distress syndrome.

c. Anesthesia.
d. β-Blocker antihypertensive agents.
e. Magnesium sulfate.

2. Neonatal drugs.
a. Anticonvulsants: phenobarbital, pentobarbital.
b. Cardiovascular drugs: prostaglandin E_1.
c. Narcotics/analgesics.
1) Fentanyl.
2) Morphine.
3) Midazolam hydrochloride.
4) Lorazepam.

H. **Metabolic disorders.**

I. **Hematopoietic disorders.**

J. **Reflex stimulation.**
1. Posterior pharyngeal stimulation.
2. Gastroesophageal reflux—recent controversial studies do not support a link. Some studies have shown apnea precedes reflux when the two are linked (Omari, 2009).

K. **Environmental factors.**

Evaluation for Apnea

A. **History**.
1. Perinatal risk factors.
a. Maternal bleeding, drugs, fever, hypertension, prolonged rupture of membranes, polyhydramnios, chorioamnionitis, decreased fetal movements, abnormal fetal presentation.
b. Fetal hypoxia, trauma.
2. Neonatal risk factors.
a. Prematurity.
b. Cardiorespiratory disease.
c. Metabolic abnormalities.
d. Temperature instability.
e. Infection.
f. Environmental causes.
g. CNS disorders.

B. **Physical examination.** A complete physical and neurologic examination should be performed. Evaluate for congenital malformations, especially those involving the airway. Evaluate for signs of respiratory distress and heart disease. Abnormal behavior, tone, or posturing may be associated with a neurologic focus. An abdominal examination should be performed, which may reveal symptoms related to obstruction, infection, necrotizing enterocolitis, or congestive heart failure.

C. **Documentation of apnea episodes.** A record of apneic episodes should be maintained as part of the infant's record. This allows the caregiver to determine a pattern, if any, to the apnea. It may also provide information about precipitating events or specific events associated with the apnea. Information documented should include the following:
1. Duration of apnea episode.
2. Time of apnea episode and any relation to feeding, activity, stooling, sleep, or procedures.
3. Infant's position: prone or supine, with head of bed elevated or flat.
4. Associated bradycardia/heart rate.
5. Associated color change and/or oxygen desaturation.
6. Type of stimulation required to resolve the episode.
a. None, self-resolved.
b. Gentle tactile stimulation.
c. Vigorous tactile stimulation.

d. Oxygen.
e. Bag-and-mask ventilation.

D. **Laboratory evaluation.**
1. Basic evaluation to look for infection, respiratory deterioration, and metabolic problems.
a. Complete blood cell count, with differential cell and platelet counts.
b. Blood gases.
c. Serum glucose, electrolytes, calcium, magnesium.
d. Blood culture, lumbar puncture for evaluation of cerebrospinal fluid, and urine culture.
2. Extensive laboratory evaluation for less common causes of apnea.
a. Toxicology screen.
b. Urine collection for detection of amino acids and organic acids.
c. Serum ammonia.
d. State screen and expanded neonatal screen for metabolic disease.

E. **Other**.
1. Echocardiogram or electrocardiogram: may detect cardiac abnormality or conduction disorders.
2. Electroencephalogram: may confirm suspected seizures.
3. Chest x-ray: may demonstrate respiratory or cardiac abnormalities.
4. Cranial ultrasound, computed tomography, or magnetic resonance imaging: may demonstrate structural abnormalities or hemorrhages.
5. Barium swallow and pH study: to evaluate pharyngeal structure and function or gastroesophageal reflux.
6. Pneumogram.
a. Measures chest wall movement, heart rate, oxygen saturation, and nasal airflow by thermistor or carbon dioxide probe (four-channel); measures esophageal pH if needed (five-channel if esophageal probe is used).
b. No predictive value for SIDS; recording monitors are as effective at detecting apnea over a prolonged period.

Management Techniques

A. **Treat underlying cause if determined.**
B. **Provide needed medical or surgical intervention.**
C. **Maintain environmental temperature at the low end of the neutral thermal zone.**
D. **Avoid triggering reflexes.**
1. Vigorous catheter suctioning.
2. Hot or cold to the face.
3. Sudden gastric distention.

E. **Positioning.** Prone positioning is associated with higher oxygen saturation, shorter gastric emptying time, and decreased incidence of regurgitation and aspiration. Historical data suggested prone positioning to decrease apneic episodes. A systematic review found no decrease in apnea, bradycardia, or desaturation with body positioning in the prone position (Bredemeyer and Foster, 2012). The only infants for whom prone positioning is recommended are those with upper airway disorders or impaired airway-protective mechanisms for whom the risk of death due to gastroesophageal reflux is greater than the risk of SIDS or other sleep-related death (Task Force on Sudden Infant Death Syndrome, 2011).

F. **Maintain the neck in a neutral position, not flexed or hyperextended. Use of a neck roll is recommended.**

G. **Avoid vigorous manual ventilation to prevent intermittent hyperoxia, hypocapnia, and blunting of the CO_2 response.**

H. **Attempt to control apnea by avoiding painful stimuli, loud noises, extremely vigorous tactile stimulation, or potent odors.** No evidence supports effectiveness of kinesthetic stimulation in reduction of apnea.

I. **Consider providing continuous positive airway pressure (CPAP).**
1. Increases end-expiratory lung volumes and splints the upper airway and weak chest wall, thereby improving compliance and oxygenation and decreasing respiratory muscle work so that diaphragmatic movements are less tiring and more effective.
2. Complicates gavage feedings and may increase risk of aspiration. Increases risk of air leak.

J. **CPAP vs. noninvasive positive pressure ventilation (NIPPV).**
1. A Cochrane review looking at CPAP vs. NIPPV for apnea of prematurity concluded that NIPPV may be a way to augment the beneficial effects of CPAP in the treatment of apnea of prematurity that is frequent or severe (Lemyre et al., 2002).
2. Additional safety and efficacy data are required before recommending NIPPV as a standard treatment for apnea of prematurity. (Lemyre et al., 2002).

K. **Pharmacologic therapy** (Table 25.3)**.**
1. Methylxanthine (aminophylline, theophylline, caffeine) administered orally or intravenously. Used to treat apnea of prematurity after pathologic causes have been eliminated.
a. Mechanisms of action include the following:
1) Stimulation of central respiratory chemoreceptors.
2) Increased ventilatory response to carbon dioxide.
3) Increased oxygenation.
4) Increased minute ventilation (theophylline).

Table 25.3

Methylxanthines Used to Treat Apnea of Prematurity

Drug	Dosage	Side Effects
Caffeine citrate	Loading dose: IV: 20 to 40 mg/kg Maintenance dosing: IV, PO: 5 to 20 mg/kg given daily, 24 hours after loading dose	Tachycardia (consider withholding dose if HR >180), dysrhythmias, diuresis, glucosuria, ketonuria, hyperglycemia, jitteriness, seizures, vomiting, hemorrhagic gastritis, necrotizing enterocolitis
Theophylline	Loading dose: PO: 5 to 6 mg/kg/dose Maintenance: PO: 2 to 6 mg/kg/day divided every 8 to 12 hours	Tachycardia, cardiac dysrhythmias, seizures, jitteriness, feeding intolerance, gastroesophageal reflux, dehydration, hyperglycemia, and hypotension

HR, Heart rate; *IV*, intravenously; *PO*, by mouth.
Data from Taketomo, C., Hodding, J., & Kraus, D. (2014). *Pediatric and neonatal dosage handbook*. Lexicomp.

5) Stabilization of oscillations in breathing (theophylline).
6) Improved diaphragmatic contractility.
7) Relaxation of bronchial smooth muscle (theophylline).
8) CNS excitation.
9) Increased respiratory drive.
10) Increased respiratory muscle activity.
11) Increased skeletal muscle activity.

b. Pharmacokinetics.
1) Half-life of aminophylline and theophylline is approximately 30 hours.
2) Half-life of caffeine is approximately 100 hours.
3) Both theophylline and caffeine are rapidly absorbed intravenously. Oral absorption of caffeine is rapid, and oral absorption of theophylline is variable.
4) Metabolism of caffeine and theophylline takes place in the liver. This is slower in the neonate than in the adult.
5) Theophylline is metabolized to caffeine by a metabolic pathway unique to the preterm infant.
6) Serum concentrations must be checked to avoid toxic levels.

c. Dosage.
1) Aminophylline.
a) Route: intravenous (IV).
b) Loading dose: 5 to 8 mg/kg.
c) Maintenance dose: 2 to 6 mg/kg/day divided every 8 to 12 hours.
d) Therapeutic level: 5 to 15 mcg/mL.
2) Caffeine.
a) Route: IV or by mouth.
b) Loading dose: 10 mg/kg, caffeine base; 20 to 40 mg/kg, caffeine citrate.
c) Maintenance dose: 2.5 mg/kg, caffeine base; 5 to 20 mg/kg, caffeine citrate; every 24 hours beginning 24 hours after loading dose (Lexi-Comp, 2018).
d) Avoid use of caffeine benzoate preparation, which can displace bilirubin from albumin-binding sites.
e) Therapeutic level: 5 to 20 mcg/mL.
f) Higher doses and therapeutic levels have been studied, with no reported adverse effects, but are not commonly used.
g) Higher doses of caffeine, both loading and maintenance, have been shown to be safe and are associated with a significant reduction of extubation failure among mechanically ventilated preterm infants, fewer apnea episodes, and reduction of days with apnea (Mohammed et al., 2015).
h) Data are lacking on when to discontinue caffeine therapy. Most centers discontinue caffeine when the infant reaches a postmenstrual age (PMA) between 32 and 34 weeks and there have been no apneic episodes requiring intervention for approximately 5 days (Martin, 2019).
i) Although controversial, most centers recommend the infant be event-free for a period of 7 days to allow caffeine to be either eliminated or reach low subtherapeutic levels (Doyle et al., 2016).

d. Side effects.
1) Caffeine: tachycardia, cardiac dysrhythmias, increased wakefulness, increased active sleep, gastrointestinal distention, gastrointestinal bleeding, and diuresis with sodium loss.
2) Theophylline: tachycardia, cardiac dysrhythmias, seizures, jitteriness, feeding intolerance, gastroesophageal reflux, dehydration, hyperglycemia, and hypotension.

e. Caffeine versus theophylline.
1) Theophylline is a more potent vasodilator.
2) Theophylline causes a more rapid and sustained tachycardia.
3) Caffeine diffuses more rapidly in the CNS.

4) Caffeine is given only once a day.
5) Caffeine has a wider therapeutic index.
6) Caffeine may be effective in apnea not responsive to theophylline and vice versa.
7) Caffeine has a longer half-life, resulting in smaller changes in its plasma concentration.
8) On the basis of its higher therapeutic ratio, more reliable enteral absorption, and longer half-life, caffeine is recommended over theophylline for treatment of apnea of prematurity (Henderson-Smart and Steer, 2010).

2. Doxapram.
   a. Potent respiratory stimulant for apnea refractory to methylxanthine therapy.
   b. Mechanism of action thought to be stimulation of the peripheral chemoreceptors at low doses (0.5 mg/kg/hr) and of the CNS at higher doses.
   c. Increases minute ventilation, tidal volume, and mean inspiratory flow and decreases P_{CO_2} (Dobson et al., 2016).
   d. Pharmacokinetics.
      1) Half-life is approximately 10 hours in the first few days of life and 8 hours at 10 days of age.
      2) Steady-state levels are reached within 24 hours.
   e. Dosage.
      1) Route: IV.
      2) Loading dose: 2.5 to 3 mg/kg followed by the dose listed next.
      3) Continuous infusion of 1 mg/kg/hr; titrate to lowest effective dose. Maximum 2.5 mg/kg/hr.
      4) Controversy exists over therapeutic and toxic plasma levels. Guidelines include the following:
         a) Therapeutic level: 1.5 to 5 mg/L.
         b) Toxic level: 5 mg/L. Levels greater than 3.5 mg/L may produce side effects.
   f. Side effects.
      1) Jitteriness, irritability, vomiting, seizures, abdominal distention, increased gastric residuals, hyperglycemia, and glycosuria.
      2) Hypertension, tachycardia, and increased cardiac output.
      3) Increased work of breathing resulting from respiratory stimulation, consequent increased oxygen consumption and carbon dioxide production, and increased tidal volume and respiratory rate.
      4) Increased risk of intraventricular hemorrhage if used in the first few days of life.
   g. Contraindication: use in newborn infant not routinely recommended because preparation contains benzyl alcohol.
      1) Benzyl alcohol is associated with "gasping syndrome," characterized by metabolic acidosis, renal failure, liver failure, and cardiovascular collapse.
      2) Cumulative doses might be toxic for the liver, kidney, or brain.
      3) Insufficient data exist on clinical benefit and long-term effects (Lexi-Comp, 2018; Spitzer, 2012).

L. **Assisted ventilation.** Used for apnea resistant to other methods of therapy.

Home Monitoring

A. **Effectiveness of home monitoring.** The American Academy of Pediatrics states that cardiorespiratory monitoring is effective in preventing death from apnea for certain selected infants but is clearly inappropriate for others, with the primary objective being to serve the best interest of the infant based on the infant's history (Task Force on Sudden Infant Death Syndrome, 2011).

B. **Indications for home monitoring.**
   1. Premature infant with symptoms of idiopathic apnea of prematurity who is otherwise ready for hospital discharge.
   2. A survivor of an apparent life-threatening event defined as apnea, cyanosis, altered muscle tone, choking, or gagging.
   3. Sibling death due to SIDS.
   4. Tracheostomy, mechanically supported ventilation.
   5. A sleep apnea syndrome caused by a neurologic disorder, periodic breathing, upper airway abnormality, or idiopathic syndromes.
   6. Other conditions of ill or high-risk infants, as determined on an individual basis.

C. **Home monitoring is not indicated in prevention of SIDS in symptom-free, healthy infants.**

D. **Monitoring technology.**
   1. Transthoracic impedance combined with electrocardiography is the current standard.
      a. Electrodes are placed on the infant's chest or inside an adjustable belt worn around the chest.
      b. A small electric current passes between the electrodes. The impedance to this current is measured as the chest wall diameter changes. The monitor senses this change and equates it with respiration.
      c. The electrocardiograph reads the cardiac activity.
      d. High and low limits for respirations and heart rate are set by the clinician.

e. Monitor is compact and portable, weighing less than 5 pounds. A battery pack is available for use outside the home.

2. Technical problems include artifacts from signal interference, false alarms caused by shallow breathing, and the monitor's inability to detect obstructive apnea. Incorrect placement of leads can result in false alarms as well.
3. Advances in technology allow recording of home monitor events for evaluation by the clinician.
   a. Recording of events allows monitoring of compliance.
   b. True events can be distinguished from false alarms.
   c. Fewer rehospitalizations are needed.
   d. Recording is as sensitive as a pneumogram for evaluating whether monitoring can be discontinued.
   e. Fewer monitor days are needed for infants without events.

E. **Follow-up care.**

1. Multidisciplinary team includes physician, nurse, social worker, case manager, and equipment company representatives.
2. Family and other caregivers of the infant are trained in cardiopulmonary resuscitation before hospital discharge. Thorough education in use of the monitor is also provided before discharge.
3. Care includes close telephone contact—within 24 hours after discharge and every week to 2 weeks afterward as needed.
4. Visiting nurse makes home visit within the first week and then as needed.
5. A team member is available 24 hours a day for answering questions and solving problems. Equipment company representative is available as needed for problems and information.
6. Home follow-up does not replace clinic visits.
7. In 80% of infants, apnea of prematurity will cease between 40 and 44 weeks of postmenstrual age; in asymptomatic infants, home monitoring can be stopped at 45 weeks of postmenstrual age (Silvestri, 2009).

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CHAPTER 26
Assisted Ventilation

Debbie Fraser and William Diehl-Jones

OBJECTIVES

1. Identify the concepts of FRC, V_T, VC, and TLC and describe their importance in the physiology of ventilation.
2. Describe the concepts of elastic recoil, compliance, resistance, and gas trapping and their importance in ventilating the lungs of the newborn infant.
3. Explain the relationship of fetal hemoglobin, pH, and temperature to the oxyhemoglobin dissociation curve.
4. List potential causes of respiratory and metabolic acid–base disturbance in the newborn infant. Identify ranges of pH, Pao_2, $Paco_2$, HCO_3^-, and base excess/deficit in various respiratory disease states in the newborn infant.
5. Identify treatment modalities for neonates in respiratory distress.
6. Describe various types of mechanical ventilation devices available for the neonate.
7. List nursing interventions required to care for ventilated infants, based on the theories of mechanical ventilation.
8. Differentiate between high-frequency jet ventilation and high-frequency oscillatory ventilation.
9. Identify the nursing interventions required for high-frequency ventilation that differ from those required for conventional ventilation.
10. Identify changes in patient status that indicate potential complications with assisted ventilation.
11. Describe various medications used to enhance lung status in the ventilated patient.

Caring for an infant requiring assisted ventilation is a challenge. The nurse should understand the normal pulmonary physiology as well as the pathophysiology of pulmonary diseases in the neonate. An understanding of the basic mechanical principles of various ventilators is important to providing optimal care for a neonate. New ventilation techniques are being developed rapidly, and there are more choices for ventilating the neonate than ever before. The focus of this chapter is to provide the basic knowledge needed to care for the infant requiring oxygen therapy or mechanical ventilation.

Physiology

A. **Definitions** (Blackburn, 2018).
   1. Tidal volume (V_T): the amount of air that moves into or out of the lungs with each breath t(4 to 6 mL/kg).
   2. Vital capacity (VC): the volume of air maximally inspired and maximally expired (40 mL/kg).
   3. Functional residual capacity (FRC): the volume of gas that remains in the lungs after a normal expiration (30 mL/kg).
   4. Total lung capacity (TLC): the amount of air contained in the lung after a maximal inspiration (63 mL/kg).
   5. Physiologic dead space: anatomic plus alveolar dead space.
      a. Anatomic dead space: the volume of gas in the pulmonary conducting airways that cannot participate in gas exchange.
      b. Alveolar dead space: the volume of inspired gas that reaches the alveoli but does not participate in gas exchange because of inadequate perfusion to those alveoli.
   6. Mechanical dead space: gas that fills the ventilator circuit for availability in inspiration, as well as exhaled gas. Minimal dead space is desirable. Excessive dead space can cause increased retention of carbon dioxide.

B. **Concepts** (Keszler and Abubakar, 2017).
   1. Elastic recoil: the natural tendency for a stretched object to return to the original resting volume. With inhalation, alveoli stretch to a certain point, and during exhalation, the alveoli return to their original size in an infant with normal lungs.
   2. Lung compliance: the change in volume that occurs with a change in pressure (elasticity of the lung). It also refers to the relationship between a given change in volume and the pressure required to produce that change. An infant with severe respiratory distress syndrome will have decreased compliance (because of lack of surfactant), requiring increased

pressure to overcome the resistance generated by the surface tension in the alveoli. The major force contributing to elastic recoil of the lung is surface tension at the air–liquid interface in distal bronchioles and alveoli. The amount of distal airway pressure needed to counteract the tendency of the alveoli and bronchioles to collapse is demonstrated by the Laplace relationship: the relationship between pressure, surface tension, and the radius of a structure. The pressure needed to stabilize an alveolus is directly proportional to twice the surface tension and inversely proportional to the radius of that alveolus.

3. Lung resistance: the result of friction between moving parts. Airway resistance is determined by the flow rate, viscosity, and density of the respiratory gases, as well as the length and diameter of the airways (Keszler and Abubakar, 2017). An increase in airway resistance increases the time needed for air to reach the alveoli. High rates of airflow increase airway resistance by creating turbulence. Resistance to gas in a 2.5-mm endotracheal tube (ETT) is higher than in a 3.5-mm ETT because of the narrow lumen of the smaller tube. It takes greater pressure to force air through a small tube. Anatomic sources of resistance in the newborn infant include nasal passages, the glottis, the trachea, and the main bronchi.
4. Gas trapping: more gas entering the lung than leaving the lung. A partially occluded ETT can cause gas trapping. Debris from meconium can allow gas into the lung but may occlude the airway during exhalation (known as a ball–valve effect).
5. Inadvertent positive end-expiratory pressure (PEEP): a result of gas trapping in which volume and pressure increase in the distal airways through end expiration. Providing oxygen by nasal cannula can result in inadvertent PEEP in the small premature infant.
6. Ventilation–perfusion ratio ($\dot{V}_A/\dot{Q}$) (Fig. 26.1). Matching pulmonary ventilation and perfusion is necessary for efficient gas exchange. The relationship between ventilation and perfusion is expressed as a ratio and describes the relationship between alveolar ventilation and capillary perfusion of the lungs. A 1:1 ratio indicates that the alveoli are in perfect contact with the pulmonary capillaries, allowing exchange of O_2 and CO_2. A $\dot{V}_A/\dot{Q}$ ratio of zero indicates a shunt whereby no ventilation occurs during the passage of blood through the lungs. Abnormalities of the $\dot{V}_A/\dot{Q}$ ratio may be due to:
   a. Reduced ventilation with normal blood flow.
   b. Reduced blood flow with normal ventilation.
   c. A combination of these.
7. Mean airway pressure (MAP): mean or average pressure transmitted to the airways throughout an entire respiratory cycle (Gardner et al., 2016). MAP is dependent on the ventilator rate, gas flow rate through the ventilator circuit, peak inspiratory pressure (PIP), PEEP, and inspiratory time. Increasing MAP can greatly influence the management of respiratory distress in decreasing atelectasis and true intrapulmonary shunting, and is a major determinant of oxygenation.
8. Permissive hypercapnia: ventilation strategy that allows carbon dioxide levels to remain elevated. This strategy is designed to minimize barotrauma by avoiding the use of mechanical ventilation or by using minimal ventilatory rates and pressures.

C. **Oxygen transport.**

1. The amount of oxygen that can be delivered to the tissues is dependent on cardiac output and the oxygen content of the blood.
2. Oxygen is transported to tissue cells bound reversibly to hemoglobin and dissolved in plasma O_2. The amount of O_2 that is dissolved in the plasma is small (0.3 mL of O_2 dissolved in 100 mL of plasma per 100 mm Hg of O_2) compared with the amount that is bound to hemoglobin (1.34 mL of O_2 per gram of 100% saturated hemoglobin).
3. The amount of oxygen carried in the blood by hemoglobin depends on the hemoglobin concentration and the percent saturation of the hemoglobin. Adequate saturation is affected by the amount of hemoglobin available. Hemoglobin is almost fully saturated at a P_{O_2} of 80 to 100 mm Hg.
4. The binding of oxygen to hemoglobin varies with the Pa_{O_2}. The relationship is nonlinear and gives rise to an S-shaped curve—the oxyhemoglobin dissociation curve. The amount of oxygen that combines with hemoglobin at a given P_{O_2} depends on the position of the hemoglobin–oxygen dissociation curve (Fig. 26.2). Factors that determine the position of the dissociation curve are:
   a. Concentration of 2,3-diphosphoglycerate and the proportion of hemoglobin A (adult) to hemoglobin F (fetal).
   b. Temperature.
   c. P_{CO_2}.
   d. pH.
5. An increase in pH and a decrease in any of 2,3-diphosphoglycerate, temperature, or P_{CO_2} shifts the curve to the left, whereas a decrease in pH and an increase in 2,3-diphosphoglycerate, temperature, or P_{CO_2} shifts the curve to the right.
6. With decreased affinity (shift to the right), hemoglobin releases O_2 more easily to the tissues.
7. With increased affinity (shift to the left), oxygen is unloaded less rapidly and efficiently in the peripheral tissues.

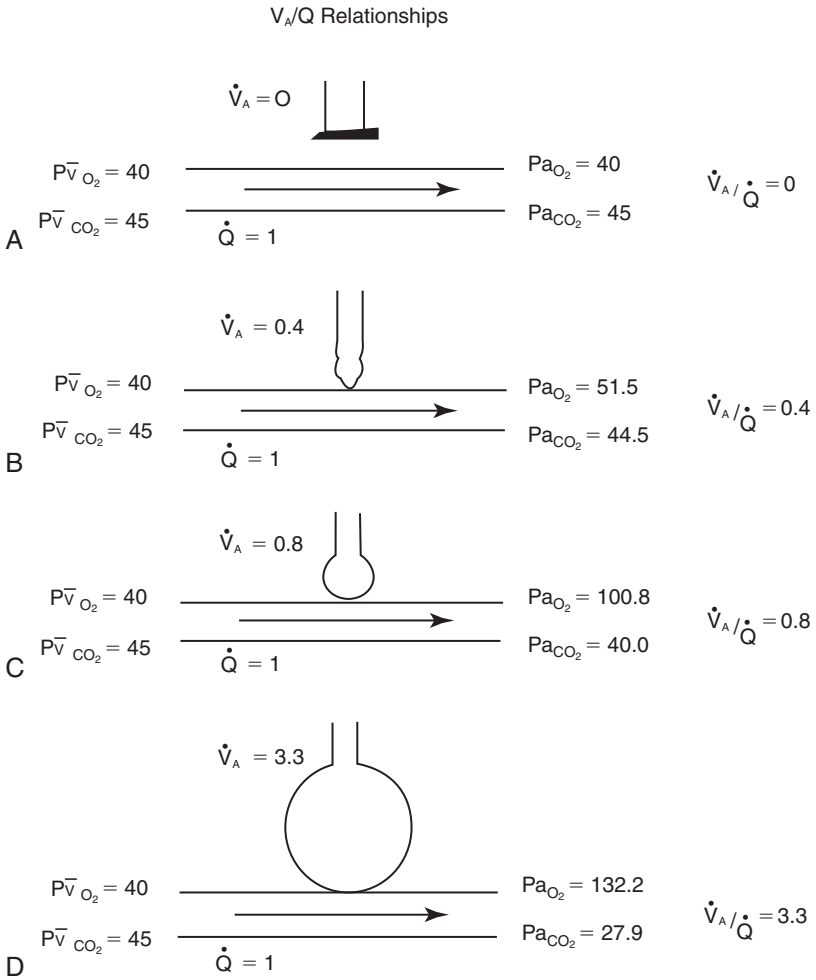

Fig. 26.1 Effects of various ventilation–perfusion ($\dot{V}_A/\dot{Q}$) ratios on blood gas tensions. **A,** Direct venoarterial shunting ($\dot{V}_A/\dot{Q} = 0$). Venous gas tensions are unaltered, and arterial blood has the same tension as venous blood. **B,** Alveolus with a low $\dot{V}_A/\dot{Q}$ ratio. Only partial oxygenation and CO_2 removal take place in this alveolus because of underventilation in relation to perfusion. **C,** Normal alveolus. **D,** Underperfused alveolus with high $\dot{V}_A/\dot{Q}$ ratio. Note that although the oxygen tension is 32 mm Hg greater than in normal alveolus (**C**), this results in only a slightly higher saturation and O_2 content. (From Thibeault, D. W., & Gregory, G. A. [1986]. *Neonatal pulmonary care*. Norwalk, CT: Appleton-Century-Crofts.)

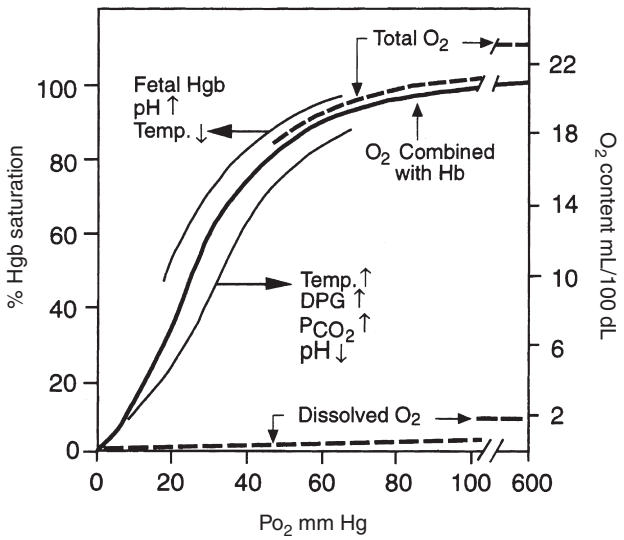

Fig. 26.2 Hemoglobin–oxygen dissociation curve. Nonlinear or S-shaped oxyhemoglobin curve and the linear or straight-line dissolved O_2 relationships between the O_2 saturation (Sao_2) and the Po_2. Total blood O_2 content is shown with division into a portion combined with hemoglobin and a portion physically dissolved at various levels of Po_2. Also shown are the major factors that change the O_2 affinity for hemoglobin and thus shift the oxyhemoglobin dissociation curve either to the left or to the right. *DPG*, 2,3-diphosphoglycerate. (Modified from West, J. B. [1979]. *Respiratory physiology: The essentials* [2nd ed., pp. 71, 73]. Baltimore, MD: Williams & Wilkins.)

Box 26.1

Factors Affecting Control of Ventilation in the Spontaneously Breathing Neonate

A. Neurologic factors
   1. "Maturity" of the CNS.
      a. Degree of myelination, which largely determines speed of impulse transmission and response time to stimuli affecting ventilation.
      b. Degree of arborization, or dendritic interconnections (synapses) between neurons, allowing summation of excitatory potentials coming in from other parts of the CNS and largely setting the neuronal depolarization threshold and response level of the respiratory center.
   2. Sleep state (i.e., REM sleep vs. quiet or non-REM sleep).
      a. REM sleep is generally associated with irregular respirations (both in depth and frequency), distortion, and paradoxic motion of the rib cage during inspiration, inhibition of Hering–Breuer and glottic closure reflexes, and blunted response to CO_2 changes.
      b. Quiet sleep is generally associated with regular respirations, a more stable rib cage, and a directly proportional relationship between P_{CO_2} and degree of ventilation.
   3. Reflex responses.
      a. Hering–Breuer reflex, whereby inspiratory duration is limited in response to lung inflation sensed by stretch receptors located in major airways. Not present in adult humans, this reflex is very active during the quiet sleep of newborn babies but is absent or very weak during REM sleep.
      b. Head reflex, whereby inspiratory effort is further increased in response to rapid lung inflation. Thought to produce the frequently observed "biphasic sighs" of newborn infants that may be crucial for promoting and maintaining lung inflation (and therefore breathing regularity) after birth.
      c. Intercostal–phrenic reflex, whereby inspiration is inhibited by proprioception (position-sensing) receptors in intercostal muscles responding to distortion of the lower rib cage during REM sleep.
      d. Trigeminal–cutaneous reflex, whereby tidal volume increases and respiratory rate decreases in response to facial stimulation.
      e. Glottic closure reflex, whereby the glottis is narrowed through reflex contraction of the laryngeal adductor muscles during respiration, "breaking" exhalation and increasing subglottic pressure (as with expiratory "grunting").

B. Chemical drive factors (chemoreflexes)
   1. Response to hypoxemia (falling Pa_{O_2}) or to decrease in O_2 concentration breathed (mediated by peripheral chemoreceptors in carotid and aortic bodies).
      a. Initially there is increase in depth of breathing (tidal volume), but subsequently (if hypoxia persists or worsens), there is depression of respiratory drive, reduction in depth and rate of respiration, and eventual failure of arousal.
      b. For the first week of life, at least, these responses are dependent on environmental temperature (i.e., keeping the baby warm).
      c. Hypoxia is associated with an increase in periodic breathing and apnea.
   2. Response to hyperoxia (increase in Fi_{O_2}) breathing causes a transient respiratory depression, stronger in term than in preterm infants.
   3. Response to hypercapnia (rising Pa_{CO_2} or $[H^+]$) or to increase in CO_2 concentration breathed (mediated by central chemoreceptors in the medulla).
      a. Increase in ventilation is directly proportional to inspired CO_2 concentration (or, more accurately stated, to alveolar CO_2 tension), as is the case in adults.
      b. Response to CO_2 is in large part dependent on sleep state: in quiet sleep, a rising Pa_{CO_2} causes increase in depth and rate of breathing, whereas during REM sleep the response is irregular and reduced in depth and rate. The degree of reduction closely parallels the amount of rib cage deformity occurring during REM sleep.
      c. Ventilatory response to CO_2 in newborn infants is markedly depressed during behavioral activity, such as feeding, and is easily depressed by sedatives and anesthesia.

CNS, Central nervous system; *REM*, rapid eye movement.

From Goldsmith, J. P., & Karotkin, E. H. (1996). *Assisted ventilation of the neonate* (3rd ed., p. 26). Philadelphia, PA: W. B. Saunders.

D. **Control of breathing** (Gardner et al., 2016). Control of ventilation (Box 26.1) is affected by both neurologic and chemical factors. The neurologic factors include central nervous system (CNS) maturity, sleep state, and reflexes. The chemoreflexes include responses to hypoxemia, hyperoxia, and hypercapnia.

E. **Hypoxia.** Delivery of O_2 to tissues is inadequate. Causes include:
   1. Heart failure.

2. Anemia. Hemoglobin available to transport oxygen is reduced, although completely saturated. Pao_2 levels are usually normal.
3. Abnormal hemoglobin. O_2 is not released to the tissues.
   a. Methemoglobin.
   b. Bart's hemoglobin.
4. Cardiogenic or hypovolemic shock.

F. **Hypoxemia.** O_2 content of arterial blood is low because of extrapulmonary or intrapulmonary shunts. The blood has bypassed adequately ventilated alveoli.
1. Intrapulmonary shunt.
   a. Ventilation–perfusion mismatch caused by lung diseases such respiratory distress syndrome, pneumonia, and MAS.
   b. Can occur with atelectasis or whenever alveoli are inadequately ventilated (hypoventilation).
2. Extrapulmonary shunt.
   a. Cyanotic congenital heart disease. Abnormal heart structure causes blood to bypass the lungs for oxygenation.
   b. Pulmonary artery hypertension. Blood shunts from the right side of the heart to the left side via a patent foramen ovale or ductus arteriosus, or both, causing blood to bypass the lungs.
      1) Comparison of the Pao_2 or O_2 saturation of preductal and postductal blood can help determine whether a right-to-left shunt is present.
      2) In the presence of shunting, preductal blood obtained from the right radial artery has a greater than 5% difference in saturation from postductal blood obtained from the umbilical artery or posterior tibial artery.

Treatment Modalities

A. **Blow-by oxygen.** Free flow of O_2 from a bag and mask or flow of O_2 through O_2 tubing near the infant's face may be useful for short-term O_2 delivery to an infant who is breathing but needs an O_2-enriched atmosphere for oxygenation (i.e., in the delivery room after a trial of room air, during caregiving activities, during placement of an intravenous [IV] line, during weighing). There is no way to determine the exact content of O_2 delivered to the infant. Oxygen content depends on O_2 concentration, flow rate, the distance of the O_2 source from the infant, and the ventilatory efforts of the infant.

B. **Nasal cannula. Humidified O_2 is delivered at a set flow rate via a cannula, with the flow directed into the nares. The exact concentration of oxygen delivered by nasal cannula cannot be measured.**
1. Conventional nasal cannula. Oxygen is delivered through the cannula and is regulated by the flow (measured in liters). Low-flow meters are capable of delivering amounts as small as 0.02 L/min. The concentration of oxygen used may be 100% or may be regulated with the use of a blender system.
2. High-flow nasal cannula (HFNC). Flow is greater than 1 L/min, with oxygen blended to a known concentration. High flow rates result in the delivery of an undetermined level of continuous positive airway pressure (CPAP), depending on the size of cannula, size of the infant, whether the infant's mouth is open or closed, and the flow rate used (Gardner et al., 2016). Adequate humidification is essential with the use of an HFNC to prevent drying and damage to the nasal passages. HFNC may be comparable to nasal CPAP in level of respiratory support supplied (Gardner et al., 2016).
3. A blender should be used to adjust the concentration of oxygen being delivered by cannula, although the amount of oxygen entering the infant's lungs cannot be accurately determined because of the entrainment of room air around the cannula.
4. Indications. A nasal cannula is used when there is a need for prolonged oxygen therapy, as in chronic lung disease, transfer or transport, and increased mobility of the infant for feedings or for other developmental activities.
5. Complications. Pressure-related tissue damage may occur because of improper or infrequent changing of the cannula, O_2 concentration may vary, hypoxemia may result from a displaced cannula, and the cannula may be occluded by nasal secretions (may cause significant respiratory distress). Flow through the cannula may result in drying of the nasal mucosa, predisposing the infant to tissue damage and thickened nasal secretions.

C. **CPAP**.
1. Mask CPAP: delivery of positive pressure (5 to 8 cm H_2O pressure) with variable amounts of O_2 via face or nasal mask. Requires appropriate-sized mask and tight seal around the nose or, in the case of face mask CPAP, the nose and mouth.
   a. Indications: atelectasis, apnea, respiratory distress, and pulmonary edema.
   b. Advantages: short-term use to assist with alveolar expansion and to inhibit alveolar collapse (atelectasis); intubation not required. May be useful in infants whose nares are too small to accommodate CPAP prongs. Alternating between nasal prong CPAP and nasal mask CPAP may help to reduce skin breakdown around the nares in low birth weight (LBW) infants (Diblasi and Courtney, 2017).
   c. Complications: carbon dioxide retention in the dead space of the mask, pulmonary hyperexpansion potentially leading to air leaks (i.e., pneumothorax, pneumomediastinum), aspiration of stomach contents, and gastric distention.

2. Nasal CPAP: generally started at 5 to 6 cm H_2O pressure and titrated up to 8 cm H_2O pressure delivered by prongs that fit into the nares, in addition to a measured concentration of oxygen.
   a. Indications: atelectasis, apnea, mild to moderate respiratory distress, and pulmonary edema.
   b. Advantage: intubation not required.
   c. Complications: ineffective ventilation, pneumothorax, variable pressure delivery when infant's mouth is open, molding of the head from securing straps, erosion of the septum from poorly fitting prongs, nasal obstruction as a result of increased secretions, agitation, dislodging of prongs by an active infant, and gastric distention and perforation.
3. Bilevel CPAP: provides continuous positive pressure at two separate CPAP levels. The background or baseline CPAP is set at 4 to 7 cm H_2O with sighs or brief periods of increased pressure set at 2 to 4 cm of H_2O higher than baseline.
   a. Indications: atelectasis, apnea, moderate respiratory distress, and pulmonary edema.
   b. Advantage: intubation not required. Higher MAPs may stabilize airways and assist in the recruitment of alveoli (Salvo et al., 2017).
   c. Complications: ineffective ventilation, pneumothorax, variable pressure delivery when infant's mouth is open, erosion of the septum from poorly fitting prongs, agitation, dislodging of prongs by an active infant, feeding intolerance, and gastric distention.
4. Nasal intermittent positive pressure ventilation (NIPPV): combines nasal CPAP with ventilator breaths delivered at a set peak pressure through nasal CPAP prongs or nasal CPAP mask.
   a. Indications: apnea, atelectasis, moderate respiratory distress.
   b. Advantages: compared with nasal CPAP, NIPPV has been shown to decrease the need for mechanical ventilation in the first 72 hours of life (Oncel et al., 2016).
   c. Complications: ineffective ventilation, pneumothorax, variable pressure delivery when infant's mouth is open, erosion of the septum from poorly fitting prongs, agitation, dislodging of prongs by an active infant, feeding intolerance, and gastric distention.
5. Mechanical ventilation: respiratory support of infant using mechanical assistance.
   a. Gas-exchange mechanisms in spontaneous and conventional mechanical ventilation.
      1) Convection (bulk flow) in large airways goes to approximately the eighth bronchial generation. Gas moves along a negative pressure gradient from the upper airways to the alveoli.
      2) Molecular diffusion occurs in terminal airways and alveoli. This is the exchange of gases in adjacent spaces.
      3) The status of alveolar ventilation is determined as follows: alveolar ventilation = respiratory rate × (tidal volume delivered − anatomic dead-space volume).
   b. Indications: respiratory failure (hypoxemia, hypercapnia, and/or acidemia), pulmonary insufficiency, need for surfactant administration, severe apnea and bradycardia episodes, cardiovascular support, CNS disease, and surgery.
   c. Advantages: consistent delivery of assisted ventilation and oxygen therapy, decreases the work of breathing, and stabilizes the airway.
   d. Disadvantages: intubation by skilled provider, x-ray examination to confirm placement, intermittent x-ray examinations to verify placement of ETT or lung status, continuous monitoring of vital signs and oxygen saturation. Exposes the neonate to potential volutrauma/barotrauma of the lung tissue and increases the risk of chronic lung disease.
   e. Complications: tube malposition or dislodgment, underventilation or overventilation, tracheobronchial injury, pulmonary air leaks, infection, intracranial hemorrhage, bronchopulmonary dysplasia (BPD), and retinopathy of prematurity.

TYPES OF ASSISTED VENTILATION

A. **Positive pressure devices.**
   1. Bag-and-mask ventilation. Positive pressure and O_2 are delivered via face mask applied with an adequate seal around the mouth and nose. Maximal pressure-relief valves should be present to prevent administration of excessive pressure. A manometer should measure pressure delivered to the patient. Device does not require intubation and can be very effective for short-term use, including initial resuscitation.
   2. T-piece resuscitator. Levels of positive pressure and PEEP are preset. Breaths are delivered by occluding the PEEP cap on the T-piece. A gas source is required to operate the T-piece resuscitator. Has the advantage of controlling the amount of pressure applied with each breath, thus eliminating variable pressure delivery inherent in bag-and-mask ventilation.
   3. Pressure-cycled ventilator. Inspiratory phase ends when a preset pressure is reached within the ventilator circuit, regardless of the volume of gas delivered during inspiration.
   4. Time-cycled, pressure-limited, continuous-flow ventilator. A predetermined pressure of gas is

administered; the duration of inspiration and expiration can be adjusted. Ventilator also allows for the infant's spontaneous respiratory efforts, facilitating a gradual reduction of support. The operator determines the rate, PIP, PEEP, inspiratory time, and flow.

5. Volume-cycled ventilator. Inspiration ends when a preset volume of gas is delivered, regardless of the pressure reached within the ventilator circuit. The pressure used to deliver the breath will vary inversely with the infant's lung compliance and respiratory effort. An increase in ventilation is achieved by increasing V_T or rate; oxygenation is improved by increasing PEEP, FiO_2, or V_T (Keszler and Chatburn, 2017).
6. Pressure support ventilator. Pressure support ventilation (PSV) supports breaths initiated by the infant by delivering a mechanical breath to a preset volume, and it uses a variable inspiratory time to allow the infant greater control and synchrony with the ventilator. PSV is flow cycled such that when inspiratory flow decreases by a certain percentage, inspiration ends. Pressure support ventilators usually have a maximum inspiratory time that is preset. PSV is often used as a weaning mode of ventilation (Gardner et al., 2016).

VENTILATOR MODES

A. **Intermittent mandatory ventilation.** "Breaths" are delivered at a predetermined rate, regardless of where the patient is in the respiratory cycle. The ventilator continues to deliver fresh gas, which allows spontaneous respirations as well. It is possible to stack a ventilator breath on top of a spontaneous breath during either inspiration or expiration. This may lead to air trapping, air leaks, CNS dysfunction, and irregularity of blood pressure and cerebral blood flow.

B. **Patient-triggered ventilation.** Mechanical breaths are delivered in response to a signal derived from the patient and detected as a spontaneous respiratory effort. The signal may be derived from a sensor that detects airflow, airway pressure, chest wall movement, esophageal pressure, or electrical activity of the diaphragm (Keszler and Mammel, 2017). The goal of patient-triggered ventilation is to avoid asynchrony of breathing by the patient and breaths given by the ventilator. Asynchrony may lead to air trapping, air leaks, CNS dysfunction, and irregularity of blood pressure and cerebral blood flow. Patient-triggered ventilation has been shown to improve gas exchange, decrease the need for and duration of ventilation, reduce the incidence of air leaks, and provide ventilation that better matches the infant's own efforts (Gardner et al., 2016; Keszler and Mammel, 2017).

1. Synchronized intermittent mandatory ventilation.
   a. Preset number of ventilator breaths is synchronized with the onset of spontaneous breaths. When the infant initiates a breath, the ventilator supports that breath according to the preset PIP and inspiratory time.
   b. Unassisted breaths occur between ventilator breaths, with continuous flow of gas from the ventilatory circuit.
   c. Partial asynchrony may occur if the patient attempts to terminate the inspiratory effort while the ventilator is in the inspiratory phase.
2. Assist/control (A/C) mode of ventilation.
   a. A synchronized breath is delivered each time a spontaneous patient breath meeting the threshold criteria is detected, or mechanical breaths are delivered at a preset regular rate if the patient does not exhibit spontaneous respiratory effort (i.e., if the patient has apnea).
   b. A detection system signals the start of inspiratory effort, which allows for synchronous initiation of inspiration.
   c. Asynchronous expiratory-phase breaths may still occur.
3. PSV.
   a. PSV is pressure limited and flow cycled. The ventilator supports each breath and terminates the breath when the inspiratory flow drops below a preset threshold, thereby varying the inspiratory time for each breath. This termination mechanism avoids prolonged inspiration and maximizes synchrony (Keszler and Mammel, 2017).
4. Neurally assisted ventilation (neurally adjusted ventilatory assist [NAVA]).
   a. NAVA uses measured electrical activity in the diaphragm to detect the onset of a breath and trigger the ventilator to support the breath.
   b. Each breath is supported in proportion to the intensity of the infant's inspiratory effort in an attempt to optimize synchrony (Colaizy et al., 2017).
5. Volume-targeted ventilation.
   a. Volume-targeted ventilation can be used in conjunction with synchronized intermittent mandatory ventilation or A/C modes in patient-triggered ventilation.
   b. A V_T is set by the operator based on the infant's weight and disease condition.
   c. The benefits of volume-targeted ventilation include reduced risk of death or chronic lung disease, air leaks, and duration of mechanical ventilation when compared with pressure-limited ventilation (Klingenberg et al., 2017).

Nursing Care of the Patient Requiring Respiratory Support or Conventional Mechanical Ventilation

A. **Care of O_2 delivery devices.**
   1. Oxygen hood. Warm, humidified (to prevent heat loss) O_2, delivered via head hood, is usually blended to select the appropriate amount needed. The percentage of O_2 in the hood must be monitored by a properly calibrated O_2 analyzer placed in the hood near the infant's nose. Ensure a hood of correct size for each infant. To prevent buildup of CO_2, do not block openings in the hood, and ensure an adequate flow of 5 to 7 L/min. Clean and change per unit protocol.
   2. Nasal cannula. Remove and clean secretions every 4 to 6 hours as needed. Inspect surrounding tissue for pressure-related injury. If sudden onset of respiratory distress occurs, inspect cannula for secretions and suction nasopharynx for mucus. Change cannula according to unit protocol. Some infants receiving oxygen by nasal cannula benefit from the administration of saline drops to moisten the mucosa. These should be administered according to unit protocol. In addition, oxygen/air flow should be warmed and humidified.
   3. Nasal prong CPAP. Ensure that CPAP device is of the correct size to decrease the incidence of pressure necrosis of the nares. Nasal CPAP units come in a variety of sizes and should be short and wide, with thin walls to allow for maximal airflow. They should be soft and flexible and should be easy to secure and maintain. Humidification of 90% to 100% should be provided in the CPAP system to prevent drying out of the mucous membranes and subsequent formation of thick secretions. Evaluate the need for suctioning every 2 to 4 hours. Inspect surrounding tissue for pressure-related injury. Secure the device to a stockinette cap or with soft straps provided by some manufacturers. Lightweight tubing is helpful for ease in securing the device and in keeping the unit in the nose. The infant can be positioned supine, on either side, or prone, generally with the head of the bed at approximately a 30-degree angle. Observe for abdominal distention resulting from excessive air entering the stomach from the CPAP device. Consider aspirating every few hours from an orogastric tube or leaving it open to continuously vent gas from the stomach. Feeding is not contraindicated during delivery of CPAP. The clinical condition must be evaluated before institution of feedings. Change prongs according to unit protocol, generally every 2 or 3 days.
   4. ETT. After correct placement has been determined, note the depth of the tube at the gum or lip and post at the bedside. This is important for future reference in case the tube slips, if reintubation is needed, or to determine suction catheter length. Secure the ETT with tape or other method. Each institution generally develops a method that works well for the staff and patients. Observe for evidence of slipping or tape loosening and secure again when necessary to prevent accidental extubation. Position the infant supine, on either side, or in the prone position, with the head in a neutral position. Be aware that the tube moves with the chin and can move several centimeters with flexion or extension of the head. Signs of extubation include sudden deterioration in clinical status, abdominal distention, crying, decreased chest wall movement, breath sounds in the abdomen, agitation, cyanosis, and bradycardia. Notify the physician or neonatal nurse practitioner if extubation is a concern, and prepare for reintubation as soon as possible. Intubation equipment should be readily available. A bag and mask with pressure manometer or a T-piece resuscitator should also be available at each bedside and should be tested during each shift. Suction the ETT when necessary. Complications of an ETT include palatal grooves (consider a palate protector, which can be made by a pediatric dentist or is commercially available), nasal erosion, subglottic stenosis, tracheoesophageal perforation during insertion of the tube, aspiration, infection, and tracheal granuloma.
   5. Tracheostomy tube. Daily changing of the dressing and weekly changing of the tube are usually adequate. Inspect the site for signs of tissue pressure and/or necrosis. Suctioning is necessary to keep the airway clear of secretions. Family members need to be included in this procedure, thus facilitating discharge.

B. **Suctioning the airway.**
   1. Nontracheal tubes.
      a. Suctioning of the mouth, nose, and tubes should be performed on an as-needed basis. The presence of a foreign body in the mouth or nose will cause an increase in secretions.
      b. Suctioning can coincide with the cleaning or changing of the tubes or with routine caregiving.
   2. ETTs.
      a. The amount of secretions will be disease related. Infants with resolving respiratory distress syndrome, patent ductus arteriosus (PDA), BPD, and pneumonia are more likely to require suctioning because of an increased production of mucus. Patients with early-stage respiratory distress syndrome and those with most types of congenital heart disease will not have much

mucus and will require less suctioning. Suctioning is done on an as-needed basis—never on a routine schedule (Gardner et al., 2016). Criteria for suctioning include evidence of secretions (audible or visible), changes in vital signs, agitation or restlessness, and changes in oxygenation or ventilation.

b. Protocols for suctioning vary from one institution to another. Administering manual breaths with the ventilator before and after suctioning may be necessary to maintain lung volumes during the procedure. Hyperoxygenation before suctioning is not recommended.

c. In-line suction devices allow suctioning while ventilation continues and are associated with a decrease in episodes of hypoxia and smaller changes in heart rate.

d. Do not advance the suction catheter farther than the distance of the ETT, and do not suction too vigorously.

e. Vacuum pressure range should be 60 to 80 mm Hg (Gardner et al., 2016). A 5F or 6F suction catheter for a 2.5- to 3.5-mm ETT, or an 8F suction catheter for a 4- to 4.5-mm ETT, is usually appropriate.

f. Complications of suctioning include hypoxemia, bradycardia, barotrauma, changes in blood pressure, alterations in cerebral blood flow, intraventricular hemorrhage, tracheal damage, atelectasis, infection, and pneumothorax.

C. **Initiating mechanical ventilation.** The goal of mechanical ventilation is to assist in providing adequate tissue oxygenation and eliminating CO_2.

1. Establish an airway. Endotracheal intubation should be performed by a skilled provider (see Chapter 15).
2. Ventilator selection. The ventilator selected for use is based on the patient's condition and disease process, the patient's response to previous ventilatory support, and staff experience and comfort with the device. Patient-triggered or synchronized ventilation is now the preferred method of mechanically ventilating neonates in most neonatal intensive care units (NICUs). A number of devices and ventilator modalities allow the operator to control the PIP or volume delivered to the neonate, as well as the rate, PEEP, flow, and inspiratory time.
3. Parameters to be set and/or monitored during mechanical ventilation.
   a. Rate of intermittent mandatory ventilation. Infants without respiratory failure have a resting respiratory rate of approximately 40/minute, whereas infants with respiratory failure may have a respiratory rate of 0/minute to more than 100/minute. A beginning ventilator rate of 40 to 50 breaths per minute for an infant with respiratory failure should be adequate. For infants without respiratory failure, a rate of 30 to 40 breaths per minute should be adequate. The ventilator rate will affect the ability to remove CO_2. The rate is adjusted to maintain the arterial tension of CO_2 in the range of 40 to 50 mm Hg and to avoid excessive respiratory effort, which would exhaust the infant. A rate greater than 40/minute may shorten the expiratory phase of ventilation and cause air trapping.
   b. PIP. PIP is the primary factor that determines the VT and affects the Pao_2 (Keszler and Chatburn, 2017). Determining the appropriate PIP requires careful and skilled assessment. The complications of excessive PIP include air leaks, decreased venous return, intraventricular hemorrhage, and decreased cardiac output. Factors such as weight, gestational age, disease process, lung compliance, and airway resistance must be considered. Auscultation of breath sounds to assess aeration and compliance is necessary. Visual inspection of chest wall movement should guide your assessment. A beginning PIP of 16 to 20 cm H_2O is appropriate for most preterm infants. The lowest PIP that will provide adequate ventilation is ideal, with the goals of preventing volutrauma and decreasing the incidence of air leaks (Gardner et al., 2016). Certain conditions may warrant the use of high PIP, including poor compliance, atelectasis, or pulmonary hypertension. Before connecting the patient to the ventilator, ensure that the inspiratory pressure is correct. Recheck after the connection has been made, and adjust as necessary.
   c. VT. VT is the primary factor affecting both oxygenation and ventilation. When using volume-targeted ventilation, the operator determines the desired volume to be delivered with each breath rather than setting the PIP. Based on averaging a series of breaths, the ventilator determines the PIP needed to deliver the desired volume of gas. An upper limit for the PIP should be set by the operator to prevent the delivery of excessive pressure. An increase in ventilation is achieved by increasing the volume of gas to be delivered (VT) or the rate. Increased oxygenation is achieved by increasing the Fio_2, the PEEP, or the VT (Keszler and Chatburn, 2017). Determination of VT is based on the infant's weight, with a beginning VT of 4 to 5 mL/kg being most common.
   d. PEEP. This measure aids in maintaining FRC, stabilizing and recruiting atelectatic areas for gas exchange, improving compliance, and improving ventilation–perfusion matching in the lung (Keszler and Abubakar, 2017). PEEP is

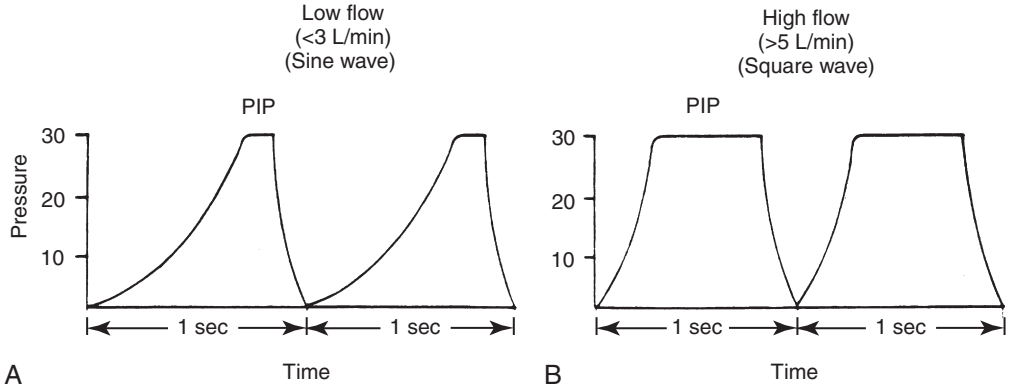

Fig. 26.3 Comparison of ventilator waveforms. **A,** Relative sine wave. **B,** Relative square wave. *PIP,* Peak inspiratory pressure. (From Goldsmith, J. P., & Karotkin, E. H. [Eds.]. [1996]. *Assisted ventilation of the neonate* [3rd ed., p. 169]. Philadelphia, PA: W. B. Saunders.)

important in assisted ventilation for infants with surfactant deficiency because of the likelihood of alveolar collapse. Physiologic PEEP is estimated at 2 cm H_2O. Levels lower than 4 cm H_2O are generally not used. In most instances, medium levels—about 4 to 7 cm H_2O—are recommended. Levels greater than 8 cm H_2O may be necessary in some infants with chronic lung disease, but are associated with pulmonary air leaks and reduction of cardiac output.

e. Inspiratory/expiratory (I/E) ratio: ratio of time spent in inspiration to time spent in expiration. Determining this time should be based on the underlying reason for ventilation. A physiologic I/E ratio in a nondisease state is equal to 1:2 or 1:3, meaning a short inspiratory time with a longer expiratory time. Prolonged expiratory time is useful during weaning, when oxygenation is not as problematic. The I/E ratio will affect the Pao_2 and $Paco_2$. Changes affect MAP and oxygenation.

f. Flow rate: flow of gas (measured in liters per minute) through the patient's circuit. The flow rate determines the ability of the ventilator to deliver the desired amount of PIP, waveform, I/E ratio, and respiratory rate. A flow rate of at least twice the infant's minute ventilation ensures that the ventilator can reach the desired pressure. Flow rates of 4 to 10 L/min are usually adequate (Harris and Fraser, 2012). With low flow rates (<3 L/min), inspiratory pressure gradually builds to a peak just before expiration, closely resembling a sine waveform (normal breaths are shaped like a sine waveform). There may be less barotrauma to the airways with a sine waveform. High flows of 4 to 10 L/min or higher are necessary with square waveform ventilation or when high rates are used. A square waveform pattern moves the ventilator breath rapidly from the resting or expiratory pressure level to the PIP. Because the PIP is reached sooner than with a sine waveform, the PIP is held for a longer period (Fig. 26.3). This may be advantageous with atelectatic areas of the lung. It may also contribute to barotrauma.

g. MAP: average distending pressure throughout a complete respiratory cycle. It is the major determinant of oxygenation. MAP is most affected by changes in PEEP, PIP, and I/E ratio. Increases in oxygenation are directly related to increases in MAP, and increased barotrauma to the lungs can result with high MAP. Close attention to the MAP during ventilation is essential, especially once the underlying disease begins to resolve.

4. For effects of different ventilator changes, see Box 26.2.

High-Frequency Ventilation

High-frequency ventilation (HFV) is any of several forms of mechanical ventilation that use small VT at rates of at least 150 breaths per minute (Golombek et al., 2016) to ventilate patients with severe respiratory failure. The advantage of HFV over conventional mechanical ventilation is the ability to deliver adequate minute volumes using small V_T with lower distal airway pressures.

A. **Gas-exchange mechanisms in HFV.** The VT used may be less than or equal to anatomic dead-space volume. According to gas-exchange theories for conventional ventilation, alveolar ventilation during HFV should be zero.

B. **Theories of gas exchange during HFV.**
   1. Augmented (facilitated) diffusion: gas molecules diffuse higher in the airways.
   2. Coaxial diffusion: fresh gases travel down the center of the airway, and CO_2 elimination occurs along the periphery of the airway (Fig. 26.4).

Box 26.2

Specific Effects of Different Ventilator Changes

Increasing PIP

1. Increases V_T and Ve
2. Adds little to MAP unless combined with a reversal of I/E ratio or prolongation of IT
3. Affects maximum dilation of alveoli already open, contributing to barotrauma
4. Opens alveoli with high critical opening pressures

Reversing I/E Ratio (for Lengthening IT While Respiratory Rate Is Kept Constant)

1. Has little effect on Vt or Ve beyond the minimum IT needed to deliver Vt or reach desired PIP level (or both)
2. Can contribute on more than one-to-one basis to MAP, depending on original PIP and degree of reversal of I/E ratio
3. Allows expansion of atelectatic alveoli at lower PIP
4. May cause inadvertent PEEP, overinflation of alveoli, and reduction of pulmonary blood flow

Increasing Background CPAP or PEEP

1. Decreases V_T and Ve unless significant atelectasis is overcome
2. Adds to MAP on a one-to-one basis
3. Holds open alveoli and terminal airways on end expiration, thus raising closing volume and aiding in equal distribution of ventilation
4. Reduces likelihood of inadvertent PEEP

CPAP, Continuous positive airway pressure; *I/E*, inspiratory/expiratory; *IT*, inspiratory time; *MAP*, mean airway pressure; *PEEP*, positive end-expiratory pressure; *PIP*, peak inspiratory pressure; V_T, tidal volume; *Ve*, expired volume per unit time.

From Goldsmith, J. P., & Karotkin, E. H. (Eds.). (1996). *Assisted ventilation of the neonate* (3rd ed., p. 62). Philadelphia, PA: W. B. Saunders.

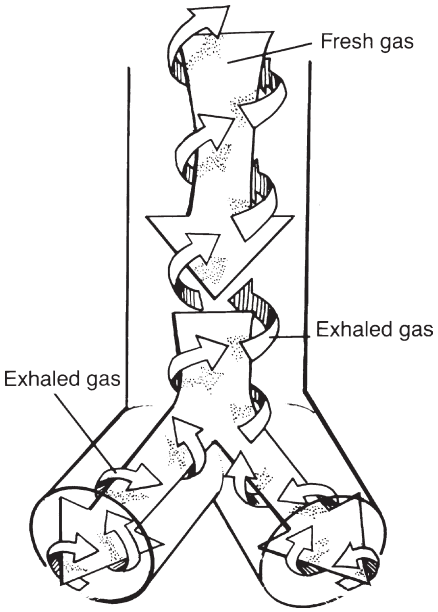

Fig. 26.4 Coaxial diffusion.

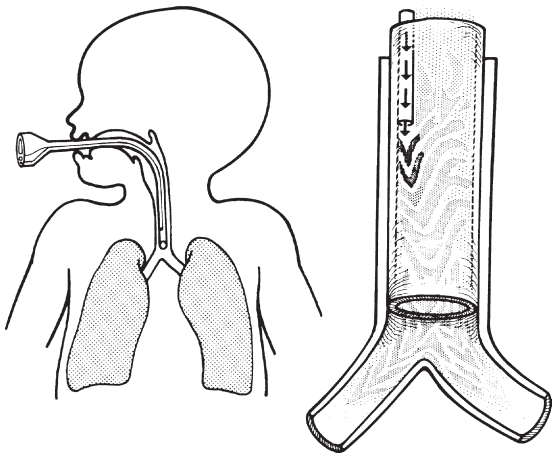

Fig. 26.5 Entrainment during high-frequency jet ventilation. Gas molecules near the jet orifice are "entrained," or dragged along with the jet pulse, whereby additional volume is delivered to the patient without substantially increasing static airway pressure. (From Harris, T. R. [1988]. Physiologic principles. In J. P. Goldsmith & E. H. Karotkin [Eds.], *Assisted ventilation of the neonate* [2nd ed.]. Philadelphia, PA: W. B. Saunders.)

3. Entrainment: gas molecules from higher in the airway are pulled into the area of low pressure created behind a high-velocity gas entry point, such as a jet cannula port (Fig. 26.5).
4. Interregional gas mixing ("pendelluft"): because of the different time constants of the respiratory units, gases in the periphery of the lung may move between alveolar units to provide better matching of ventilation and perfusion.

C. **Effectiveness of gas exchange.** All forms of HFV produce gas exchange with lower distal PIPs and small tidal volumes, theoretically reducing the risk of barotrauma and volutrama.

D. **Types of high-frequency ventilators.**
   1. High-frequency jet ventilation (HFJV): Bunnell Life Pulse Jet Ventilator (Bunnell Inc., Salt Lake City, Utah).

a. A jet injector delivers short, rapid, high-velocity pulses from a humidified, pressurized gas source directly into the trachea via a special jet ETT adapter ("jet nozzle") that attaches to a standard ETT.
b. Servo-controlled driving pressure: continuously adjusts the pressure of the gas supply to the jet nozzle to maintain desired peak airway pressure. Solenoid valve: opens and closes gas supply to the jet nozzle.
c. Humidification system: built in-line.
d. Proximal airway pressures: monitored and continuously displayed; used in servo-control of pressure delivery.
e. Conventional ventilator: used in tandem to provide gas for patient's spontaneous breathing, PEEP, and background ventilation (sighs).
f. Exhalation: passive.
g. Ventilation (CO_2 removal) is primarily determined by the amplitude (PIP − PEEP) or size of the breath.
h. Oxygenation is related to MAP, which is generated primarily by the tandem conventional ventilator PEEP but includes all the pressure sources (HFJV PIP, rate, and I-time) and the rate, PIP, PEEP, and inspiration time (I-time) provided by the conventional ventilator if conventional breaths are used (Fraser, 2012).
i. Indications for use: effective with disorders in which CO_2 elimination is the major problem. Severe atelectatic disorders, such as respiratory distress syndrome, may also benefit from HFJV, as do obstructive disorders, such as meconium aspiration syndrome and restrictive lung diseases and air leaks (Mammel and Courtney, 2017).
j. Parameters to be set and/or monitored.
   1) PIP: set on both the HFJV and the conventional ventilator.
      a) HFJV PIP is usually initially set at the same PIP required during conventional ventilation, and the conventional ventilator PIP is set based on the lowest PIP needed to achieve lung inflation. There is no fixed relationship between the two PIPs.
      b) A higher conventional PIP may cause interruption of the HFJV breaths.
   2) Servo-controlled pressure: internal adjustment of driving pressure by the ventilator as patient compliance and pressure settings change.
      a) Lower servo-pressure reflects worsening lung disease, airway obstruction, pneumothorax, or kinked ventilator tubing.
      b) Higher servo-pressure indicates improved lung compliance or a leak in the patient/system.
   3) PEEP: set on conventional ventilator; displayed on HFJV ventilator. Value displayed may be lower than value set, because of where and how it is measured. The PEEP provided by the conventional ventilator assists in lung recruitment when atelectasis is a problem.
   4) Jet valve "on" time is the time that the jet valve is open; similar to inspiratory time, usually 0.02 second.
   5) Rate set on jet and conventional ventilators.
      a) The HFJV rate is usually 240 to 420 breaths per minute; Bunnell default setting of 420/minute is a typical starting rate for this ventilator. Decreasing the HFJV rate lengthens the exhalation time and improves the I/E ratio. Slower HFJV rates are critical for larger patients (>2 kg) and patients with hyperinflation.
      b) The rate for conventional intermittent mandatory ventilation is usually set between 0 and 5 breaths per minute to provide background ventilation (sigh breaths), which helps recruit lung volume and to prevent atelectasis.
   6) FiO_2: set on HFJV and conventional ventilators.
k. Weaning from HFJV is usually accomplished as the acute phase of the illness resolves. Air leaks should be resolved for 1 or 2 days before switching back to nasal CPAP or conventional mechanical ventilation. Weaning is accomplished by decreasing the PIP and reducing the HFJV rate to 240 to 300 breaths per minute. Support from conventional mechanical ventilation is increased using small V_T breaths if the patient cannot be supported on nasal CPAP.
l. Patient assessment and care.
   1) Patient will require a special jet ETT adapter that is attached to the standard ETT (Fig. 26.6).
   2) Suctioning may be performed with HFJV on or off.
      a) Placing the HFJV ventilator on stand-by mode during suctioning is the preferred method because it eliminates the potential for pressure fluctuations.
      b) Suctioning with the HFJV ventilator running may help decrease respiratory decompensation during the procedure in some patients.
   3) Humidification of gases is important with HFJV in preventing obstruction of the ETT.
      a) Main port of ETT is suctioned as usual.

Fig. 26.6 LifePort endotracheal tube adapter. (Courtesy Bunnell Inc., Salt Lake City, Utah.)

4) Tubing to the conventional ventilator must never be kinked because overpressurization of the circuit and alveolar rupture may occur if expiratory gas cannot escape.
5) Vibration of the chest wall is an indicator of lung compliance, airway patency, and effectiveness of ventilator settings.
   a) Chest wall vibration must be assessed after head position changes to ensure that the jet port of the ETT has not been occluded by the tracheal wall.
   b) Sudden decrease in chest wall vibration may indicate a plugged ETT or a pneumothorax.
6) Vibration may interfere with electrical monitoring of heart rate and respiratory rate.
   a) Use pulse from arterial line or pulse oximeter to monitor heart rate, if necessary.
   b) Spontaneous respiratory rate can be counted and trended if breathing effort is adequate.
7) HFJV ventilation is efficient at CO_2 elimination and at oxygenation.
   a) MAP is the major determinant of oxygenation.
   b) Increasing the PEEP to raise MAP improves oxygenation. Conventional ventilator breaths can be used to recruit lung volume, but PEEP must be high enough to maintain lung volume.
   c) Pressure difference between PIP and PEEP is the major determinant of ventilation.
8) Patients are generally weaned to a low PIP and adequate MAP before being switched to nasal CPAP. Some patients are switched back to conventional ventilation before extubation if nasal CPAP is not tolerated.

m. Complications and problems.
   1) Airway obstruction, which may be indicated by decreased chest wall vibration, increased P_{CO_2}, and decreased servo-pressure.
   2) Air trapping occurs when the HFJV rate is too fast or when too many conventional breaths are used (>5 bpm) or the conventional breaths are too large, or both.

2. High-frequency oscillatory ventilation (HFOV). In the United States, the majority of HFOV is provided by the SensorMedics 3100 (Sensor Medics Inc., Yorba Linda, Calif.). In Canada and the United Kingdom, the Dräger Babylog (Dräger Medical, Lübeck, Germany) HFOV is more commonly used.
   a. Piston, or vibrating diaphragm, moves a small volume of gas toward and then away from the patient.
   b. The amount of gas moved is referred to as the *amplitude*.
   c. Oscillators deliver very little bulk gas. A continuous flow of fresh gas flows past the source that powers the oscillations, producing bias gas flow in a resulting push–pull fashion and thereby eliminating CO_2 buildup and delivering O_2. A low-pass filter allows gas to exit the system while maintaining vibration of gas in the airway.
   d. MAP is governed by the rate of gas flow into the circuit and the resistance to flow out of the circuit (Mammel and Courtney, 2017).
   e. Amplitude is determined by the driving pressure or stroke volume of the piston or vibrating diaphragm.
   f. Proximal airway pressure is monitored by the ventilator, but clinical relevance is questionable because it probably does not reflect alveolar pressure.
   g. HFOV allows for the use of higher MAP with less barotrauma compared with conventional mechanical ventilation and ventilation with small V_T.
   h. Exhalation is active, assisted by the oscillating device.
   i. Oxygenation is determined by MAP. Ventilation (CO_2 removal) is governed by amplitude or MAP.
   j. Indications for use are as follows:
      1) Severe lung disease that is unresponsive to conventional ventilation.
      2) Pulmonary air leaks, pulmonary interstitial emphysema, pneumothorax, and bronchopleural fistula.

3) Pulmonary hypoplasia and diaphragmatic hernia: treated with limited success. HFV can be used to stabilize the condition of these patients.
4) Persistent pulmonary hypertension and meconium aspiration syndrome: treated with mixed results. The improved CO_2 exchange may lead to a respiratory alkalosis that would result in dilation of the pulmonary vascular bed.
5) Failure of conventional mechanical ventilation.

k. Parameters to be set or monitored.
1) MAP: affects oxygenation.
2) Amplitude or stroke volume: size of pressure wave produced by oscillator (another way to describe volume delivered).
3) Fio_2: set on the ventilator as with conventional ventilation.
4) Frequency: 180 to 900 breaths per minute (3 to 15 Hz where 1 Hz = 60 breaths).

l. Patient care and assessment.
1) No special ETT is required.
2) Suctioning procedure is performed as usual. Infants on HFV often benefit from the use of an in-line suctioning device to minimize postsuctioning atelectasis.
3) Chest wall vibration is assessed, rather than breath sounds, to determine the effectiveness of ventilator settings and lung compliance changes. Breath sounds are not audible during HFOV.
4) Vibration may interfere with electrical monitoring of heart rate and respiratory rate.
a) Use pulse from arterial line or pulse oximeter for heart rate monitoring if necessary.
b) Respiratory rate cannot be monitored.
c) Sighs help reduce microatelectasis and improve oxygenation.
5) Complications and problems.
a) Microatelectasis, poor oxygenation.

m. Studies evaluating the use of HFOV have demonstrated mixed results depending on the volume strategy used. A Cochrane review comparing HFOV to conventional ventilation for preterm infants found that in 19 studies involving 4096 infants, elective HFOV resulted in a small reduction in chronic lung disease. Inconsistencies in the protocols used in the studies were thought to explain some of the variation in results (Cools et al., 2015).

Nursing Care During Therapy

A. **Physical assessment.**
1. Observation. One of the most valuable tools in assessing an infant's respiratory status is observation. Does the infant appear to be comfortable while breathing, or does the infant show signs and symptoms of distress by grunting, flaring, and retracting? The Silverman–Andersen score is a screening tool that uses five signs or symptoms to assess respiratory distress in the newborn infant (Fig. 26.7). Assess the skin color of the infant. It should be uniformly pink. Skin color that is blue, dusky, or pale needs to be evaluated further. A dramatic change in skin color needs to be investigated immediately to rule out a pneumothorax versus a mechanical obstruction. Observe the infant's respiratory rate. Is it within the normal range (40 to 60 breaths per

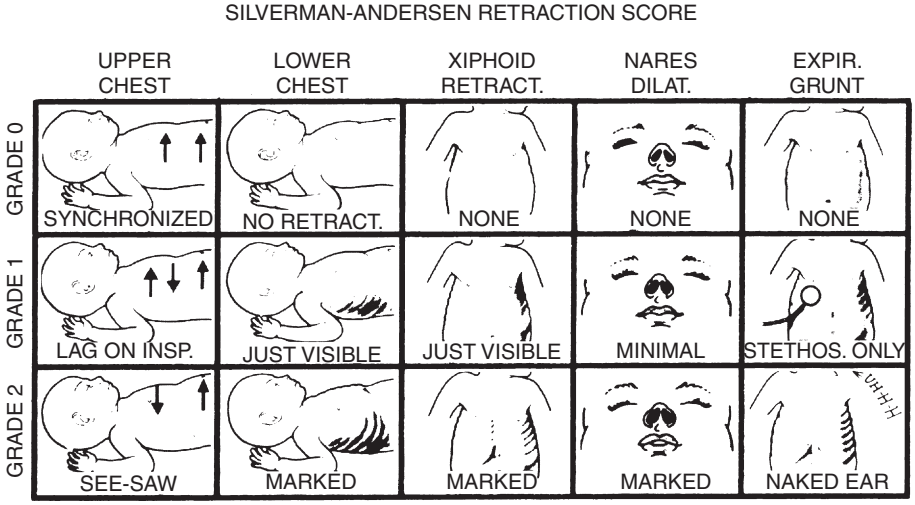

Fig. 26.7 Silverman–Andersen scale to assess respiratory distress in the newborn infant. (Adapted from Silverman, W. A., & Andersen D. H. [1956]. A controlled clinical trial of effects of water mist on obstructive respiratory signs, death rate, and necropsy findings among premature infants. *Pediatrics*, *17*[1], 1–10.)

minute)? When observing the respiratory rate, consider variables such as environment, temperature, and the infant's state of activity or inactivity, which can increase or decrease the respiratory rate. Observe whether the chest rises symmetrically; if asymmetrical, suspect a possible pneumothorax, diaphragmatic hernia, or phrenic nerve palsy. With accidental extubation, chest movement may not be observable or may be decreased from previous observations.

2. Auscultation. Listen to the breath sounds carefully to determine differences in the upper and lower lung fields and differences in the left and right lung fields. Is aeration equal bilaterally? Are fine coarse crackles evident? Are other abnormal sounds audible? A finding in a ventilated infant may be louder breath sounds on the right; if so, suspect that the ETT may have slipped into the right bronchus or that a pneumothorax may have occurred, necessitating evaluation. Rule out other noises and their points of origin. Bowel sounds heard in the chest may be an indication of a diaphragmatic hernia. In the patient receiving HFV, chest wall vibration is an indicator of lung compliance, airway patency, and effectiveness of ventilator settings. Chest wall vibration must be assessed after repositioning. A sudden decrease in chest wall vibration may indicate a plugged ETT or a pneumothorax.
3. ETT observation. Fogging or condensation in the ETT is a sign that the infant is intubated. The condensation occurs on exhalation and is visible in the ETT. Observation of the tube position more than 1 cm from its desired location may indicate extubation or placement in the right mainstem bronchus.
4. Signs of extubation.
   a. Audible crying.
   b. Absent or decreased breath sounds.
   c. Cyanosis.
   d. Bradycardia.
   e. Hypoxemia.
   f. Agitation, restlessness.
   g. Increased abdominal distention.

B. **Equipment function.** All ventilators used for conventional mechanical ventilation should have been approved by the U.S. Food and Drug Administration (FDA) and should display rate (intermittent mandatory ventilation), PIP, PEEP, V_T (where applicable), inspiratory time, I/E ratio, MAP, and O_2 concentration. Ventilators must be plugged into an electrical outlet that provides emergency power in the event of a power failure.
   1. All mechanical ventilators should have the following:
      a. Alarms activated to alert caregivers to ventilator malfunction or disconnection.
      b. Preset pressure-relief valves to ensure against administration of excessive PIP and PEEP.
      c. Frequently scheduled inspections by licensed respiratory therapists.
      d. Ventilator tubing changed routinely per unit policy.
      e. O_2 concentration analyzed routinely and documented in the patient record.
      f. Routine cleaning between patient use.
   2. The following equipment, to be located in the immediate area of all infants requiring mechanical ventilation, should be checked for proper functioning and replaced as needed:
      a. Laryngoscope with blade.
         1) Size 0 for infants weighing less than 3 kg.
         2) Size 1 for infants weighing more than 3 kg.
      b. Sterile ETTs.
         1) Size 2.5 for infants weighing less than 1000 g.
         2) Size 3 for infants weighing 1000 to 2000 g.
         3) Size 3.5 for infants weighing 2000 to 3000 g.
         4) Size 3.5 or 4 for infants weighing more than 3000 g.
      c. Sterile stylet (plastic coated).
      d. Suction tubing and catheters (suction control gauge set at 60 to 100 mm Hg).
      e. Sterile orogastric tubes.
         1) Size 5F or 6F for infants weighing less than 1 kg.
         2) Size 8F for infants weighing more than 1 kg.
      f. Self-inflating bag or anesthesia bag with manometer and mask or T-piece resuscitator capable of delivering blended O_2, and O_2 source.
      g. Tape, scissors.
      h. Carbon dioxide detector.

C. **Noninvasive monitoring.**
   1. All infants receiving O_2 therapy should be considered potential candidates for mechanical ventilation and should be monitored with the following:
      a. Heart rate monitor: audible beat-to-beat capability and alarm device for bradycardia (<100 beats per minute [bpm]) or tachycardia (>180 bpm); should provide a visual display of electrocardiogram and actual heart rate.
      b. Respiratory monitor: visual display of respiratory wave pattern and actual respiratory rate; should include alarm device for apnea and tachypnea. Respiratory rate trend mode is preferred.
      c. Blood pressure monitoring: peripheral (cuff) blood pressure or arterial blood pressure monitoring, performed on a scheduled interval, and documented on the permanent record.
      d. O_2 analyzer: continuous monitoring of O_2 content of the gas delivered to the patient, with mandatory alarm device for O_2 concentration greater than or less than the desired range.
      e. Pulse oximetry: continuous monitoring for critically ill infants; intermittent checks with

documentation of peripheral O_2 saturations indicated for infants not critically ill.

f. Additional requirements for all infants requiring mechanical ventilation, based on clinical condition.
   1) Arterial access (usually via umbilical artery catheter) for:
      a) Blood gas sampling.
      b) Blood pressure monitoring.

2. Pulse oximetry.
   a. Pulse oximetry is a noninvasive and continuous method of measuring hemoglobin O_2 saturation. With the use of red and infrared light, the saturation of hemoglobin bound to O_2 is determined and displayed by a digital readout on the monitoring device. The main advantage of pulse oximetry is the short response time in determining O_2 saturation in a neonate. It also reduces the number of invasive blood gas measurements necessary for a particular infant. It can be used in various settings outside the NICU (e.g., in neonatal transport, delivery room care, and surgery). The alarm device will alert attendants if O_2 saturations are at less or greater than the desired range. **Pulse oximetry does not eliminate the need for blood gas analysis because clinical signs of ventilation and acid–base balance must still be evaluated.**
   b. An accurate reading is dependent on several factors, a primary factor being the perfusion status of the infant. The accuracy of pulse oximetry decreases with low perfusion states. Phototherapy, motion artifact, dyes (ink from footprints), and vasoconstricting drugs (dopamine) can affect saturation readouts. Research has shown that the incidence of severe retinopathy of prematurity in LBW infants can be reduced by lowering the oxygen saturation alarm limits and implementing oxygen targeting guidelines and educational programs (Cayabyab et al., 2016).
3. End-tidal CO_2 monitoring.
   a. Measures CO_2 tension through gas analysis during respiration.
   b. Most accurate when infants have normal lung function and a normal $\dot{V}_A/\dot{Q}$ ratio.
   c. Markedly less accurate in infants with severe lung disease (large alveolar–arterial gradient) and cannot be relied on for accuracy.
   d. May be useful in premature infants with mild to moderate lung disease and in infants with normal lung function.

D. **Blood gas measurement.** Blood gas measurement is the standard method for monitoring oxygenation, ventilation, and acid–base balance in the ill neonate. Different methods are available for obtaining the blood sample, with umbilical arterial catheterization being the most common. Other methods for sampling include the use of indwelling peripheral arterial catheters, intermittent arterial puncture, and capillary sampling. Arterial samples are preferred over capillary samples (heel stick), because arterial samples are more reliable in obtaining an accurate Pa_{O_2} value. Capillary samples are useful for measuring P_{CO_2} and pH in infants with chronic lung disease. All these methods are invasive, with potential for complications (see Chapter 15).

Medications Used During Ventilation Therapy

A. **Surfactant:** a deficiency of surfactant in the lungs of premature infants results in impaired gas exchange and increased work of breathing. Administration of exogenous surfactants is routine in preterm infants with evidence of respiratory distress syndrome. Surfactant therapy may also be indicated for more mature infants with meconium aspiration or pulmonary hypertension (Polin et al., 2014). Exogenous surfactant may be in a natural form taken from the lungs of pigs or calves (Beractant [Survanta], Bovine Lung Exogenous Surfactant, Curosurf, Infasurf) or synthetic surfactant (Surfaxin). Exogenous surfactant is a liquid preparation administered directly into the ETT.
   1. Dose: depends on the product used; approximately 4 or 5 mL/kg.
   2. Administration: ensure that the ETT is in the proper position before beginning surfactant administration. Follow the manufacturer's recommendations regarding positioning for administration.
   3. Monitor continuous cardiac, respiratory, and oxygen saturation during and after administration; frequent vital signs and blood pressure; and ongoing assessment of air entry and chest excursion.
   4. Considerations: infants may become hypoxic, bradycardic, or distressed during surfactant administration. Rapid changes in lung compliance may occur during and immediately after dosing. Changes in lung compliance increase the risk of pulmonary hemorrhage in infants with a PDA.
   5. Endotracheal suctioning is delayed for at least 1 to 2 hours after dosing to avoid removing the drug.
   6. Results: a Cochrane review of natural surfactant use in preterm infants found an improvement in respiratory status and a decreased risk of pneumothorax, BPD, and mortality (Ardell et al., 2015).

B. **Bronchodilators.**
   1. Methylxanthines: theophylline and caffeine citrate are used to stimulate respirations in preterm neonates (see Chapter 25). In addition to improving respiratory drive, methylxanthines increase the

contractility of the diaphragm and enhance chemoreceptor sensitivity to carbon dioxide. Theophylline has largely been replaced by caffeine, which has a lower risk of toxicity.

a. Caffeine: preferred by many clinicians over theophylline because it is given once daily and has fewer adverse effects. Caffeine does not have as great a bronchodilator or diuretic effect as theophylline.
   1) Dose: loading dose, 10 mg/kg of caffeine base; maintenance 2.5 to 5 mg/kg of caffeine base every 24 hours, beginning 24 hours after loading dose (Johnson, 2011).
   2) Serum drug concentrations are not routinely monitored.
   3) Adverse effects: usually well tolerated. Tachycardia, jitteriness, and mild glycosuria may occur at higher serum concentrations.

C. **Diuretics**.

1. Furosemide (Lasix): affects chloride transport in the loop of Henle; causes loss of chloride, sodium, potassium, and calcium. Diuresis may decrease pulmonary blood flow, decrease vascular resistance, and increase pulmonary compliance.
   a. Dose: 1 to 2 mg/kg IV (Kandasamy and Carlo, 2017); a higher oral dose may be required because of reduced bioavailability. Interval: premature infant, every 24 hours; term, every 12 hours; full-term greater than 1 month, every 6 to 8 hours. Long-term therapy: consider a dose every other day.
   b. Monitor: accurate intake and output; specific gravity to evaluate response; frequent electrolyte values to monitor losses and replacement.
   c. Considerations: ototoxic, with transient and permanent hearing losses reported; renal calculi reported with long-term use.
2. Spironolactone (Aldactone): exerts an inhibitory effect of aldosterone on the tubules, with resultant increase in sodium losses and sparing of potassium.
   a. Dose: 1.5 mg/kg/dose every 12 hours by mouth (Kandasamy and Carlo, 2017).
   b. Monitor: accurate intake and output; specific gravity to evaluate response; electrolyte values after 48 to 72 hours to detect hyperkalemia.
   c. Considerations: may cause rash, vomiting, and diarrhea. Use with caution in infant with impaired renal function.
3. Hydrochlorothiazide with spironolactone (Aldactazide): thiazides inhibit sodium reabsorption in the distal nephron, resulting in increased excretion of sodium chloride. Spironolactone is an aldosterone antagonist that helps prevent potassium excretion and hypokalemia.
   a. Dose: 1 to 3 mg/kg/day given as a single daily dose or divided every 12 hours.
   b. Monitor: accurate intake and output when first starting spironolactone, signs of dehydration, serum electrolytes.
   c. Considerations: may cause hyperglycemia or altered glucose tolerance; hypokalemia may result despite the potassium-sparing effect of spironolactone.
4. Chlorothiazide (Diuril) acts on the distal tubule to inhibit chloride reabsorption. It also decreases calcium excretion.
   a. Dose: 10 to 20 mg/kg/day (Kandasamy and Carlo, 2017).
   b. Monitor: accurate intake and output when first starting chlorothiazide; serum electrolytes.

D. **Corticosteroids**.

1. Dexamethasone (Decadron): a long-acting antiinflammatory medication used in the treatment of chronic lung disease and tracheal edema before and after extubation. Studies have documented an increased risk of adverse neurodevelopmental outcomes in infants receiving systemic steroid therapy. These findings have resulted in the following recommendations developed by the American Academy of Pediatrics, Committee on Fetus and Newborn (2010, reaffirmed 2014):
   a. Routine use of corticosteroids for the prevention or treatment of chronic lung disease in LBW infants is not recommended.
   b. Therapy with high-dose dexamethasone is not recommended.
   c. There is not enough evidence to make a recommendation regarding low-dose dexamethasone therapy.
2. Monitor serum and urine glucose, blood pressure, and gastric aspirates for blood. Echocardiogram is indicated if treatment continues longer than 7 days.
3. Considerations: adverse effects—hyperglycemia, glycosuria, hypertension, cardiac effects, sodium and water retention, poor weight gain, hypokalemia, hypocalcemia, and increased risk of sepsis.

E. **Paralytic agents.**

1. Pancuronium (Pavulon): pharmacologic relaxation/paralysis of the skeletal muscle to promote improved mechanical ventilation with improved oxygenation/ventilation, decreased barotrauma, decreased fluctuations in cerebral blood flow.
   a. Dose: 0.04 to 0.15 mg/kg IV push. Interval: every 1 to 4 hours as needed for paralysis (Kandasamy and Carlo, 2017).
   b. Monitor vital signs, including blood pressure, continuously.
   c. Considerations: mandatory use of mechanical ventilation, adequate pulmonary toilet mandatory because no swallow or gag reflex is present, eye lubricant necessary. Signs of toxicity: tachycardia, hypertension, or hypotension.

2. Vecuronium (Norcuron): similar to pancuronium but shorter acting. Dose: 0.03 to 0.15 mg/kg IV push every 1 to 2 hours as needed for paralysis. Can be given by infusion at a dose of 0.05 to 0.1 mg/kg/hr (Kandasamy and Carlo, 2017).

F. **Pain control/sedation** (see Chapter 16).

G. **Inhaled nitric oxide (iNO):** Endogenous nitric oxide is released from the endothelium and is responsible for vascular smooth muscle relaxation. iNO is used to promote relaxation of the pulmonary smooth muscle to facilitate perfusion of the lung and gas exchange. iNO has been approved by the FDA for the treatment of late preterm, near-term, and term infants with persistent pulmonary hypertension of the newborn (Gardner et al., 2016). Use of iNO in preterm infants less than 34 weeks remains experimental.
   1. Dose: initial 20 parts per million (ppm); after 4 hours, reduce dose to 6 ppm. iNO is then weaned in a stepwise fashion to a dose of 1 ppm before discontinuation (Kinsella, 2017).
   2. Duration of therapy: usually less than 5 days.
   3. Monitor vital signs, including blood pressure, continuously; also complete blood count, methemoglobin levels, and environmental levels of nitric oxide.
   4. Considerations: may cause methemoglobinemia, decreased platelet aggregation.
   5. Term, near-term, and late preterm infants—significant reduction in the need for extracorporeal membrane oxygenation (ECMO) (Barrington et al., 2017). A Cochrane review concluded that enough evidence exists to recommend iNO for this population of infants with hypoxic respiratory failure who do not have a diaphragmatic hernia (Barrington et al., 2017).
   6. Premature infants: a meta-analysis of iNO in preterm infants demonstrated a significant reduction in the risk for BPD (Yang et al., 2016).

Weaning From Conventional Ventilation

A. **Indications**.
   1. Clinical status of infant consistent with beginning resolution of pulmonary condition.
   2. Ventilation becomes easier with less support and may result in hypocapnia.
   3. Less inspiratory pressure is required to achieve desired Vt.

B. **Techniques**.
   1. Physical assessment of respiratory status: breath sounds, aeration, chest wall excursion, and spontaneous respiratory rate. Physical assessment of cardiovascular status: color, perfusion, heart rate, pulses, blood pressure, and presence or absence of murmur. Physical assessment of neurologic status: presence of spontaneous respirations, tone, irritability, and reflexes.
   2. Radiographic evaluation: useful in documenting improved lung status and absence of pathologic changes.
   3. Laboratory analysis: fluid, electrolyte, and hematologic stability.
   4. Blood gas analysis: primary information for weaning an infant from conventional mechanical ventilation. If all other assessments indicate improvement, blood gas analysis provides information about the appropriate ventilator settings to adjust. To decrease the Pao_2, alter the Fio_2 or the MAP: reduce PIP, I/E time ratio, or PEEP. To increase $Paco_2$, decrease ventilation: decrease rate or Vt. During weaning, it is important to try to decrease the most injurious parameters first. Toxic effects from free O_2 radicals damage lung tissue, and O_2 is associated with retinopathy of prematurity. Therefore, it is important to keep O_2 use at a minimum. PIP, PEEP, I/E time ratio, and rate are all associated with barotrauma, so weaning should be achieved as soon as possible.
   5. Extubation score: in an effort to facilitate weaning and extubation from mechanical ventilation, a variety of scoring tools have been developed. Recent work has focused on validating cardiorespiratory behavior gathered and analyzed through monitoring equipment (Shalish et al., 2017).

C. Extubation from mechanical ventilation. When low ventilator parameters have been achieved (intermittent mandatory ventilation, 10 to 20/minute; PIP, 14 to 18 cm H_2O; Vt 3.5 to 5 mL/kg; Fio_2, 21% to 30%), the infant should be evaluated for extubation. Some infants may need a transition to nasal CPAP, nasal prong, cannula, or O_2 hood.

NURSING CARE DURING THE WEANING PROCESS

A. **Airway management, equipment function, and monitoring of the infant do not change during the weaning process.**

B. **Frequent assessment of the infant's vital signs, blood pressure, O_2 saturation, and neurologic status is essential.** Documentation of this assessment will facilitate appropriate changes in ventilator support.

C. **Be alert for decompensation of respiratory or cardiovascular status during this time, and notify the appropriate personnel when necessary.**

D. **Preparation for extubation.**
   1. Equipment for reintubation available at the bedside.
   2. Suction of ETT and oropharynx.
   3. Postextubation equipment ready for use.
   4. Blood gas determination after extubation, if warranted.
   5. X-ray examination of chest to rule out atelectasis if decompensation occurs.
   6. Frequent physical assessment every 1 to 2 hours after extubation for 24 hours.

7. Frequent position changes; suctioning as needed.
8. Explanation of the plan and process to the family before extubation.

Interpretation of Blood Gas Values

The purpose of obtaining blood gas values is to determine whether the patient has adequate ventilation and perfusion. Blood gas values also facilitate analysis of oxygenation and acid–base status. Oxygenation is determined by the Pao_2 value. The Pao_2 is the amount of O_2 dissolved in the serum—3% of the total O_2 content. The remainder of the body's O_2 is bound to hemoglobin. Acceptable arterial blood gas values are illustrated in Table 26.1. Capillary Pao_2 reliability is uncertain. The value is lower than with an arterial specimen. Acid–base balance is indicated by the pH and the base deficit or excess. Ventilation is measured by Pco_2.

A. **Acidosis and alkalosis.** Changes in the pH from the normal range indicate a change in the acid–base status of the infant. An elevated pH, greater than 7.45, is alkalosis, which is caused by excess base or decreased acid level in the blood. A decreased pH, less than 7.35, is acidosis, which is caused by decreased base or increased acid level in the blood.
   1. Respiratory acidosis ($Paco_2$ >45 mm Hg; pH <7.35), caused by the accumulation of CO_2, the respiratory acid, results from hypoventilation.
   2. Respiratory alkalosis ($Paco_2$ <35 mm Hg; pH >7.45), caused by the decrease of CO_2, results from hyperventilation.
   3. Metabolic alkalosis (HCO_3^- >26 mEq/L, base excess >+2, pH >7.45) is caused by a failure to excrete HCO_3^-, which is controlled by kidney function.
   4. Metabolic acidosis (HCO_3^- <22 mEq/L, base deficit >−2, pH <7.35) is caused by failure to retain HCO_3^- or by an increase in blood acid, which is controlled by the kidney.
   5. For causes of acidosis and alkalosis, see Table 26.2.

Table 26.1

Normal Arterial Blood Gas Values

pH	7.35 to 7.45
$Paco_2$	35 to 45 mm Hg
Pao_2	50 to 80 mm Hg
HCO_3^-	22 to 26 mEq/L
Base excess	−2 to +2

Part 3

Table 26.2

Causes of Acidosis and Alkalosis

Cause	Mechanism
Respiratory Acidosis (↑ $Paco_2$, ↓ pH)	
CNS depression	Maternal narcotics during labor, asphyxia, intracranial hemorrhage, neuromuscular disorder, CNS dysmaturity (apnea of prematurity)
Decreased ventilation–perfusion ratio	Obstructed airway, meconium aspiration, choanal atresia
Decreased lung compliance	Respiratory distress syndrome, pulmonary insufficiency, diaphragmatic hernia
Injury to the thorax	Phrenic nerve paralysis, pneumothorax
Metabolic Acidosis (↓ HCO_3^-, pH, and Base Deficit [Negative Value])	
Decreased tissue perfusion	Increased lactic acid production
Sepsis, congestive heart failure	Increased lactic acid production
Renal failure	Increased organic acids
Renal tubular acidosis	Renal loss of base
Diarrhea	Gastrointestinal loss of base
Respiratory Alkalosis (↓ $Paco_2$, ↑ pH)	
Iatrogenic	Excessive mechanical ventilation
Hypoxemia	Increase in alveolar ventilation
CNS irritation (pain)	Increase in alveolar ventilation
Metabolic Alkalosis (↑ HCO_3^-, pH, and Base Excess [Positive Value])	
Gastric suction	Loss of acid
Vomiting	Loss of acid
Diuretic therapy	Renal losses of H^+ ion
Iatrogenic	Administration of HCO_3^- (base added)

CNS, Central nervous system.

B. **Disorders of acid–base balance (see** Chapter 8**).**
C. **Interpreting a blood gas value.**
   1. Evaluate the pH. Is there an acidosis or an alkalosis?
   2. Evaluate the $PaCO_2$. If it is not normal, does it contribute to the acid–base status? Or is it a compensating factor?
   3. Evaluate the HCO_3^- and the base excess or deficit. If they are not normal, do they contribute to the acid–base status? Or are they compensating factors?
   4. Evaluate the PaO_2. Is there hypoxia or hyperoxia?
   5. From this information, you can attempt to identify the specific cause of the abnormal acid–base status and treat as indicated.

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CHAPTER 27

Extracorporeal Membrane Oxygenation

Leigh Ann Cates-McGlinn

OBJECTIVES

1. Examine briefly common neonatal extracorporeal membrane oxygenation (ECMO) pathophysiology.
2. Discuss indications and contraindications for neonatal ECMO.
3. Discuss the criteria used to determine an infant's need for neonatal ECMO.
4. Examine common perfusion techniques in neonatal ECMO.
5. Review the technical and mechanical aspects of the neonatal ECMO procedure.
6. Review the physiology of neonatal extracorporeal circulation.
7. Discuss the general care given to infants undergoing the ECMO procedure and the support provided to their families.
8. Review follow-up and outcome of neonatal ECMO survivors.

ECMO: A Historical Perspective

Extracorporeal life support (ECMO) was developed initially by surgeon John Gibbon as a heart–lung bypass machine for use in adult open heart surgeries. Currently, neonatal ECMO has been in use for over four decades and has transitioned from a rarely utilized lifesaving modality to a routine practice in major children's centers across the nation. Employed initially to manage newborn respiratory failure in 1975 (Fortenberry and Lorusso, 2017), neonatal ECMO presently aids in the management of multiple pathologies from cardiac anomalies to overwhelming sepsis. In fact, the Extracorporeal Life Support Organization (ELSO), founded in 1989, has created a national registry for ECMO cases; ELSO reported in 2017 that almost half of the over 78,397 ECMO cases were newborns (Thiagarajan et al., 2017). With this increase in use and understanding, survival rates have improved with advancements in neonatal ECMO technology, including membrane lungs, safe centrifugal pumps, and vascular access. There has been a shift resulting in nearly half of the neonatal ECMO centers using centrifugal pumps and polymethylpentene (PMP) oxygenators (Lawson et al., 2011).

A. ELSO International Registry report.
   1. Since 2009 there has been a 55% increase in neonatal ECMO centers, resulting in a total of 467 ECMO centers worldwide. Survival to discharge was as follows: meconium aspiration syndrome (MAS), 93%; persistent pulmonary hypertension of the newborn (PPHN)/persistent fetal circulation, 74%; respiratory distress syndrome/hyaline membrane disease, 79%; sepsis, 55%; congenital diaphragmatic hernia (CDH), 50%; and other diagnoses, 59% (Barbaro et al., 2017).
   2. Since 2009 the number of neonatal ECMO cases totals 38,859, with 30,062 of respiratory origin, 7243 cardiac in nature, and 1554 in support of cardiopulmonary resuscitation. The survival rate has declined from 75% in 2012 to 61%. This decline in both cases and survival reflects a change in the kinds of neonates who require ECMO support, having failed the more sophisticated ventilator management, surfactant, and use of inhaled nitric oxide that is currently standard practice (Barbaro et al., 2017).

B. **Current technology.**
   1. In 2008 roller pumps began to be replaced by safer centrifugal pumps (Toomasian et al., 2017).
   2. A new generation of membrane lungs developed: PMP oxygenators.
   3. Increased capabilities of vascular access.

Common Neonatal ECMO Pathophysiology

When discussing neonatal ECMO, the practitioner must keep in mind a strong understanding of fetal circulation, including the three primary shunts: the ductus venosus, patent ductus arteriosus (PDA), and patent foramen ovale (PFO). Additionally, the practitioner should have a firm understanding of the most common disease processes associated with the utilization of neonatal ECMO, including but not limited to the management of the underlying pulmonary hypertension related to sepsis, MAS, pneumonia,

CDH, or idiopathic PPHN (Short and Soghier, 2017). Pulmonary hypertension in the newborn period is characterized by elevated pulmonary vascular resistance forcing deoxygenated blood to shunt right to left through a PDA or PFO. Subsequently, there is mixing of oxygenated and deoxygenated blood in the aorta followed by systemic hypoxia and acidosis, resulting in a persistent state of increased pulmonary vascular resistance (Short and Soghier, 2017). Pulmonary vascular resistance can be decreased primarily through an increase in arterial oxygenation (Pao_2), use of nitric oxide, and a correction in acidosis. Additionally, the patient may require correction of polycythemia, hypocalcemia, and systemic hypotension, as well as the need for gentle ventilation and sedation. Once these methods have been employed and failed, the patient may require being placed on ECMO (Short and Soghier, 2017).

Criteria for Use of ECMO

The goal is to properly identify patients who would benefit from ECMO while simultaneously limiting those patient populations in which the potential risks outweigh the benefits. Thus, inclusion criteria were developed to aid centers in ECMO candidate selection. These criteria are guidelines and are not mandates (Suttner, 2017).

A. **Neonatal ECMO patient criteria.**
   1. Gestational age greater than 34 weeks.
   2. Birth weight greater than 2000 g; small-for-gestational-age infants should not be excluded. This guideline is the most debated. There are recent reports of placing patients less than 2 kg on ECMO, but survival rates were significantly lower (Suttner, 2017).
   3. Reversible lung disease.
   4. No significant coagulopathy or uncontrolled bleeding—if present, this should be corrected before initiating ECMO, if possible.
   5. Intracranial hemorrhage grade 2 or less (must monitor more closely).
   6. Failure of optimal medical management.
   7. No lethal anomalies or brain injuries.
   8. No major cardiac malformations (except in infants requiring stabilization and life support before or after surgery).
   9. Must have decision to provide "full support" (Suttner, 2017).

B. **Acute and reversible pathology.**
   1. Respiratory distress syndrome (RDS).
   2. MAS.
   3. PPHN.
   4. CDH.
   5. Sepsis/pneumonia.
   6. Life support before or after cardiac surgery.

C. **Cranial and cardiac ultrasonography findings** ruling out severe intracranial hemorrhage and cyanotic congenital heart disease.

Box 27.1

Neonatal ECMO Patient Qualifying Criteria

Alveolar–Arterial Difference in Partial Pressure of Oxygen ($AaDo_2$):

600 to 624 mm Hg for 4 to 12 hours at sea level

$$AaDo_2 = \frac{\text{Atmospheric pressure} - 47 - (Paco_2 + Pao_2)}{Fio_2}$$

Note: 47 is the partial pressure of water vapor.

Oxygenation Index (OI):

≥40 for 30 minutes to 6 hours or >20 without improvement (>24 hours) on maximal medical therapy or persistent episodes of decompensation

$$OI = \frac{MAP \times Fio_2 \times 100}{Pao_2}$$

where MAP is mean airway pressure.

Pao_2:

<40 mm Hg for 2 to 12 hours—unresponsive to intervention

Acute Deterioration

pH ≤7.25 for 2 hours or more

Intractable hypotension

From Suttner, D. M. (2017). Indications and contraindications for ECLS in neonates with respiratory failure. In T.V. Brogran, L. Lequire, R. Lorusso, G. MacLaren, & G. Peek (Eds.), *Extracorporeal life support: The ELSO red book* (5th ed., pp.151–158). Ann Arbor, MI: Extracorporeal Life Support Organization.

D. **Objective criteria for final selection predictive of greater than 80% mortality rate** (Box 27.1). To achieve specificity, each ECMO center must determine its own mortality indicators and criteria. Criteria may differ in different disease states, such as septic shock, CDH, or severe air leak caused by barotrauma.

E. **Pre-ECMO stabilization, including optimal ventilatory management and trial of high-frequency ventilation, volume support, vasopressors, vasodilator medications, surfactant, and nitric oxide if indicated.** These should be used at a center where ECMO can be initiated quickly if the infant does not respond adequately (Suttner, 2017).

ECMO Perfusion Techniques

Before placing a patient on ECMO, a multidisciplinary team must decide what modality of perfusion delivery will be best for the patient and the patient's particular disease

process. The two most common approaches are venoarterial (VA) and venovenous (VV). VA support, the most widely used ECMO modality in the United States, is a technique whereby the cannulas are inserted to permit drainage of deoxygenated blood from a large vein or veins (Heard et al., 2010). Subsequently, the blood is circulated through an artificial lung for oxygenation and returned to the body through a major artery such as the aorta. Conversely, VV ECMO utilizes only the venous system for both drainage and return of blood to the patient, yet can be converted to VA ECMO if the patient requires it (Davis and Walker, 2017). See Table 27.1 for a comparison of VA and VV ECMO.

Circuit Components and Additional Devices

Neonatal care and equipment are constantly being modified and improved. Rather than use the circuits utilized for short runs of cardiac bypass, novel biocompatible circuits are emerging. In addition, over 50% of neonatal centers have shifted away from traditional roller pumps to the use of centrifugal pumps controlled by highly advanced, computerized, servo-regulated systems (Lawson et al., 2011). Finally, vascular access cannulas are being improved to provide reliable care and enhance outcomes.

Table 27.1

Comparison of VA and VV ECMO

	VA Perfusion	VV Perfusion
Technique	• Deoxygenated blood is drained from the right side of the heart through a cannula placed in the RA via the right internal jugular vein • Oxygenated blood is returned through a cannula placed into the ascending aorta via the right common carotid artery • Achieves approximately 60% to 80% of normal cardiac output (Heard et al., 2010)	• Deoxygenated blood is drained from the venous limb, positioned in the RA • Blood returned through the arterial limb in RA, with side holes positioned at the tricuspid valve • Blood flow is directed across the valve, into the RV, through pulmonary circulation. • Blood returns to the LA before entering the systemic circulation via the aorta
Cannula specifics	• Venous cannula size must deliver pump flow range of 80 to 150 mL/kg/min • Cannulas of largest possible internal diameter 8F to 14F • May also use 16F on babies larger than 3.4 kg (Davis and Walker, 2017) • Must use a cannula that is reinforced if using a centrifugal pump to handle the negative pressures generated	• Double-lumen cannula 12F, 14F, or 15F
Advantages	• Provides both respiratory and cardiac support by decompressing pulmonary circulation • Decreases pulmonary artery and pulmonary capillary filtration pressure • Supports circulation by augmenting the pumping action of the heart • Positive pressure ventilation can be reduced to minimal parameters • PIP 15 to 25 cm H_2O • PEEP 4 to 5 cm H_2O • RR 10 to 20/minute • Fio_2, 21% to 30%	• No ligation of the carotid artery is necessary • Oxygenated blood flows through pulmonary circulation, which may help reverse pulmonary hypertension • Oxygenated blood is provided to the coronary arteries • Emboli (air or particulate) are less likely to result in severe compromise to the infant because blood is not returned directly to the arterial circulation • May eliminate potential for left ventricular cardiac stun (Guiang, 2015)
Disadvantages	• Emboli (air or particulate) could be infused directly into the arterial circulation • Ligation of carotid artery may be permanent and subsequently affect cerebral perfusion • Greater potential for left ventricular cardiac stun (Beke et al., 2014) • Increased incidence of neurologic events (Tinku, 2016)	• Can be used only with adequate cardiac function—systemic flow is dependent on cardiac output • In the event of cardiac stun or decreased function, emergent conversion to VA ECMO may be needed • Recirculation of oxygenated blood can occur • Oxygenated blood returned to the RA may be emptied again into the venous side of the double-lumen cannula, rather than across the tricuspid valve • Use of somewhat higher ventilatory support may be required because lower flow rates are achieved with the smaller lumens of the double-lumen cannula • Vasopressor therapy may need to be continued to support blood pressure and ECMO flow • Greater potential for RV cardiac stun (Guiang, 2015)

ECMO, Extracorporeal membrane oxygenation; Fio_2, fractional concentration of oxygen in inspired gas; *LA*, left atrium; *PEEP*, positive end-expiratory pressure; *PIP*, peak inspiratory pressure; *RA*, right atrium; *RR*, respiratory rate; *RV*, right ventricle; *VA*, venoarterial.

A. The **ECMO circuit** (Fig. 27.1).
   1. The ECMO circuit consists of polyvinyl chloride tubing, Luer-Lock connectors, stopcocks, and infusion sites. The tubing is made more flexible by a plasticizer known as Diethylhexylphthalate (DEHP). There is concern for preterm, specifically male, neonates, on their reproductive systems, and thus non–DHEP-containing circuits should be used on male neonates when available (Center for Devices and Radiological Health, 2001).
   2. Some manufacturers have developed surface bonding materials for circuit tubing and cannulas to minimize the activation of complement, platelets, and inflammatory mediators, and these are thought to be less thrombogenic (Murphy et al., 2015).
   3. Blood circulates throughout all components of the ECMO circuit; parenteral fluids, medications, and blood products are administered into the venous side of the circuit (before the membrane oxygenator).
   4. Only platelets are infused on the arterial side of the circuit, or into the patient directly, to prevent adherence to the membrane oxygenator.
   5. Precautions and guidelines for placing medications and blood products into the circuit are the same as those for safely administering medications and blood products directly to patients.

B. **Pumps** (Table 27.2).
   1. Roller/occlusive: uses the principle of fluid displacement utilizing two rollers placed opposite one another to pull blood from the right atrium and

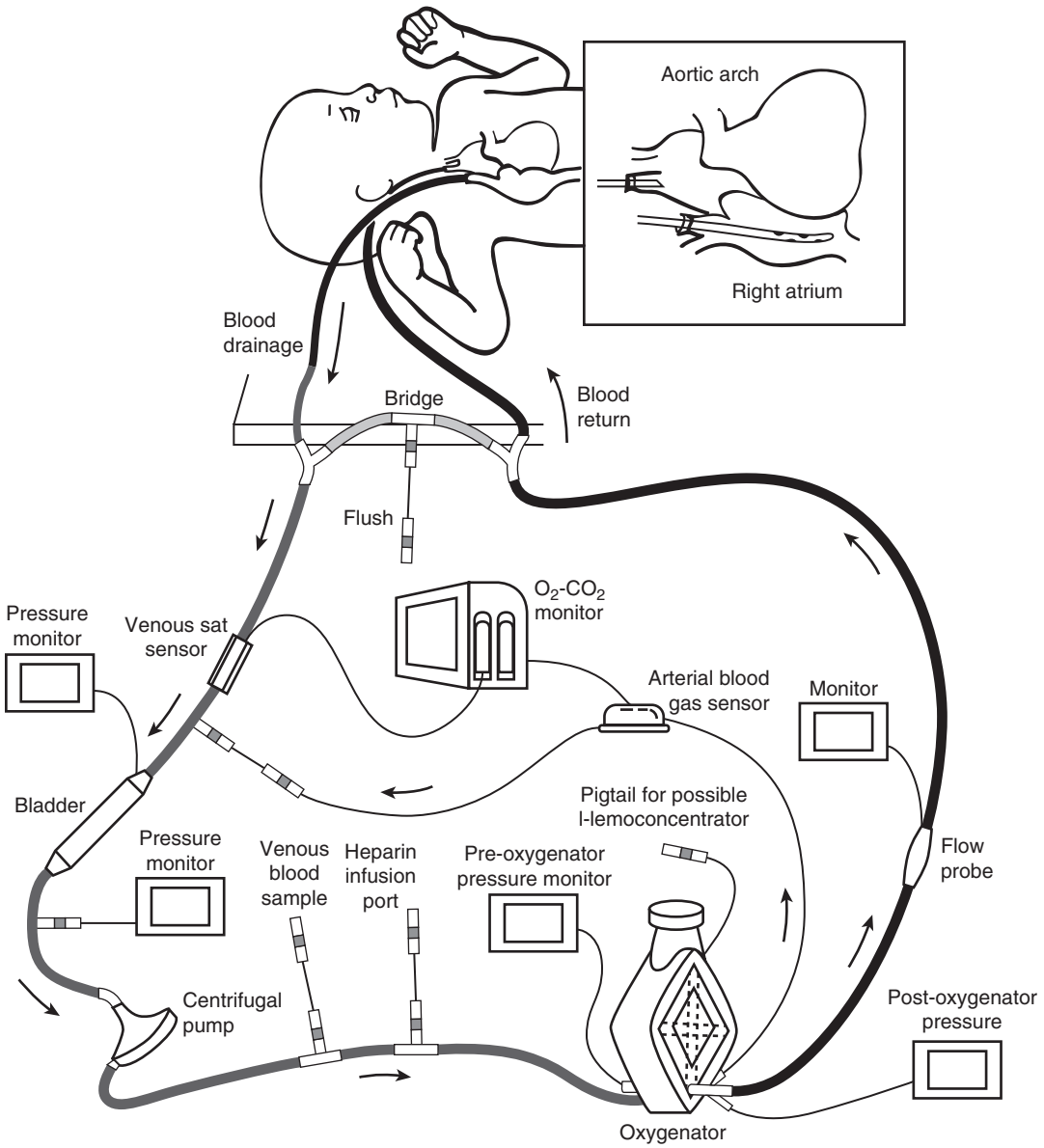

Fig. 27.1 Configuration of neonatal centrifugal ECMO circuit. (Adapted with permission from Short, B., & Williams, L. [Eds.]. [2010]. *ECMO specialist training manual* [3rd ed.]. Ann Arbor, MI: Extracorporeal Life Support Organization.)

Table 27.2

Comparison of ECMO Pumps

	Roller/Occlusive Pump	Centrifugal
Process	Uses two rollers to pull blood from RA and push blood through the circuit's tubing	Uses constrained vortex in which an object spins in a fluid environment
Flow regulation	Venous return to collapsible bladder and servo-control	The device's RPMs
Major limitation	Inadequate venous return to bladder causes pump to stop	Potential for very high negative pressures resulting in ICH in neonates
Advantages	Manual operation (power failure) Reduced cost Less initial blood for priming circuit Flow independent of patient afterload Increased provider experience	Manual/short-term battery (power failure) Decreased provider experience
Disadvantages	Discharge of plastic particles: emboli Requires servo-regulation Total delivered pressure critical Limited circuit availability	Inaccuracy of flow measurements at low RPMs

ICH, Intracranial hemorrhage; *RA*, right atrium; *RPM*, revolutions per minute.

push blood forward through the circuit's tubing (Toomasian et al., 2017).

a. Servo-regulation of venous return: bladder reservoir, pressure monitoring with roller pump.
b. Collapsible silicone bladder distends with returning venous blood.
c. If using a roller head pump, inadequate flow (decreased venous return) into the ECMO circuit causes the bladder to collapse, which triggers a microswitch and an audible alarm and stops the roller head pump.
d. When the bladder re-expands, the microswitch engages the pump and normal pump operation continues.
e. Adequate venous return is critical for maintaining cardiorespiratory support; therefore, the cause of decreased return must be recognized and corrected immediately.
f. Servo-mechanism regulation of ECMO flow can also be achieved by transducers placed in the circuits. Premembrane (venous) pressure and postmembrane (arterial) pressure may be monitored continuously to signal extracorporeal flow problems before collapse of the silicone bladder. This allows for early detection and timely intervention.
    1) Fall in premembrane pressure indicates decreased venous return.
    2) Rise in postmembrane pressure indicates malfunction of membrane oxygenator or heat exchanger.
g. Other devices have been recently introduced to regulate venous flow, including a thin-walled section of tubing encased in a rigid housing that is mounted vertically in the circuit and does not have the clotting issues associated with the conventional silicone bladder (Toomasian et al., 2017).
h. Advantages.
    1) Can be operated manually in case of power failure.
    2) Lower cost.
    3) Less initial volume of blood needed to prime circuit.
    4) Flow not dependent on patient's afterload status.
    5) Used for more than 20 years and can equate to greater experience and comfort level of ECMO providers.
i. Disadvantages.
    1) The discharge of plastic particles into the patient's circulatory system resulting in embolization.
    2) Requires use of servo-regulated bladder box or pressure servo-regulator.
    3) Total pressure delivered by the rollers to the circuit is critical in delivery calculations.
    4) Limited availability of circuits due to transition of many ECMO centers to the centrifugal pump.

2. Centrifugal/constrained vortex/nonocclusive pump: works on the principle of a constrained vortex in which an object spins in a fluid environment. The spinning results in an area of low pressure at the nucleus of the vortex, and an area of high pressure results at the periphery. The centrifugal pump contains a plastic housing composed of a single inlet located in the center low-pressure region and outlet positioned along the high-pressure outer border (Toomasian et al., 2017).

a. Advantages.
   1) Flow manipulated by the device's revolutions per minute (RPMs—the rate at which the pump spins).
   2) If the patient's volume fluctuates, the RPMs remain steady, resulting in less negative (volume decrease) or positive pressure (volume increase) on the atrium.
   3) Can be operated by hand or short-term battery backup.
b. Disadvantages.
   1) Inaccuracy of flow measurements at low RPMs.

C. **Gas-exchange devices.**
1. Silicone membrane oxygenator—made of a solid silicone polymer membrane envelope with a plastic space screen that is wrapped spirally around a spool; encased in a silicone rubber sleeve.
   a. Maximizes gas exchange across the membrane.
   b. Only oxygenator currently approved by the U.S. Food and Drug Administration for long-term use.
   c. No direct blood-to-gas interface.
2. Polypropylene (microporous) hollow-fiber oxygenator—contains small tubes with tiny pores through which gas exchange takes place (Toomasian et al., 2017).
   a. Potential advantage during priming; can have bioactive coating.
   b. Direct blood-to-gas interface.
   c. Designed for short-term use (≈2 hours).
   d. Good for rapid response scenarios.
3. PMP hollow-fiber oxygenator—contains microporous tubes with tiny pores through which gas exchange takes place (Toomasian et al., 2017).
   a. Potential advantage during priming; can have bioactive coating.
   b. Direct blood-to-gas interface.
   c. Can be used for up to 6 hours.
   d. Good for rapid-response scenarios.

D. **Heat exchanger.**
1. Located after the oxygenator or incorporated into the oxygenator.
2. Can add or subtract heat from the blood before returning it to the infant's circulation.
3. Heat loss occurs from cooling effect of ventilating gases inside the oxygenator and circuit exposure to ambient air temperature.
4. Important for maintenance of homeostasis of clotting functions and physiologic functions.

E. **The ECMO console.**
1. Monitors circuit pressure on both the venous and arterial sides of the circuit.
2. Provides bubble detection.
3. Thorough automated alarm system, including servo-regulation of the pump when aberrant conditions are discovered.

F. **Bubble detector.**
1. Placed beyond the heat exchanger to detect air in blood flowing through the arterial side of the pump as the blood is returned to the patient.
2. In some systems, when air is detected, the roller head pump is shut off and flow to the patient ceases.
3. Critical importance in VA ECMO.

G. Activated clotting time (ACT) monitoring.
1. Because heparin is used to prevent clotting, ACT is the most common bedside method to measure anticoagulation in the ECMO patient (Murphy et al., 2015).
2. Use to titrate heparin infusion based on ECMO center's desired ACT ranges and required effects.
3. Initial bolus of heparin during cannulation (usually 100 units/kg).
4. Infusion pump for continuous infusion of heparin solution at 25 to 100 units/kg/hr into ECMO circuit.
5. Titration of heparin solution to keep ACT within the desired range (usually 180 to 220 seconds, but acceptable at 160 to 250 seconds).
6. For control of heparin administration, no heparin added to any other medications or fluids (an exception may be the fluids being infused into umbilical or peripheral arterial lines).
7. Factors that influence heparin requirements: thrombocytopenia, abnormal clotting studies, urinary output, and infusions of blood products that contain clotting factors.

H. **Blood gas monitoring.**
1. Mixed venous oxygen saturation (Svo_2), monitored continuously, is the optimal parameter to assess tissue oxygen delivery. It can be measured through fiberoptic catheters or by using optical reflectance technology. Correlation with co-oximeter values measured by a blood gas machine is required.
2. Arterial blood gas measurements obtained beyond the membrane oxygenator in the ECMO circuit reflect the function of the membrane lung.
3. Patient blood gas values and noninvasive oxygen saturation monitoring are used to assess the recovery of lung function and the infant's acid–base balance.

I. **Cannulas**.
1. Cannulas are surgically placed in large blood vessels to remove deoxygenated venous blood and return oxygenated blood to the circulation.
2. Before insertion of the cannula, the infant is paralyzed and given opiates to prevent respiratory movement and air embolism, and systemic heparin is given to prevent clotting of the cannulas and the circuit; this is because when circulating blood comes into contact with artificial surfaces, coagulation is activated (Davis and Walker, 2017).

3. In VA ECMO, the venous cannula tip is positioned in the right atrium to drain blood flow from the inferior vena cava and the superior vena cava. The arterial cannula tip reaches just to the aortic arch.
4. In VV ECMO, the double-lumen cannula is commonly placed in the internal jugular vein and is positioned in the right atrium, with the arterial side directed toward the tricuspid valve.
5. Double-lumen cannulas are now available that could potentially avoid cannulation of two vessels to avoid the carotid artery (Davis and Walker, 2017).

J. **ECMO transport.**
Patients can be transported on ECMO both within an ECMO center and between two facilities. Because of the extreme risks and technical difficulty involved, extensive planning and coordination of a highly skilled team are required.
1. There may be several reasons to transport a patient on ECMO from one facility to another, including delivery at a non-ECMO center or need for interventions not provided at the current ECMO center.
2. Cannulation and subsequent ECMO transport at a non-ECMO center poses the most risk, such as issues with oxygen delivery, mechanical ventilation, and electrical complications (Blum et al., 2017). There is also the added complication of movement of an extremely fragile patient in an unfamiliar environment. Finally, because of the extreme high-risk nature, there are very few teams, such as the Wilford Hall United States Airforce Medical Center, that provide remote neonatal cannulation and transport on ECMO.
3. Interfacility transport on ECMO may be required. The most common occurrences being EXIT to ECMO, where the fetus is delivered and cannulated to ECMO before umbilical cord separation, such as with prenatal diagnosis of severe CDH. Additionally, there may be a need to perform vital diagnostic or therapeutic interventions at delivery or postoperatively (Frenckner et al., 2017).

Physiology of Extracorporeal Circulation

The primary goal behind ECMO is to sufficiently supply the body with oxygen so that metabolic requirements are met while removing subsequent waste by-products from the body (Bartlett and Conrad, 2017). The body naturally exchanges gases at the alveolar and tissue levels. Oxygenation of the blood is achieved during ECMO through the use of a membrane oxygenator. The arterial partial pressures of oxygen (Pao_2) and carbon dioxide (CO_2) are the primary forces in the diffusion of gases across the membrane. CO_2 exchange is independent of blood flow and dependent on gas diffusion gradient, sweep gas flow rate, and membrane surface area. Conversely, Pao_2 is independent of sweep gas flow rate, yet dependent on blood flow rate, blood path thickness, membrane diffusion thickness, Pao_2 concentrations, and membrane surface area. ECMO improves Pao_2 delivery by improving Pao_2 content through stabilization of the saturation of hemoglobin, taking 60% of the cardiac output away from native lung, and providing a stable source of delivery via the membrane oxygenator (Bartlett and Conrad, 2017).

A. **Blood flow.**
1. VA bypass is instituted by draining venous blood into the ECMO circuit; a like amount of oxygenated blood is returned to the arterial circulation.
2. As bypass flow increases, flow through the pulmonary artery decreases faster than bypass flow and reduces total flow in the systemic circulation, causing peripheral and pulmonary hypotension.
3. Blood volume replacement is required for optimal tissue perfusion.
4. ECMO perfusion is nonpulsatile (pulse contour decreases as flow rate increases); kidneys interpret this as inadequate flow and promote the release of renin and aldosterone, which causes sodium retention, extracellular fluid expansion, and a decreased total body potassium concentration.
5. Total patient flow is the sum of ECMO flow and pulmonary blood flow; adequate flow is reached when oxygen delivery and tissue perfusion result in normoxia, normal pH, normal Svo_2, and normal organ function.
6. Total gas exchange and support are achieved at a flow rate of 120 to 150 mL/kg/min.

B. **Gas exchange.**
1. Oxygen diffuses into the blood because of a pressure gradient between the elevated oxygen pressure in the gas compartment and the low oxygen pressure in the venous blood.
2. Carbon dioxide diffuses from the blood compartment to the gas compartment as a result of a pressure gradient between venous carbon dioxide pressure and the ventilating gas. The carbon dioxide transfer rate is 6 times greater than that of oxygen transfer. The ventilating gas mixture is usually enriched with carbon dioxide to prevent hypocapnia.

C. **Blood–surface interface.**
1. During ECMO, up to 80% of the cardiac output is exposed to a large artificial surface each minute.
2. Clot formation is prevented by systemic heparinization; platelet destruction is minimized by preexposure of the circuit to albumin.
3. Platelets show the greatest effect of exposure to a foreign surface, as evidenced by decreased platelet count (thrombocytopenia) and function.
4. Hemolysis is monitored regularly by measuring plasma-free hemoglobin levels. The level is usually

not significantly altered by ECMO flow, although increases may indicate problems with red blood cell destruction in the membrane oxygenator or small-lumen cannula.
5. All types of white blood cells decrease in concentration, and phagocytic activity is significantly decreased.
6. After cessation of ECMO, platelets and white blood cell counts return to normal.

Care of the Infant Requiring ECMO

The neonate requiring ECMO requires a collection of highly trained personnel, each with unique skills and training. The team composition minimally consists of the pediatric surgical team, neonatologist specializing in the management of ECMO, and an ECMO specialist (physician [MD], registered nurse [RN], registered respiratory therapist [RRT], or perfusionist) to operate and manage the circuit, as well as the bedside nurse (Faulkner and Hickey, 2017). The following is an outline of the responsibilities of the ECMO specialist and the bedside nurse in the care of the infant during ECMO (Faulkner and Hickey, 2017).

A. Cannulation.
   1. Cannulation requires the initiation of systemic anesthesia and analgesia; the operating room staff is in attendance.
   2. See Table 27.3 for nursing responsibilities and interventions.
   3. ECMO specialist responsibilities.
      a. Maintain and monitor ECMO circuit.
      b. Assess physiologic stability.

Table 27.3

Nursing Responsibilities and Interventions for ECMO

Responsibility	Intervention
Before Cannulation	
Obtain and document baseline physiologic data.	• Record weight, length, and head circumference. • Draw blood samples for CBC, electrolytes, calcium, glucose, BUN, creatinine, PT/PTT, platelet count and function, ABGs, ACT. • Record vital signs: heart rate; respiratory rate; systolic, diastolic, and mean blood pressure; and temperature.
Ensure adequate supply of blood products for replacement.	• Draw, type, and cross-match samples for 2 units of packed red blood cells and fresh frozen plasma. • Keep 1 unit of packed cells and fresh frozen plasma always available in the blood bank and a separate set at the bedside.
Diagnostic examinations.	• Pre-ECMO CXR. • Pre-ECMO HUS. • Pre-ECMO ECHO.
Maintain prescribed pulmonary support.	• Maintain ventilator parameters. • Administer muscle relaxants if indicated.
Assemble and prepare equipment.	• Prepare infusion pumps to maintain arterial lines and infusion of parenteral fluids and medications into the ECMO circuit. • Place the infant on a radiant warmer with the head positioned at the foot of the bed to provide thermoregulation and access for cannulation. • Attach infant to physiologic monitoring devices to monitor heart rate, intra-arterial blood pressure, transcutaneous oxygen, and other parameters.
Circuit priming medications and fluids.	• 2 units PRBCs; Plasmalyte A, 1000 mL; albumin 25%, 50 mL; heparin, 200 units; sodium bicarbonate, 20 mEq; calcium gluconate, 200 mg.
Laboratory tests drawn from prime.	• ABGs, whole blood sodium, whole blood potassium, whole blood ionized calcium, whole blood glucose, hemoglobin, and hematocrit. • Insert urinary catheter and NG tube; place to gravity drainage. • Remove IV lines just before heparinization (optional). • Prepare loading dose of heparin (50 to 100 units/kg). • Prepare heparin solution for continuous infusion (100 units in 30-mL syringe to be infused into circuit at 25 units/kg/hr). • Prepare and infuse pain medication: morphine sulfate 0.03 mg/kg/hr or fentanyl 1 mcg/kg/hr. • Prepare paralyzing drug (pancuronium bromide, 0.1 mg/kg, or succinylcholine, 1 to 4 mg/kg). • Assist in insertion of arterial line (umbilical or peripheral). • Administer prophylactic antibiotics.

Continued

Table 27.3

Nursing Responsibilities and Interventions for ECMO—cont'd

Responsibility	Intervention

Additional medications/ fluids to have on hand.	• $D_{10}W$, 250-mL bag.
	• D_5W, 250-mL bag.
	• NS, 250-mL bag.
	• Optional to be administered by surgeon:
	  • Cryoprecipitate, 10 mL.
	  • Calcium chloride 10%, 5 mL.
	  • Bovine thrombin, 5000 units/5 mL.

Be prepared to administer cardiopulmonary support.	• Have medications and blood products available to correct:
	  • Hypovolemia.
	  • Bradycardia.
	  • Acidosis.
	  • Cardiac arrest.

During Cannulation	
Monitor cardiopulmonary status during procedure.	• Monitor heart rate and intra-arterial blood pressure continuously. • Obtain blood gas values after paralysis and during cannulation, as indicated by the infant's response to the procedure.
Administer medications.	• Give loading dose of heparin systemically when vessels are dissected free and are ready to be cannulated. • Give paralyzing drug systemically just before cannulation of internal jugular vein if infant has not been previously paralyzed. • Give analgesia for anesthetic effect.
Reduce ventilator parameters to minimal settings.	• Once adequate bypass is achieved, reduce PIP to 16 to 20 cm H_2O, PEEP to 4 cm H_2O, ventilator rate to 10 to 20 breaths per minute, and Fio_2 to 21% to 30%. • Patients undergoing VV bypass may require greater respiratory support.
During ECMO Run	
Monitor and document physiologic parameters.	• Record hourly and PRN: heart rate, blood pressure (systolic, diastolic, mean), respirations, temperature (skin, axilla), oxygen saturation, ECMO flow. • Measure hourly accurate intake and output of all body fluids (urine, gastric contents, blood). • Test all stools for occult blood. • Assess hourly: color, breath sounds, heart tones, murmurs, cardiac rhythm, arterial pressure waveform, peripheral perfusion. • Assess hourly: level of consciousness, reflexes, tone, and movement of extremities. • Assess neurologic status every 8 to 12 hours (e.g., fontanelle tension, pupil size, and reaction). • Assess weight and head circumference daily. • Circuit check per ECMO perfusion flow sheet.

Routine laboratory tests.	• All other blood specimens are drawn from ECMO circuit by ECMO specialist.
	  • ABGs until stable hourly.
	  • ACT every 2 hours.
	  • Platelets every 6 hours.
	  • aPTT every 6 hours × 48 hours, then daily.
	• Daily: plasma-free hemoglobin, heparin assay, fibrinogen, D-dimer; electrolytes, calcium, platelets, Chemstrip, creatinine, total and direct bilirubin.
	• Record ventilator parameters hourly.

Administer medications.	• Remove air bubbles and double-check dosages before infusion. • Place all medications and fluids (except heparin drip) into the venous side of the ECMO circuit or central venous line. • Prepare and administer the arterial line (umbilical or peripheral) infusion. • NPO, OG to gravity, and administer parenteral alimentation.
Provide pulmonary support.	• Perform gentle endotracheal suctioning according to individual assessment and need. • Maintain patent airway; be alert to extubation or plugging. • Obtain daily chest films, head ultrasounds, and tracheal aspirate cultures as indicated. • Maintain ventilator parameters.
Heparin (bleeding) precautions.	• ***Avoid*** all of the following: rectal probes, injections, venipunctures, heel sticks, NG tubes (oral only), nasal suctioning, administration of medications intramuscularly or by venipuncture. • Avoid invasive procedures. Do not change OG tube, urinary catheters, or endotracheal tube unless absolutely necessary; use gentle premeasured endotracheal tube suction technique. • Observe for blood in urine, stools, and endotracheal OG tubes.

Table 27.3

Nursing Responsibilities and Interventions for ECMO—cont'd

Responsibility	Intervention
Maintain excellent infection control.	• Change all fluids and tubing daily. • Change dressings daily and as needed. • Maintain closed system for urinary catheter drainage. • Maintain strict aseptic and handwashing techniques. • Use universal barrier precautions.
Provide physical care.	• Keep skin dry, clean, and free of pressure points. • Monitor blood loss from cannula site. • Give mouth care as needed. • Provide ROM every 8 hours or as indicated. • Turn side to side every 1 to 2 hours. • Nonnutritive sucking every 4 hours, if stable.
Provide pain management, sedation, stress reduction.	• Minimize noise level. • Cluster patient care to maximize sleep period. • Administer analgesia: fentanyl or morphine as continuous IV drip. • Manage iatrogenic physical dependency by following dose reduction regimen.
Be alert to complications and emergencies.	• See text. • Social services consult.
After ECMO Run	
	• Head CT and MRI before discharge.

ABGs, Arterial blood gases; *ACT*, activated clotting time; *aPTT*, activated partial thromboplastin time; *BUN*, blood urea nitrogen; *CBC*, complete blood cell count; *CT*, computed tomography; *CXR*, chest x-ray; D_5W, 5% dextrose in water; $D_{10}W$, 10% dextrose in water; *ECHO*, echocardiogram; Fio_2, fractional concentration of oxygen in inspired gas; *HUS*, hemolytic–uremic syndrome; *IV*, intravenous; *MRI*, magnetic resonance imaging; *NG*, nasogastric; *NPO*, nothing by mouth; *NS*, normal saline; *OG*, orogastric; *PEEP*, positive end-expiratory pressure; *PIP*, peak inspiratory pressure; *PRBCs*, packed red blood cells; *PRN*, as needed; *PT/PTT*, prothrombin time/partial thromboplastin time; *ROM*, range of motion; *VV*, venovenous.

Adapted from Nugent, J., & Matranga, G. (1997). Extracorporeal membrane oxygenation. In D. F. Askin (Ed.), *Acute respiratory care of the newborn* (2nd ed., pp. 341–368). Petaluma, CA: NICU Ink.

c. Maintain physiologic parameters such as blood gas values, blood pressure, platelet count, Svo_2 and arterial oxygen saturation (Sao_2), and ACT.
d. Assist nurse in the general care of the infant.
e. Be prepared for circuit emergencies.

B. **During ECMO "run."**
1. Bypass is gradually instituted until approximately 80% (120 to 150 mL/kg/min) of cardiac output is diverted through the ECMO circuit.
2. At maximal flow, blood gas values should normalize and Svo_2 is maintained at greater than 70%.
3. Svo_2 is an excellent indicator of adequate flow during VA ECMO because it is a measure of tissue perfusion and efficiency of extracorporeal circulation in meeting metabolic demands.
4. Oxygenation during VV ECMO is assessed by the infant's arterial blood gas values and continuous oxygen saturation monitoring via pulse oximetry. Svo_2 is not an accurate reflection of deoxygenated blood because of recirculation; Svo_2 is used as a trending parameter during VV ECMO.
5. Ventilator settings are reduced to a minimum; vasopressor therapy and chemical paralysis are usually discontinued; enteral feedings are generally withheld because of concern about hypoxic injury to the gastrointestinal tract; and blood loss is quantified and replaced.
6. Emergencies during ECMO (Faulkner and Hickey, 2017).
   a. Circuit emergencies.
      1) Air embolism.
      2) Tubing rupture.
      3) Oxygenator malfunction.
      4) Accidental decannulation.
      5) Power failure.
      6) Gas source failure.
      7) Equipment malfunction.
   b. Responsibilities of the nurse during a circuit emergency (Shelley and Rees, 2010).
      1) Notification of physician.
      2) Ventilation.
      3) Anticoagulation.
      4) Chemical resuscitation.
      5) Blood loss replacement.
   c. Responsibilities of the ECMO specialist during a circuit emergency (Shelley and Rees, 2010).
      1) Clamp catheters.
      2) Open bridge.
      3) Remove gas source.
      4) Repair circuit.

C. **ECMO patient complications** (Gokalp et al., 2015).
1. Electrolyte/glucose/fluid imbalance: sodium requirements decrease; potassium requirements increase because of the action of aldosterone.

Calcium replacement may be needed if citrate–phosphate–dextrose anticoagulated blood is used. Hyperglycemia may necessitate a decrease in the glucose concentration of IV fluids.

2. Central nervous system (CNS) deterioration: cerebral edema, intracranial hemorrhage, and seizures. Deterioration results from initial hypoxia, acidosis, hypercapnia, or vessel ligation.
3. Generalized edema: the extracellular space is enlarged by the distribution of crystalloid solution and the action of aldosterone and antidiuretic hormone. The use of diuretics or hemofiltration may be necessary if edema causes brain or lung dysfunction.
4. Renal failure: acute tubular necrosis may result from pre-ECMO hypotension and hypoxia. Indicators of renal failure are abnormal blood urea nitrogen and creatinine values. Low-dose dopamine therapy and/or hemodialysis may be necessary.
5. Hemorrhage due to thrombocytopenia, coagulopathy.
6. Decreased venous return and/or hypovolemia due to inadequate circulating blood volume, pneumothorax, and/or partial venous catheter occlusion or malposition.
7. Hypertension due to overinfusion of blood products, renal ischemia, and excretion of renin–angiotensin.
8. PDA: Left-to-right shunting may cause increased blood flow to the lung, necessitating high pump flows without the expected increase in Pao_2. Ligation may be necessary.
9. Cardiac stun: transient loss of ventricular contractility (1 to 3 days) is manifested by hypotension, decrease in aortic pulse pressure, poor peripheral perfusion, and decreased Pao_2. It is possibly due to a mismatch between afterload and ventricular contractility during ECMO.
10. Mechanical complications: these include incorrect catheter placement or accidental displacement, oxygenator failure, power failure, air entrainment, and accidental decannulation.

D. **Weaning/decannulation.**

1. Signs of improvement and indicators that the infant is ready to be weaned are as follows:
   a. Improvement of lung fields on chest x-ray examination.
   b. Clinical findings: improved breath sounds, rising Pao_2 on fixed ECMO flow, improvement in lung compliance.
2. Once improvement has been ascertained, flow rate is decreased slowly in 10- to 20-mL increments until ECMO support is no longer needed to maintain adequate gas exchange at low ventilator settings (Harvey, 2017). Ventilator settings are usually increased during weaning from the settings used during ECMO.
3. When flow rate is 50 to 100 mL/kg/min, a state of "idling" is achieved; the infant remains at this lowest possible flow rate for 4 to 8 hours.
4. If improvement in lung function remains stable, cannulas are clamped, heparin is infused directly into the infant, and the circuit is recirculated via a bridge. If blood gas values deteriorate, the cannulas are unclamped and ECMO support is resumed.
5. In VV ECMO, the cannulas are not clamped during the "trial off" procedure; gas flow to the membrane oxygenator is discontinued. Low flow rates are maintained, and patient response is assessed by measurement of blood gases.
6. Decannulation proceeds if blood gas values remain satisfactory.
7. Before decannulation, the infant undergoes chemical paralysis, and ventilator parameters are increased to compensate for loss of spontaneous respiratory function.
8. After adequate anesthesia and analgesia have been administered, the cannulas are removed. Both the internal jugular vein and the carotid artery are ligated. In some ECMO centers, carotid reconstruction is attempted (Harvey, 2017). The efficacy of this procedure is debatable because of clot formation at the site of reconstruction.
9. After decannulation, the infant is weaned as tolerated from the ventilator, and routine neonatal intensive care unit (NICU) care is resumed.

Post-ECMO Care

A. **Lung recovery is achieved through weaning of the infant from assisted ventilation.** Occasionally the use of steroids and/or diuretics is necessary to improve recovery.

B. **Assessment of neurologic recovery involves clinical evaluation and computed tomography scan.** It may be difficult to assess neurologic status during opiate use or while the infant is recovering from significant illness, so assessment may be deferred until the infant is ready for discharge.

C. **Weaning from opiate analgesics and sedatives involves a gradual reduction of doses and careful monitoring for withdrawal symptoms.** Infants receiving ECMO therapy require opiate infusions or scheduled dosing of opiates and sedatives throughout their course of ECMO to prevent excessive movement, which can dislodge the cannulas (Guaman and Garcia-Prats, 2017).

D. **Establishing oral feedings may be difficult.** Prolonged respiratory compromise, the effect of opiates on state control, alterations in swallowing caused by neck dissection during cannula placement, and gastroesophageal reflux, particularly in infants with CDH,

are some of the causes of feeding problems in the post-ECMO infant. Feeding difficulties are generally more common in infants with CDH than in those with other diagnoses such as MAS or PPHN.

Parental Support

A. **The ECMO candidate's parents are in crisis.** They are aware that ECMO is a method of last resort with no guarantee of positive result, and the technology is overwhelming.
B. **Parents need concise, accurate, understandable information about their child's condition and the required procedures.**
C. **Parent-to-parent support, using parents of "ECMO graduates," is efficacious and a positive experience.**
D. **Parents should have access to their infant.** ECMO candidates have an increasingly positive outcome, and every effort should be made to encourage involvement and bonding.

Follow-Up and Outcome

For some neonatal ECMO patients, their postcannulation status mirrors that of an infant with moderate to severe hypoxic–ischemic encephalopathy, thus appearing hypotonic, lethargic, and hyporeflexive (Glass, 2010). Additionally, these infants may require weaning from narcotics or sedative medications.

Cashen et al. (2017) determined the presence of a chronic condition, development of a neurologic event or renal failure, and longer durations of NICU and hospital stay were associated with worse overall functional status at hospital discharge among survivors. Those neonates requiring ECMO for less than 2 days had better overall functional status (Cashen et al., 2017). Table 27.4 depicts the potential determinants of impaired outcomes of neonates previously requiring ECMO (IJsselstijn et al., 2017).

Table 27.4

Risk Factors Related to Adverse Outcomes After Neonatal ECMO

Adverse Outcome	Risk Factors
Lung performance Airflow obstruction	RDS, CDH, CLD, BPD, Lengthy duration on ECMO
Exercise capability	None reported
Physical development	CDH
Sensorineural hearing loss	CDH, lengthy duration on ECMO, clinical seizures before ECMO
Development of motor function	Low familial socioeconomic status, intracranial abnormalities, length of hospitalization
Intellect	Intracranial abnormalities, low familial socioeconomic status, length of hospitalization
Neuropsychological outcome	Intracranial abnormalities, highest MAP before ECMO
Conduct	Need for added assistance with schoolwork

BPD, Bronchopulmonary dysplasia; *CDH*, congenital diaphragmatic hernia; *CLD*, chronic lung disease; *MAP*, mean airway pressure; *RDS*, respiratory distress syndrome.

Adapted from IJsselstijn, H., Madderom, M. J., & Hoskote, A. (2017). Outcomes, complications, and followup of neonates with respiratory failure. In T. V. Brogran, L. Lequire, R. Lorusso, G. MacLaren, & G. Peek (Eds.), *Extracorporeal life support: The ELSO red book* (5th ed., p. 219). Ann Arbor, MI: Extracorporeal Life Support Organization.

A. **Critical scrutiny of survivors is essential to assess the value and safety of ECMO.** Survivors should be evaluated at 4 to 6 months and then yearly until school age.
   1. Growth and development.
   2. Cardiorespiratory development.
   3. Cerebrovascular status.
   4. Neurologic and psychological functioning.
B. Medical morbidity includes poor somatic growth, feeding problems, chronic lung disease, and rehospitalizations (Table 27.5).

Table 27.5

Long-Term Follow-Up Guidelines

	Evaluation	Primary Foci	Intervention
INFANCY 0 to 2 years	Growth Hearing Neurologic Mental Motor	MRI Brain	Dietician Referral. Early Audiology Examination Early Rehabilitation Early Referral Early PT
PRESCHOOL 2 to 5 years	Growth (*CDH) Neurologic Language Motor		Dietician Referral. Rehabilitation ST PT

Continued

Table 27.5

Long-Term Follow-Up Guidelines—cont'd

	Evaluation	Primary Foci	Intervention
SCHOOL AGE ≥6 years	Growth (*CDH) Lung Performance Motor Exercise Tolerance Neuropsychological Behavior	 Spirometry Intelligence (once) Cognition Memory Concentration Hyperactivity Somatic Issues	Dietician Referral. Examine Correction of Airflow PT Sports Involvement/Training Cognitive Rehabilitation/Training Counseling/Support Groups
ADOLESCENCE >12 years	Growth (*CDH) Motor Exercise Tolerance Neuropsychological Behavior	 Gross Motor Function Cognition Memory Concentration Hyperactivity Depression Social Interaction Problems Somatic issues	Dietician Referral. PT Sports Involvement/Training School Support Career/Profession Counseling Cognitive Rehabilitation/Training Counseling/Support Groups

CDH, Congenital diaphragmatic hernia; *MRI*, magnetic resonance imaging; *PT*, physical therapy; *ST*, speech therapy.

Adapted from IJsselstijn, H., Madderom, M.J., & Hoskote, A. (2017). Outcomes, complications, and followup of neonates with respiratory failure. In T.V. Brogran, L. Lequire, R. Lorusso, G. MacLaren, & G. Peek (Eds.), *Extracorporeal life support: The ELSO red book* (5th ed., pp. 219). Ann Arbor, MI: Extracorporeal Life Support Organization.

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CHAPTER 28
Cardiovascular Disorders

Sharyl L. Sadowski and M. Terese Verklan

OBJECTIVES

1. Describe how to differentiate between cyanosis that is cardiac in origin and that which is pulmonary in origin.
2. Discuss the importance of universal pulse oximetry screening.
3. Name the major classifications of congenital heart disease, and list two anomalies in each.
4. Discuss the importance of environmental teratogens and their link to cardiac defects.
5. Discuss the link between congenital heart disease and genetics, including the use of available tests.
6. Describe the anatomy, clinical manifestations, and the possible medical and/or surgical treatment of tetralogy of Fallot (TOF), coarctation of the aorta (CoA), patent ductus arteriosus (PDA), ventricular septal defect (VSD), atrial septal defect (ASD), and hypoplastic left heart syndrome (HLHS).
7. Describe the basic medical rationale for care of the newborn infant with a suspected or identified cardiac defect.
8. Describe the basic surgical rationale for treatment of major cardiovascular defects.
9. List signs and symptoms of congenital heart abnormalities in the newborn infant.
10. Discuss available diagnostic modalities and the congenital cardiac defects they are used to diagnose.
11. List the signs and symptoms of PDA and the current medical, transcatheter, and surgical interventions.
12. Discuss the treatment modalities used in congestive heart failure, including the risks and benefits to the neonate.
13. Define the three classifications of shock, and list one cause under each category.
14. Discuss the major complications and sequelae of open heart surgery, and list two factors that contribute to the sequelae.
15. Discuss pregnancy implications for women with a history of complex congenital heart defects (CHDs).

Until the 20th century, there was limited clinical interest in congenital heart disease. In the majority of cases, the cardiac anomaly was incompatible with life; in the others, no treatment existed either to remedy the condition or to relieve its symptoms. Today, with advances in prenatal and early postnatal diagnosis and treatment of congenital heart defects (CHDs), the survival and quality of life of infants with congenital heart disease have markedly improved; many patients survive into childbearing ages and beyond. Before universal pulse oximetry screening, 20% to 30% of neonates with critical CHDs were not diagnosed before discharge from the hospital. Additional directives have been published recommending the screening be performed as close to discharge as possible and after 24 hours of age. With universal pulse oximetry screening, the number of infants missed has been reduced by 60% to 70% (Kumar, 2016). A delay in diagnosis leads to increased morbidity and mortality (Altman, 2013).

Advances in fetal echocardiography have resulted in a significant increase in the prenatal diagnosis of many CHDs, allowing for extensive parental counseling, thus providing time for parents to make decisions about treatment options before birth (Dorfman et al., 2008) and delivery at a tertiary hospital (Donofrio et al., 2013). Fetal echocardiography has been found to be most reliable between 18 and 22 weeks' gestation with a 71% to 100% detection rate in the United States when performed by university-based practices (Kumar, 2016). Telemedicine has also made a big impact on CHD, allowing for accurate diagnosis at remote hospitals and thus quicker implementation of care (Grant et al., 2010). In addition, advancements in angiography, interventional catheterization, and the advent of three-dimensional (3-D) and four-dimensional (4-D) echocardiography, coupled with a more complete understanding of newborn physiology, have led to improvements in diagnostic and treatment capabilities with decreased risk (Vernon and Lewin, 2018). The latest innovation is fetal magnetic resonance imaging (MRI), which provides detailed information on the fetal heart (Espinoza, 2019). In addition, more fetal medicine centers are offering early fetal intervention in certain cardiac defects to mitigate associated severity and complications. The most common procedure is fetal valvuloplasty, which is used for severe aortic stenosis with intact atrial septum,

pulmonary atresia or stenosis with intact ventricular septum, and complete heart block with hydrops fetalis (Moon-Grady, 2017). Transcatheter repairs have been rare in the neonatal and infancy periods due to the small size of vessels in which catheters needed to deploy devices are too large. Further development of transcatheter biomaterials and devices holds promise for biodegradable vascular stents, patches for muscular ventricular septal defects (VSDs) with a microstapler, and nontoxic bioinspired adhesive that allows for attachment of biodegradable patches to close any intracardiac defect in neonates and infants (Sizarov and Boudjemline, 2016a, 2016b). In addition, research is being done to develop stents to create intervascular communications that would allow for bidirectional Glenn anastomosis percutaneously (Sizarov and Boudjemline, 2016c). Newer surgical techniques that limit time spent in deep hypothermia with circulatory arrest or on continuous cardiopulmonary bypass, use of normothermic cardiopulmonary bypass, and surgery on beating hearts not only permits the total correction of many forms of CHDs in the neonatal period but also increases survival and decreases morbidities (Nevvazhay et al., 2012). In most cases, early intervention is essential to minimize and prevent long-term morbidity or early death (Knowles et al., 2012).

Whereas these advances have allowed for correction of many CHDs with dramatic decreases in mortality, neurodevelopmental morbidities are still found (Stone, 2010). Multiple clinical trials reported in the literature substantiate earlier findings of neurodevelopmental impairments in patients after neonatal cardiac surgery (Newburger et al., 2012). Although overall intelligence has been spared, 50% of school-age patients do not function at age-appropriate levels, 37% have moderate disabilities, and 6% have severe disabilities. The disabilities were identified as motor and cognitive impairments, including attention deficit, speech and language delays; gross and fine motor deficiencies; and visual–motor delays. Many studies have linked these outcomes to deep hypothermic cardiac arrest and continuous cardiopulmonary bypass that is used during open heart surgery. Some poor neurocognitive outcomes result from prenatal or fetal factors as opposed to postsurgical factors (Morton et al., 2017). Many infants with CHDs have immature brains, white matter injury, hemorrhages, and stroke at delivery (Wernovsky and Licht, 2016). Over 20% of neonates and infants who require surgical intervention have abnormal brain development, felt to be related to the severity of their cardiac defect and associated genetic syndromes and the presence of extracardiac abnormalities (Verall et al., 2019). Due to the number of patients with complex congenital heart disease reaching adulthood and beyond, new medical specialties have been developed in the field of adult congenital heart disease, as these patients require subspecialty care. Many of the patients who would have died 50 years ago are now living and bearing children. Pregnancy in congenital heart disease is not uncommon in today's world.

Cardiovascular Embryology and Anatomy

CARDIAC DEVELOPMENT

Fetal cardiac development occurs rapidly from day 18 to the 12th week of fetal life (Sedmera, 2011).

A. **Cardiac tube.**
   1. Heart development is first identified at 18 to 19 days of fetal life with formation of a heart tube (Table 28.1; Fig. 28.1, *A*).
   2. The heart tube elongates and develops dilatations and contractions that will later form the ventricles, bulbus cordis, and outflow tracts (Fig. 28.1, *B*). Molecular studies are beginning to identify that the heart tube actually becomes the left ventricle, but more studies are needed (van de Berg and Moorman, 2009).
   3. The pairs of aortic arches develop from the cephalic, extracardial portion of the heart tube. The caudal end will form the early ventricle (Fig. 28.1, *C*).
   4. Abnormal development during this time will include corrected transposition and dextrocardia (Snarr et al., 2017).

B. **Cardiac septation:** begins in the middle of the fourth week and is complete by the end of the fifth week of fetal life (Fig. 28.1, *D*).
   1. Atrial septum and foramen ovale are formed from two septa and endocardial cushions.

Table 28.1

Timeline for Fetal Heart Development

Age (Days)	Cardiovascular Morphogenesis
18	Angiogenic tissue appears
19 to 20	Endothelial heart tubes appear
21	Fusion of endothelial heart tubes
23 to 25	Differentiation of atria, ventricles, and bulbus cordis; heart begins to beat
25	Fusion of atria, dorsal mesocardium regresses, formation of bulboventricular loop
26 to 27	Circulation is established
32	Appearance of septum primum
33	Intraventricular septum begins to form
35	Foramen secundum present
36 to 37	Fusion of atrial endocardial cushions
43	Ridges form in the bulbus cordis
46	Closure of ventricular septum, formation of coronary arteries
47	Septum secundum appears

Data from Collins-Nakai, R., & McLaughlin, P. (2002). How congenital heart disease originates in life. *Cardiology Clinics*, *20*(3), 367–383; Park, M. K. (2008). *Pediatric cardiology for practitioners* (5th ed.). Philadelphia, PA: Elsevier Mosby; Theorell, C. (2002). Cardiovascular assessment of the newborn. *Newborn and Infant Nursing Reviews*, *2*(2):111–127.

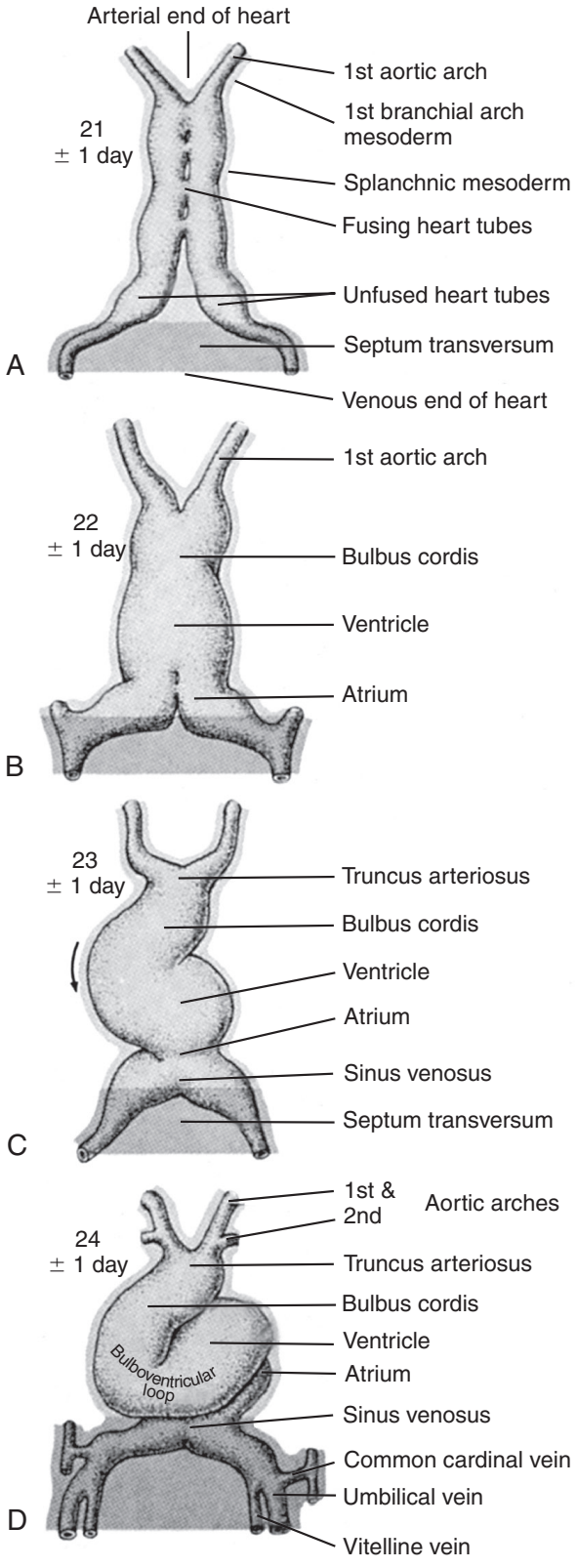

Fig. 28.1 Sketches of ventral views of the developing heart (at 20 to 25 days), showing fusion of endocardial heart tubes to form a single heart tube. Bending of the heart tube to form a bulboventricular loop is also illustrated. (Adapted from Moore, K. L., & Persaud, T. V. N. [2008]. *The developing human: Clinically oriented embryology* [8th ed.]. Philadelphia, PA: Elsevier Saunders.)

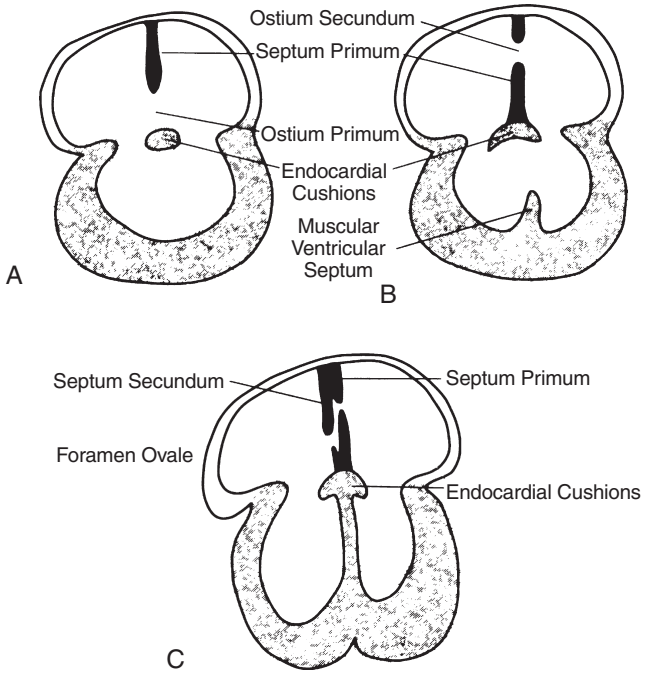

Fig. 28.2 Atrial septation. **A**, Septum primum begins to form, extending toward endocardial cushion (note ostium primum). **B**, Ostium primum is closed and perforation (called *ostium secundum*) forms in the septum primum. **C**, Septum secundum forms, creating the foramen ovale. (From Hazinski, M. F. [1983]. Congenital heart disease in the neonate. *Neonatal Network*, *21*[3], 31–42.)

   a. Atrial septum primum is formed by unidirectional growth from the top of the atrium toward the endocardial cushions, resulting in formation of the septum.
   b. A second septum (septum secundum) appears to the right of the septum primum and grows to overlap the ostium secundum. Thus, the flapped opening, the foramen ovale, is created (Fig. 28.2).
2. Ventricular septation results from fusion of the endocardial cushions and dilation and fusion of the ventricles (Fig. 28.3).

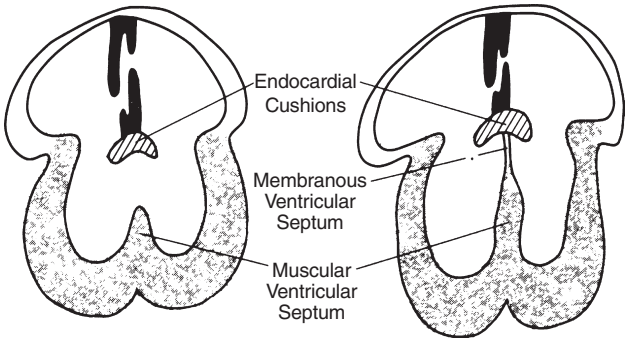

Fig. 28.3 Ventricular septation (with muscular and membranous septum). (From Hazinski, M. F. [1983]. Congenital heart disease in the neonate. *Neonatal Network*, *21*[3], 31–42.)

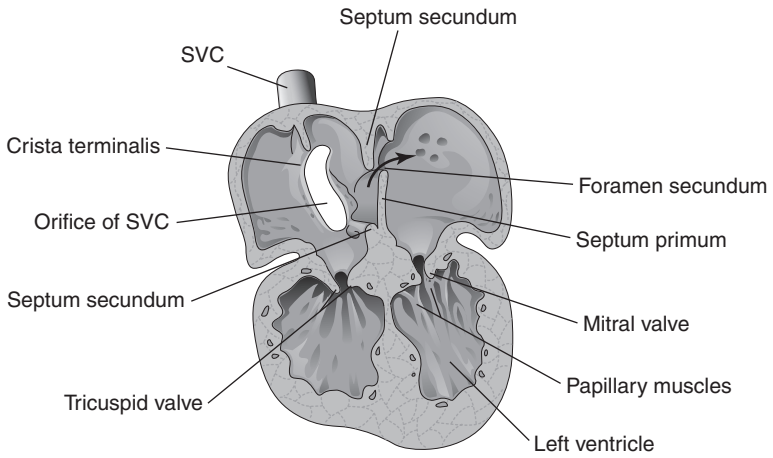

Fig. 28.4 The developing heart at about 8 weeks, showing the heart after it is partitioned into four chambers. *Arrow* indicates flow of well-oxygenated blood from right to left atrium. *SVC*, superior vena cava. (From Moore, K. L., & Persaud, T. V. N. [2008]. *The developing human: Clinically oriented embryology* [8th ed.]. Philadelphia, PA: Elsevier Saunders.)

3. Tissue of endocardial cushion forms the atrioventricular valves (Fig. 28.4).
   a. Tricuspid valve: between right atrium and ventricle.
   b. Mitral valve: between left atrium and ventricle.
4. Abnormal development during cardiac septation can lead to the following:
   a. VSD, atrial septal defect (ASD), and endocardial cushion defect (atrioventricular canal).
   b. Absence, deformation, stenosis, or atresia of the tricuspid and/or mitral valves.

GREAT VESSEL DEVELOPMENT

A. **Single vessel (truncus arteriosus)** extends from the ventricles until the fourth week of fetal life. It will then separate into the aorta and the pulmonary artery (Fig. 28.5).

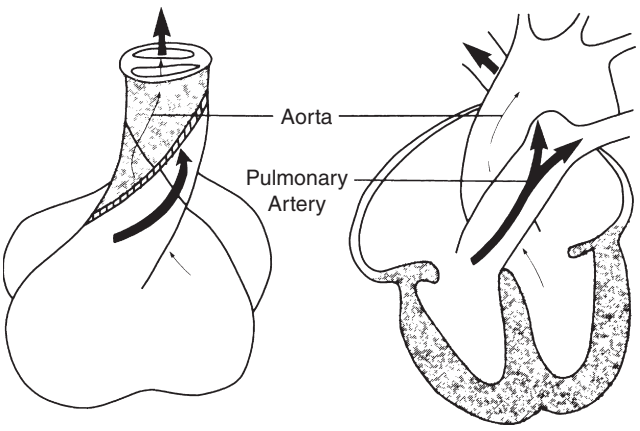

Fig. 28.5 Closing of the truncus arteriosus and division into the pulmonary artery and aorta. (From Hazinski, M. F. [1983]. Congenital heart disease in the neonate. *Neonatal Network*, *21*[3], 31–42.)

1. The semilunar valves (aortic and pulmonic valves) develop from three ridges of tissue at the opening to the aorta and pulmonary trunk.

B. **Development of aorta and aortic branches** (Table 28.2). The truncus arteriosus connects with the aortic sac, which in turn connects with the paired aortic branches.

Table 28.2

Development of Aorta and Aortic Branches

Embryonic Vessel	Results In
Truncus arteriosus	Aorta and pulmonary artery
First pair of aortic arches	Pieces remain as stapedial arteries
Second pair of aortic arches	Pieces remain as stapedial arteries
Third pair of aortic arches	Common carotid arteries and proximal portion of internal carotid arteries
Fourth pair of aortic arches	
Right	Proximal portion of the right subclavian artery
Left	Aortic arch segment between left common carotid and left subclavian artery
Fifth pair of aortic arches	Regresses totally
Sixth pair of aortic arches	
Left	Proximal portion of the left pulmonary artery and ductus arteriosus
Right	Proximal portion of the right pulmonary artery

Data from Collins-Nakai, R., & McLaughlin, P. (2002). How congenital heart disease originates in life. *Cardiology Clinics*, *20*(3), 367–383; Park, M. K. (2008). *Pediatric cardiology for practitioners* (5th ed.). Philadelphia, PA: Elsevier Mosby; Theorell, C. (2002). Cardiovascular assessment of the newborn. *Newborn and Infant Nursing Reviews*, *2*(2), 111–127.

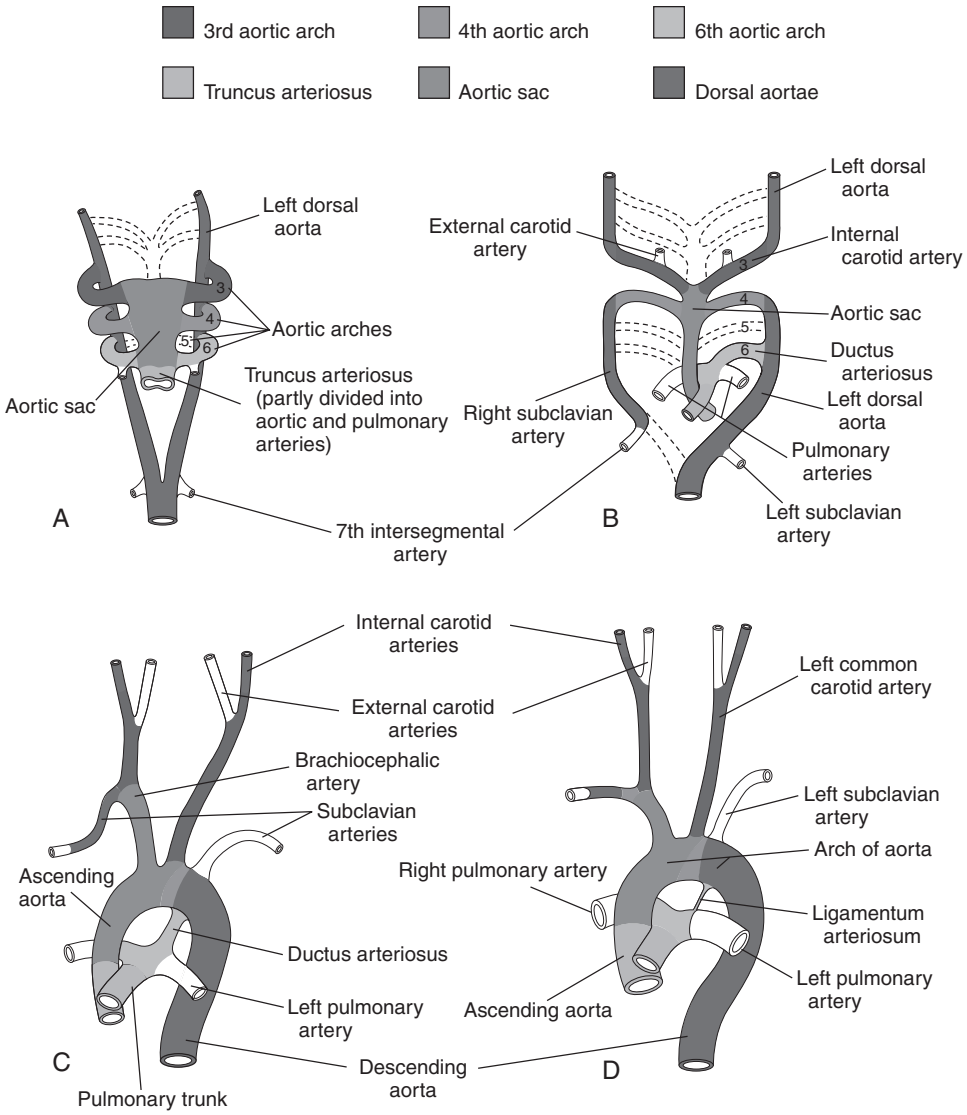

Fig. 28.6 Schematic drawings illustrating arterial changes that result during transformation of the truncus arteriosus, aortic sac, aortic arches, and dorsal aortas into the adult arterial pattern. **A**, Aortic arches at 6 weeks. **B**, Aortic arches at 7 weeks. **C**, Arterial arrangement at 8 weeks. **D**, Sketch of arterial vessels of 6-month-old infant. (From Moore, K. L., Persaud, T. V. N., & Torchia, M. G. [2013]. *The developing human: Clinically oriented embryology* [9th ed.]. Philadelphia, PA: Elsevier Saunders.)

A series of six paired aortic arches then form in succession (Fig. 28.6).

1. The third arches become part of the common carotid arteries.
2. The right fourth arch becomes the proximal portion of the right subclavian artery.
3. The left fourth arch becomes the aortic arch segment between the left common carotid artery and left subclavian artery.
4. The left sixth arch becomes part of the left pulmonary artery and the ductus arteriosus.
5. The right sixth arch forms the right pulmonary artery.
6. Abnormalities include interrupted aortic arch and coarctation of the aorta (CoA).

C. **Developmental abnormalities of truncal septation include** (Snarr et al., 2017):
   1. Truncus arteriosus.
   2. Tetralogy of Fallot (TOF).
   3. Pulmonary and/or aortic valve atresia or stenosis.
   4. Transposition of the great vessels (dextroposition).
   5. Double-outlet right ventricle.

CIRCULATORY DEVELOPMENT

A. **Heart contractions begin around 21 days;** the atrium and ventricle muscle layers are continuous. Contractions result in a rhythmic peristalsis.

B. **Electrical conduction system** is functional around 10 weeks, with normal sinus rhythm seen by 16 weeks (Blackburn, 2018).

C. **Establishment of fetal circulation:** With completion of atrial and ventricular septation, development of valves between chambers and outflow tracts, and separation of the truncus arteriosus into the great vessels, fetal circulation is established.
D. **Fetal circulation is anatomically and physiologically different from adult circulation,** and adaptation after birth is necessary (Blackburn, 2018). For a full discussion of fetal circulation and cardiopulmonary adaptation at birth, see Chapter 4.

CARDIOVASCULAR PHYSIOLOGY

A. **Normal circulation** (see Fig. 4.2).
   1. Oxygen-poor blood enters the right atrium and passes through the tricuspid valve into the right ventricle, where it is pumped through the pulmonary artery to the lungs.
   2. As the blood flows through the lungs, it gives up carbon dioxide and gains oxygen.
   3. Oxygen-rich blood returns from the lungs through the pulmonary veins. It enters the left atrium and then passes through the mitral valve into the left ventricle, which pumps it through the aortic valve and into the aorta.
   4. The aorta then delivers oxygenated blood to all body organs and tissues.

B. **Cardiac depolarization.**
   1. Results from the electrical discharge across the myocardial cell (total net movement of ions across the cell wall) and is measured by the electrocardiograph.
   2. Shortening of muscle fibers (contraction) usually follows cardiac depolarization. Strength of cardiac (ventricular) contraction is measured by blood pressure or arterial pulse palpation.
   3. Cardiac electrical activity does not ensure adequate cardiac function.
      a. Congenital defects or surgical injury to the conduction system may result in arrhythmias or heart block.
      b. Electrolyte disturbance (i.e., altered fluid composition surrounding the cells) can affect electrical activity.
         1) Hypokalemia and hyperkalemia.
         2) Hypocalcemia and hypercalcemia.
         3) Hypoxia.
         4) Acidosis.

C. **Cardiac output.**
   1. Cardiac output is the volume of blood ejected by the heart in 1 minute. Approximations vary from 120 to 200 mL/kg/min.
   2. Cardiac output = stroke volume × heart rate (in liters per minute).
      a. As heart rate fluctuates, so will cardiac output.
         1) Normal term newborn heart rate is 120 to 160 beats per minute (bpm), although it may range from 80 to 180 bpm on an individual basis, depending on activity levels.
      b. Tachycardia seems to be an effective mechanism for improving cardiac output as long as the tachycardia does not compromise diastolic filling time and decrease coronary artery perfusion.
   3. Stroke volume is relatively fixed at 1.5 mL/kg and is affected by three factors: preload, contractility, and afterload.
      a. Preload: the volume of blood in the ventricles before contraction.
         1) Clinically, preload is a measurement of pressure, rather than volume, in the ventricles before contraction.
         2) Increasing the volume in the ventricles, consequently lengthening the myocardial fibers before contraction, should result in improved stroke volume (Frank–Starling law). The newborn infant is capable of increasing stroke volume, provided there is no increase in systemic vascular resistance (SVR) or rapid rise in aortic pressure. Given the neonate's smaller contractile mass, less compliant myocardium, and normal maximization of myocardial fiber length, volume infusions are likely to increase aortic pressure and afterload, resulting in a decline in stroke volume (Scholz et al., 2018).
      b. Contractility: speed of ventricular contraction.
         1) Cardiac cycle consists of ventricular contraction (systole), followed by ventricular relaxation (diastole). As contraction time decreases, relaxation time (diastole) increases, with an increase in ventricular filling volume (preload) before contraction.
         2) Ventricular contractility cannot be directly measured. Measurements of cardiac shortening fractions and ejection fraction provide an indirect assessment of contractility.
         3) Contractility in neonates is influenced by the following:
            a) Exogenous catecholamine (dopamine/dobutamine) use, which increases blood pressure and cardiac output.
            b) Factors that decrease contractility.
               (1) Acidosis, which impairs myocardial response to catecholamines.
               (2) Hypoxia.
               (3) Electrolyte disturbances.
               (4) Hypoglycemia.
      c. Afterload: the resistance to blood leaving the ventricle.
         1) Dependent on SVR and pulmonary vascular resistance (PVR); if SVR or PVR increases, afterload increases.

2) The neonate's myocardium is very sensitive to increased afterload; with small increases in afterload, stroke volume can fall significantly.
3) Afterload can be reduced by intravenous (IV) infusion of vasodilators (e.g., nitroglycerin, amrinone, and nitroprusside). Inhaled nitric oxide and phosphodiesterase inhibitors, such as sildenafil, can be used to decrease PVR (Steinhorn and Abman, 2018).

4. Concepts of blood flow.
   a. Flow is directly proportional to pressure/resistance.
   b. Blood flow will always take the path of least resistance.
   c. If heart action (pressure) remains unchanged but vasoconstriction or dilation or obstruction to flow (resistance) changes, flow will change (i.e., cardiac output will vary).
   d. PVR starts to fall by almost 80% after delivery, resulting in a dramatic increase in pulmonary blood flow and subsequent increase in systolic blood pressure (Blackburn, 2018). This normal decline is influenced by prematurity, low birth weight, and hypoxia episodes.

Congenital Heart Defects

For a list of abbreviations used for cardiac defects, see Table 28.3.

OCCURRENCE

A. **Incidence:** 10% of all stillbirths. Three to nine per 1000 live births (Fahed et al., 2013); the incidence in premature infants is 2 to 3 times that of term infants (Altman, 2013).
   1. 85% of cases are due to multifactorial causes.
   2. 10% to 12% are due to chromosomal factors.
   3. 1% to 2% are due to genetic factors.
   4. 1% to 2% are due to exposure to maternal or environmental teratogens (Lott, 2014).
   5. 14.5% to 66% are in conjunction with other structural anomalies.

B. **Genetic factors:** Chromosomal abnormalities: overall incidence of CHD in patients with a chromosome aberration is 30%. Isolated cardiac defects result from multiple genes and their interaction with factors in the environment. Major advances in genomic technologies have shifted the numbers for inheritance factors of many of these defects (Edwards and Gelb, 2016).
   1. Incidence of CHD varies with chromosomal abnormality. Syndromes with an entire extra chromosome or syndromes with a missing chromosome are detected with normal chromosomal studies (Zaidi and Brueckner, 2017).
      a. Trisomy 21: 40% to 50%.
      b. Trisomy 18: 100%.
      c. Trisomy 13: 100%.
      d. Turner's syndrome: 20% to 50% (45,X0 karyotype or mosaic 46,XX).
   2. Syndromes requiring fluorescence in-situ hybridization (FISH) analysis include those with mosaicism and those with deletions in a chromosome.
      a. Chromosome deletion syndromes 18, 13, 5, and 4: 25% to 50%.
      b. Mosaic Turner's syndrome: X and Y chromosome. FISH probe needed to rule out Y chromosome (Bishara and Clericuzio, 2008).
   3. Microdeletions that are detected through FISH and multiplex ligation-dependent probe amplification (MLPA).
      a. 22q11 deletion syndrome: 80% to 85%.
      b. Williams syndrome: 55% to 80% (deletion of elastin gene at 7q11.23).
      c. Alagille syndrome: 90% (*JAGI* deletion on 20p12).
      d. Noonan's syndrome: 80% (12q24.1, *PTPN11* gene) (Zubani et al., 2017).
      e. DiGeorge deletion: greater than 50% (22q 11.2).
   4. Single-mutant-gene syndromes: 1% to 2% of all cardiovascular abnormalities in newborn infants. Both autosomal dominant and recessive syndromes have been associated with CHD. According to Fahed et al. (2013), these are defined as copy number variants and are identified on tests for genetic mutation analysis via array comparative genomic hybridization (aCGH) and FISH. This type of testing can detect smaller imbalances in the genome, allowing for detection of mutations, insertions, deletions, and imprinting abnormalities.
      a. Holt–Oram syndrome: more than 75% (*TBX5* gene found at 12q24.1).
      b. X-linked situs inversus Xq25, *ZIC3* gene.

Table 28.3
Abbreviations Used for Cardiac Defects

AS	Aortic stenosis
ASD	Atrial septal defect
CoA	Coarctation of the aorta
HLHS	Hypoplastic left heart syndrome
IAA	Interrupted aortic arch
PA	Pulmonary atresia
PDA	Patent ductus arteriosus
PFO	Patent foramen ovale
PS	Pulmonary stenosis
TA	Truncus arteriosus
TAPVR	Total anomalous pulmonary venous return
TGV or TGA	Transposition of the great vessels or arteries
VSD	Ventricular septal defect

c. Kartagener's syndrome (Fleiner, 2006): 100% (*DNAI1* on 9p21-p13, *DNAH5* on 5p15-p14).
d. Beckwith–Wiedemann syndrome: 10% to 35%, imprinting defects of *KIP2*/*LIT1* and paternal *IGF2* genes at 11p15.5 (Haldeman-Englert et al., 2018).

5. Multifactorial: approximately 90% due to genetic predisposition coupled with a causative factor.
   a. Cornelia de Lange's syndrome: approximately 30%.
   b. VACTERL (*v*ertebral anomalies, *a*nal atresia/stenosis, *c*ardiac defects [73%], *t*racheo*e*sophageal fistula, *r*adial defects, *l*imb anomalies) (Zubani et al., 2017).
   c. CHARGE (8q12.1, *c*oloboma, *h*eart defects [71% to 92%], choanal *a*tresia, *r*estriction of growth and development, *g*enital anomalies, *e*ar anomalies) (Zubani et al., 2017).
6. Genetic counseling is done to evaluate cause and recurrence risk. The risk of having another child with a cardiac lesion is 1% to 6% if the cause is unknown (Zaidi and Brueckner, 2017). However, this risk may be as much as 13% higher in specific syndromes.
   a. DiGeorge syndrome: Chromosomal microarray analysis should be recommended as first-line test if the infant has developmental disabilities.
      1) 7% of parents carry the deletion.
      2) Recurrence risk is up to 50% (Zubani et al., 2017).
      3) Prenatal diagnosis in future pregnancies via chorionic villus sampling (CVS) or amniocentesis, with FISH requested specifically.
   b. Trisomies 13, 18, and 21 all carry recurrence risk of 1%, and prenatal diagnosis in future pregnancies is done using CVS or amniocentesis. The recurrence risk for trisomy 21 increases after maternal age 40.

C. **Environmental factors and teratogens** can include fetal exposure to drug, chemical, infectious, or physical agents; maternal disease or altered metabolic state with the period of greatest risk at 14 to 50 days of fetal life (Lott, 2014).
1. Cardiac teratogenesis is associated with maternal ingestion of the following:
   a. Thalidomide: dramatically illustrated the extraordinarily deleterious effects of prescribed drug on a developing fetus; included patent ductus arteriosus (PDA), ASD, VSD, and pulmonary stenosis (Lynch and Abel, 2015).
   b. Anticonvulsants: 2% to 3% of infants exposed to anticonvulsants will have associated congenital cardiac defects such as pulmonary stenosis, CoA, and PDA. Glickstein (2007) reported the following defects with use of specific anticonvulsants in pregnancy:
      1) Phenytoin (fetal hydantoin syndrome): VSD, D-transposition of the great vessels (D-TGV), TOF, hypoplastic left heart syndrome (HLHS), pulmonary atresia, ASD, aortic stenosis, and pulmonic stenosis.
      2) Carbamazepine (Tegretol): VSD, TOF.
      3) Valproic acid: VSD, CoA, interrupted aortic arch, TOF, HLHS, aortic stenosis, ASD, pulmonary atresia.
      4) Trimethadione (fetal trimethadione syndrome): VSD, TGV, TOF, HLHS, double-outlet right ventricle, pulmonary atresia, ASD, aortic stenosis, pulmonic stenosis.
      5) Pentobarbital: no confirmed specific embryopathy but may potentiate the effects of other drugs taken concurrently.
   c. Anticoagulants.
      1) Warfarin (Coumadin): abortion or fetal embryopathic development in weeks 6 to 9 of gestation. Cardiac malformations have been identified, but no consistent cardiac defect has been noted.
      2) Heparin: because of its larger molecular weight, does not cross the placenta.
   d. Antineoplastic medications.
      1) Aminopterin: cardiac manifestations include dextroposition but are not as prominent as other defects resulting from drug ingestion.
      2) In general, the disorders for which antineoplastic agents are used are serious enough to preclude pregnancy.
   e. Lithium: approximately 10% of infants exposed will have defects such as Ebstein's anomaly, ASD, and tricuspid atresia.
   f. Retinoic acid: aortic arch abnormalities, other congenital heart malformations.
   g. Isotretinoin.
   h. Alcohol: fetal alcohol syndrome (FAS) is accompanied by a variety of cardiac lesions (e.g., VSD with or without subpulmonic and subaortic stenosis, ASD, CoA, TOF).
   i. Amphetamine: 5% to 10% will have congenital cardiac defects such as VSD, PDA, ASD, and TGV (Swanson and Erickson, 2016).
   j. Selective serotonin reuptake inhibitors: ASD, VSD, and increased left outflow tract defects (Lynch and Abel, 2015).
   k. Immunosuppressants: Mycophenolate mofetil is contraindicated in pregnancy (Lynch and Abel, 2015).
   l. Tobacco and smoking: correlation between first-trimester smoking and defects such as pulmonary valve stenosis, TGV, ASD, right ventricular outflow tract defects, and PDA in term newborns (Alverson et al., 2011). This association is higher when both parents smoke (Nicoll, 2018).

m. Marijuana: studies suggest an increased risk of VSD and Ebstein's anomaly (Lynch and Abel, 2015).

2. Exposure to environmental hazards such as radiation, heat, and gases may produce teratogenic effects, but there are no specific associated cardiac malformations.
   a. Agricultural pesticides have an increased risk of septal defects (Nicoll, 2018).
   b. Air pollution with nitrogen dioxide (NO_2) has increased risk of CoA, and pulmonary valve stenosis.
   c. Insecticides, herbicides, and fungicides have an increased risk of HLHS, TOF, CoA, and septal defects. The association is higher when exposure occurs one month before conception through the first trimester.
   d. Heavy metals like arsenic, lead, and aluminum are associated with septal defects, conotruncal defects, and outflow tract obstructions.
   e. Living in close proximity to a landfill or hazardous waste site carries an increased risk for defects of the septum, great arteries, and veins.
   f. Paternal exposure to welding and ionizing radiation were associated with increases in endocardial cushion defect, lead soldering exposure has been associated with increases in pulmonary atresia, and paint strippers with an increased risk of HLHS (Nicoll, 2018).
3. Assisted reproductive technology is highly linked to cardiac defects (Swanson and Erickson, 2016).

D. **Maternal disease and viral infections** (Box 28.1).
1. Women with diabetes mellitus, especially insulin-dependent, have a 5 times greater risk of their children being born with cardiac anomalies than the general population of pregnant women have. Disorders include hypertrophy of the septum and myocardium, VSD, double-outlet right ventricle, TGV, truncus arteriosus, and CoA.
2. Maternal lupus erythematosus may be linked to complete congenital heart block and dilated cardiomyopathy.
3. Untreated maternal phenylketonuria (PKU) increases risk by six-fold (Lynch and Abel, 2015).
4. Rubella and cytomegalovirus (CMV) produce clinically significant heart disease (Swanson and Erickson, 2016). Disorders seen are PDA, pulmonary stenosis and branch pulmonary artery stenosis, VSD, and ASD.
5. Maternal obesity has been linked to congenital heart disease, with severe obesity leading to risk being twice as high (Persson et al., 2019).
6. Maternal infections have been linked to CHD. Parvovirus, coxsackievirus, adenovirus, and CMV have been linked to fetal myocarditis (Swanson and Erickson, 2016).

Risk Assessment and Approach to Diagnosis of Cardiac Disease

SEX PREFERENCES ASSOCIATED WITH CARDIAC LESIONS

A. **Males**.
1. CoA.
2. Aortic stenosis.

Box 28.1

Classification of Maternal Diseases Affecting the Fetal Cardiovascular System

Category I: Maternal Diseases That Directly Affect the Fetal Cardiovascular System (Excluding Teratogenic Effects)

Pheochromocytoma
Hyperthyroidism
Diabetes mellitus
Collagen vascular disease (e.g., Ro antibody)
Rubella
Cytomegalovirus
Enterovirus infection
Toxoplasmosis
Listeriosis
Maternal group B streptococcal colonization with fetal invasion
Syphilis
Inherited metabolic diseases

Category II: Maternal Diseases That May Indirectly Affect the Fetal Cardiovascular System as a Result of Abnormalities of Uteroplacental Function

Neoplastic diseases
Diabetes mellitus
Maternal cardiac disease
Anemia (including the hemoglobinopathies)
Hypertensive disorders
Collagen vascular disease (e.g., lupus anticoagulant and systemic lupus erythematosus)
Renal disease (associated with hypertension)
Asthma
Cholestatic jaundice of pregnancy
Cytomegalovirus
Bacterial infections

From Katz, V., & Bowes, W. (1990). Maternal diseases affecting the fetal cardiovascular system. In W. Long (Ed.), *Fetal and neonatal cardiology* (p. 135). Philadelphia, PA: W. B. Saunders.

3. TGV.
4. HLHS.

B. **Females.**
1. ASD.
2. PDA.

HISTORY (SWANSON AND ERICKSON, 2016)

A. **Gestational age.**
1. Preterm. Infants born prematurely are much more likely to have pulmonary problems resulting in cyanosis than to have congestive heart failure (CHF), but they do have a higher incidence of:
   a. PDA.
   b. Left-to-right shunts (e.g., VSD or atrioventricular canal).
2. Term. The majority of infants with CHF are term infants.

B. Maternal history (see Box 28.1).
1. Infants of mothers with uncontrolled diabetes have an increased risk of:
   a. TGV.
   b. VSD.
   c. Cardiomyopathy.
   d. Complex congenital heart disease.
2. Lupus may cause congenital heart block and cardiomyopathy.
3. Viral and bacterial illnesses may directly and indirectly affect the fetal cardiovascular system.
4. Seizures or coagulation disorders can be linked to CHDs because the medications used may be teratogens.
5. Maternal congenital heart disease can lead to an increased risk of the same defect in the infant.
6. Maternal age greater than 35 years increases risk.
7. Alcohol consumption: increase in cardiac defects seen with FAS.

C. **Familial.**
1. Incidence of CHDs more than doubles if a sibling or parent has CHD (Scholz et al., 2018). Risk increases by 10-fold if two first-order relatives have congenital heart disease (Table 28.4).

D. **Perinatal history.**
1. Intrauterine growth pattern and birth weight.
2. Prenatal diagnosis with ultrasound.
3. Mode of delivery.
   a. Vaginal delivery most common for CHD, and initial Apgar scores are usually good.
   b. History of cesarean section and poor Apgar scores more indicative of asphyxia and respiratory distress.

E. **Universal pulse oximetry screening in well-baby nursery** (Mathur and Mathur, 2017).
1. Standard of care throughout the United States.
2. Endorsed by American Academy of Pediatrics and National Association of Neonatal Nurses.
3. Used to identify newborns at risk for HLHS, TOF, TGV, total anomalous pulmonary venous return (TAPVR), pulmonary atresia, critical aortic stenosis, and truncus arteriosus.
   a. 100% sensitivity to ductal dependent lesions.
   b. 50% to 70% of all undiagnosed cases will be detected by universal screening.
4. Cost per infant is approximately $15 (Kumar, 2016).
   a. Should be done as close to discharge as possible and after 24 hours of age in well-baby and intermediate care nurseries.
      1) Earlier screening may lead to false-positive results.

Table 28.4

Familial Recurrence Risks

Cardiac Anomaly	Family Member With Congenital Heart Defect	Risk (%)
Overall	Parent	3.2
	Grandparent	1.8
	Aunt/Uncle/Cousin	1.1
PDA—patent ductus arteriosus	Mother	3.5 to 4
	Father	2.5
	Sibling	3
VSD—ventricular septal defect	Mother	6
	Father	2
	Sibling	3
ASD—atrial septal defect	Mother	4 to 4.5
	Father	1.5
	Sibling	2-3
AVC—atrioventricular canal	Mother	14
	Father	1
	Sibling	3-4
Tetralogy of Fallot	Mother	6 to 10
	Father	1.5
	Sibling	2.5
Aortic stenosis	Mother	13 to 18
	Father	3
	Sibling	2
Pulmonary stenosis	Mother	4 to 6.5
	Father	2
	Sibling	2
Coarctation of the aorta	Mother	4
	Father	2
	Sibling	2
Other defects (TGA, tricuspid atresia, truncus arteriosus, HLHS)	Sibling	1.4 (average)

HLHS, Hypoplastic left heart syndrome; *TGA*, transposition of the great arteries.
Data from Park, M. K. (2008). *Pediatric cardiology for practitioners* (5th ed.). Philadelphia, PA: Elsevier Mosby; Theorell, C. (2002). Cardiovascular assessment of the newborn. *Newborn and Infant Nursing Reviews*, *2*(2), 111–127; Altman, C. A. (2013). Congenital heart disease (CHD) in the newborn: Presentation and screening for CHD. Retrieved from www.uptodate.com.

b. Simultaneously monitor pulse oximetry of both the right hand (RH; preductal) and either foot (postductal).
   1) Negative screen pulse oximetry reading is greater than 95% in both RH and either foot—discharge home.
      a) If pulse oximeter reading is greater than 95% in RH or foot and difference between RH and foot is less than 3%.
   2) Suspicious screen—repeat screen in 1 hour.
      a) If reading is 90% to 95% in RH and foot or there is ≥3% difference between RH and foot, repeat in 1 hour.
      b) If second reading is the same, then repeat again in 1 hour. If pulse oximeter readings indicate positive test, then refer for further testing.
   3) Positive screen—refer for further testing via echocardiography:
      a) If pulse oximeter reading in RH or foot is less than 90%, further testing is warranted.

F. **Universal pulse oximetry screening in the neonatal intensive care (NICU) setting.**
   1. Oxygen saturation at room air or on oxygen less than 90% and/or greater than 3% difference between RH and foot. Using the standard 95% will result in many more false-positives.
   2. Abnormal pulse oximetry at all three attempts that are an hour apart.
      a. False-positives are more common in the NICU (Mathur and Mathur, 2017).

CLINICAL PRESENTATION

A. Cyanosis (in the first week may be sole evidence of a heart lesion).
   1. With cardiovascular problems, cyanosis is unexpected or gradual in onset.
   2. Cyanosis observation.
      a. Dependent on hemoglobin levels; at least 5 g of desaturated hemoglobin per deciliter is necessary before cyanosis becomes apparent.
      b. Will be influenced by presence of anemia or polycythemia and the levels of 2,3-diphosphoglycerate.
   3. Differentiation between central and peripheral cyanosis:
      a. Peripheral or acrocyanosis results from sluggish movement of blood through the extremities and increased tissue oxygen extraction.
         1) Persists from birth and can last several days.
         2) Does not involve mucous membranes.
         3) May be caused by peripheral vasomotor instability.
      b. Central cyanosis results from desaturated blood leaving the heart.
         1) Seen as bluish discoloration of tongue and mucous membranes, reflecting arterial desaturation.
         2) Central cyanosis may present difficulties in making a differential diagnosis between respiratory and cardiac origin.

B. **Respiratory pattern.**
   1. Useful in the differentiation of cyanosis.
   2. Tachypnea (respiratory rate >60) without dyspnea is an important, often subtle, clue to cardiac anomalies. In the absence of cyanosis, it may indicate a left-to-right shunt lesion. Tachypnea is significant if coupled with feeding difficulty. It is suggestive of CHF if the infant must stop feeding to catch its breath.
   3. Hyperpnea (increased respiratory depth) is observed in congenital heart lesions resulting in diminished pulmonary blood flow.
   4. Crying may exacerbate cyanosis in neonates with CHD because of increased oxygen consumption by the tissues.

C. **Heart sounds.**
   1. First heart sound (S_1) represents closure of the mitral and tricuspid valves at the onset of ventricular systole.
      a. Best heard at the fourth intercostal space in the left midclavicular line (mitral) and at the fourth intercostal space at the sternal borders (tricuspid).
      b. S_1 is accentuated with the following:
         1) Increased cardiac output.
         2) Increased flow across atrioventricular valves.
         3) Specific conditions such as the following:
            a) PDA.
            b) VSD with increased mitral flow.
            c) TAPVR.
            d) Arteriovenous malformation.
            e) TOF.
            f) Anemia.
            g) Fever.
      c. Conditions decreasing S_1 include the following:
         1) Decreased atrioventricular conduction.
         2) CHF.
         3) Myocarditis.
   2. Second heart sound (S_2) occurs at the end of ventricular systole from closure of aortic and pulmonic valves.
      a. Heard best at upper left sternal border.
      b. Split S_2 is a normal occurrence, reflecting closure of aortic valve before the pulmonic valve.
         1) Increases on inspiration.
         2) Single S_2 is often heard in the first 2 days of life because of increased PVR.
         3) Splitting of S_2 is influenced by:
            a) Abnormalities of aortic or pulmonic valves.
            b) Conditions altering PVR or SVR.

c. Conditions widening the S_2 are influenced by the following:
   1) ASD.
   2) TAPVR.
   3) TOF.
   4) Pulmonary stenosis.
   5) Ebstein's anomaly.
d. Absent S_2 splits occur in the following:
   1) Pulmonary atresia and severe pulmonary stenosis.
   2) Aortic stenosis/atresia.
   3) Persistent pulmonary hypertension.
   4) *l*-TGV.
   5) Truncus arteriosus.

3. Third heart sound (S_3) is due to increased flow across the atrioventricular valves from rapid, passive ventricular filling from the atria.
   a. Follows S_2 and is a low-pitched, broad sound.
      1) Left-to-right shunts (e.g., ASD, VSD, PDA).
      2) Anemia.
      3) Mitral valve insufficiency.
4. Fourth heart sound (S_4) occurs at the final phase of ventricular filling and active atrial contraction during late diastole.
   a. Occurs just before S_1 and is low pitched.
   b. Rarely heard in the newborn infant.
   c. Always pathologic and indicates decreased ventricular compliance.
5. Ejection clicks are heard as snapping sounds just after the first heart sound in the first 24 hours of life.
   a. Abnormal (except during first 24 hours of life) and indicate cardiac disease.
   b. Audible for short duration after S_1.
   c. Associated with dilation of the great vessels or deformity of aortic or pulmonic valve.
   d. Other conditions associated with ejection clicks include the following:
      1) Aortic valve stenosis.
      2) Truncus arteriosus.
      3) TOF (severe).
      4) Pulmonary valve stenosis.
      5) HLHS.
      6) CoA.
6. Murmurs.
   a. Murmurs are audible vibrations resulting from turbulence of blood flow and may be due to:
      1) Abnormal valves.
      2) Septal defects.
      3) Regurgitated flow through incompetent valves.
      4) High blood flow across normal structures.
   b. Innocent, or functional, murmurs have been noted in 60% of neonates in the first 48 hours of life (Narvey and MacDonald, 2016). Generally, these murmurs are due to:
      1) Transient left-to-right flow via the ductus arteriosus.
      2) Increased flow over the pulmonary valve associated with a fall in PVR.
      3) Mild bilateral peripheral pulmonary arterial stenosis because of size and pressure differences between the main pulmonary trunk and the left and right pulmonary arterial branches.
   c. Absence of murmur does not indicate absence of significant cardiac disease.
   d. Evaluation of murmurs includes the following:
      1) Intensity of sound.
         a) Murmurs are graded 1 to 6. Grade 3 or less generally presents no hemodynamic problems (Goff, 2020).
            (1) Grade 1: barely audible, only after careful auscultation.
            (2) Grade 2: soft, easily audible on auscultation.
            (3) Grade 3: moderately loud, not associated with a thrill.
            (4) Grade 4: loud murmur associated with a thrill.
            (5) Grade 5: very loud. May be heard with stethoscope just touching the chest wall.
            (6) Grade 6: extremely loud. Can be heard with stethoscope off the chest wall.
         b) Presence of a thrill on palpation is associated with a loud murmur of at least grade 4.
      2) Timing within cardiac cycle.
         a) Systolic: heard during ventricular systole (i.e., between S_1 and S_2) or, if feeling the pulse during auscultation, at the upstroke of the pulse.
            (1) Identified as early, mid-, or late systolic.
            (2) Pansystolic (holosystolic): heard throughout systole. Heard in mitral or tricuspid insufficiency and VSD.
            (3) Ejection murmurs: turbulence of blood flow leaving the heart; noted in aortic or pulmonic valve stenosis, TOF, ASD, and TAPVR.
         b) Diastolic: heard during period of ventricular filling (i.e., between S_2 and S_1) and is usually indicative of a cardiac disorder.
            (1) Early: results from aortic or pulmonic valve insufficiency.
            (2) Mid: increased blood flow across normal mitral or tricuspid valve.
            (3) Late: associated with stenotic mitral or tricuspid valve.

c) Continuous: audible throughout cardiac cycle but can be louder in systole or diastole (e.g., PDA).

3) Quality and pitch.
   a) Pitch: reflects frequency of vibrations.
      (1) High-pitched sound from turbulent blood flow from a high-pressure area to a low-pressure area. Generally reflects valve insufficiency on the left side of the heart, whereas a low-pitched sound reflects right-sided valve insufficiency.
      (2) Low-pitched sound is from a low-pressure difference in turbulent blood flow reflecting right-sided valve insufficiency.
   b) Quality is described as:
      (1) Harsh.
      (2) Blowing.
      (3) Musical.
4) Location: in terms of maximal intensity described by anatomic location on chest wall.
5) Radiation if present.

D. **Peripheral pulses.**
1. Pulses should be synchronous with equal intensity.
2. Upper and lower extremity pulses should be palpated simultaneously and differences documented.
3. Discrepancies (e.g., pulses that are greater in upper than in lower extremities) raise the possibility of an abnormal aortic arch.
4. Right brachial artery pulse should be compared with pulses in lower extremities because the right subclavian is always preductal.
5. Pulse volume graded from 0 to 4. A grade of 2 is assigned to "normal" pulses (Walker, 2018).
   a. 0 = absent.
   b. 1+ = weak.
   c. 2+ = weak to average.
   d. 3+ = strong.
   e. 4+ = bounding.
6. Weak pulses indicate low cardiac output, as seen in:
   a. Left heart outflow obstructive lesions.
   b. Myocardial failure.
   c. Shock.
7. Bounding pulses indicate aortic runoff.
   a. PDA.
   b. Aortic insufficiency.
   c. Systemic-to-pulmonary shunts.
8. Visible precordial impulse persisting after the first 12 hours of life occurs in defects with volume overload and is suggestive of left-to-right shunt (Breinholt, 2017).

E. **Blood pressure.**
1. Normal values are dependent on birth weight and gestational age. Typically, the mean arterial pressure (MAP) is reported as being the same as the gestational age of the infant. However, if the neonate is large for gestational age, the MAP may be higher than gestational age, and if small for gestational age, the MAP may be lower than gestational age (Gardner and Hernandez, 2016).
2. Blood pressure values may also be affected by postnatal age, body weight, body temperature, infant's behavioral state, and cuff size.
3. Cuff width should be 25% greater than the width of the extremity. If the width is too narrow, the blood pressure will have a false high reading. If the cuff width is too wide, the blood pressure will have a false low reading (Frost et al., 2011).
4. Compare upper and lower extremity pressures using four-point blood pressures—measuring blood pressure in all four extremities. Measurements done after the second day of life improve sensitivity and specificity. Systolic blood pressure of the upper extremities 20 mm Hg above that of lower extremities is suggestive of the following (Pantankar et al., 2016):
   a. CoA. PDA may mask these pressure differences.
   b. Aortic arch abnormalities.
      1) In addition, blood pressure differences between the upper extremities are seen with aortic arch abnormalities.
      2) To evaluate, simultaneously measure blood pressure in both arms and one leg. Either leg can be evaluated because the blood supply to both legs comes from the descending aorta below the level of the defect.
5. In a term infant, neonatal hypertension is defined as a systolic blood pressure greater than 90 mm Hg and a diastolic pressure greater than 60 mm Hg.
   a. In a premature infant, systolic pressure greater than 80 mm Hg and diastolic pressure greater than 50 mm Hg indicate hypertension.
   b. Structural and/or functional renal abnormalities are the most common causes of hypertension.

DIAGNOSTIC ADJUNCTS

A. **Arterial blood gas values** are used primarily to help differentiate lung disease versus heart disease as the cause of cyanosis.
1. $Paco_2$: generally normal in CHD and elevated in pulmonary parenchymal disease.
2. Hyperoxia test: should be performed on all neonates with suspected CHD.
   a. Sample arterial Po_2 with infant breathing room air if tolerated. Have the patient breathe 100% oxygen for at least 10 minutes and repeat the arterial Po_2. Measurements should be taken from the right radial artery (Swanson and Erickson, 2016).
      1) Umbilical artery sample may detect right-to-left shunts via PDA. The lowered Pao_2 is

usually a reflection of lung disease and not of primary heart disease.
2) Administration of oxygen to infants with cardiac disease resulting in high pulmonary blood flow and CHF will improve oxygen levels (i.e., increased Pao_2) through decreased PVR and increased pulmonary blood flow.
3) Most accurate assessment of cardiac versus pulmonary disease can be made if the right radial or temporal (preductal) and umbilical artery samples (postductal) are taken simultaneously.
4) Monitoring of preductal and postductal transcutaneous oxygen pressure or pulse oximetry provides a noninvasive evaluation for cardiac versus pulmonary disease.

b. Preductal Pao_2 will rise to greater than 100 mm Hg with pulmonary disease, whereas an increase to less than 100 mm Hg is consistent with cardiac disease. The response of arterial Po_2 in the hyperoxia test should be interpreted in view of the clinical picture (Swanson and Erickson, 2016).

B. **Pulse oximetry** is noninvasive and cost-effective.
1. The combination of pulse oximetry and clinical examination has a sensitivity of 76.5% and specificity of greater than 90%% in detecting CHD (Kumar, 2016).

C. **Chest x-ray examination is used to** (Swanson and Erikson, 2016):
1. Rule out pulmonary parenchymal disease.
2. Identify increased pulmonary vascular markings, as seen in lesions with left-to-right shunting.
3. Evaluate aortic arch.
4. Evaluate cardiac size, shape, and position.
a. Cardiomegaly: defined as cardiac/thoracic ratio greater than 0.6.
b. See Chapter 14 for chest x-ray findings in heart disease.

D. **Electrocardiography (ECG).**
1. Reflects abnormal hemodynamic burdens placed on the heart.
2. Used to determine severity of disease by assessing the degree of atrial or ventricular hypertrophy. Right ventricular predominance is normal shortly after birth. (In utero, the right ventricle does most of the cardiac work.)
3. Changes in ST segments or T waves may suggest myocardial ischemia.
a. Tall, peaked P waves are common in right-sided heart failure.
b. Wide, notched P waves are seen with left-sided heart failure.
4. ECG is the major diagnostic tool for evaluating arrhythmias and the impact of electrolyte imbalances (e.g., potassium and calcium) on electrical conductivity.
5. Normal ECG values in term neonates (Flanagan et al., 2016; Scholtz and Reinking, 2018).
a. Heart rate: 120 to 160 bpm in first week.
b. Normal sinus rhythm: P wave precedes QRS complex.
c. P wave: duration 0.04 to 0.08 second.
d. P-R interval: 0.09 to 0.12 second. Prolonged interval is seen in first-degree heart block and is usually benign.
e. Rightward deviation of the QRS complex with a maximum of −180 degrees and duration of 0.03 to 0.07 second. Prolonged complex indicates interventricular conduction delay.
f. Occasional Q waves in V_1.
g. Premature infants have higher resting heart rates with greater variation. Duration of P wave is shorter. P-R and QRS intervals are decreased (0.10 and 0.04 second, respectively).

E. **Echocardiography** (Vernon and Lewin, 2018).
1. Provides rapid, noninvasive, and relatively painless evaluation of cardiovascular anatomy and function by use of ultrasonic sound waves. Used to estimate pressures, measure gradients, and evaluate cardiac function. The soft tissue and fluids that comprise the heart provide clear windows for cardiac imaging using echocardiography. Although advances in technology and decrease in the size of transducers have increased the sensitivity of echocardiography, it does have some limitations.
a. There are three types of echocardiograms (echo).
1) Transthoracic echo: most common.
2) Transesophageal echo: small transducer is placed in the esophagus in neonates weighing ≥2.5 kg. Used to visualize structures in the posterior chest such as the pulmonary veins. It is also used to guide interventional procedures.
3) Fetal echo: conducted on the pregnant mother to examine the fetal heart and major blood vessels for structural defects and arrhythmias before birth. A family history of CHD, fetal abnormalities detected during routine obstetric ultrasound, abnormal amniocentesis, abnormal fetal heart rhythm, maternal insulin-dependent diabetes mellitus, and exposure to known teratogens are all indications for a fetal echocardiogram. Detects 30% to 50% of severe CHD before birth.

b. M-mode (single-dimension) echocardiography permits evaluation of anatomic relationships of heart and vessels, including relative sizes of each. It is also used to evaluate the motion of the cardiac valves and detect pericardial fluid. Most commonly used to determine ventricular function.

c. Two-dimensional (real-time) echocardiography provides more specific information regarding anatomic relationships. This mode is used to diagnose PDA or ventricular dysfunction in premature infants.
d. Color-flow Doppler echocardiography shows:
   1) Patterns of blood flow (i.e., right-to-left vs. left-to-right shunting).
   2) Location of restrictions and/or regurgitation.
   3) Direction of motion (i.e., warm colors indicate movement toward the transducer and cool, away from the transducer).
e. Continuous-wave Doppler echocardiography shows the quantity of flow across an obstruction, giving an estimate of pressure gradients, which is beneficial in aortic, pulmonary, and mitral stenosis. It is used to detect the direction of shunting, to estimate cardiac output, and to assess ventricular diastolic function.
f. Contrast echocardiography is accomplished by rapid injection of sterile contrast solution, saline, or dextrose in water solution in a vein while conducting an ultrasonographic examination. It allows for greater evaluation of flow patterns throughout the heart and identifies the presence of shunts.
g. 3-D echocardiography provides a great number of cross-sectional images. The newest technique in pediatric echocardiography is matrix-array 3-D, which enhances the ability to identify spatial relationships and assess function, and can record a large amount of image data using limited examination times.
h. 4-D echocardiography, also known as *real-time 3-D echocardiography*, allows for accurate left ventricular volumes, ejection fraction measurements, assessments of structure and function of cardiac valves, and guidance of catheterization interventions (Kwon and Gopal, 2017).

F. **MRI**.
1. Three-dimensional, providing high-resolution images of the heart and great vessels. Used in conjunction with echocardiograms and cardiac catheterization to evaluate pulmonary arteries and veins and systemic veins. It has become the gold standard to quantify mass, volume, and function of both ventricles. Newer modalities that combine both echocardiography and contrast-enhanced MRI are being used to assess ventricular function and volumes (Parra and Vera, 2012).

G. **Cardiac catheterization** (Ofori-Amanfo and Cheifetz, 2013).
1. The focus of this invasive procedure has changed over the past 10 years from a diagnostic modality to an interventional procedure. However, noninterventional cardiac catheterization remains an important tool in presurgical hemodynamic evaluation and reevaluation of previously repaired defects and biopsies of transplanted hearts to detect rejection.
   a. Measures pulmonary artery pressure, detects pulmonary artery stenosis.
   b. May be used in palliative treatment (e.g., in the use of balloon atrial septostomy to treat TGV).
   c. Radiofrequency perforation of atrial septum and atretic valves.
   d. Balloon valvuloplasty.
   e. Acyanotic heart lesions; catheterization can be delayed until the full effect of medical management of CHF is seen.
   f. Treatment modalities during catheterization include coil placement to close the ductus arteriosus, placement of stents after balloon dilation of stenotic heart valves or narrow vessels, and implantation of devices to close ASDs and VSDs, valvuloplasty, and, recently, percutaneous valve implantation, as well as post–cardiac transplantation biopsy.
2. Procedure: advancement of a catheter through the umbilical, subclavian, femoral, or right internal jugular vessels and into the heart.
   a. If balloon septostomy is anticipated, a large vessel will be needed.
   b. Pressure measurements are made of all chambers and outlet tracts.
3. Concomitant angiography (injection of contrast medium): often performed to achieve maximal cardiac information.
4. Interventional techniques have replaced conventional surgery for many lesions.
   a. Objective is improvement or preservation of cardiac function and improvement in quality and quantity of life.
   b. Common procedures (Dodge-Khatami, 2016).
      1) Dilation of valvular lesions (mitral stenosis).
      2) Balloon valvuloplasty for critical aortic or pulmonary valve stenosis.
      3) Dilation and stent placement of CoA.
      4) Dilation and stent placement of pulmonary artery stenosis.
      5) Balloon atrial septostomy.
      6) Transcatheter defect occlusion for PDA.
      7) Catheter-delivered devices for ASD closure and certain muscular VSD closures.
      8) Percutaneous valve implantation.
5. Complications.
   a. Mortality risk is related to the defect, severity of symptoms, and the patient's condition.
   b. High sodium content of contrast medium contributes to myocardial depression and exerts an osmotic effect, temporarily increasing intravascular volume.

c. Hemorrhage with catheter insertion or removal may lead to hypotension, shock, and cardiac tamponade if bleeding is in the pericardial sac.
d. Dysrhythmias are not uncommon (e.g., premature atrial and ventricular beats, heart block, and tachycardia) because of catheter manipulation.
e. In infants younger than 4 months of age, the rate of nonfatal serious complications is 12%.

H. **Laboratory data** (Kunanithy, 2011).
1. Arterial blood gases.
a. Arterial Po_2 to confirm central cyanosis.
b. Pco_2 to rule out pulmonary or central nervous system (CNS) disorders.
2. Complete blood cell count with differential cell count.
a. Rules out anemia or polycythemia as cause of CHF.
b. Decreased number of neutrophils and presence of left shift: possible indication of sepsis. Group B β-hemolytic streptococci can mimic HLHS.
3. Blood glucose concentration. Used to evaluate hypoglycemia as potential cause.
4. Electrolytes (especially potassium and calcium). Both potassium and calcium are major cations in electrical conductivity. Alterations can adversely affect cardiac contractility.

Defects With Increased Pulmonary Blood Flow (Table 28.6)

PATENT DUCTUS ARTERIOSUS

A. **Incidence:** fourth most common lesion.
1. Isolated PDA in term gestations: 1 per 2000 live births.
2. In preterm gestations (Clyman, 2018):
a. Incidence is inversely related to gestational age and weight.
b. Appears in 30% of infants weighing less than 1500 g at birth.
c. Is apparent in 40% of infants weighing 751 to 1000 g at birth.
d. Seen in 50% of infants weighing 500 to 750 g at birth.
3. Occurs 3 times more commonly in females than in males.

B. **Anatomy:** persistent patency of the ductus arteriosus or failure of the ductus arteriosus to close within 72 hours after birth (Fig. 28.7).
1. In-utero patency of this structure is functional, diverting blood to the placenta for gas exchange. About 90% of right ventricular outflow is through the ductus arteriosus.
2. Persistent patency is influenced by several factors.
a. Improvement in oxygenation causes the pulmonary vascular resistance to drop rapidly.

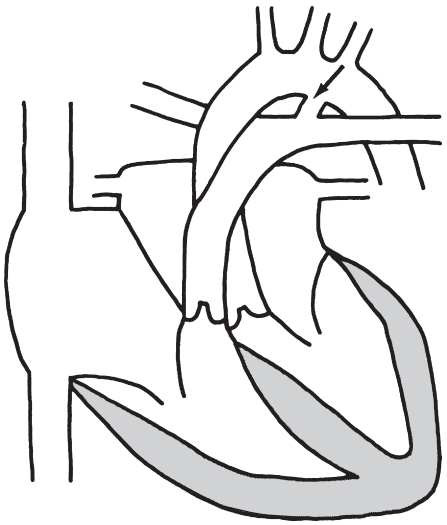

Fig. 28.7 Patent ductus arteriosus (PDA).

Although increased oxygen tension is a potent stimulant of smooth muscle contraction, which should decrease patency, premature infants have an immature response to oxygen; thus, the PDA remains open.
b. Lack of ductal smooth muscle (e.g., in premature infants) prolongs patency.
c. Prostaglandins inhibit closure of ductus.

C. **Hemodynamics.**
1. As PVR falls and SVR rises, a left-to-right shunt via the PDA results in blood flow from the aorta into the pulmonary artery, increasing pulmonary blood flow. The increased pulmonary artery pressure and increased left ventricular pressure and volume lead to bilateral CHF.
2. Because left-to-right flow is dependent on a drop in PVR, infants with pulmonary disease (e.g., respiratory distress syndrome) will show symptoms when lung disease improves. Before this time, PVR greater than SVR leads to a right-to-left shunt via the patent ductus (commonly referred to as *persistent pulmonary hypertension of the neonate*).

D. **Clinical manifestations.**
1. Presents at 4 to 7 days of life with inability to wean from the ventilator or has a need for increased ventilatory and oxygen support. May present with apneic and/or bradycardic spells if not on a ventilator.
a. Increased pulmonary vasculature and cardiomegaly.
b. Bounding peripheral pulses and hyperactive precordium.
c. Widening pulse pressure (>20 mm Hg).
d. Low diastolic blood pressure.
e. Unexplained metabolic acidosis.
2. Continuous murmur may be present at the upper left sternal border, but may be "silent" in 10% to

20% of the preterm infants despite hemodynamically significant shunt.

3. Radiographic findings consist of normal size or mild cardiomegaly (cardiothoracic ratio >0.60), pulmonary edema, and increased pulmonary vascularity. These "typical" signs may be absent if the infant is receiving positive pressure ventilation.
4. Echocardiography is the gold standard for diagnosis. Two-dimensional echocardiography will provide anatomic information about the diameter, length, and shape of the ductus. Doppler flow will provide information on the ductal shunt magnitude and patterns and pulmonary artery pressure.
5. Clinical cardiovascular distress scoring system evaluates five variables, and score ≥3 is associated with hemodynamically significant PDA (Mezu-Ndubuisi et al., 2012).
   a. Heart rate.
   b. Peripheral arterial pulses.
   c. Precordial pulsations.
   d. Duration of murmur.
   e. Cardiac silhouette on chest x-ray.
6. B-type natriuretic peptide (BNP) levels between 70 and 100 pg/mL are used to identify a symptomatic PDA (Mezu-Ndubuisi et al., 2012). Some studies have reported specificity of 100% and sensitivity of 93% using a cutoff value of 132.5 pg/mL (Davlouros et al., 2011). In a recent study, N-terminal (NT)–proBNP levels on the second day of life were found to predict need for early indomethacin therapy (Kim, 2018).

E. **Management**.

1. Dependent on whether shunt is hemodynamically significant. In premature infants, the PDA may prolong ventilator use beyond the dictates of the initial lung disease.
2. Hemodynamically significant ductus arteriosus includes the following:
   a. Heart rate greater than 170 bpm.
   b. Respiratory rate greater than 70/minute.
   c. Hepatomegaly greater than 3 cm below costal margin.
   d. Bounding pulses.
3. Conservative measures are generally employed initially, which may minimize exposure to pharmacologic agents. However, delaying treatment may decrease response to nonsteroidal antiinflammatory drugs (NSAIDs).
   a. Fluid restriction to less than 130 mL/kg/day.
   b. Diuretics: used cautiously with fluid restriction, may lead to electrolyte imbalance, dehydration, and caloric deprivation.
   c. Positive end-expiratory pressure: useful in reducing left-to-right shunt via PDA.
4. Medical management using an NSAID that inhibits cyclooxygenase-1 (COX-1) and/or cyclooxygenase-2 (COX-2). Treatment choices are indomethacin and ibuprofen lysine, both manufactured by Ovation Pharmaceuticals, Inc. Success rate is 65% (Kim, 2018).
   a. Ibuprofen lysine (NeoProfen) gained U.S. Food and Drug Administration approval in 2006 for treatment of clinically significant PDA in neonates with birth weight 500 to 1500 g and gestational age ≤32 weeks at time medication is given (Overmeire, 2007). Inhibits both COX-1 and COX-2 enzymes but has less COX-1 inhibition than indomethacin.
      1) Initial dose 10 mg/kg IV, followed by two doses of 5 mg/kg IV at 24 and 48 hours after the first dose (Kim, 2018).
      2) Reduced rates of necrotizing enterocolitis and transient renal insufficiency when compared with indomethacin (Clyman, 2018).
      3) Does not affect mesenteric blood flow and does not decrease cerebral blood flow (Clyman, 2018).
      4) Monitor serum creatinine, blood urea nitrogen, platelet count, and urine output during treatment course.
   b. Indomethacin management includes the following (Clyman, 2018; Swanson and Erickson, 2016):
      1) As a prostaglandin inhibitor, indomethacin can constrict and close the PDA in some premature infants.
      2) Initial dosage is 0.2 mg/kg IV, followed by two doses of 0.1 mg/kg IV every 12 to 24 hours, for a total of three doses.
      3) Prophylactic treatment in the extremely low birth weight premature neonate in the first 24 hours after birth showed a decrease in intraventricular hemorrhage when compared with placebo.
      4) Complications related to indomethacin being a stronger COX-1 inhibitor are as follows:
         a) Transient oliguria and decreased renal blood flow.
         b) Increased incidence of gastrointestinal bleeding.
         c) Inhibition of platelet aggregation for 7 to 9 days, with potential for intracerebral hemorrhage.
      5) Contraindications (Swanson and Erickson, 2016).
         a) Renal failure (blood urea nitrogen concentration >30 mg/dL, serum creatinine concentration >1.8 mg/dL, urine output <0.5 mL/kg/hr).
         b) Active bleeding or platelet count <50,000.
         c) Suspected necrotizing enterocolitis.
         d) Thrombocytopenia.
         e) Sepsis: suspected or proven.

5. Surgical management: ligation of the PDA should be reserved for those patients with need for escalating respiratory support or inotrope-dependent hypotension (Clyman, 2018).
   a. Standard approach is surgical ligation via posterolateral thoracotomy incision.
   b. New techniques include placement of a stainless-steel spring coil or Amplatzer PDA occlusion device via interventional cardiac catheterization, with complete occlusion rates of approximately 90% at 24 hours after the procedure and 98% at 6 months. However, this therapy is only approved for older infants and children. A newer device, the Amplatzer Duct Occluder II, is available in Europe for all types of PDAs (Kim, 2018). Minimally invasive video-assisted thoracoscopic surgery allows for PDA closure using two titanium clips that are placed using surgical instruments (Stankowski et al., 2017).

F. **Prognosis:** Surgical ligation is associated with unilateral vocal cord paralysis, postligation hypotension, bronchopulmonary dysplasia, and abnormal cognitive development, especially in the extremely low birth weight infant. Avoiding/delaying ligation is associated with a decrease in adverse events (Clyman, 2018).

VENTRICULAR SEPTAL DEFECT

A. **Incidence:** At 2 per 1000 live births, VSDs are the most common of all CHDs, accounting for 37% of all congenital heart disease (Wael and Oliver, 2019).

B. **Anatomy:** Abnormal opening in the septum between the right and left ventricles. Sizes range from pinhole to almost complete absence of the ventricular septum (Fig. 28.8).

C. **Hemodynamics.**
   1. The degree of hypertrophy of ventricles and the pressure relationships are dependent on the size of the defect. A small defect allows pressure differences between ventricles.
   2. PVR less than SVR results in a left-to-right shunt, producing increased pulmonary blood flow and leading to decreased pulmonary compliance and pulmonary edema.
   3. Excessive pulmonary artery blood flow eventually results in pulmonary artery hypertrophy and stenosis.
   4. High pulmonary artery pressure can delay maturation of pulmonary arterioles.

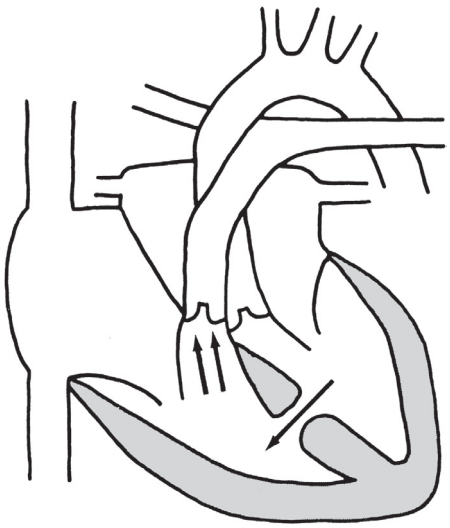

Fig. 28.8 Ventricular septal defect (VSD).

D. **Clinical manifestations.**
   1. Size dependent.
   2. Small VSD.
      a. Asymptomatic.
      b. High-pitched pansystolic murmur along the left sternal border 4 to 10 days after birth.
   3. Moderate VSD: asymptomatic except for murmur, fatigue with feeding, and recurrent respiratory infections.
   4. Large VSD.
      a. Present at 1 to 2 months of age with CHF, hepatomegaly, recurrent pulmonary infections, and increased precordial activity.
      b. Loud, blowing pansystolic murmur at the left lower sternal border.
      c. Chest x-ray examination: cardiomegaly and increased pulmonary vascular markings.
      d. Two-dimensional echocardiography is capable of identifying 90% of VSDs. Doppler and/or color-flow mapping increases the accuracy of diagnosis of VSD. Color flow is extremely useful in identifying multiple VSDs and the direction of blood flow across the VSD.

E. **Management**.
   1. Close to 90% of small defects will close spontaneously during the first year of life; 20% of large defects become smaller or close (Wael and Oliver, 2019).
   2. Plasma BNP is useful in the diagnosis of CHF, although levels may vary for different defects; following trends in the levels may help estimate cardiac stress and predict outcomes (Swanson and Erickson, 2016). With mild CHF, treatment consists of digoxin and diuretics.
   3. Surgery is indicated if patient has failure to thrive or intractable CHF.
      a. Palliative: surgical banding of pulmonary artery to reduce pulmonary blood flow, decrease CHF, and prevent pulmonary vascular resistance.
      b. Surgical: repair by suturing defect or patching defect through a median sternotomy. The defect is approached via the right atrium and tricuspid valve through ventriculotomy. Indicated in the first 6 months of life if failure to thrive develops and medical management fails to control CHF.

Also indicated in the 6- to 12-month-old who has a large VSD without symptoms of CHF. Pulmonary artery banding is falling out of favor. Use of new hybrid approaches when the cardiac surgeon and interventional cardiologist work as a team is growing (Sholtz and Reinking, 2018).

c. Transcatheter devices, such as the clamshell, double-umbrella, and buttoned devices, and patch may be used but are unpopular in the United States (Wael and Oliver, 2019).

F. **Prognosis:** excellent. Mortality rate is less than 1% in infants. Complications from surgical closure may include a residual VSD (persistent shunt), right bundle-branch block, third-degree heart block, and aortic and/or tricuspid insufficiency (Swanson and Erickson, 2016).

ATRIAL SEPTAL DEFECT
(SWANSON AND ERIKSON, 2016)

A. **Incidence:** 1 per 5000 live births, 7% to 10% of all cardiac defects. Female-to-male ratio 2:1 (Kensey et al., 2011).

B. **Anatomy:** defect in formation of septum, resulting in a communication between right and left atria. Defect may be an ostium primum defect, an ostium secundum defect (most common), or a partial endocardial cushion defect (Fig. 28.9). By definition, a patent foramen ovale (PFO) is generally excluded, although symptoms can be the same.

C. **Hemodynamics.**
1. Immediately after birth, right ventricular pressure is greater than left ventricle pressure, so there is no shunt or only a small right-to-left shunt.
2. As PVR decreases, left-to-right shunt develops with concomitant right ventricular volume overload and hypertrophy.

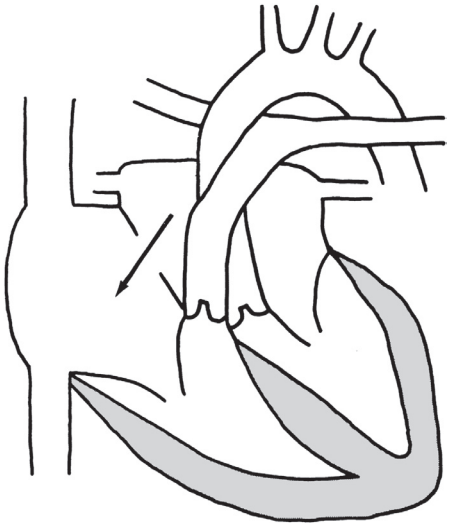

Fig. 28.9 Atrial septal defect (ASD).

D. **Clinical manifestations.**
1. The isolated defect is generally asymptomatic and unrecognized. If ASD is diagnosed in infancy, greater than 50% of the patients will be symptomatic.
2. CHF from left-to-right shunt with mitral valve insufficiency.
3. Failure to thrive.
4. Recurrent respiratory infections.
5. Systolic murmur at the second intercostal space at the left sternal border, persistent split S_2 if shunt is large, diastolic murmur heard at the left lower sternal border.
6. Chest x-ray examination: increased pulmonary vascular markings with enlarged right atrium and ventricle.

E. **Management**.
1. If defect is small, clinical follow-up is indicated; it may close spontaneously (Carr, 2017).
2. ASD with CHF: medical treatment of CHF and delay surgical repair.
3. ASD with intractable CHF or if defect is very large or lacks significant borders for positioning of closure device: early surgical repair (i.e., suturing or patching of defect).
4. Surgical repair is required for the ASD that can't be closed by cardiac catheterization interventions. Complete atrioventricular septal defects require surgical repair at about 4 to 6 months. CHF may need to be treated with Lasix, afterload reduction, and digoxin. It is rare that palliative banding will be used to control blood flow through the pulmonary artery (Schlotz and Reinking, 2018).
5. Transcatheter closure devices are now commonly used for secundum ASD closure. Device sizes range from 6 to 48 mm. The larger the device, the larger the infant needs to be. Implantation of the device is guided by transthoracic echocardiography. One type of device has two sides, with one side of the device placed on the left side of the septum and the other on the right, which forms a sandwich over the defect. This acts as a framework for normal tissue to grow over the defect (Chen et al., 2012). Benefits are quick recovery time and avoiding cardiopulmonary bypass and sternotomy (Carr, 2017).

F. **Prognosis**.
1. Spontaneous closure occurs in up to 80% of small secundum ASDs during the first 2 years of life.
2. Surgical or device closure of the defect requires long-term follow-up by cardiology.

ENDOCARDIAL CUSHION DEFECT (CANAL)

A. **Incidence:** 1 per 9000 live births. Most common heart defect found in Down syndrome.

B. **Anatomy.**
1. Endocardial cushions form the lower portion of the atrial septum, the upper portion of the ventricular

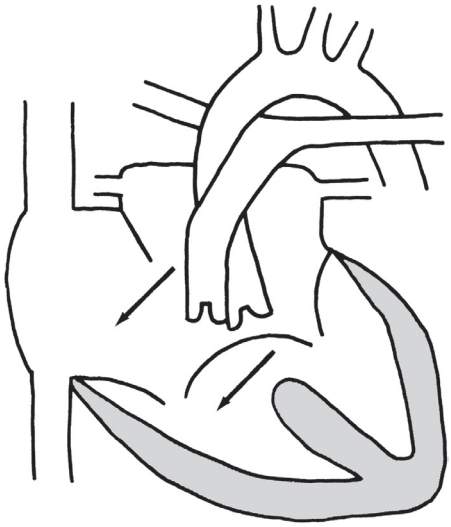

Fig. 28.10 Atrioventricular canal (AVC).

septum, and septal portions of the mitral and tricuspid valves.

2. A wide range of defects is possible, from simple cleft of the mitral and/or tricuspid valves to complete absence of the lower atrial and upper ventricular septa with common atrioventricular valve (i.e., atrioventricular canal) (Fig. 28.10).

C. **Hemodynamics**.
1. With PVR less than SVR, blood dependently shunts left to right via the ASD and the VSD.
2. Higher pressure of the left ventricle creates obligatory left-to-right shunting via the atrioventricular valve (atrioventricular valve regurgitation). Blood flows from the left ventricle to the mitral portion of the atrioventricular valve to the left atrium, to the ASD, and to the right atrium.

D. **Clinical manifestations.**
1. Isolated ostium primum atrial defect: rarely identified in the neonatal period.
2. Isolated ventricular defect: see clinical features of VSD.
3. Complete atrioventricular canal.
   a. Atrioventricular valve regurgitation controls age at presentation.
      1) Severe: seen at 1 to 2 weeks of age with CHF.
      2) Valves competent: seen in first or second month of life.
   b. Respiratory distress.
   c. Active precordium with a thrill at the left lower sternal border.
      1) Single S_1 and split S_2 (Pettersen, 2016).
   d. Variable murmurs; usually loud pansystolic murmur at the lower left sternal border, radiating to left back.
   e. Recurrent respiratory infections.
   f. Chest x-ray examination: cardiomegaly, bilateral atrial and ventricular hypertrophy, increased pulmonary markings.

E. **Management**.
1. Objective: avoid development of pulmonary vascular obstructive disease.
2. Medical management: prevent or control CHF with digoxin, angiotensin-converting enzyme (ACE) inhibitors, and diuretics only for a few weeks.
3. Single-stage complete repair preferred using a pericardial patch to repair the tricuspid and to create a functional mitral valve. A newer approach uses a pericardial patch to close the ASD, a polytetrafluoroethylene patch to close the VSD, and closure of the mitral valve cleft.
4. Palliative pulmonary artery banding to decrease pulmonary overload in low birth weight infants or those with muscular VSDs. Does not influence obligatory shunting of the atrioventricular valve (Pettersen, 2016).

F. **Prognosis**.
1. Prognosis is dependent on details of anatomic form and on the presence of significant associated noncardiac anomalies and significant pulmonary obstructive vascular disease.
2. Best results are seen with ostium primum defect or common atrium; long-term prognosis is good.
3. Outlook for complete atrioventricular canal without operation is poor.
4. Mortality rate for surgical repair is under 5%. Up to 20% will develop mitral regurgitation; 9% will require another surgical procedure (Pettersen, 2016).

Obstructive Defects With Pulmonary Venous Congestion (see Table 28.6)

COARCTATION OF THE AORTA

A. **Incidence:** 7% of congenital heart lesions (Swanson and Erickson, 2016).
1. Neonate becomes critically ill after ductal closure.
2. Mild coarctation does not present in neonatal/infancy period (Scholtz and Reinking, 2018).
3. Male dominance: 2:1.
4. Ten percent of those with Turner's syndrome will have this defect.

B. **Anatomy:** constriction of aorta at the junction or the transverse aortic arch or the vicinity of the ductus arteriosus (Fig. 28.11) (Scholtz and Reinking, 2018).
1. Most common site is below the origin of the left subclavian artery.
2. Preductal coarctation is associated with hypoplasia of the aortic arch. Defects such as VSD, PDA, and TGA will be found in 40%.
3. Seventy percent of infants with coarctation will have a bicuspid aortic valve.

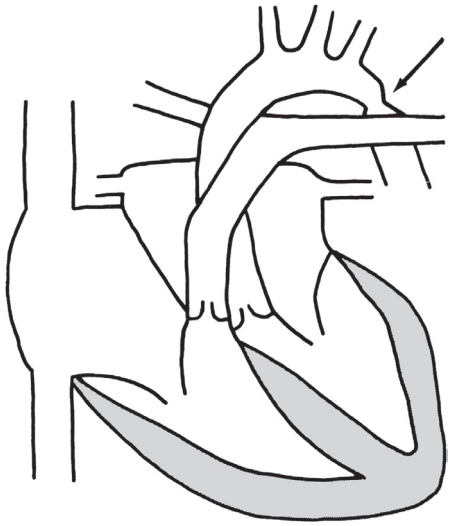

Fig. 28.11 Coarctation of aorta.

C. **Hemodynamics**.
   1. Isolated coarctation: obstruction to left ventricular outflow, leading to increased left ventricular, left atrial, and pulmonary venous pressures. Pulmonary venous congestion develops.
   2. Coarctation with VSD: elevated left ventricular pressure, shunting blood left to right via VSD and causing pulmonary overload.
   3. Preductal coarctation: dependent on PDA for distal aorta and lower body blood flow.

D. **Clinical manifestations.**
   1. CHF as a result of pressure overload on the left ventricle.
      a. If severe, will result in cardiovascular collapse after ductus closes.
   2. Decreased or absent pulses in the lower extremities.
   3. Lower extremities cool to touch.
   4. Higher blood pressure (>15 mm Hg) in upper extremities is the most consistent factor in critical coarctation and is present in 97%. If blood pressures are lower in the upper extremities, the following applies:
      a. Decreased blood pressure in left arm: indicative of left subclavian artery as site of coarctation.
      b. Decreased blood pressure in right arm: right subclavian artery arises below coarctation (rare).
      c. Pulses that "wax and wane": related to increase or decrease in PDA blood flow.
   5. Heart sounds.
      a. Postductal: no murmur or short systolic ejection click in axilla or back.
      b. Preductal with VSD: harsh pansystolic murmur at the left lower sternal border.
      c. Gallop rhythm possible.
   6. Systolic thrill heard at the suprasternal notch.
   7. Chest x-ray examination: enlarged heart with left ventricular hypertrophy and increased pulmonary vascular markings.
   8. Echocardiogram will define the location of the coarctation and identify the extent of aortic narrowing (Scholtz and Reinking, 2018).

E. **Management**.
   1. Intubation and mechanical ventilation (Scholtz and Reinking, 2018).
   2. Aggressive medical management of CHF.
   3. Use of dopamine and/or dobutamine for inotropic support (Swanson and Erickson, 2016).
   4. Prostaglandin E_1 (PGE_1) to dilate ductus arteriosus (preductal lesion).
      a. Dose: 0.05 to 0.1 mcg/kg/min IV infusion, titrate dose.
      b. Response: ductus arteriosus will reopen 30 to 120 minutes after infusion starts.
      c. Adverse effects: apnea, fever, hypotension.
   5. Surgical management (Scholtz and Reinking, 2018).
      a. Indicated at time of diagnosis, even if the neonate is asymptomatic.
      b. Lateral thoracotomy performed, coarctation is excised, and an end-to-end anastomosis is done.
      c. A patch to enhance the aortic arch will be used if long-segment narrowing is found. A more extended end-to-end anastomosis will be used.
      d. Balloon angioplasty not typically performed due to high risks of aneurysm, vascular injury, and recoarctation.

F. **Prognosis**.
   1. Outcome is dependent on complexity of coarctation, with mortality rates at 1 month ranging from zero for simple coarctation to 4%; can be higher for complex coarctation associated with VSD or other left-sided obstruction (Sen et al., 2018).
   2. Long-term prognosis after coarctation repair is determined by the presence of residual or recurrent coarctation, aortic aneurysm, persistence of pulmonary hypertension, and residual cardiovascular lesions (Swanson and Erickson, 2016).
      a. Ten to 15% of children will have a recurrence of the coarctation, which is typically managed with balloon angioplasty (Scholz et al., 2018).
      b. Incidence of recurrence necessitating reintervention after surgical correction is 17% in the neonatal period and 42% in postneonatal period.
      c. Surgical mortality is approximately 5% (Scholtz and Reinking, 2018).
   3. The most common complication is hypertension.

CRITICAL AORTIC STENOSIS

A. **Incidence:** 1 per 24,000 live births, accounts for 5% to 6% of all cardiac anomalies.
   1. Four times more likely in males.

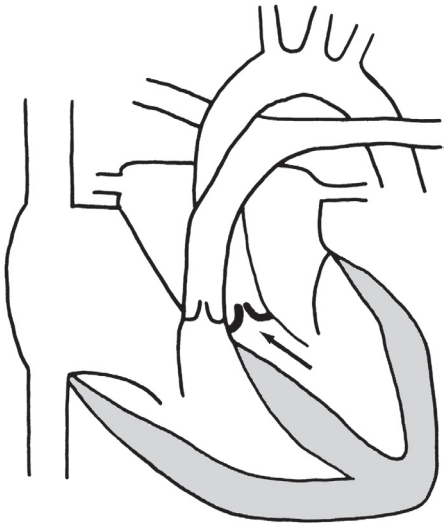

Fig. 28.12 Aortic stenosis.

B. **Anatomy:** may be subvalvular, valvular, or supravalvular, with valvular stenosis being the most common form. The myocardium of the left ventricle is hypertrophied (Fig. 28.12).
   1. Valvular stenosis usually has a bicuspid aortic valve.
   2. Supravalvular stenosis is the least common and is seen with Williams syndrome.
C. **Hemodynamics:** obstruction to left ventricular outflow leads to increased left ventricular pressures and hypertrophy. If aortic stenosis is severe in utero, blood flow through the ventricle is decreased, resulting in left ventricular hypoplasia and left-sided heart syndrome.
D. **Fetal treatment:** several centers throughout the United States perform fetal balloon aortic valvuloplasty procedures in select patients in an attempt to maximize ventricular growth in utero (Moon-Grady, 2017).
E. **Clinical manifestations** (Swanson and Erickson, 2016).
   1. When PDA begins to close, the neonate will quickly become pale/gray with cool skin.
   2. Decreased perfusion.
   3. Decreased peripheral pulses.
   4. Heart sounds include a grade II to IV/VI harsh systolic murmur in upper right sternal border, radiating to the neck and lower left sternal border.
   5. Ejection click heard at apex.
   6. Suprasternal notch thrill may be palpable.
   7. CHF develops because of pressure overload of left ventricle.
   8. Metabolic acidosis due to decreased cardiac output.
   9. Chest x-ray examination shows cardiomegaly with normal pulmonary vascular markings.
F. **Management**.
   1. Medical management is usually not successful.
   2. Initially, CHF is treated with fluid restriction, diuretics, digoxin, inotropic medications, acidosis management, positive pressure ventilation, and antibiotic prophylaxis.
   3. Begin PGE_1 to prevent hypoxia.
   4. The treatment of choice in neonates is balloon valvuloplasty. Early mortality rate is 5%. However, 20% will develop significant aortic insufficiency at 2 years (Rossi et al., 2011). Using retrograde catheterization via the right carotid artery can be done at the bedside using continuous transesophageal echocardiography (Weber, 2018).
   5. Surgery is reserved for patients who fail balloon valvuloplasty and involves either open aortic valvotomy while patient is on cardiopulmonary bypass or transventricular valvotomy without bypass or valve replacement, with mortality less than 10% (Hraska et al., 2012; Weber, 2018). The number of aortic valvotomies has declined substantially since balloon valvuloplasty has gained favor.
   6. The modified Ross–Konno procedure may be used in children with complex left ventricular outflow obstruction (Sames-Dolzer et al., 2018). The pulmonary valve is removed and placed into the aortic position. The pulmonic value is replaced by a homograft. Eventually, the child will outgrow the homograft, which will need to be surgically replaced.
G. **Prognosis**.
   1. Success rate of balloon valvuloplasty is very high.
   2. Critical aortic stenosis accounts for 1% of all sudden death in children with heart disease.

Obstructive Defects With Decreased Pulmonary Blood Flow (see Table 28.6)

TETRALOGY OF FALLOT

A. **Incidence:** 1 per 5000 live births. Most common cyanotic heart lesion, accounting for 10% of all defects.
B. **Anatomy:** classified as a combination of four defects, although numbers 3 and 4, next, are consequences of numbers 1 and 2, shown next (Fig. 28.13).
   1. Pulmonary stenosis: obstruction of outflow tract.
   2. VSD.
   3. Aorta overriding VSD.
   4. Right ventricular hypertrophy.
C. **Hemodynamics**.
   1. Dependent primarily on degree of pulmonary stenosis and to a lesser extent on VSD size.
   2. In severe pulmonary stenosis, blood flow passes from right to left via the VSD, with resulting hypoxia and cyanosis.
   3. In mild pulmonary stenosis, blood flows from left to right via the VSD, with CHF resulting.
   4. In mild to moderate pulmonary stenosis, blood flow via the VSD may be minimal as long as PVR

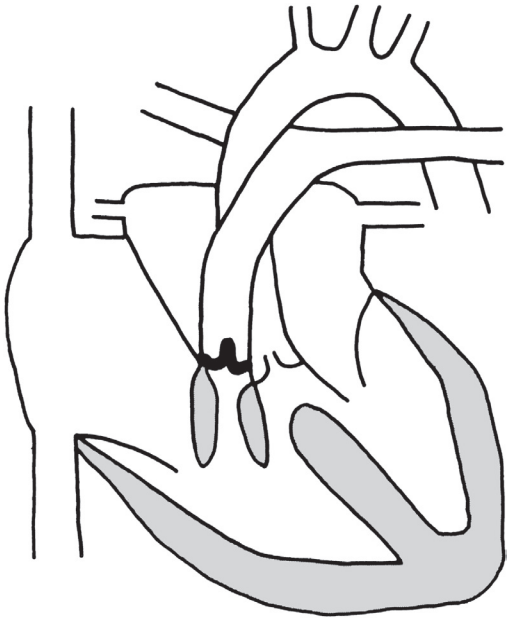

Fig. 28.13 Tetralogy of Fallot (TOF).

and SVR are balanced. With crying, right-to-left shunting occurs.

D. **Clinical manifestations.**
   1. Presentation is a function of the degree of pulmonary stenosis.
   2. Severe obstruction presents in the first days of life with severe cyanosis, hypoxia, and dyspnea as ductus begins to close.
   3. Milder pulmonary obstruction presents in the first days of life with mild cyanosis.
   4. Harsh grades II to IV/VI systolic murmur with thrill present at mid- to upper left sternal border.
   5. Chest x-ray examination shows normal-sized boot-shaped heart with normal or decreased pulmonary vascular markings.
   6. Traditional "Tet spells" (paroxysmal dyspnea and severe cyanosis) are common in infants and can occur in neonates.

E. **Management**.
   1. Medical (Swanson and Erickson, 2016).
      a. Majority of neonates are stable and require no medical management.
      b. If there is severe right ventricular outflow tract obstruction, PGE_1 is used to maintain patency of the ductus arteriosus until the infant can be taken to surgery.
      c. Propranolol is the drug of choice for treating hypercyanotic infants.
      d. Hypercyanotic or Tet spells: place the neonate in the knee–chest position. Oxygen, morphine, and fluid boluses may be needed (Swanson and Erickson, 2016).
   2. Corrective surgery involves closure of the VSD with a patch and eliminating the pulmonary stenosis by resection. The pulmonary outflow tract may be enlarged by a patch.
      a. If the neonate has severe pulmonary stenosis or atresia, a Blalock–Taussig procedure is generally performed, with full correction at a later time. More commonly, complete correction is being done earlier in symptomatic neonates (Scholtz and Reinking, 2018).
      b. Early complete repair reduces secondary damage to the major organs and has lower mortality (Yang et al., 2019).

F. **Prognosis** (Swanson and Erickson, 2016).
   1. Prognosis without surgery is very poor.
   2. Ventricular arrhythmias and sudden death due to right ventricular dilatation.
   3. Because of the patch across the pulmonary annulus, the pulmonary valve is dysfunctional, leading to pulmonary regurgitation. Eventually (after decades), right ventricular dilation develops and adversely affects right ventricular function (Swanson and Erickson, 2016).
   4. Long-term follow-up is necessary, as most will require future surgery/intervention for pulmonary valve replacement.
   5. Repair under 30 days of age has a higher rate of morbidity and mortality but has better overall physical growth. Repair over 91 days of age has lower mortality and morbidity (Yang et al., 2019).

PULMONARY STENOSIS

A. **Incidence:** 1 per 14,000 live births, 5% to 8% of all CHDs.

B. **Anatomy:** narrowed opening either in pulmonary valve as a consequence of pulmonary valve cusp fusions (Fig. 28.14) or above or below the valve because of tissue hypertrophy.

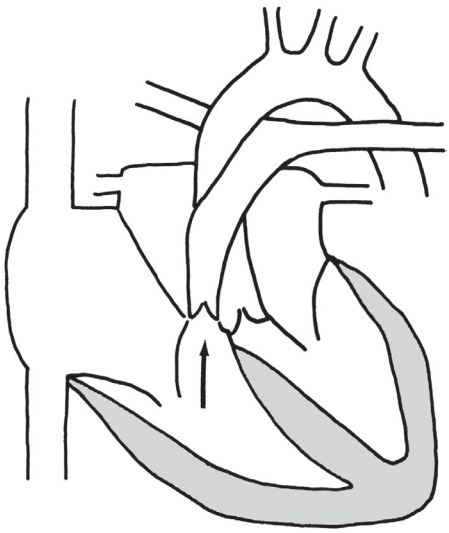

Fig. 28.14 Pulmonary stenosis (PS).

C. **Hemodynamics.**
   1. In utero, right ventricular hypoplasia can develop, depending on the degree of pulmonary valve stenosis and subsequent decrease in right ventricular blood flow.
   2. After birth, the combination of right ventricular hypoplasia and severe pulmonary valve stenosis redirects blood flow from right to left at the atrial level via the foramen ovale. Pulmonary blood becomes dependent on a left-to-right flow via the PDA.
   3. In mild stenosis, the pulmonary blood flow is not excessively restricted and is PDA independent. As PVR decreases, atrial right-to-left shunt will decrease, improving systemic hypoxia.

D. **Clinical manifestations.**
   1. Mild pulmonary stenosis: loud systolic murmur at left upper sternal border is the only finding.
   2. Moderately severe stenosis.
      a. Harsh grade II to III/VI heard left upper sternal border. Murmur of tricuspid insufficiency may be noted. Ejection click may be auscultated at left sternal border (Swanson and Erikson, 2016).
      b. If critical pulmonary stenosis, right-sided CHF will present due to increased pressure overload (Swanson and Erickson, 2016).
      c. Cyanosis is present and increases with PDA closure.
      d. Generally, hepatomegaly is present.
   3. Chest x-ray examination: mild cardiomegaly with bulging right heart border and decreased pulmonary vascular markings.
   4. Two-dimensional echocardiography used to make anatomic and physiologic diagnosis (Vernon and Lewin, 2018).

E. **Management**.
   1. Cyanotic neonate.
      a. Initial management: oxygen, bicarbonate, and PGE_1.
      b. Nonsurgical treatment has the highest safety with transcatheter balloon valvuloplasty and stent implant in neonates and infants.
         1) Few complications; effective.
         2) Treatment of choice for most lesions.
         3) Is 96% successful in neonatal patients.
      c. Surgical valvotomy or tissue excision is reserved for specific cases or when valvuloplasty fails and patient is symptomatic.
   2. Noncyanotic neonate: conservative management includes catheterization at 6 to 12 months if stenosis is severe, with subsequent surgery if right ventricular pressure exceeds systemic.
      a. Hybrid approach combining catheterization and surgical approach is more effective and safer in patients with complex lesions (Kang and Benson, 2018).

F. **Prognosis:** excellent for both balloon and operative procedures. Pulmonary insufficiency may occur as a late complication of balloon valvuloplasty requiring pulmonary valve replacement (Rao, 2019). Operative mortality rate for valvuloplasty is less than 1%.

PULMONARY ATRESIA

A. **Incidence:** 1 per 14,000 live births, accounting for less than 1% of cardiac defects.

B. **Anatomy:** complete obstruction of the pulmonic valve, resulting in a hypoplastic right ventricle and tricuspid valve (Fig. 28.15). In the presence of a VSD, the right ventricle may be of adequate size.

C. **Hemodynamics.**
   1. Venous blood returning to the right atrium goes across the foramen ovale into the left atrium, into the left ventricle, and out the aorta.
   2. Blood flow to the lungs is derived entirely from a left-to-right shunt at the ductus arteriosus, which is generally small and tortuous. As the PDA closes, severe hypoxemia ensues.
   3. Regurgitant blood flow occurs at the tricuspid valve.

D. **Clinical manifestations.**
   1. Mild cyanosis at birth, progressing to intense cyanosis by 24 hours.
   2. Tachypnea.
   3. Heart sounds.
      a. PDA murmur is present.
      b. Soft systolic murmur is heard at the upper left sternal border, and harsh systolic murmur at the lower right and upper left sternal border if tricuspid insufficiency is present.
   4. Chest x-ray examination shows increased heart size with decreased pulmonary markings. Right atrial hypertrophy is seen in 70%.

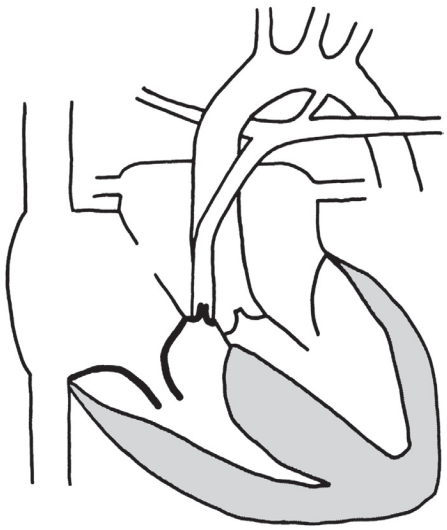

Fig. 28.15 Pulmonary atresia.

5. Two-dimensional echocardiography with Doppler and color-flow mapping and 3-D echocardiography are used to determine absence of blood flow across the pulmonary valve and are standard for diagnosis (Parra and Vera, 2012).

E. **Management**.
1. Initial treatment is use of fluid, oxygen, and bicarbonate for metabolic acidosis and PGE_1 to maintain patency of the ductus arteriosus.
2. Digitalis and diuretics to manage CHF.
3. Cardiac catheterization is done with balloon atrial septostomy in infants with pulmonary atresia.
4. Balloon valvuloplasty with or without stent placement is used in small neonates and infants (Chubb et al., 2012).
5. Percutaneous valve placement is a newer treatment option with favorable outcomes (Balzer, 2012).
6. Mild right ventricle hypertrophy: surgical valvotomy may be effective. With severe hyperplasia of right ventricle and tricuspid valve, usually a Blalock–Taussig shunt to provide systemic-to-pulmonary shunting in the neonatal period that may be converted at 3 to 6 months to a bidirectional Glenn procedure. These infants will later require definitive repair via completion of the Fontan procedure, resulting in communication between the right ventricular outflow tract and the pulmonary artery (Rodriguez-Cruz, 2015).
7. Heart–lung transplant may be needed in patients with complete atresia of left and right pulmonary arteries.

F. **Prognosis**.
1. Without surgery, the mortality rate is 100%. If reconstruction of the right ventricular outflow tract is needed and the ductus arteriosus is closed, the mortality rate is 25%.
2. Long-term complications are arrhythmias, CHF, infective endocarditis, brain abscesses, delayed growth, and sudden death (Rodriguez-Cruz, 2015).
3. Increased mortality after Blalock–Taussig shunt with ductal closure is noted.

TRICUSPID ATRESIA

A. **Incidence:** 1 per 10,000 live births. Most are diagnosed prenatally via ultrasound and fetal echocardiography (Centers for Disease Control and Prevention [CDC], 2018).

B. **Anatomy:** agenesis of the tricuspid valve development with associated PFO or ASD (Fig. 28.16).
1. VSD is often associated with the hypoplastic right ventricle.
2. Pulmonary atresia or stenosis typically present.
3. TGV occurs in 30% of cases.

C. **Hemodynamics**.
1. Systemic venous blood is shunted from the right atrium across the foramen ovale or ASD into the left atrium. With an isolated defect, the pulmonary blood flow is supplied by the left ventricular outflow via the PDA.
2. In the presence of a VSD, some of the blood entering the left ventricle shunts across into the hypoplastic right ventricle and out the pulmonary artery—or out the aorta in the case of coexisting transposition. If severe pulmonary stenosis or atresia is present, blood does not flow through the VSD (see also item C.1).

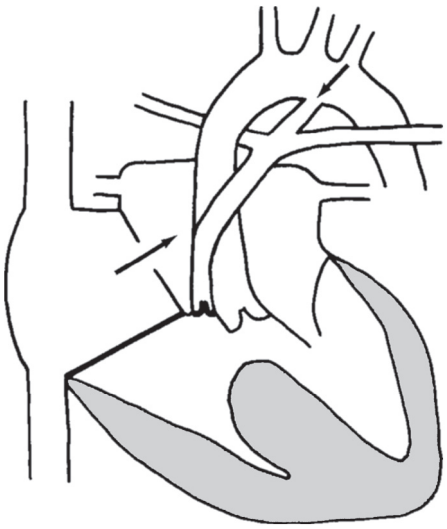

Fig. 28.16 Tricuspid atresia. *Arrows* identify shunting through the patent foramen ovale and the patent ductus arteriosus.

D. **Clinical manifestations.**
1. Cyanosis usually presents soon after birth with an isolated defect or coexisting VSD and pulmonary outflow tract obstruction. Increasing cyanosis occurs with closure of the ductus.
2. Dyspnea; tachypnea may be present.
3. CHF ensues with large VSD and absent pulmonary stenosis, usually within the first month of life.
4. Murmur is absent unless associated with pulmonary stenosis, VSD, or PDA.
5. Chest x-ray examination shows variable heart size, depending on the degree of pulmonary stenosis; size is generally nondiagnostic.
6. Cardiac catheterization to perform a balloon septostomy to improve intra-atrial mixing of blood.

E. **Management**.
1. Primary treatment: depends on decreased vs. increased pulmonary blood flow.
   a. Decreased pulmonary blood flow: oxygen, bicarbonate, and PGE_1 for severe hypoxia.
   b. Increased pulmonary blood flow: diuretics and digoxin.
2. Palliative treatment will allow 50% to survive into teen years (Mancini, 2016).
   a. Systemic-to-pulmonary artery shunt, including Blalock–Taussig procedure.

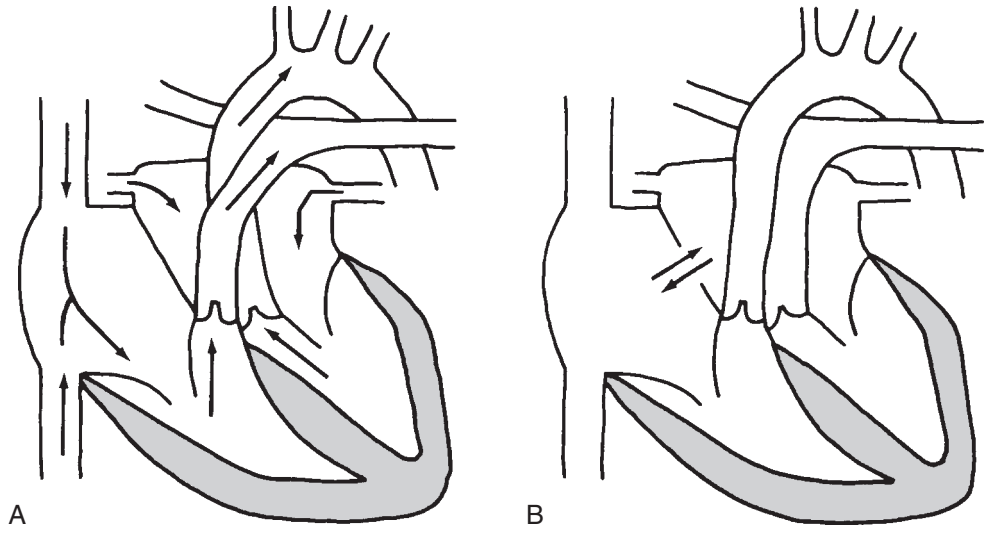

Fig. 28.17 Transposition of great vessels (TGV). **A**, Normal anatomy. **B**, Appearance of heart with TGV.

b. Large VSD with no pulmonary stenosis: pulmonary artery banding is performed to control CHF.

3. Reparative surgery.
   a. Right atrium is connected to either the right ventricular outflow tract or the pulmonary artery (Fontan or modified Fontan procedure) so that the right atrium forces blood into the lungs. Closure of the ASD and VSD is done at this time if they are present.
   b. Modified Fontan procedure separates oxygenated and unoxygenated blood inside the heart but does not restore normal hemodynamics or anatomy.
   c. Bidirectional Glenn procedure (superior vena cava to pulmonary artery anastomosis) at 6 months of age for those who have adequate pulmonary blood flow. The Fontan procedure will be completed at about 3 years of age (Scholz et al., 2018).

F. **Prognosis:** Survival is 82% at 1 year, 75% at 5 years, and 70% at 20 years. Complications include heart failure, persistent shunts, and dysrhythmias.

Mixed Defects

TRANSPOSITION OF THE GREAT VESSELS

A. **Incidence:** 1 per 5000 live births; 60% to 70% male predominance. Most common cardiac cause of cyanosis in neonates (Charpie, 2017).

B. **Anatomy:** positions of the great arteries are reversed (i.e., the pulmonary artery arises from the left ventricle and the aorta from the right ventricle). Without other intracardiac defects (e.g., VSD, ASD), an independent, parallel circuit exists (Fig. 28.17). In dextroposition (D-presentation), the aorta is situated to the left of the pulmonary artery. Forty percent to 45% have an associated VSD (Scholz et al., 2018).

C. **Hemodynamics.**
1. Oxygenated blood returns from the lungs to enter the left atrium and ventricle, then recirculates to the lungs by way of the pulmonary artery.
2. Unoxygenated blood returns to the right atrium and ventricle and is returned through the aorta to the body.
3. Mixing of oxygenated and unoxygenated blood occurs at the ductus arteriosus (as long as patency exists) or through any existing septal defects (ASD, VSD).
   a. Mixing is required for survival.
   b. Shunting occurs from left to right through septal defects or the PDA, ameliorating the degree of cyanosis and hypoxia.

D. **Clinical manifestations.**
1. Cyanosis is present within the first 24 hours of life and becomes progressively more intense.
2. Prominent murmurs are uncommon; VSD (if present) will have a loud murmur.
3. Chest x-ray findings are usually normal; the heart may have an "egg-on-a-string" appearance. Pulmonary vasculature may be increased or decreased.
4. Echocardiography is the standard diagnostic test to examine the transposed vessels, determine the size of the PDA and PFO, and look for any other cardiac defects (Scholz et al., 2018).

E. **Management: TGA is a cardiac emergency** (Scholz et al., 2018).
1. Maintain communication between pulmonary and systemic circulations.

2. PGE_1 to maintain patency of the PDA.
3. Correction of metabolic acidosis.
4. Palliation of choice: catheter-introduced balloon atrial septostomy for neonates with a restrictive PFO or insufficient flow through the PDA.
   a. Balloon catheter is inserted into the femoral or umbilical vein; it is advanced across the foramen ovale into the left atrium. The balloon is inflated and pulled across the atrium, creating an ASD.
   b. Procedure rapidly improves systemic and pulmonary circulation admixing, thus increasing Pao_2 (40s) and saturation (80s).
5. Corrective surgery.
   a. Arterial switch operation (Jatene procedure) is the treatment of choice: detaches aorta, coronary arteries, and pulmonary artery, reattaching to correct ventricles. Procedure is generally performed within the first week of life and provides both anatomic and physiologic correction (Swanson and Erikson, 2016).
   b Rastelli procedure: intraventricular repair combined with placement of an extracardiac shunt from the right ventricle to the pulmonary artery. Used for TGV with large VSD and extensive left ventricular outflow tract obstruction (Costello and Nguyen, 2016).
   c. Type of surgical repair is variable and depends on how complex the TGA is.

F. **Prognosis**.
1. Without surgery, 30% will die in first week, 50% in first month, and 90% within the first year.
2. Survival outcomes are greater than 97% at 25 years if arterial switch is performed (Charpie, 2017).
3. Complications are myocardial ischemia and infarction, aortic and/or pulmonary supraventricular stenosis, and dysrhythmias (Swanson and Erikson, 2016).

TRUNCUS ARTERIOSUS

A. **Incidence:** 1 per 33,000 live births, 1% to 2% of cardiac defects.
B. **Anatomy:** a single great artery arises from both ventricles, overriding a VSD (Fig. 28.18).
1. Type I: most common, short pulmonary artery arising from the base of the common trunk, then divides into the right and left arteries.
2. Type II: right and left pulmonary arteries arise from the posterior surface of the common trunk.
3. Type III: right and left pulmonary arteries have separate origins in the lateral walls of the common trunk (Jones et al., 2006; Scholz et al., 2018).

C. **Hemodynamics**.
1. Both ventricles pump blood into the common trunk supplying the systemic and pulmonary circulation. As PVR drops, preferential shunting to the pulmonary circulation occurs, increasing blood flow to the lungs and workload of the left ventricle.
2. If pulmonary arteries are stenotic or hypoplastic, blood flow to the lungs is restricted.

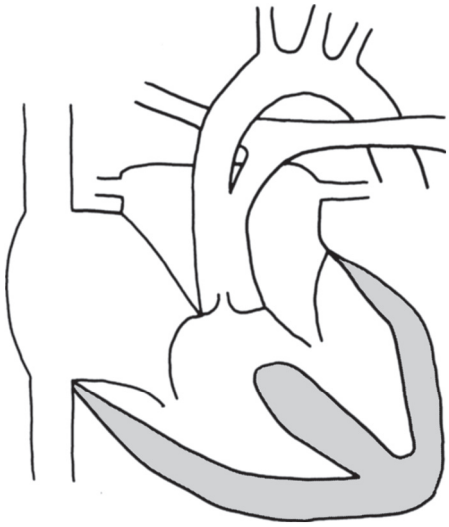

Fig. 28.18 Truncus arteriosus.

D. **Clinical manifestations.**
1. CHF with bounding pulses and widened pulse pressure.
2. Intermittent cyanosis: severe cyanosis with pulmonary artery stenosis.
3. Heart sounds: harsh systolic murmur at the mid- to lower left sternal border and systolic ejection click with single S_2.
4. Chest x-ray examination: cardiomegaly with increased pulmonary vascular markings. (Exception: If pulmonary artery stenosis exists, decreased pulmonary markings are seen.)
5. Echocardiography details the anatomy (to identify the number of truncal valve leaflets and presence of pulmonary stenosis and to assess the aortic arch) and evaluates for associated defects (Scholz et al., 2018).

E. **Management**.
1. Medical management is temporary and is directed toward treating CHF.
   a. Diuretics, digoxin, and ACE inhibitors are used to control pulmonary overload and decrease systemic resistance, which leads to a decrease in PVR.
2. Complete operative repair at a few days to 4 weeks of age is the treatment of choice.
   a. Homograft between the right ventricle and the pulmonary artery.
   b. VSD closure using a patch.
   c. Separation of the pulmonary arteries from the truncus (McElhinney, 2015).

3. Homografts are preferred to synthetic because they are more flexible, easier to use during surgery, and less prone to obstruction.
4. A newer therapy still undergoing research is tissue-valve engineering to find the ideal conduit for the right ventricular outflow tract.

F. **Prognosis**.
1. Mortality rate ranges from 70% to 95% in the first year of life if left unrepaired.
2. Postsurgical long-term mortality is 10% to 30%. Those infants needing truncal valve repair have the highest mortality.
3. Increased risk of necrotizing enterocolitis in early infancy (McElhinney, 2015).

TOTAL ANOMALOUS PULMONARY VENOUS RETURN

A. **Incidence:** 1 per 17,000 live births, 1% of all cardiac defects.

B. **Anatomy:** Pulmonary veins drain into the right atrium either directly or indirectly via a systemic venous channel (Fig. 28.19).
1. Presence of a PFO or true ASD is required for survival.
2. Varying degrees of pulmonary venous obstruction occur.
3. Three types of TAPVR occur.
   a. Supracardiac: pulmonary veins attach above the diaphragm, often to the superior vena cava (common form).
   b. Cardiac: pulmonary veins attach directly to the coronary sinus and drain into the right atrium.
   c. Infracardiac: pulmonary veins attach below the diaphragm into the portal venous system, draining into the inferior vena cava (most severe form).

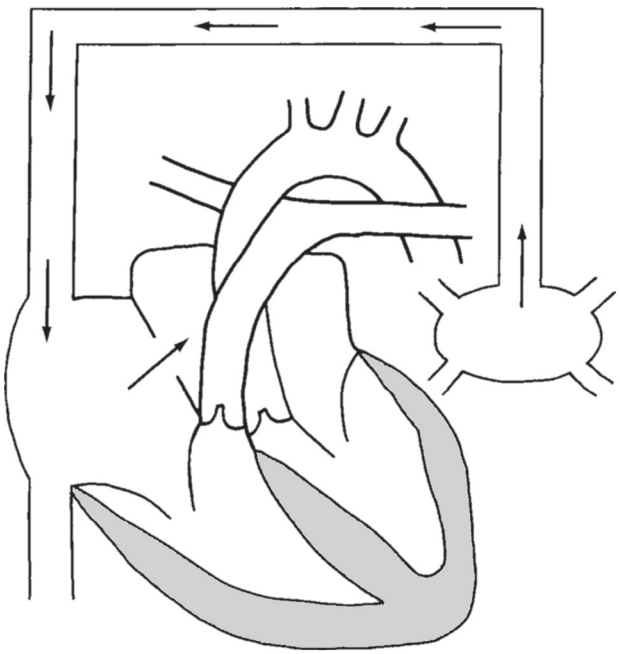

Fig. 28.19 Total anomalous pulmonary venous connection (TAPVR).

C. **Hemodynamics**.
1. Oxygenated blood from the lungs drains into the right atrium, mixing with the systemic venous return. Part of this flow passes into the left atrium via the PFO or ASD, into the left ventricle, and out the aorta. With the normal decrease in PVR, pulmonary blood flow will increase.
2. If obstruction to pulmonary venous return exists, the resulting increase in PVR leads to pulmonary edema and diversion of blood from the pulmonary artery to the aorta via the PDA. Closure of the PDA then increases right-to-left atrial shunting.

D. **Clinical manifestations.**
1. Nonobstructed.
   a. CHF.
   b. Mild cyanosis.
   c. Heart sounds: systolic murmur at the upper left sternal border, diastolic rumble at the lower left sternal border. Wide split S_2 may be present but is generally nonspecific.
   d. Chest x-ray examination: right ventricle dilation, increased pulmonary vascular markings, and "snowman" appearance after 4 months of age.
   e. Moderate restriction to pulmonary blood flow: may have cyanosis although typically there is sufficient mixing of venous return to permit oxygen delivery to tissues. Supplemental oxygen and mechanical ventilation may be needed. Consider sedation to decrease oxygen consumption (Scholz et al., 2018).
2. Obstructed.
   a. Profound cyanosis present.
   b. Respiratory distress unresponsive to mechanical ventilation.
   c. Electrocardiography will show right ventricular hypertrophy with a right-axis deviation.
   d. Chest x-ray examination: normal size, with pulmonary edema.
   e. Two-dimensional echocardiography and color Doppler: difficult to detect pulmonary veins due to low blood flow and will demonstrate a right ventricular dilation (Scholtz and Reinking, 2018).

E. **Management: Surgical treatment of obstructed TAPVR is an emergency.**
1. Medical management of nonobstructed TAPVR is rare. The neonate is usually stable enough for elective surgery (Swanson and Erickson, 2016).
2. Surgical management of both nonobstructed and obstructed:
   a. Cardiac catheterization may be omitted to speed time to operation, with surgery based on echocardiography.

b. Anomalous veins are detached and transplanted to the left atrium.
c. ASD is repaired.

F. **Prognosis.**
1. Mortality rate for infants with TAPVR who undergo surgery is 10% to 38% in infancy (Khan et al., 2015); the highest mortality is in patients with single-ventricle physiology.
2. Reoperation in the immediate postoperative group for pulmonary vein stenosis occurs in 4% of patients.
3. For those surviving surgical correction, long-term prognosis is excellent.

HYPOPLASTIC LEFT HEART SYNDROME

A. **Incidence:** Reported 1.4% to 3.8% of all cardiac defects. Responsible for 23% of cardiac-related deaths in first week of life and 15% of cardiac-related deaths in the first 30 days of life (Scholz et al., 2018).

B. **Anatomy.**
1. Hypoplastic left ventricle, aortic arch, and ascending aorta.
2. Atretic or hypoplastic mitral and aortic valves (Fig. 28.20).

C. **Hemodynamics**.
1. Obstruction of blood flow through the left side of the heart due to hypoplastic aorta and ventricle leads to pulmonary venous congestion and edema.
2. Blood supply to the descending aorta and to the aortic arch and coronary arteries (retrograde flow) is dependent on the PDA.
3. CoA is present in 75% of patients.

D. **Clinical manifestations.**
1. Asymptomatic at birth.
2. Tachypnea and dyspnea with increasing pulmonary blood flow.
3. CHF: usually presents at 24 to 48 hours of life.
4. Cyanosis: rarely permanent despite mixing of systemic and pulmonary circulations.
5. Rapid deterioration as PDA closes (Scholtz and Reinking, 2018).
   a. Severe mottling.
   b. Gray pallor of skin.
   c. Markedly diminished pulses.
   d. Cardiovascular collapse and shock.
   e. Systolic murmur present in two thirds.
6. Chest x-ray examination: cardiomegaly with increased pulmonary blood flow and pulmonary edema.
7. Prenatal diagnosis by fetal echocardiography: abnormal four-chamber view of heart. Delivery should occur at a tertiary facility (Scholz et al., 2018).
8. Fetuses with aortic stenosis and evolving HLHS or with HLHS and intact or restrictive atrial septum may benefit from fetal intervention at 18 to 30 weeks using ultrasound-guided percutaneous approach to perform balloon dilation and stent placement in areas of restriction, or aortic valvuloplasty (Moon-Grady, 2017). This allows for improved chamber development and function but does not prevent the need for postnatal management. Contraindications to fetal intervention are serious preexisting maternal diseases, multiple gestation pregnancy, and chromosomal and noncardiac structural anomalies in the fetus (Moon-Grady, 2017). A newer procedure being studied is the creation of a VSD in-utero to establish communication between left and right ventricles and preserve normal growth of the left ventricle and myocardium. It is hypothesized that this may provide a potential cure for HLHS (Hattam, 2018).
9. Postnatal diagnosis with echocardiography details the anatomy and estimates the degree of restriction to the blood flow across the foramen ovale (Scholz et al., 2018).

Fig. 28.20 Hypoplastic left heart syndrome (HLHS).

E. **Management**.
1. Treatment options include a multistage surgical approach, cardiac transplantation, and, though not as common in the present decade, comfort care.
2. Initial management.
   a. PGE_1 to maintain ductus arteriosus patency and systemic circulation.
   b. Systemic afterload-reducing agents.
   c. Aggressive management of acidosis.
   d. Transcatheter balloon atrial septostomy to decompress the left atrium if not taken to surgery immediately after birth.
3. Staged surgical repair ("Norwood" procedure): Mortality rate is 10% to 20% in the low-risk patient (Scholtz and Reinking, 2018). It is expected that about 70% of neonates will now survive all three

stages of repair, but longer-term survival is not as optimistic (Swanson and Erickson, 2016).

a. First (Norwood) stage can be performed on infants with birth weights as low as 1.5 kg and has a 15% mortality, with 3- to 5-year survival around 70% (National Institutes of Health [NIH], 2018).
   1) Division of the main pulmonary artery and ligation of the ductus arteriosus.
   2) Minimized Gore-Tex shunt is placed to maintain pulmonary blood flow and prevent CHF.
   3) Atrial septectomy to ensure pulmonary venous return to the right atrium.
   4) Connection of the right pulmonary artery and the aorta using an aortic allograft.
   5) Newer Sano procedure for first stage includes placement of a conduit between the right ventricle and left and right pulmonary arteries. This has led to improved early survival and improved coronary and systemic perfusion (Scholtz and Reinking, 2018).
   6) "Hybrid" approach: combines interventional cardiac catheterization with surgery off cardiopulmonary bypass. It involves balloon or surgical atrial septostomy along with bilateral pulmonary artery banding. This is done in a special suite that has catheterization and surgery capabilities. Complications include narrowing of the ductus, which requires balloon dilation, and increased pulmonary blood flow (Yabrodi and Mastropietro, 2017).

b. Second stage: bidirectional Glenn procedure (anastomosis of the superior vena cava to the right pulmonary artery) done between 4 and 6 months of age to reduce volume overload to the right ventricle. Most infants will have developed severe cyanosis from limited pulmonary circulation. Mortality rate for this stage is less than 7%.

c. Third stage, or modified Fontan procedure (Swanson and Erikson, 2016).
   1) Separates the pulmonary and systemic circulations.
   2) Connects the inferior vena cava to the pulmonary arteries.
   3) Done about 3 to 5 years of age.

d. Disadvantages.
   1) Two or three open surgeries in the first 2 years of life.
   2) Single right ventricle supplies the systemic circulation.
   3) Higher systemic venous pressures resulting in liver dysfunction.
   4) Many of these patients will go on to need a transplant.

e. Contraindication: significant tricuspid valve or pulmonic valve dysplasia associated with functional disturbances.

4. Cardiac transplantation.
   a. Provides a structurally and physiologically normal heart in one operation.
   b. About 39% of infants die while waiting for a donor. This number still remains high, but newer modalities to provide support while waiting for a heart include extracorporeal membrane oxygenation (ECMO) and the Berlin Heart. ECMO may only be used for short-term support. About 45% of the infants placed on ECMO will survive to transplantation using palliative procedures as a bridge to transplant, thereby increasing waiting list survival (Daly, 2016). The Berlin Heart EXCOR and ventricular assist devices (VADs) have been used as a bridge to transplant (Arnold et al., 2014).
   c. Complications.
      1) Increased susceptibility to infections as a result of immunosuppression.
      2) Allograft rejection, with acute rejection the leading cause of death in the first year after transplantation.
      3) Systemic hypertension: usually seen only in the first year after transplantation.
      4) Recurrent or residual coarctation: managed with angioplasty or surgical repair.
      5) Abnormal neurologic findings in as many as 19%, including seizures.
      6) Post-transplantation death, with one in nine infants dying before discharge, seen primarily in those who needed ECMO or ventilator support (Gandhi et al., 2011).

5. Comfort care: Although offered at some centers, there is an ethical debate among experts regarding whether it should be offered at all. Those arguing in favor report that there is no guarantee of survival and those who do survive will need repeated procedures, develop comorbidities, and have neurodevelopmental delays. Up to one third will die waiting for transplant if that is chosen. Those arguing in favor of repair or transplant report survival rates approaching 90% for those surviving surgical correction (NIH, 2018).

F. **Prognosis.**
1. Comparison of staged repair with heart transplantation outcomes requires evaluation of numbers of surviving children who completed procedures and numbers of those "lost" through death awaiting procedure or death between stages of the procedure.
2. According to websites that list survival data, survival after transplantation has improved to 89% at discharge from hospital, 84% at 1 year, and 70% to 80% at 3 years, not including deaths while awaiting

transplant, which can approach 40%. Recent advancements in ABO-incompatible transplant and use of VADs have increased survival rates (Tweddell et al., 2012).

3. Overall, 1-year survival after completion of the staged procedure is 75%. However, survival at 10 years is only 50% to 60% for patients who complete the staged repair (Yabrodi and Mastropietro, 2017).
4. Right ventricular failure is a long-term complication of the staged repair, especially when there is anterior prolapse of the tricuspid valve. This may lead to necessity for cardiac transplant (Arnold et al., 2014).

Congestive Heart Failure

ETIOLOGY

A. **CHF is a set of clinical signs and symptoms** that reflect the heart's inability to deliver adequate oxygen to meet the metabolic requirements of the body.
   1. Cardiac output is unable to meet the body's metabolic requirements.
   2. Right and/or left ventricular end-diastolic pressures are elevated, impeding systemic and/or pulmonary venous returns.

B. **Although structural heart defects are the most common cause of CHF** in neonates, other causes, such as birth asphyxia, severe anemia, dysrhythmias, and sepsis, should be considered.
   1. Timing of detection is often helpful in predicting causes because the diseases causing CHF characteristically show up at certain ages. Table 28.5 indicates conditions associated with CHF and their time of onset.

Table 28.5

Causes of Congestive Heart Failure and Time of Onset

Age at Onset of Symptoms	Underlying Cause
At birth	Hypoplastic left heart syndrome (HLHS)
	Severe tricuspid or pulmonary regurgitation
	Systemic arteriovenous fistula
In first week of life	Patent ductus arteriosus (PDA) in premature infants
	Transposition of the great vessels (TGV)
	Total anomalous pulmonary venous return (TAPVR) with pulmonary venous obstruction
1 to 4 weeks after birth	Coarctation of the aorta
	Critical aortic or pulmonary stenosis
	All other lesions listed here

Data from Park, M. K. (2008). *Pediatric cardiology for practitioners* (5th ed.). Philadelphia, PA: Elsevier Mosby.

   2. CHF in utero (hydrops fetalis) that is detected at birth may be due to the following:
      a. Profound anemia: erythroblastosis fetalis or twin-to-twin transfusion.
      b. Arrhythmia: supraventricular tachycardia or congenital heart block.
      c. Intrauterine infection with myocarditis.
      d. Arteriovenous malformations.
      e. Absent pulmonary valve.
      f. Premature ductus arteriosus closure: maternal use of prostaglandin inhibitor (e.g., aspirin, ibuprofen).
      g. Volume overload: twin-to-twin or mother-to-infant transfusion.

C. Diagnosis and management still challenging, and mortality remains high.

D. Underlying fetal pathophysiology will determine treatment options.
   1. Fetal arrhythmias: treatment may be nothing, administration of medications to the mother or to the fetus via intraperitoneal or cordocentesis, or fetal pacing. Mixed results have been attained with implantation of fetal pacemakers (Moon-Grady, 2017).
   2. Fetal anemia: intrauterine or intravascular fetal transfusion of packed red blood cells (RBCs) when hematocrit is <30%.
      a. Goal is to raise hematocrit to 45% to 55%. May be repeated every 3 to 5 weeks.
      b. Survival rate is 89% with a 3% complication rate.
   3. Fetal hemorrhage: from vascular tumors.
      a. Investigative treatments: radiofrequency ablation and photocoagulation are showing success in animal studies.
   4. Masses: treatment aimed at removing or debulking the mass if immediate delivery is not an option.
   5. Fluid collections: pericardial, pleural, and ascites treated with single or serial taps to drain excess fluid.
   6. Fetal anomalies: fetal surgery for bronchopulmonary sequestration and cystic adenomatoid malformations.
      a. Delivery should be at a level III or IV perinatal center with a skilled delivery team (neonatologist, neonatal nurse practitioner, nurse, respiratory technician, and ultrasonographer present).
         1) Have O-negative, CMV-negative, irradiated blood available at delivery for immediate transfusion through an emergency umbilical catheter.
         2) Monitor arterial pressure, venous pressure, and blood gases.
         3) Manage metabolic acidoses and hypoglycemia.
         4) Administer surfactant and ventilate as necessary.
         5) Drain any pleural, pericardial, or abdominal cavity fluid collections that interfere with adequate ventilation and circulation.
   7. Autopsy recommended in all nonimmune hydrops fetalis cases.

CLINICAL MANIFESTATIONS

A. **Common signs** (Satou, 2019).
   1. Tachypnea (60 to 100 respirations per minute at rest) is the first clinical sign of pulmonary edema.
   2. Tachycardia (160 to 180 bpm at rest) from compensation for decreased cardiac output.
   3. Four-limb blood pressure may yield a higher blood pressure in the right arm than in either leg, indicating an aortic obstruction.
   4. Central or prolonged peripheral cyanosis due to poor perfusion.
   5. Arrhythmias.
   6. Poor feeding—may take up to 45 minutes to complete a feeding.
   7. Cardiomegaly on x-ray.
      a. Dilational or hypertrophic cardiomyopathy.
      b. Diminished or engorged pulmonary vasculature.
   8. Hepatomegaly (3 to 5 cm below coastal margin): one of the most useful signs.
   9. Pulmonary fine rales and coarse rales (rhonchi).

B. **Less common signs.**
   1. Peripheral edema: usually not obvious unless CHF is present for some time.
   2. Diaphoresis.
   3. Gallop rhythm.
   4. May have mottling of the extremities from redistribution of blood flow to vital tissues.
   5. Electrocardiogram indicating the following:
      a. Hypertrophy of one or more chambers.
      b. Abnormal mean QRS axis.
      c. Rhythm disturbances.
   6. Laboratory biomarker tests for BNP and NT-proBNP are elevated and may be linked to poor outcomes (Price, 2019).
   7. Grading the severity of CHF is difficult and not standardized. Several tools have been reported in the literature with collaboration by the International Society for Heart and Lung Transplantation (ISHLT), American College of Chest Physicians, and Heart Rhythm Society producing a tool in 2013 that was endorsed by the Heart Failure Society of America (Price, 2019).

MANAGEMENT OF CONGESTIVE HEART FAILURE

A. **General measures** (appropriate for any heart disease).
   1. Use semi-Fowler's or prone position to achieve maximal diaphragmatic excursion and lung expansion.
   2. Decrease oxygen consumption.
      a. Maintain neutral thermal environment.
      b. Minimize stimulation (e.g., heel sticks, radial sticks).
      c. Provide sedation with morphine or fentanyl for agitated infant.
      d. Consider assisted ventilation to reduce work of breathing and decrease pulmonary edema if present.
   3. Provide supplemental oxygen. The amount is dictated by the Pao_2 and the presence of CHD with admixing of arterial and venous blood.
   4. Correct acidosis and any metabolic derangements (e.g., hypoglycemia or hypocalcemia).

B. **Specific measures.**
   1. Fluid and nutritional support.
      a. During acute phase, volume intake is reduced, generally to two thirds of maintenance levels.
      b. Use of glucose polymers or medium-chain triglyceride (MCT) oil enhances caloric content without significant volume increase.
      c. IV infusions of up to 50% fat emulsions can also be used to increase caloric intake with minimal intake volume.
   2. Pharmacologic therapy.
      a. Digoxin therapy (see Table 28.6).
         1) Inotrope to achieve maximal cardiac output; use in patients with left-to-right shunt is controversial.

Table 28.6

Digoxin Dosages and Common Side Effects

Digitalizing Schedule	Common Side Effects
Preterm infant Oral (PO) route: 20 mcg/kg total dose*	Total dose is usually divided into three doses giving one half, then one fourth, then one fourth of the total dose every 8 hours. Check electrocardiogram rhythm strip for rate, P-R interval, and dysrhythmias before each dose.
Term infant PO route: 30 mcg/kg total dose*	
Maintenance Schedule	
Preterm infant PO route: 5 to 10 mcg/kg/day*	Total dose should be divided to give twice daily. Allow 12 to 24 hours between last digitalizing and first maintenance doses. It takes about 6 days to "digitalize" a patient with maintenance doses alone. The sign of digitalis effect is usually prolongation of the P-R interval. The first sign of digitalis toxicity is usually vomiting, dysrhythmia, or bradycardia.
Term infant PO route: 5 to 10 mcg/kg/day	Drugs such as quinidine, amiodarone, and diuretics predispose to digoxin toxicity. The clearance of digoxin is directly related to renal function. Dosage must be reduced in patients with impaired renal function.

*Intravenous dose is 75% of PO dose.

2) Digitalize patient and observe for bradycardia (discontinue if heart rate <100 bpm).
   a) Arrhythmias or heart block.
   b) Hypokalemia.
   c) Toxic effects: increased in premature infants because of a longer serum half-life (61 to 170 hours) for digoxin than in term or older infants (18 to 45 hours) (Takemoto et al., 2011).

b. Diuretic therapy.
   1) Used to eliminate excess intravascular fluid.
   2) Furosemide (Lasix) 1 to 2 mg/kg every 12 hours IV or 1 to 3 mg/kg every 12 hours by mouth; may increase to four times a day if needed (Satou, 2019).
      a) In severe CHF, the IV route is preferable for its rapid onset of action.
      b) Hypokalemia and hypochloremia are side effects that can result in metabolic alkalosis.
      c) May cause hypocalcemia, with urinary loss of calcium leading to nephrocalcinosis.
      d) Use is contraindicated in renal failure.
   3) Chlorothiazide (Diuril) 20 to 40 mg/kg/day in two divided oral doses (Takemoto et al., 2011).
      a) Administered when less acute oral diuresis is required.
      b) IV dose 2 to 8 mg/kg/day divided in two doses.
      c) Does not produce the profound potassium losses seen with furosemide; may reduce urinary calcium losses seen with furosemide.
   4) Spironolactone (Aldactone) 1 to 3.3 mg/kg/day by mouth.
      a) Potassium sparing; must monitor for hyperkalemia.

c. Inotropic agents.
   1) May be necessary in severe CHF or cardiogenic shock.
   2) Most commonly used are dopamine, dobutamine, and isoproterenol.
   3) Milrinone (short term, <48 hours only).
      a) IV dose 0.3 to 1 mcg/kg/min.
      b) Loading dose of 50 to 75 mcg/kg IV over 15 minutes if needed.
   4) Carvedilol dose of 0.05 mg/kg every 12 hours, titrating dose upward over several weeks (Price, 2019).
   5) Nesiritide dose 0.01 to 0.03 mcg/kg/min IV drip to reduce afterload (Satou, 2019).

C. **Cardiology consultation to rule out or establish presence of congenital heart lesion.** Cardiac catheterization, angiocardiography, and surgery may be indicated.

Postoperative Cardiac Management

NONINVASIVE MONITORING

A. **Electrocardiography**.
   1. Continuous display of a limb lead, which shows P wave and QRS complex, should be monitored.
      a. Tachycardia.
      b. Bradycardia.
      c. Fibrillation.
      d. Asystole.
   2. Lead II: assessment of amplitude, axis, and presence and absence of P waves.
   3. Lead V_5 changes: septal or lateral wall ischemia.

B. **Blood pressure: manual.**
   1. Cuff can be used to occlude an arterial catheter leak.
   2. Measurement of upper and lower extremities after repair of CoA gives pressure gradient across repair site.
   3. Avoid extremity for blood pressure measurement when an artery has been used for surgical repair (e.g., subclavian patch for CoA, Blalock–Taussig shunt).

C. **Pulse oximetry.**
   1. Decreasing oxygen saturations may indicate:
      a. Decreased cardiac output.
      b. Increasing intracardiac shunting.
      c. Increased intrapulmonary shunting.
   2. Continuous monitoring is useful in pulmonary hypertension. Small decreases in saturation may be the first sign of increased pulmonary artery pressure with onset of right-to-left shunting.

D. **Urinary output.**
   1. Hourly output rate of 1 to 2 mL/kg/hr is a good clinical indicator of renal perfusion.
      a. Invalid in first 2 hours postoperatively after diuretic administration.
      b. Urinary retention can be induced by analgesics.
      c. A sudden decrease in urine output may indicate renal failure.
   2. Oliguria may persist for up to 48 hours after cardiopulmonary bypass.
   3. It is common to see increased urine output secondary to osmotic diuresis in the initial postoperative period, followed by decreased urine output after 6 to 8 hours.

E. **Cerebral near-infrared spectroscopy** (Noorie et al., 2018).
   1. Assesses cerebral oxygenation and regional tissue oxygenation (rSo_2).
   2. Use for tracking patient trends.

INVASIVE MONITORING

For pressure values from cardiac catheterization, see Table 28.7.

A. **Arterial pressure.**
   1. Mandatory for timely vasoactive medication adjustments.

Part 3

Table 28.7

Pressure Values From Cardiac Catheterization

Pressure	Normal Neonatal Values
Systemic arterial pressure	60 to 90/20 to 60 mm Hg (birth to 5 days of age)
Right atrial pressure	3 mm Hg
Right ventricular pressure	30/3 mm Hg
Pulmonary artery occlusion pressure/pulmonary wedge pressure	6 to 10 mm Hg
Left atrial pressure	8 mm Hg
Left ventricular pressure	100/6 mm Hg

2. Arterial tracing provides information for analysis of waveform and calculation of pulse pressure.
3. Pronounced phasic variations during mechanical ventilation may indicate hypovolemia or heart failure.

B. **Right-sided cardiac pressures.**
1. In patients with normal cardiac anatomy: right atrial pressure = right ventricular end-diastolic pressure = central venous pressure.
2. Increasing values seen with:
   a. Right ventricular overload.
   b. Poor ventricular function.
   c. Elevated pulmonary artery pressure resulting from reactive pulmonary hypertension.
   d. Tricuspid regurgitation.
   e. Cardiac tamponade.
   f. Residual shunting.
3. Particularly useful for evaluating the following:
   a. Right-sided cardiac lesions.
      1) Pulmonic stenosis.
      2) TOF.
   b. Those lesions requiring high right atrial pressures, such as in the Fontan procedure.
4. Right-sided line may be used to give vasoactive and inotropic medications and to provide parenteral nutrition.

C. **Pulmonary artery pressure.**
1. Surgical placement using a purse-string structure or transthoracic placement of a pulmonary artery catheter into the right ventricular outflow tract is indicated for those neonates at risk for pulmonary hypertension (Steinhorn and Abman, 2018).
2. Measurements guide the medical management of pulmonary hypertension and are most frequently used in conditions in which postoperative pulmonary hypertension is anticipated, as in endocardial cushion repair, truncus arteriosus, TAPVR, and HLHS with intact atrial septum and mitral valve stenosis (Kameny et al., 2016). Incidence of severe pulmonary hypertension after pediatric cardiac surgery found to be 2% to 7%.
3. Mixed venous oxygen saturation (So_2) monitoring can be obtained from pulmonary artery catheters with continuous oximetry capabilities in high-risk patients.
   a. $S\bar{V}o_2$ reflects a balance between oxygen delivery and consumption.
   b. Alterations are seen in:
      1) Anemia.
      2) Shock.
      3) Left-to-right or right-to-left shunts.
   c. Change in $S\bar{V}o_2$ generally precedes detectable hemodynamic changes by several minutes.

D. **Left-sided cardiac pressures are monitored using a left atrial line.**
1. In patients with normal cardiac anatomy: left ventricular end-diastolic pressure = left atrial pressure = pulmonary artery occlusion pressure = pulmonary artery wedge pressure.
2. Used to monitor systemic ventricular function and pulmonary shunting.
3. Useful in patients with mitral valve dysfunction, as seen in post–endocardial cushion repair.
4. Requires meticulous line care because the risk of air or particulate embolization is high.
5. Usually removed 1 to 2 days postoperation.

E. **Epicardial pacing wires.**
1. Usually attached to right atrium and/or right ventricle.
2. Provide temporary backup pacing for up to 10 days.
3. Access to dual-chamber pacing is most important after surgical repairs near the cardiac conduction system. For example:
   a. Cardiac resynchronization.
   b. VSD.
   c. TGA.
   d. Truncus arteriosus.
   e. Endocardial cushion defects.

HEMODYNAMIC MANAGEMENT

Neonates experience wide swings in physiologic responses, namely, heart rate, temperature, glucose metabolism, and systemic and pulmonary vascular resistance.

A. **Bradycardia**.
1. Common result of intraoperative cooling; proportional to degree of hypothermia.
2. After extensive atrial surgery, such as arterial switch procedure, TAPVR repair.
3. After injury to sinoatrial node.
4. With conducting problems.
   a. Sinoatrial block.
   b. Sinus asystole.
   c. Atrioventricular block is of most concern in the postoperative period.
5. As a consequence of edema around conduction system (generally resolves in 3 to 4 days).

B. **Tachycardia:** Observed as a consequence of or in response to the following:
   1. Pain.
   2. Anxiety/agitation.
   3. Fever.
   4. Hypovolemia.
   5. Junctional conduction disturbance.

Postoperative Disturbances

HEART FAILURE

ETIOLOGY

A. **Most common postoperative event** resulting from decreased neonatal cardiac reserve, limited by the following:
   1. Decreased myofilament numbers.
   2. Decreased ventricular compliance.
   3. Greater oxygen consumption, cardiac output, and resting heart rate in the neonate.
   4. Nearly maximal neonatal cardiac performance in the absence of stress.

B. **Causes** (Bronicki and Chang, 2011).
   1. Cardiopulmonary bypass adversely affects myocardial performance.
      a. Causes inflammatory response, which may be decreased by pre-bypass glucocorticoids.
   2. Residual anatomic lesions.
      a. Transesophageal echocardiography in the operating room has minimized the incidence.
   3. Pulmonary artery hypertensive crisis.
      a. Life-threatening right heart failure may be caused by an acute increase in pulmonary artery pressure.
   4. Arrhythmias.

C. **Preload or diastolic filling.**
   1. Hypovolemia.
      a. Inadequate volume replacement.
      b. Inadequate mechanical hemostasis.
      c. Impaired clotting.
   2. Iatrogenic volume overload.
   3. Left ventricular dysfunction.
   4. Cardiac compression.

D. **Afterload**.
   1. In the postoperative period, the neonatal heart is extremely sensitive to increased afterload.
   2. Evidenced by peripheral vasoconstriction.
      a. Vasodilators are used to enhance the reduction of ventricular afterload.

E. **Contractility**.
   1. Decreased peripheral perfusion.
   2. Decreased urine output.
   3. Treat with inotropic medications.

F. **Inadequate systemic venous return.**
   1. Excessive positive end-expiratory pressure.
   2. Tension pneumothorax.
   3. Atrial baffle obstruction.
   4. Postpericardial effusions.

G. **Increased pulmonary vascular resistance.**

H. **Decreased cardiac contractility**, resulting from the following:
   1. Accidental discontinuation of vasoactive drugs.
   2. Electrolyte disturbances.
   3. Hypoglycemia.
   4. Surgical manipulation or damage.

RECOGNITION OF LOW CARDIAC OUTPUT

A. **Frequently seen with changes in preload, afterload, and contractility** in the postoperative period, identified by impaired multiorgan system perfusion and elevated filling pressures (Noori et al., 2018).

B. **Factors that influence the severity of low cardiac output.**
   1. Age less than 1 month.
   2. Weight less than 2.5 kg.
   3. Preoperative condition.
   4. Type of defect.

C. **Observation: "just not doing well."**
   1. Noninteractive or becoming less interactive with environment.
   2. Lack of or decreasing vigor of cry.
   3. Awake but "floppy."

D. **Color**.
   1. Violet color of mucosa.
   2. Gray skin or mottling of skin.

E. **Extremities**.
   1. Cool to touch.
   2. Lack of or decrease in pedal pulses.
   3. Capillary refill time longer than 3 seconds.
   4. Edema: often seen postoperatively as "third spacing," but also indicative of fluid overload.

F. **Oliguria (urine output <0.5 to 1 mL/kg/hr).**
   1. Transient acute renal failure may occur in 5% of neonates who require cardiopulmonary bypass during cardiac surgery.

G. **Tachycardia**.
   1. Gallop rhythm.
   2. Distant heart sounds: possible indication of pericardial effusions.

H. **Low arterial blood pressure.**

I. **Respiratory distress.**
   1. Retractions, tachypnea, grunting, and/or stridor in infant after extubation.
   2. Rales: often heard after bypass procedure.

J. **Weight gain disproportionate to caloric intake.**
   1. May be early indicator of fluid retention.

K. **X-ray findings.**
   1. Excessive cardiac size or enlargement of specific chamber.
   2. Large cardiac silhouette or "bag-of-waters" appearance may indicate pericardial effusions.

3. Increased fluffy densities; these are not seen if elevated positive end-expiratory pressure is used in ventilation.

L. **Metabolic derangement.**
1. Metabolic acidosis, generally resulting from low bicarbonate levels and lactic acid buildup that results from diminished tissue perfusion.
2. Low sodium value, in part due to excessive free water.
3. Hypokalemia related to diuretics.

MANAGEMENT OF LOW CARDIAC OUTPUT

A. **Use blood for volume replacement.**
1. Maintain hemoglobin greater than 7 g/dL for hemodynamically stable patients with noncyanotic lesions and greater than 9 g/dL for cyanotic lesions (Lacroix et al., 2015).

B. **Volume challenge is appropriate in light of cardiopulmonary-bypass third spacing.**
1. Close monitoring required.
2. Strict intake and output.
3. Neonates are easily fluid overloaded when given excessive fluids (Noori et al., 2018).

C. **Provide correction of metabolic disorders.**
1. Hypocalcemia, hyponatremia, and hypoglycemia.
2. Acid–base balances.
   a. Acidosis may result from poor tissue perfusion, prolonged hypovolemia, or impaired renal function. Correction depends on the underlying cause.

D. **Reduce right ventricular afterload.**
1. Hyperventilation.
2. Pulmonary vasodilating agents (Kameny et al., 2016).
   a. Inhaled nitric oxide.
   b. Sildenafil.
3. Provide sedation and analgesia.

E. **Treat rate or rhythm disturbance.**
1. Increased heart rate.
   a. Rate of 200 to 210 bpm is tolerated well, with acceptable myocardial work and oxygen consumption.
   b. Cardioversion can be used for supraventricular tachycardia, atrial flutter/fibrillation, and ventricular tachycardia (Hay et al., 2003).
2. Atrial or atrioventricular pacing is often necessary.

F. **Consider pharmaceutical agents.**
1. Milrinone: reduces afterload in neonates with congenital heart disease. In the term neonates with persistent pulmonary hypertension treated with inhaled nitric oxide, oxygenation index improves without systemic hypotension. Most common adverse effects are thrombocytopenia and arterial hypotension (Noori et al., 2018). In adult patients, studies have shown increases in episodes of hypotension and arrhythmias (Price, 2019).
2. Nitroprusside and nitroglycerin reduce afterload.
3. Nesiritide is a venous and arterial dilator with diuretic properties (Satou, 2019).
4. Volume replacement: often necessary because of vasodilation (maintain preload). Central venous pressure is useful in determining volume needs.
5. Vasopressors (dopamine, epinephrine, or dobutamine). Potential for increasing PVR. Careful monitoring of effects is necessary.

G. **Mechanical circulatory support** (Daly, 2016).
1. Berlin Heart EXCOR can be used as bilateral or single ventricular support.
2. VAD.
3. ECMO.

H. **Monitor blood pressure.**

BLEEDING

A. **Provide sedation.** Avoid agitation, prevent hypertension and pressure at active and potential bleeding sites, which may aggravate or disrupt clot formation.

B. **Assess and treat coagulopathy.**
1. Blood clotting proteins mature at different rates: activated partial thromboplastin (aPTT) may be at adult levels at birth, but the preterm baby may not achieve normal values for about 2 months. Fibrinogen levels are at adult levels at birth for both preterm and term neonates. Evaluate the coagulation system by a hemostasis screen: aPTT, prothrombin time, thrombin time, platelet count, and fibrinogen concentration (Manco-Johnson et al., 2016).
2. Use 10 mL/kg of RBCs over 2 to 3 hours that are less than 7 days old for volume and clotting (Manco-Johnson et al., 2016).
   a. Consideration should be given for RBC transfusion of 15 to 20 mL/kg over 2 to 4 hours in the neonate with cyanotic heart disease with a hemoglobin less than 12 g/dL or hematocrit less than 36% (Christensen, 2018).
3. Use cryoprecipitate for fibrinogen (aids clotting).
4. Evaluate platelets: count is low and function is inadequate because of "bypass" and deep hypothermia.
   a. Give platelet infusion.
   b. Give desmopressin (DDAVP) 0.3 mcg/kg to increase levels of von Willebrand's factor, which stimulates platelets to aggregate.

PULMONARY HYPERTENSION/PULMONARY VASOSPASM (SEE CHAPTER 24)

A. Avoid hypoxemia and acidosis.
1. Hypoxia increases PVR and acidosis.
2. Neonates at risk for postoperative pulmonary hypertension need to be identified on return from the recovery room (Steinhorn and Abman, 2018).
   a. Large VSD.
   b. Complete atrioventricular canal.
   c. Truncus arteriosus.
   d. TAPVR.
   e. D-TGA.

MAINTENANCE OF FLUID AND ELECTROLYTE BALANCE (SEE CHAPTER 8)

A. **Hypoglycemia, hypokalemia, and hypocalcemia are potential problems.**
   1. All result in decreased myocardial function.
   2. Potential for seizures is present.
      a. Poor cardiac output to the brain may cause seizures.
      b. Cardiopulmonary bypass and circulatory arrest also predispose an infant to seizures.

SHOCK

ETIOLOGY

A. **Shock is a complex state of inadequate circulating blood volume,** resulting in insufficient perfusion, oxygenation, and nutrients to the tissues. Several varieties of shock are recognized.
B. **Hypovolemic shock** may be caused by (Noori et al., 2018):
   1. Blood loss from placental abnormalities (e.g., umbilical cord rupture, abruptio placentae, placenta previa, and twin-to-twin transfusion syndrome).
   2. Acute blood loss postnatally (such as intracranial or pulmonary hemorrhage).
   3. Acute or chronic blood loss postsurgically.
   4. Plasma and fluid losses.
      a. Skin integrity losses (e.g., myelomeningocele, gastroschisis).
      b. Pleural effusions (e.g., erythroblastosis fetalis or nonimmune hydrops).
      c. Body water loss from persistent vomiting/continuous gastric suctioning, diarrhea, or evaporative skin losses.
      d. Capillary leak syndrome resulting in third spacing.
C. **Cardiogenic shock** may be caused by (Noori et al., 2018):
   1. Myocardial failure due to severe hypoxemia, hypoglycemia, hypocalcemia, or acidosis.
   2. Congenital heart lesions.
   3. Cardiac arrhythmias.
      a. Sustained supraventricular tachycardia.
      b. Complete atrioventricular block (third degree).
   4. Restriction of cardiac function by:
      a. Tamponade.
      b. Tension pneumothorax.
      c. Excessive levels of ventilatory distending pressures.
   5. Myocarditis: often associated with sepsis.
D. **Septic shock.**
   1. Results from impaired peripheral arterial resistance usually caused by sepsis (i.e., release of bacterial toxins). The toxins cause capillary leak, which then leads to hypovolemic shock (Noori et al., 2018).
   2. Typically is associated with gram-negative organisms; however, gram-positive organisms may be the causative agent.
   3. **Cardiac signs include pulmonary hypertension, decreased cardiac output, and hypoxemia in the early phase, followed by uncompensated decrease in cardiac output, bradycardia, and hypotension. As it progresses, poor muscle tone, pallor, prolonged capillary refill, and edema are present** (Gollehon, 2019)**.**
   4. **Metabolic signs include hypoglycemia, hyperglycemia, metabolic acidosis, and jaundice. Hypothermia may be present.**
   5. Occurs in 15% to 20% of patients who have had cardiac surgery and is associated with poor neurodevelopmental outcomes (Sidhu et al., 2015).
   6. A recent tool, Vasoactive-Inotropic Score (VIS), for use in infants who develop shock after cardiac surgery has been shown to correlate with increased length of stay and more ventilator days, with higher scores predictive of poor outcomes (McIntosh et al., 2017).

CLINICAL INDICATORS

A. **Signs of shock are frequently nonspecific.** (Cardiogenic shock may be indistinguishable from CHF.)
B. **Cardiopulmonary status changes.**
   1. Tachycardia at rest.
   2. Bradycardia.
   3. Tachypnea, increased work of breathing, dyspnea.
   4. Poor peripheral perfusion.
      a. Pallor (especially with acute blood loss).
      b. Capillary refill time longer than 3 seconds.
      c. Mottling.
      d. Weak, thready pulses.
      e. Cool extremities.
   5. Hypotension (blood pressure may be normal in early stages).
   6. Hypotonia, lethargy that may progress to a comatose state.
C. **Decreased urinary output.**
D. **Metabolic disturbances.**
   1. Metabolic acidosis.
   2. Hypoglycemia.
   3. Hypothermia.
E. **Evidence of coagulation defects.**
   1. Oozing from IV sites, suture lines, etc.
   2. Coagulopathy: abnormal prothrombin time, partial thromboplastin time, fibrinogen.
F. **Indicators of blood volume** (or effective blood volume).
   1. Change in hemoglobin and hematocrit values.
   2. Response to fluid challenge of 10 mL of saline solution per kilogram of body weight, while blood pressure and urine output are monitored.
   3. Positive Kleihauer–Betke test result indicates fetal-to-maternal transfusion in utero. This test examines the maternal blood for the presence of fetal erythrocytes.
G. **Indicators of cardiac function.**
   1. See B. Cardiopulmonary Status Changes, earlier.
   2. Echocardiogram establishes anatomic defects and/or specific myocardial function abnormalities.

3. Central venous pressure is generally elevated, except during hypovolemic shock.

H. **Indicators of septic shock.**
1. Clinical signs of sepsis or positive culture results.
2. Normal blood pressure in the face of prominent hypoperfusion.
3. Edema or sclerema from capillary protein and fluid leakage.
4. Oliguria, proteinuria.
5. Persistent pulmonary hypertension of the neonate (common).
6. Hypothermia.

MANAGEMENT OF SHOCK

A. **Depends largely on prevailing pathogenesis.** A large proportion of the care is supportive.

B. **Supportive care.**
1. Maintain oxygenation and ventilation as dictated by arterial blood gas values.
   a. Give ventilatory support if concurrent pulmonary disease exists.
   b. Provide neutral thermal environment to decrease oxygen consumption.
   c. Decrease external stress (i.e., handling, peripheral blood sampling).
   d. Consider sedatives, analgesics, and neuromuscular blockade to decrease stress.
2. Promptly treat acidosis to avoid adverse effects on myocardial contractility. Sodium bicarbonate is often necessary.
3. Maintain fluid and electrolyte balance.

C. **Specific therapies.**
1. Increase blood volume and erythrocyte mass.
   a. Maintain blood pressure and maximize oxygen content.
   b. Treatment of acute blood loss may require large-volume transfusion.
   c. Monitoring arterial blood pressure is essential; monitoring of central venous pressure ideally should be included.
   d. Caution: In cardiogenic shock, added volume may increase the myocardial workload.
2. Treat the infectious process in septic shock.
   a. Antibiotic therapy should be initiated.
   b. Fluid resuscitation with crystalloids.
3. Maximize cardiac output.
   a. Inotropic agents such as epinephrine are used as first-line vasoactive agents in cardiogenic and septic shock to increase cardiac output and support circulation. Start early in septic shock if evidence of oliguria, hypotension, or acidosis exists. Norepinephrine may prove useful in warm shock (Weiss, 2018).
   b. Isoproterenol (Isuprel): increases heart rate and contractility (β_1-adrenergic effects). Simultaneous effects produce bronchodilation and smooth muscle relaxation (β_2-adrenergic effects). Usual dose is 0.05 to 2 mcg/kg/min. Observe for ventricular arrhythmias and tachycardia.
   c. Dopamine: increases cardiac contractility and cardiac output, affecting preload, contractility, and afterload—all three components of cardiovascular function (Noori et al., 2018). Effects are dose dependent. At low doses (1 to 3 mcg/kg/min IV), selective vasodilation of the renal, mesenteric, cerebral, and coronary vascular beds occurs, with little effect on heart rate or blood pressure. With moderate doses (5 to 10 mcg/kg/min), increased blood pressure and improved tissue perfusion can be observed. Beneficial effects are largely dependent on adequate blood volume. Correct hypovolemia before the dopamine infusion. At higher doses (>10 mcg/kg/min IV), vasoconstriction occurs and includes vasoconstriction of the pulmonary vasculature, increased right ventricular afterload, reduction in pulmonary blood flow, right-to-left shunting through fetal structures, increased blood pressure, and increased hypoxemia. Tachycardia, dysrhythmias, and ectopic beats can occur as a consequence of dopamine infusion.
   d. Dobutamine: increases cardiac contractility and heart rate while exerting limited effects on vasculature. Cardiac output increases, depending on myocardial catecholamine stores. Dose is 5 to 10 mcg/kg/min as a continuous IV infusion (Noori et al., 2018).
   e. Milrinone decreases afterload in neonates with congenital heart disease who demonstrate low cardiac output syndrome postoperatively (Noori et al., 2018). Milrinone should be given for less than 72 hours. In term neonates, a loading dose of 75 mcg/kg IV is given over 60 minutes, followed by an infusion of 0.5 to 0.75 mcg/kg/min. In preterm neonates of less than 30 weeks of gestational age, loading dose is 0.75 mcg/kg/min for 3 hours, followed by 0.2 mcg/kg/min IV infusion (Swanson and Erickson, 2016).
   f. Corticosteroids have been used in infants to treat hypotension in fluid-refractory, catecholamine-resistant shock (Pasman, 2019). More randomized controlled studies are needed to determine safety and efficacy for use in shock (Kawasaki, 2017).
   g. Digitalis should be considered and used selectively, especially in the face of hypoxia or toxic myocardiopathy.
4. Correct any tension pneumothorax or cardiac tamponade.
5. In refractory shock, venoarterial ECMO should be considered. Survival rates for newborns are as high as 80% (Weiss, 2018).

D. **Treatment goals.**
   1. Reduce morbidity.
   2. Normalize hemodynamic status.
   3. Halt progression of the shock state.

PAIN CONTROL AND SEDATION
(SEE CHAPTER 16)

A. **Pain assessment is the fifth vital sign;** however, assessment of pain in newborn infants remains a major challenge for health care providers. Immaturity of the nervous system limits the neonate's ability to differentiate noxious and nonnoxious stimuli consistently. They are not able to modulate their pain responses and do not consistently display signs/symptoms of pain to facilitate an accurate assessment of pain levels (Fleishman and Mayock, 2018).

DEVELOPMENTAL CARE
(SEE CHAPTER 11)

A. **Measures taken to facilitate developmentally appropriate care.**
   1. Decrease noise and lighting.
   2. Decrease hands-on care; cluster tasks.
   3. Provide nonnutritive sucking.
   4. Use positional devices and facilitated tucking.
   5. Administer analgesics and sedatives.
   6. Involve the family (Gardner et al., 2016).

LONG-TERM OUTCOMES

A. In 2010, there were approximately 1.4 million adults living with complex congenital heart disease who required surgery in the first month of life. In addition, about 1 million children are living with complex congenital heart disease (CDC, 2018).

B. **Mortality has decreased dramatically over the last decade;** between 1979 and 1993, mortality was 33% at 1 year of age; between 1994 and 2005, mortality was only 17% at 1 year of age (CDC, 2018). Expected survival of all CHDs is 96% (Dodge-Khatami, 2016).

C. **Neurodevelopmental outcomes.**
   1. Adverse outcomes are well documented in the literature and are linked to the complexity of the defect. Although survival has increased, the incidence of poor neurodevelopmental outcomes remain unchanged at 50% (Children's National Health System, 2017).
   2. Abnormal prenatal and postnatal cerebral development is of significant concern and may explain why the incidence remains relatively constant (Mebius et al., 2017).
      a. Infancy.
         1) Feeding issues are present in 50% of infants.
         2) Delay in milestones by several months.
      b. Childhood.
         1) Learning difficulties.
         2) Attention deficit.
         3) Problems with communication.
         4) Impaired visual-spatial skills.
         5) Fine and gross motor delays (CDC, 2018).
   2. Damage to CNS as a result of inability to autoregulate cerebral blood flow, especially in the preterm neonate (Noori et al., 2018).
      a. Forty-four percent of all who had surgery before 8 weeks of age.
      b. Equally common with or without cardiopulmonary bypass during surgery.
      c. Most frequently seen in patients who had circulatory arrest or arch surgery.
      d. Current research and imaging have demonstrated cerebral lesions exist before any procedures on the heart, with many lesions present at birth (Dodge-Khatami, 2016).

D. **Factors associated with poor outcomes.**
   1. Preoperative factors.
      a. Gestational age (inversely related).
      b. Type of defect; increased risk of aneurysms with CoA.
      c. Brain anomaly or injury.
      d. Age at time of repair.
      e. Presence of major extracardiac malformations, syndromes, or chromosomal abnormality (Bensemlali et al., 2016).
      f. Non-white race and ethnicity (Oster et al., 2011).
      g. Lower socioeconomic class (Tabbutt et al., 2012).
      h. Reduced quality of life for children and their families (Wernovsky and Licht, 2016).
   2. Operative factors.
      a. Type of circulatory support during surgery (Caputo et al., 2011).
         1) Deep hypothermic circulatory arrest.
            a) Period of cerebral ischemia followed by reperfusion leading to inflammatory response.
         2) Continuous cardiopulmonary bypass.
      b. Hemodilution.
      c. Degree of cooling.
   3. Postoperative.
      a. Seizures within 48 hours of surgery.
         1) Linked to increase in cerebral palsy and neurodevelopmental delays.
         2) Hypoxemia, low cardiac output; cardiac arrest.
         3) CHF.

CONGENITAL HEART DISEASE AND PREGNANCY

A. Advancements in the management of CHDs over the past 50 years have led to the majority of females with CHDs and disease surviving and thriving into childbearing years. Overall, 2% of all pregnancies will be complicated by cardiac issues, with most of these being related to CHD.

B. For many of these patients, pregnancy is successful with mild to moderate risks; however, it is dependent on the lesion and effects it has on the woman pre-pregnancy (American Heart Association, 2017). The World Health Organization (WHO) has divided these into four levels of disease.
   1. Class I: no increased risk of death to the mother; no or mild increase in morbidity.
   2. Class II: mild risk of maternal death; moderate risk of morbidity.
   3. Class III: significant risk of mortality and severe risk of morbidity—requires expert counseling
   4. Class IV: extremely high risk of maternal death and morbidity—pregnancy is contraindicated (Warnes, 2015).

C. Preconceptual counseling is highly recommended for all women with congenital heart disease, regardless of the class, and should include a cardiac examination complete with ECG, chest x-ray, and exercise testing; discussion regarding risk to mother and fetus, whether time and treatment will affect risk, need for high-risk pregnancy care, and alternative options such as surrogacy and adoption.

D. Any woman in class III and IV needs a delivery plan that is developed by an interdisciplinary team consisting of CHD cardiologist, maternal-fetal medicine physician, neonatology, anesthesia, and nursing, with delivery planned at a tertiary perinatal center.

E. It may be necessary for the woman to labor in left or right lateral position to avoid compression of the vena cava. Maternal monitoring during labor and delivery should include continuous ECG and pulse oximetry monitoring with adequate IV access. In some patients, central venous pressure catheter and arterial catheters are required to adequately monitor cardiac function (Warnes, 2015).

F. In a study of 17,729 deliveries in women with CHD, these women experienced longer hospital stays, which resulted in increased costs. The women were more likely to have CHF and coronary artery disease as co-morbidities and experienced more adverse outcomes, such as arrhythmias, thromboembolic events, heart failure, pre-eclampsia, and placenta previa. In addition, there was an increase in the number of deliveries by induction, forceps- or vacuum-assisted vaginal, and cesarean routes (Schlichting et al., 2019). Other complications of pregnancy that have been reported include 44% tachyarrhythmias, 12% to 15% spontaneous abortions, 4% to 8% intrauterine growth restriction, 17% to 21% preterm delivery, and 20% adverse fetal events (American Heart Association, 2017).

G. Women with complex congenital heart disease have the worst outcomes and require more care. Specific lesions identified are (Warnes, 2015):
   1. Cyanotic lesions: fetal outcomes are related to maternal oxygen saturation. If saturation is ≥90%, 96% are born alive; if saturation is ≤85%, only 12% are born alive.
   2. Aortic stenosis: exercise testing should be performed before pregnancy. If left ventricular function is impaired and the patient is symptomatic, the patient should be counseled to avoid pregnancy until valvuloplasty or valve replacement is completed. Without repair, there is a risk of low birth weight, prematurity, and fetal death.
   3. Coarctation of the aorta: usually able to sustain pregnancy to delivery. Increased risk of impaired fetal growth and maternal aortic dissection.
   4. Mechanical valves: due to need for anticoagulation therapy, there is an increased risk of maternal, fetal, and placental hemorrhage. Anticoagulants need to be stopped for delivery. Warfarin is more effective but crosses the placenta and is linked to birth defects. Heparin is not as effective, which increases the risk of valve thrombus or embolus; however, it does not cross the placenta.
   5. TGA: if ventricular function is adequate before conception, pregnancy may be successful in some patients. Increased risk of morbidity and mortality. Maternal ventricular function may not return to baseline if pregnancy results in worsening ventricular dilatation and tricuspid regurgitation.
   6. Single-ventricle/Fontan surgery: risk of miscarriage is 55%. Increased risk of heart failure and arrhythmias to mother, sudden maternal decompensation in third trimester resulting in early delivery via cesarean section.

PARENTAL SUPPORT AND EDUCATION
(SEE CHAPTER 17)

GENERAL INFORMATION. Whether made prenatally or postnatally, the diagnosis of a CHD or disease is stress-inducing for parents and other family members. Having the diagnosis made prenatally does not lessen the stress experienced after birth. It is imperative that families be given support, accurate education, decision-making capability (Kon et al., 2016), and skills to care for their newborn. Postoperatively, parents focus on feeding, weight gain, and caregiver sleep deprivation. Education must be directed toward these issues and may be facilitated by a family-centered approach to care (Gardner et al., 2016).

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CHAPTER 29
Gastrointestinal Disorders

Wanda T. Bradshaw

OBJECTIVES

1. Discuss normal and abnormal abdominal assessment findings.
2. Discuss common laboratory and diagnostic tests used to evaluate the gastrointestinal system.
3. Differentiate between omphalocele and gastroschisis.
4. Identify four common associations in infants with intestinal obstruction.
5. Identify the clinical presentation of a neonate with tracheoesophageal fistula.
6. Describe radiographic findings in an infant with duodenal atresia.
7. Identify one gastrointestinal disorder that is considered a surgical emergency.
8. Identify the gastrointestinal presentation of infants with cystic fibrosis.
9. Describe the defect in Hirschsprung's disease.
10. Identify the three mechanisms involved in the pathogenesis of necrotizing enterocolitis.
11. Describe the clinical presentation of an infant with biliary atresia.
12. Identify at least three management strategies for the infant with cholestasis.
13. Identify at least three management strategies for the infant with gastroesophageal reflux.
14. Identify the triad of anomalies occurring in prune-belly syndrome.
15. Describe the symptoms of diaphragmatic hernia.
16. Differentiate between unconjugated and conjugated bilirubin.
17. Compare and contrast physiologic and nonphysiologic jaundice.
18. Describe the management of an infant receiving phototherapy.
19. Define hydrops.

Unique embryologic features of the gastrointestinal (GI) tract, such as the obliteration and recanalization of the GI tract, midgut herniation into the umbilical cord, and rotation of the intestines, make the GI tract prone to a variety of congenital anomalies. Anomalies may affect any part of the GI tract, from the mouth to the anus. Atresias, stenoses, and functional obstructions account for the majority of congenital defects. As for acquired defects, necrotizing enterocolitis (NEC) is the most common serious GI illness in neonates. This chapter will review the more common GI anomalies and a variety of multisystem disorders that have significant GI involvement, such as prune-belly syndrome, congenital diaphragmatic hernia (CDH), hyperbilirubinemia, and hydrops.

Gastrointestinal Embryonic Development

A. **Week 3.** Tubular intestine begins to form; omphalomesenteric (yolk stalk) duct forms; mesentery is forming; major digestive (salivary, liver, pancreas, gallbladder) and endocrine (thyroid) gland formation is initiated.
B. **Week 4.** Intestine is present; esophagus and trachea separate and are distinct; stomach becomes obvious; liver is present.
C. **Week 5.** Esophagus, stomach, and proximal duodenum present; intestine elongates into a loop and begins to rotate.
D. **Week 6.** Stomach rotates into adult position; distal duodenum, jejunum, ileum, cecum, ascending colon, and proximal two thirds of transverse colon present; rapidly developing midgut herniates into umbilical cord.
E. **Week 7.** Rapid endothelial proliferation results in temporary duodenal occlusion; intestinal loops herniate into umbilical cord, lengthen, and rotate; and urorectal septum fuses with cloacal membrane, separating rectum from the developing urinary bladder.
F. **Week 8.** Small intestine recanalizes; intestinal villi develop; diaphragm complete.
G. **Weeks 9 and 10.** Intestines begin to reenter the abdominal cavity and continue counterclockwise rotation around the axis of the superior mesenteric artery.

H. **Week 12.** Muscular layers of intestine are present; active transport of amino acids begins; pancreatic islet cells appear; bile appears; lactase appears.
I. **Week 16.** Meconium is present; swallowing is observed.
J. **Week 24.** Ganglion cells are detected in the rectum.
K. **Week 26.** Random peristalsis begins.
L. **Weeks 34 to 36.** Sucking and swallowing become coordinated.
M. **Weeks 36 to 38.** Maturity of GI system completed.
N. **Weeks 5 to 40.** Intestine elongates approximately 100-fold (small intestine is 6 times the length of the colon).

Functions of the Gastrointestinal Tract

A. **Absorption and digestion of nutrients.**
B. **Elimination of waste products.**
C. **Maintenance of fluid and electrolyte balance.**
D. **Protection of host from toxins and pathogens.**

Assessment of the Gastrointestinal System

A. **History**.
1. Family: presence of GI disease.
2. Presence of genetic syndrome: major syndromes associated with GI defects include (Stevenson and Hall, 2016):
a. Apert's syndrome: pyloric stenosis, tracheoesophageal fistula/esophageal atresia (TEF/EA), CDH.
b. Beckwith–Wiedemann syndrome: umbilical defects, diastasis recti, posterior diaphragmatic eventration, pancreatic hyperplasia resulting in hypoglycemia.
c. Fetal hydantoin syndrome: umbilical hernia, duodenal atresia.
d. Meckel–Gruber syndrome: liver defects (bile duct proliferation, fibrosis, cysts), single umbilical artery, patent urachus, omphalocele, intestinal malrotation, imperforate anus.
e. Sirenomelia: imperforate anus, anal agenesis.
f. Trisomy 13: umbilical defects, intestinal malrotation, CDH.
g. Trisomy 18: umbilical defects, pyloric stenosis, intestinal malrotation, TEF/EA, CDH, single umbilical artery.
h. Trisomy 21: Hirschsprung's disease, pyloric stenosis, duodenal atresia, intestinal malrotation.
i. VATERR association (*v*ertebral defects, imperforate *a*nus, *t*racheo*e*sophageal fistula and/or esophageal atresia, and *r*adial and *r*enal dysplasia). Additional: single umbilical artery.
j. VACTERL association (*v*ertebral defects, *a*nal atresia, *c*ardiac abnormalities, *t*racheo*e*sophageal fistula and/or esophageal atresia, *r*enal agenesis or dysplasia, and *l*imb defects).
3. History of present illness.
a. Fetal ultrasonography.
1) Abdomen can be seen by 10 weeks of gestation, stomach by 13 weeks.
2) Abdomen can be assessed for intactness of abdominal wall, umbilical cord insertion, stomach as fluid-filled chamber, bowel dilation, or indication of obstruction.
3) Polyhydramnios (>2000 mL) may indicate interference with fetal swallowing or intestinal obstruction.
4) Oligohydramnios (<500 mL) may indicate renal agenesis or dysgenesis.
b. Birth weight, weight loss/gain, reflux, gastric aspirates, vomiting (bilious vs. nonbilious, projectile), timing of passage of first meconium stool, stool color, presence of blood, diarrhea, constipation, abdominal distention or tenderness, jaundice (LaBronte, 2019).

B. **Abdominal assessment** (Goodwin, 2019).
1. Inspection.
a. Size, shape, and color.
1) Normal: rounded, soft, symmetrical, pink.
2) Abnormal: erythematous, dusky, mottled.
3) Distended: intestinal obstruction, infection, organomegaly, ascites.
4) Scaphoid: associated with CDH.
5) Asymmetrical: mass, organomegaly, intestinal obstruction.
b. Muscular development.
1) Flat, flabby, lumpy: prune-belly syndrome.
2) Gap between rectus muscles: diastasis recti.
3) Externalization of abdominal contents: omphalocele, gastroschisis, bladder exstrophy.
4) Hernias: protrusions of an organ or tissue through an abnormal opening. Common in three areas:
a) Umbilical: common in African Americans, low birth weight males, trisomy 21, hypothyroidism, and mucopolysaccharidosis.
b) Inguinal.
1) More common in males, especially very low birth weight.
2) Frequently bilateral.
3) May not be evident until second or third month of life.
4) Usually readily reducible.
c) Femoral.
1) Rare but more common in females.
2) Located just below inguinal ligament on anterior aspect of thigh.

c. Umbilicus/umbilical cord.
1) Normally pearly white.
2) Normally three vessels: two ventrally situated arteries and one dorsally situated vein.
3) Usually dries and spontaneously detaches in 10 to 14 days.
4) Green or yellow staining suggests in-utero meconium passage.
5) Wet, foul-smelling cord or periumbilical redness: omphalitis.
6) Persistent clear drainage: patent urachus.
7) Ileal fluid drainage: omphalomesenteric duct.
8) Serous or serosanguineous drainage: granuloma.
9) Abnormally thick: single herniated loop of intestine.
10) Thick, gelatinous: large for gestational age.
11) Thin, small: intrauterine growth restriction.

d. Bowel loops.
1) Normally not visible.
2) Presence: obstruction.

e. Movements.
1) Should move in synchrony with respirations.
2) Movements not in synchrony may represent respiratory distress, peritoneal irritation, or central nervous system (CNS) disease.
3) Peristalsis: not normally seen.
a) May be seen in premature infants with thin abdominal walls.
b) Presence: associated with hypertrophic pyloric stenosis.

f. Veins.
1) Superficial veins become more prominent with abdominal distention.
2) Dilated veins: venous obstruction.

g. Perineum: inspected for patency of anus and presence of fistulas.

2. Auscultation.
a. Done before palpation (to avoid altering sounds).
b. Bowel sounds.
1) Become audible within 15 to 30 minutes after birth (Goodwin, 2019).
2) Should have a metallic clicking quality.
3) Hyperactive or hypoactive does not necessarily represent pathologic change. Other historical or clinical findings should be taken into consideration when interpreting bowel sounds.
4) Increased sounds.
a) Malrotation.
b) Hirschsprung's disease.
c) Diarrhea.
5) Decreased or absent sounds.
a) Ileus.
b) Starvation.
c) Medication administration: opiates, magnesium, anesthesia.

c. Vascular sounds: bruit, similar to murmur. Caused by turbulent blood flow through an artery, especially if heard despite position change of infant. Bruits may indicate partial vascular obstruction.
d. Friction rub: peritoneal inflammation, splenic involvement, hepatic tumor, abscess.

3. Percussion.
a. Provides information regarding size and location of organs, presence of masses, fluids, gases. Not a significantly useful tool in the newborn infant.
b. Two main sounds to listen for:
1) Tympanic: low-pitched, heard over gas-filled structures (stomach).
2) Dullness: high-pitched, short, heard over dense or solid organs (liver, spleen).

4. Palpation.
a. Performed to assess the following:
1) Abdominal tone.
2) Organ position.
a) Liver should be 1 to 2 cm below right costal margin, midclavicular line.
b) Spleen rarely palpable. Tip should not be more than 1 cm below left costal margin.
c) Kidneys are about 4 to 5 cm in length. Right kidney is easier to palpate and is lower than left.
3) Organomegaly.
4) Masses.
5) Pulsations.
6) Fluid.
b. Technique: start in lower quadrants and progress to upper quadrants using a bimanual approach. Place one hand under infant's back; using free hand, start with light palpation, then progress to deep palpation.
c. Hints to relax infant.
1) Use warm hands.
2) Flex legs.
3) Use gentle circular motion.
4) Slowly increase depth of palpation.
5) Palpate any known areas of tenderness last.

C. **Diagnostic tests.**
1. Gastric tests.
a. Gastric aspirate. Measure pH of gastric contents.
b. Apt test.
1) Differentiates swallowed maternal blood from fetal blood. Fetal hemoglobin remains pink; adult hemoglobin turns yellow-brown.
2) Can be done on gastric fluid or stool.

2. Stool examination.
a. Normal: initially meconium followed by soft, yellow stool after milk introduction.

b. Examined for color, consistency, odor, blood, mucus, pus, tissue fragments, bacteria, and parasites.
c. Color may be influenced by diet, dyes, drugs, pathology.
   1) Green: indomethacin, meconium.
   2) Greenish black: iron, meconium.
   3) Black: iron, swallowed blood, blood from high GI tract lesion.
   4) Pale: biliary atresia.
   5) White: antacids, barium.
   6) Red: bright red indicates blood from low GI tract lesion or anal fissure; currant jelly indicates intussusception.
d. Odor.
   1) Sweet, yeasty, or acidic in odor suggests carbohydrate (CHO) malabsorption typical of osmotic diarrhea of viral enteritis.
   2) Purulent odor suggests colitis.
e. CHO malabsorption.
   1) pH less than 5 in infants is suggestive.
   2) Newborn screen tests for galactosemia.
f. Guaiac.
   1) Detects occult blood.

3. pH probe test: 24-hour pH probe study to diagnose GI reflux. Detects acid reflux only; does not detect nonacid (milk) or gas reflux.
4. Radiologic studies.
   a. Plain radiograph (see Chapter 14).
      1) Bowel gas pattern (Iyer and Chapman, 2016).
         a) At birth, GI tract is fluid filled and gasless.
         b) Within 30 minutes, gas should be in stomach.
         c) By 3 to 4 hours, gas should be in small intestine.
         d) After 6 to 8 hours, gas should be in entire intestine.
      2) Absence of gas below pylorus: possible indication of obstruction.
   b. Upper GI series: done to assess structure and function of esophagus and evaluate for pyloric stenosis, malrotation, and strictures.
      1) Contrast material such as barium or a water-soluble product is administered via a nasogastric tube and observed by fluoroscopy.
      2) Water-soluble products are preferred in cases of suspected perforation.
   c. Lower GI series: may be used to detect presence of malrotation, Hirschsprung's disease, meconium ileus, and meconium plug syndrome. May be therapeutic in meconium ileus and meconium plug syndrome.
5. Ultrasonography: may be used to diagnose suspected cases of pyloric stenosis, duplications, gastroesophageal reflux (GER), or biliary atresia.
6. Scintigraphy (nuclear scan): used to evaluate gastric emptying, aspiration with swallowing, reflux with aspiration, and liver excretory function. Radionuclide-tagged formula is fed to the infant and recorded by a gamma camera.
7. Endoscopy: used to directly visualize the upper or lower GI mucosa. Endoscopic retrograde cholangiopancreatography (ERCP) visualizes the biliary pancreatic ducts.
8. Fecal fat: used to diagnosis malabsorption syndromes. Fecal fat content greater than 6 g/24 hours is associated with malabsorption syndrome.
9. Culture: helpful in differentiating bloody diarrhea caused by infection versus hypoxic insult to intestine.

D. **Laboratory tests** (Table 29.1) (Pagana and Pagana, 2018).
   1. Albumin.
      a. Synthesized in the liver; it is the most abundant plasma protein.
      b. Decreased levels occur in hepatocellular injury; usually a late finding.
   2. Alkaline phosphatase (ALP).
      a. ALP is derived from the epithelium of the intrahepatic bile ducts and excreted into the bile. It is also found in the bone, kidney, and small intestine.
      b. Elevated levels occur in obstructive liver disease (e.g., biliary atresia) and hepatitis, as well as in bone disease.
   3. Aminotransferase activity.
      a. Alanine aminotransferase (ALT) catabolizes the reversible transfer of the α-amino group of aspartic acid to the α-keto group of α-ketoglutaric acid, leading to the formation of pyruvic acid.
      b. Aspartate aminotransferase (AST) catabolizes the reversible transfer of the α-amino group of aspartic acid to the α-keto group of α-ketoglutaric acid, leading to the formation of oxaloacetic acid.
      c. ALT and AST are the most sensitive tests of hepatocyte necrosis. ALT is more specific than AST because it is not found in high concentrations in other tissues.
      d. High elevations occur in hepatocellular injury. Slight elevations occur in cholestasis. Serum ALT greater than 300 units coupled with jaundice signals a liver disorder and not a hemolytic disorder.
      e. ALT-to-AST ratio is often performed to help differentiate types of liver disease.
   4. Ammonia.
      a. Produced from the deamination of amino acids during protein metabolism and is a by-product of colonic bacteria protein breakdown. Liver is responsible for metabolizing ammonia.

Table 29.1

Laboratory Tests Used to Evaluate the Gastrointestinal System

Test	Preterm	Term	Reference
Alanine aminotransferase (ALT) (units/L)	—	10 to 33	1
Aspartate aminotransferase (AST) (units/L)		24 to 81	1
Alkaline phosphatase (ALP) (units/L)	207 ± 60 to 320 ± 142	164 ± 68	1
Albumin (g/dL)	—	2.8 to 4.4	2
Bile acids	⅙ of adult value	½ of adult value	3
Bilirubin, total (mg/dL)			1
Cord	<2.8	<2.8	
24 hours	1 to 6	2 to 6	
48 hours	6 to 8	6 to 7	
3 to 5 days	10 to 12	4 to 6	
≥1 month	<1.5	<1.5	
Bilirubin, direct (mg/dL)	<0.5	<0.5	
Ammonia (mcg/dL)	—	90 to 150	1
γ-Glutamyltransferase (GGT) (units/L)	—	14 to 131	1
5′-Nucleotidase (5′N, 5′NT) (units/L)	—	5 to 10	4
Prothrombin time (PT) (seconds)	—	13 to 18	2

Adapted from [1]Blackburn, S. T. (2013). *Maternal, fetal, and neonatal physiology: A clinical perspective* (4th ed.). St. Louis, MO: Elsevier Mosby; Martin, R. J., Fanaroff, A. A., & Walsh, M. C. (Eds.). (2006). [2]*Fanaroff and Martin's neonatal-perinatal medicine: Diseases of the fetus and infant* (8th ed.). Philadelphia, PA: Elsevier Mosby; [3]Malarkey, L. M., & McMorrow, M. E. (2005). *Saunder's nursing guide to laboratory and diagnostic tests*. St. Louis, MO: Elsevier Saunders; [4]Simone, S. (2001). Gastrointestinal critical care problems. In M. C. Curley & P. A. Moloney-Harmon (Eds.), *Critical care nursing of infants and children* (2nd ed., pp. 765–804). Philadelphia, PA: Saunders.

   b. Elevated in liver failure.
   c. Elevations occur in acute or chronic liver disease.
5. Bilirubin.
   a. By-product of heme breakdown.
   b. Increased indirect bilirubin occurs when liver function is reduced (prematurity, injury) or when there is an excessive load of unconjugated bilirubin (hemolysis).
   c. Increased direct bilirubin occurs when the liver cannot excrete conjugated bilirubin into the bile ducts or biliary tract (biliary atresia, cholestasis).
6. Prothrombin time (PT).
   a. Measures the time required for prothrombin (factor II) to be converted to thrombin.
   b. In cases of obstructive liver disease in which bile acids do not reach the intestine, fat-soluble vitamins are not absorbed (required for coagulation factors).
   c. Prolonged PT occurs in patients with hepatocellular injury and biliary obstruction.
7. International normalized ratio (INR): ratio of a patient sample PT to a normal PT.
8. Serum bile acids.
   a. In the absence of abnormalities of the ileum, normal serum values reflect functioning of the enterohepatic circulation.
   b. Elevations occur in acute and chronic liver disease.

Abdominal Wall Defects (O'Connell et al., 2016; Raymond et al., 2018)

A. **Omphalocele (exomphalos).**
   1. Definition: central defect with herniation of the abdominal viscera into the umbilical cord covered by a thin, avascular membranous sac composed of amnion and peritoneum with a small amount of Wharton's jelly. Umbilical arteries and veins insert into the apex of the defect (Fig. 29.1).
   2. Etiology: multifactorial, including environmental, chromosomal (recessive and dominant forms), and folding abnormality of the germ disc, with failure to close the ventral abdominal wall.
   3. Incidence: 2.5 per 10,000 live births.
   4. Associated conditions: many will have associated anomalies or be part of a syndrome.
      a. Prematurity; small for gestational age.
      b. Cardiac defects (50%).
      c. Intestinal malrotation and/or atresia.
      d. Pentalogy of Cantrell: upper abdominal omphalocele above the umbilical cord, diaphragmatic hernia, sternal cleft, pericardial defect, ectopia cardiac defect.
      e. Neurologic anomalies, neural tube (40%).
      f. Genitourinary anomalies.
      g. Skeletal anomalies.

Fig. 29.1 Omphalocele.

h. Chromosomal anomalies (50% to 65%). Common anomalies include trisomy 13, 18, and 21, with 18 being the most frequent. Frequent in infants with Beckwith–Wiedemann syndrome (chromosome 11).

5. Diagnosis.
   a. Maternal serum markers: elevated serum α-fetoprotein to detect open defects.
   b. High-resolution prenatal ultrasound.
   c. Amniocentesis: chromosome analysis for associated defects; amniotic fluid α-fetoprotein and acetylcholinesterase levels to evaluate for defects associated with abnormal values.
   d. Inspection at birth.
      1) Small defect: contains few loops of intestine, slightly enlarged umbilical ring. Any umbilical cord that is unusually fat should be inspected carefully before clamping to prevent intestinal trauma.
      2) Large defect: may contain intestines, stomach, liver, spleen, bladder, uterus and ovaries, testicles; deficient upper musculature of the umbilical ring.
      3) The thin, avascular membranous sac may rupture before or at time of delivery; must be differentiated from gastroschisis because of the high rate of associated anomalies with omphalocele.
6. Prognosis.
   a. Mortality rate is related to size of defect and severity of associated anomalies.

B. **Gastroschisis** (Beaudoin, 2018).

1. Definition: herniation of abdominal contents through an abdominal wall defect lateral to the umbilical ring; umbilical ring and cord are normal; right-sided predominance (Fig. 29.2). See Table 29.2 for a comparison of omphalocele and gastroschisis.
2. Etiology: unclear; theories include rupture of umbilical stalk, right periumbilical ischemia due to atrophy or persistence of the right umbilical vein, or a vascular accident of the right omphalomesenteric artery.
3. Incidence: overall 1 per 10,000 live births, with 7 per 10,000 in women less than 20 years old, of low socioeconomic status, and with exposure to vasoconstrictors (decongestants, nonsteroidal antiinflammatory drugs, cocaine).
4. Associated conditions.
   a. Prematurity.
   b. Intestinal malrotation (100%) and atresia (5% to 25%).
   c. Other anomalies are uncommon.
5. Diagnosis.
   a. Maternal serum markers: elevated serum α-fetoprotein to detect open defects.
   b. Prenatal ultrasonography, including a high-resolution method.
   c. Amniocentesis: chromosome analysis for associated defects; amniotic fluid α-fetoprotein and acetylcholinesterase levels to evaluate for defects associated with abnormal values.
   d. Inspection at birth.
      1) Eviscerated abdominal organs without a thin, avascular membranous sac to protect the viscera.
      2) Usually includes small and large intestines and rarely the liver.

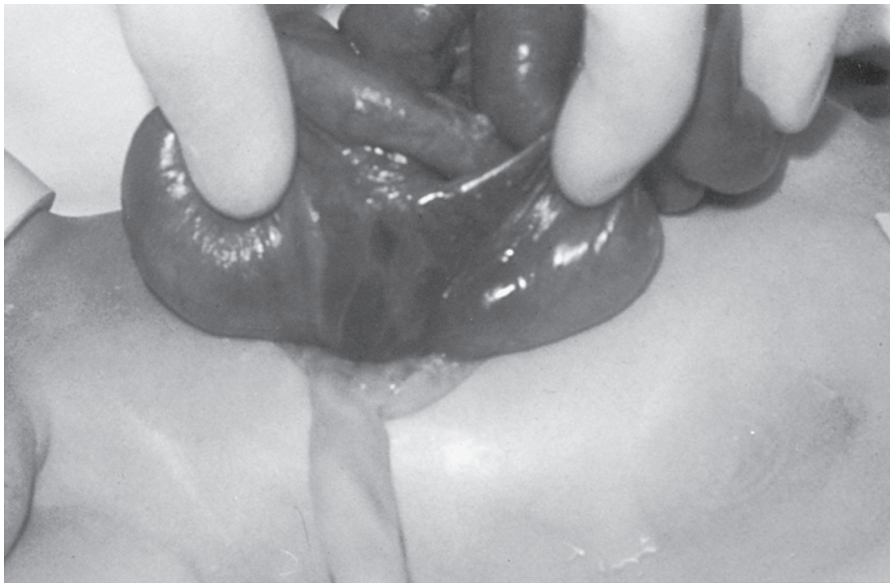

Fig. 29.2 Gastroschisis.

Table 29.2

Comparison of Omphalocele and Gastroschisis

	Omphalocele	Gastroschisis
Incidence	1:5000 to 1:6000	1:30,000 to 1:50,000
Covering	Present, may be ruptured	None
Site	Umbilical	Paraumbilical, usually to the right
Fascial defect	Small or large	Small
Herniated organs	Intestines; stomach, liver, spleen sometimes	Intestines; rarely liver
Appearance of herniated bowel	Normal, unless sac is ruptured	Often edematous, matted
Associated anomalies	45% to 55%	10% to 15%
IUGR	Less common	Common

IUGR, Intrauterine growth restriction.

3) Intestine may be thickened, edematous, and inflamed as a result of amniotic fluid exposure.
4) Fascial defect is smaller than with omphalocele.
5) Umbilical cord is intact.
6) Must be differentiated from ruptured omphalocele because of the high rate of associated anomalies with omphalocele.

6. Prognosis.
   a. Mortality rate is related to size of defect and severity of associated anomalies.
   b. Morbidity almost entirely related to intestinal dysfunction (impaired absorption, reduced enzymes, dysmotility) as a result of in-utero injury to eviscerated, unprotected bowel.

C. **Care of the neonate with an abdominal wall defect (omphalocele and gastroschisis).**
1. No research has demonstrated the efficacy of delivering infants with omphalocele or gastroschisis early.
2. Goals.
   a. Prevent hypothermia and hypovolemia (heat and evaporative fluid loss).
      1) At the time of delivery, if there are exposed viscera, place infant in a sterile bowel bag from the feet to the axilla. Secure drawstring around torso at axilla. The bowel bag maintains a sterile environment for, and allows visualization of, the exposed viscera. If bowel bag is not available, cover the exposed defect and viscera with warm, sterile normal saline dressings. Then cover the dressing with plastic. Gauze dressings require rehydration to prevent drying, adherence to viscera, and tissue trauma when removed. Such dressings may contribute to hypothermia as the gauze cools over time. Close assessment for adequate perfusion is imperative.

2) Begin intravenous (IV) fluid as soon as possible. Add amino acids and electrolytes as needed. IV fluid may need to be increased to approximately 150 mL/kg/day because of increased fluid loss through exposed bowel. Ideally, IV infusions should not be started in the lower extremities due to postoperatively increased intra-abdominal pressure and venous stasis.

b. Nutrition: nothing by mouth (NPO).

c. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid. Bowel distention restricts normal intestinal blood flow and makes primary surgical repair more difficult.

d. Maintain perfusion to the viscera; prevent vascular compromise from torqued viscera.
   1) Position infant side lying or support viscera with a small roll.

e. Prevent infection.
   1) Maintain sterile environment. Minimize handling of viscera, wear sterile gloves.
   2) Administer antibiotics.

3. Laboratory studies: complete blood count (CBC) with manual differential; electrolytes; acid–base and blood gas values; clotting studies; and blood type and cross-match.
4. Assess for associated anomalies, syndromes, or malformations.
5. Most newborn infants with abdominal wall defects require surgical repair. The types of repair include:
   a. Primary repair: all contents are returned to the abdominal cavity, and the fascia and skin are closed. The infant may require prolonged respiratory support because of increased intra-abdominal pressure. Preferred repair, but not possible in all cases.
   b. Staged repair: not all the organs are returned to the abdominal cavity during the primary surgery.
      1) The viscera remaining outside the cavity are managed three ways.
         a) Placement in an extra-abdominal prosthetic compartment (typically a mesh-reinforced, Silastic-covered Marlex sac [silo]). The sac is either sutured to the edge of the defect or secured underneath the fascia, allowing gradual reduction of the intestines on a daily basis. The silo must be supported at a 90-degree angle to the infant to promote reduction by gravity and prevent vascular compromise. This technique is employed with infants with large defects and for those who cannot tolerate primary repair.
         b) A variation of the silo technique is the insertion of a spring-loaded silo over the exposed viscera under the fascia, performed in the delivery room or in the neonatal intensive care unit (NICU) with subsequent closure on an elective basis. This latter technique is gaining in popularity and has been associated with fewer complications, fewer ventilator days, and shorter hospital stays.
         c) The umbilical turban, where the amnion is coiled over the defect and fixed into place with an adhesive dressing that reduces the defect until surgical repair (Kogut and Fiore, 2018).
      2) Reduction minimizes the stress on the respiratory and vascular systems by allowing these systems to adjust slowly to the increased pressure of the organs as they are slowly returned to the abdominal cavity.
      3) Reduction can usually be accomplished during a period of 10 days or less, after which infection becomes a major consideration.
      4) Assess perfusion of herniated contents frequently. Compromise of mesenteric vasculature can occur within the silo.
      5) The abdominal wall is closed after the reduction is completed.
   c. Skin flap closure. Only the skin is pulled over the exposed organs. This method is not a long-term solution and is used when the fascia cannot be initially repaired.
      1) Definitive repair done at 6 to 12 months of age.
   d. Closure by porcine small intestinal submucosal graft using a biomaterial (collagen, proteins, and biomolecules) such as Alloderm (LifeCell Corp., Branchburg, NJ), Surgisis ES (Cook, Bloomington, IN), or Permacol (Tissue Science Laboratories, Hampshire, UK). The graft is sewn to the fascia. Complete epithelialization and vascularization over the graft occur, closing the abdomen (Jiang et al., 2016).
   e. Nonsurgical repair. The omphalocele defect is painted with an escharotic agent such as silver nitrate or silver sulfadiazine and allowed to air dry and epithelialize.
      1) This uncommon procedure is used only if the defect is large, if the infant cannot tolerate surgery or has uncorrectable congenital anomalies, or if the reduction fails.
      2) Systemic side effects are associated with most of the escharotic agents. The health care team should be aware of such effects and assess the infant for them.

6. Postoperative care.
   a. Pain management (see Chapter 16).
   b. Prevent infection: dressing changes are performed with aseptic technique; administer antibiotics.
   c. Oxygen saturation, urine output, and blood pressure are monitored continuously. Other parameters to watch closely include fluid and electrolyte balance, pH, and clotting times.
   d. Observe for complications: respiratory distress, sepsis, intestinal obstruction, abdominal compartment syndrome, skin necrosis over repaired defect, and venous stasis distal to the repair.
   e. When staged reduction is employed, the silo must be supported to prevent tilting or torsion of the enclosed viscera. Sterile gauze may be wrapped around the base of the silo for this purpose.
   f. Gastric suction is required postoperatively until the gastric output is minimal. Gastric losses should be replaced with physiologic IV solutions. To prevent dehydration, measure gastric suction drainage every 4 hours and replace this volume over the ensuing 4 hours with physiologic IV fluid.
   g. Establish long-term IV access: percutaneously inserted central line, subclavian catheter, central venous catheter. Total parenteral nutrition (TPN) is provided until the infant tolerates full enteral feedings.
   h. Bowel sounds are assessed to determine readiness to feed. A prolonged ileus is a common complication in gastroschisis, but relatively uncommon in omphalocele.
   i. Feeding is begun very slowly when gastric output is minimal and bowel sounds are active.
      1) Low-osmolality feeding, such as half-strength formula, human milk, or mineral–electrolyte solution (Pedialyte, Abbott, Abbott Park, IL), is usually preferred. Feedings are frequently stopped and started because of reduced intestinal function.
      2) Soy-based and elemental formulas are used for infants who exhibit signs of feeding intolerance or malabsorption.
   j. Support parents through the often long recovery process (see Chapter 17).

Obstructions of the Gastrointestinal Tract

A. **General considerations** (Janek et al., 2019; Johncilla and Yantiss, 2018).
   1. Obstructions may be either mechanical (in which there is a specific point of obstruction) or functional (usually related to motility) in nature and can be found anywhere from the esophagus to the anus.
   2. Obstruction occurs because of an intrinsic or extrinsic blockage (Table 29.3).
   3. Common associations in infants with intestinal obstruction.
      a. History of polyhydramnios.
         1) Occurs more often in proximal obstructions.
         2) Fifteen percent to 20% of polyhydramnios cases are associated with fetal GI obstructions.
      b. Failure to pass meconium within 24 to 48 hours: 95% of term infants pass meconium by 24 hours (Goodwin, 2019).
      c. Abdominal distention: occurs more often in distal obstructions and TEF.
      d. Bilious vomiting: occurs when obstruction is distal to the ampulla of Vater, located in the duodenum.
   4. General preoperative management.
      a. NPO.
      b. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
      c. Correct fluid, electrolyte, and acid–base status (see Chapter 8).

Table 29.3

Causes of Intestinal Obstruction in the Newborn Infant

MECHANICAL		
Congenital	**Acquired**	**Functional**
Intrinsic		
Atresias	Necrotizing enterocolitis	Hirschsprung's disease
Stenoses	Intussusception	Meconium plug syndrome
Meconium ileus	Peritoneal adhesions	Ileus
Anorectal malformations		Peritonitis
Enteric duplications		
Extrinsic		
Volvulus		Intestinal pseudo-obstruction syndrome
Peritoneal bands		
Annular pancreas		
Cysts and tumors		
Incarcerated hernias		

From Gleason, C. A., & Devaskar, S. U. (2012). *Avery's diseases of the newborn* (9th ed.). Philadelphia, PA: Saunders.

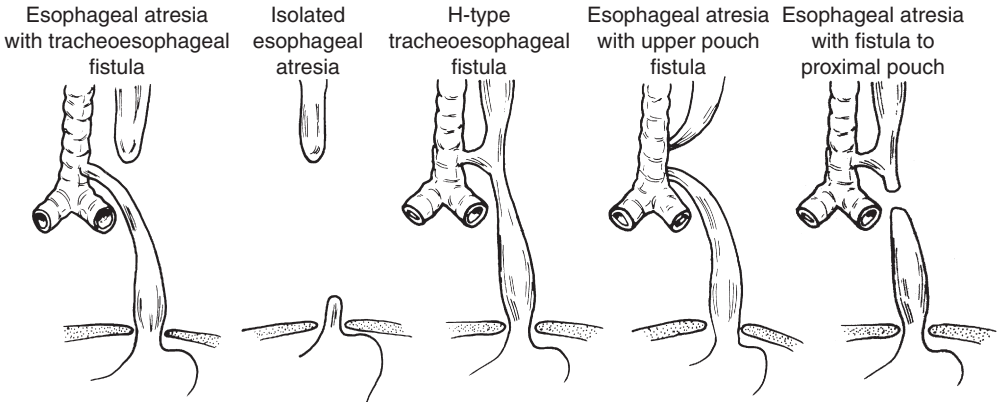

Fig. 29.3 Esophageal malformations.

d. Maintenance IV therapy (may include TPN).
e. Antibiotics.

B. **EA and TEF** (Conforti et al., 2018; Holmquist et al., 2018; Perin et al., 2017; Salik and Paul, 2019).
1. Definitions: EA, an interruption in the esophagus; TEF, an abnormal communication between the esophagus and trachea. EA and TEF may occur as separate defects or, more commonly, in association with each other.
   a. Types of TEFs (Fig. 29.3).
      1) EA (blind proximal pouch) with distal esophageal communication with the trachea (85%).
      2) Isolated EA (blind proximal pouch), no esophageal–tracheal communication (8%).
      3) H-type: communication between normal esophagus and normal trachea (5%).
      4) EA (blind proximal pouch) with proximal or proximal and distal communication with trachea (2%).
2. Etiology: hedgehog signaling abnormality and other genetic factors leading to incomplete elongation and separation of esophagus and trachea during the fourth week of gestation.
3. Incidence: approximately 1 per 1000 to 2500 live births.
4. Associated anomalies.
   a. Low birth weight is associated with other malformations and poor outcome.
   b. Cardiac defects: primarily atrial septal defects and ventricular septal defects.
   c. GI anomalies: pyloric stenosis, duodenal obstruction, and imperforate anus.
   d. EA/TEF are components of both VATERR and VACTERL associations. Infants with EA/TEF should have a cardiac, renal, and skeletal evaluation. TEF in infants with VATERR/VACTERL associations close to the carina are associated with a longer gap between esophageal segments.
   e. Esophageal abnormalities are also seen in the CHARGE (*c*olobomata, *h*eart disease, choanal *a*tresia, mental *r*etardation (preferred term now is intellectual disability), *g*enital hypoplasia, and *e*ar anomalies with deafness) association.
5. Diagnosis.
   a. Fetal ultrasound showing small or absent stomach.
   b. History of polyhydramnios.
   c. Clinical presentation.
      1) Dependent on the type of tracheoesophageal anomaly.
      2) Accumulation of oral secretions in mouth, drooling.
      3) Coughing, choking, respiratory distress, or cyanosis.
      4) Inability to pass gastric tube. Passage terminates in proximal esophageal pouch at approximately 10 cm. On radiographic examination, gastric tube appears coiled in the proximal esophageal pouch. In addition, air in the GI tract indicates the presence of a TEF. A gasless abdomen indicates an isolated EA (see Chapter 14).
      5) Abdominal distention if fistula between distal esophagus and trachea.
      6) Recurrent pneumonia (especially with communication between normal esophagus and normal trachea [H-type]).
      7) Use of contrast studies is not recommended because of the risk of aspiration and subsequent chemical pneumonitis.
6. Prognosis: survival rate excellent for healthy term infants. Prognosis is dependent on birth weight; presence of other congenital anomalies, especially cardiac; and preoperative condition. Highest mortality occurs in infants less than 1500 g and those with associated cardiac or chromosomal abnormalities. Quality of life in childhood and beyond can

be diminished by GER, esophagitis, decreased esophageal motility, and respiratory issues.

7. Preoperative care.
   a. See A. "General considerations."
   b. Manage airway; prevent aspiration-induced lung injury.
      1) EA/TEF: elevate head of bed 30 to 45 degrees to avoid reflux and aspiration of gastric secretions.
      2) EA without TEF: normal positioning.
      3) Evacuate EA pouch using a Replogle (Kendall, Covidien, Mansfield, MA) tube to low continuous suction. Replogle is the desired tube because evacuation holes are near the distal end. Assess and maintain patency of tube. If tube appears clogged, move tube slightly, as it may have adhered to the esophageal mucosa, or inject air only (to prevent aspiration) into the pigtail.
      4) Use comfort measures to prevent crying, which leads to increased swallowed air, abdominal distention, and increased risk of gastric content reflux into the trachea.
      5) Medications: gastric acid blockade and antibiotics.
      6) For lung disease requiring ventilatory support: avoid nasal continuous positive airway pressure; for endotracheal ventilation, use low mean airway pressures or use high-frequency oscillation. These techniques minimize shunting of tidal volume from the trachea to the stomach, which results in inadequate ventilation and may result in a ruptured viscus.
   c. Perform complete evaluation for associated anomalies. A high percentage of infants with EA demonstrate laryngotracheal abnormalities. These abnormalities result in an increased risk for tracheostomy and death (Conforti et al., 2018).
8. Surgical repair.
   a. Primary repair.
      1) EA: end-to-end anastomosis of the esophagus.
      2) TEF: ligation of the TEF.
   b. Staged repair is used with infants who are very premature, who have pneumonia or other coexisting life-threatening problems, or in whom the gap between the two esophageal segments is great (more than four vertebral bodies, with both segments in a neutral position).
      1) Initial surgery: ligation of TEF, placement of gastrostomy tube for gastric decompression, minimize risk of aspiration of gastric contents, and provide route for enteral feedings.
      2) Continue suction of proximal esophageal pouch until final surgery.
      3) Final surgery is usually delayed for 6 to 12 months.
   c. When end-to-end anastomosis is impossible because the gap between the esophageal pouches is too great or a previous repair has failed, various methods are utilized to support esophageal lengthening and tension-free anastomosis.
      1) The upper segment may be elongated surgically.
      2) The stomach can be pulled up into the mediastinum.
      3) A section of intestine may be spliced between the proximal and distal esophageal segments.
      4) Traction mechanical procedures foster esophageal segment growth.
      5) Researchers are engineering esophageal tissue using acellular scaffolds. These tissue grafts will need innervation, and research is being done using enteric neural stem cells and pluripotent stem cells to generate nerves.
9. Postoperative care.
   a. Provide pain management (see Chapter 16).
   b. Prevent aspiration: continue elevation of head of bed and gastric acid blockade.
   c. Prevent infection: administer antibiotics.
   d. Protect anastomosis site.
      1) Ventilate using low mean airway pressure.
      2) Suction length of endotracheal tube (ETT) only. Prevent suction catheter extrusion beyond the ETT.
      3) Do not extubate until certain that reintubation will not be necessary.
      4) If accidental extubation occurs, do not bag-and-mask ventilate; only experienced personnel should reintubate if needed.
      5) Suction posterior pharynx using a premeasured catheter to limit the distance.
      6) If the orogastric/nasogastric tube placed during surgery is dislodged, do not attempt to reinsert.
   e. Monitor: extrathoracic drain, gastric drainage. Note amount, color, and consistency.
   f. Gastrostomy tube care.
   g. Nutrition.
      1) TPN is used until sufficient enteral intake is established.
      2) Enteral nutrition is initiated when the anastomosis site has healed. Confirmation may be obtained by esophagram.
10. Postoperative complications.
   a. Aspiration.
   b. Infection, pneumonia.
   c. Anastomosis site complications.
      1) Leak: delays feeding, may result in infection.
      2) Stricture: suspect in infants exhibiting dysphagia, inability to handle secretions,

or respiratory distress after the immediate postoperative period. Strictures require long-term periodic dilation.

d. Dysmotility of lower esophageal segment. Most often a problem with long-gap atresia and when oral intake is delayed for a prolonged period.
e. Recurrent fistula, usually resulting from a leak.
f. Unilateral diaphragmatic paralysis.
g. Tracheomalacia. This complication is occasionally severe enough to require a tracheostomy. Caused by deformation and softening of tracheal cartilages from compression of posterior trachea by enlarged proximal esophageal pouch.
h. TEF cough. Characterized by stridor, brassy cough, and bronchospastic airway symptoms.
i. GER (common).

C. **Pyloric stenosis** (Fidanza and Sables-Baus, 2019; Galea and Said, 2018).

1. Definition: obstruction of pylorus caused by hypertrophy of the pyloric musculature.
2. Etiology: unknown but higher incidence in infants whose mothers had increased gastrin secretion in the third trimester of pregnancy or infants who received prostaglandin E administration. The pyloric muscle demonstrates both hypertrophy and hyperplasia.
3. Incidence: overall 3 per 1000 live births.
   a. Predominance: males 5 per 1000 live births; females 1 per 1000 live births.
   b. Prevalence: more common in infants who are white, full term, and have trisomy 21.
   c. Occurs in approximately 20% of males and 10% of females who had affected mothers.
4. Associated conditions: uncommon.
5. Diagnosis.
   a. Presence of signs and symptoms usually between 3 weeks and 5 months of age.
   b. Clinical presentation.
      1) Nonbilious vomiting that becomes projectile over time.
      2) Visible peristaltic waves in epigastrium.
      3) Palpable pyloric "olive" in right upper quadrant. The incidence is decreasing due to the early increased use of ultrasound for diagnosis.
      4) Dehydration, electrolyte imbalances, acid–base disturbance (hypochloremia, hypokalemia, metabolic alkalosis).
      5) Chronic weight loss, malnutrition, and failure to thrive (late sign).
   c. Ultrasound (almost exclusively).
   d. Upper GI tract contrast study.
6. Prognosis: excellent. Generally, complete recovery with no residual effects; some continued vomiting possible in the first few days after surgery, followed by quick resolution.
7. Preoperative care.
   a. See A. "General considerations."
   b. Prevent aspiration-induced lung injury: use gastric decompression.
8. Medical repair.
   a. Pyloric stenosis may resolve spontaneously before 1 year of life. Infant requires medical and nutritional support. Procedure is associated with slow improvement and higher mortality.
9. Surgical repair.
   a. Pyloromyotomy: pyloric muscles are split/separated either by laparotomy or laparoscopic techniques.
10. Postoperative care.
    a. Pain management (see Chapter 16).
    b. Routine wound care.
    c. Nutrition: initially NPO for a few hours, then rapid progression of enteral feeds leading to full volume and discharge 24 hours after surgery.
    d. Prevention of perforation of the mucosa at the pyloromyotomy site by avoiding placement of a gastric tube postoperatively.

D. **Duodenal atresia and stenosis** (Eovaldi and Cohen, 2018; Miscia et al., 2019).

1. Definition: congenital obstruction of the duodenum. The defect usually occurs distal to the ampulla of Vater. The obstruction can be partial or complete and is further stratified as intrinsic or extrinsic. Duodenal atresia exhibits three forms: a membranous web causes obstruction in type I and is associated with common bile duct anomalies; a fibrous atretic cord connects two segments of the duodenum in type II; and type III exhibits discontinuous segments of the duodenum.
2. Etiology: During early gestation, the duodenal epithelium proliferates rapidly and completely obliterates the bowel lumen. Obstruction is thought to be a failure of recanalization during weeks 8 to 10 of fetal life. With extrinsic obstruction, anomalies outside the duodenum affect patency. These anomalies include malrotation with Ladd's bands, annular pancreas, and supraduodenal portal vein.
3. Incidence: approximately 1 per 7000 live births.
4. Associated conditions.
   a. Trisomy 21 syndrome (approximately 30%).
   b. Congenital heart disease (approximately 30%).
   c. Intestinal malrotation (approximately 20%).
   d. Tracheoesophageal abnormalities (10% to 20%).
   e. Anorectal defects (10% to 20%).
5. Diagnosis.
   a. Fetal ultrasound showing classic "double bubble" echogenicity.
   b. History of polyhydramnios.
   c. Clinical presentation.
      1) Abdominal distention.
      2) Absence of stools.

3) Bilious vomiting within the first 24 hours; nonbilious vomiting does not rule out duodenal atresia or obstruction.
4) Jaundice.

d. Plain radiograph showing double bubble pattern (see Chapter 14).

6. Prognosis: excellent. Long-term outcome is primarily dependent on associated anomalies and malformations.
7. Preoperative care.
   a. See A. "General considerations."
   b. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   c. Perform complete evaluation for associated anomalies.
8. Surgical repair.
   a. For intrinsic lesions, surgery is performed to excise the atretic or stenosed portions and perform primary reanastomoses. For extrinsic etiology, surgery removes or redirects the tissue causing duodenal blockage.
   b. Surgery may be by open laparotomy or laparoscopy assisted.
9. Postoperative care.
   a. Pain management (see Chapter 16).
   b. Prevent infection.
      1) Routine wound care.
      2) Continue antibiotics.
   c. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   d. Gastrostomy tube care if placed (rare).
   e. Nutrition: initially NPO for 3 to 10 days. Initiate enteral feeding and progress slowly as tolerated. Expect possible intolerance due to delayed gastric emptying and microcolon distal to repair site. Continue TPN until adequate enteral nutrition is established.

E. **Jejunal or ileal atresia** (Peng et al., 2018; Stanescu et al., 2017).
1. Definition: congenital obstruction of the jejunum, ileum, or both. Type I: membranous web; type II: segments connected by fibrous cord; type IIIa: segments separated by V-shaped mesenteric defect; type IIIb: apple-peel defect, with distal small-bowel corkscrewing around the ileocecal artery; type IV: multiple atresias (Fig. 29.4).
2. Etiology: two proposed etiologies: failure of recanalization during weeks 8 to 10 of fetal life or, second—and most supported hypothesis—is a mesenteric vascular insult with subsequent necrosis and resorption of the affected segment or segments.
3. Incidence: 1 per 1000 live births. Males and females are equally affected. Anatomic distribution: jejunal (50%), ileum (50%).
4. Associated conditions.
   a. Intestinal malrotation (10% to 18%).
   b. Meconium peritonitis (12%).
   c. Meconium ileus (10%).
5. Diagnosis.
   a. Fetal ultrasound showing distended intestinal loops.
   b. History of polyhydramnios.
   c. Clinical presentation.
      1) Abdominal distention. The lower the obstruction, the greater the distention.
      2) Absence of stools.
      3) Bilious vomiting within the first 24 to 48 hours.
      4) Jaundice.
   d. Radiologic studies.
      1) Plain radiograph showing dilated bowel loops and multiple air–fluid levels (see Chapter 14). With proximal jejunal atresia,

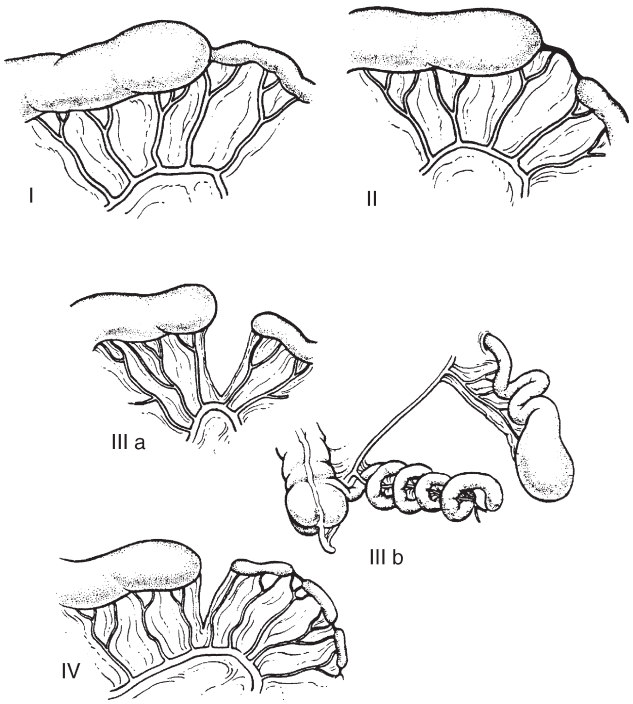

Fig. 29.4 Types of jejunal atresia. Type I—mucosal atresia with intact muscularis. Type II—atretic ends are separated by a fibrous band. Type IIIa—atretic ends are separated by a V-shaped gap defect. Type IIIb—apple-peel deformity of the distal atretic segment with retrograde blood supply from the ileocolic or right colic artery. Type IV—multiple atresias ("string-of-sausage" effect). (From Rowe, M. I., O'Neill, J. A., Grosfeld, J. L., et al. [1995]. *Essentials of pediatric surgery* [p. 511]. St. Louis, MO: Mosby.)

classic "triple bubble" is noted. With in-utero bowel perforation, peritoneal calcifications may be visible.
2) Barium enema reveals a microcolon.

6. Prognosis: generally good, with return to normal bowel function within 10 days. Mortality is usually related to short-bowel syndrome and complex defects (types IIIb and IV). Morbidity includes ileus, peritonitis, and prolonged intestinal dysfunction.
7. Preoperative care.
   a. See A. "General considerations."
   b. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   c. Perform complete evaluation for associated anomalies.
8. Surgical repair.
   a. Surgery may be by open laparotomy or laparoscopy assisted.
   b. Dependent on location of atresia and amount of intestinal involvement.
   c. Atretic intestinal portion is often resected proximally to the point of normal bowel dimensions and then connected to the distal segment using an end-to-oblique-side anastomosis.
   d. Occasionally, exteriorization of the proximal and even distal ends may be necessary with reanastomosis later (secondary versus primary repair).
9. Postoperative care.
   a. Pain management (see Chapter 16).
   b. Prevent infection.
   c. Routine wound care.
   d. Continue antibiotics.
   e. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   f. Nutrition: initially NPO until motility returns. Initiate enteral feeding with human milk or elemental formula and progress slowly as tolerated. Expect possible intolerance due to delayed gastric emptying and microcolon distal to repair site. Continue TPN until adequate enteral nutrition is established.

F. **Malrotation** (Burge, 2016; Ferrero et al., 2017).
1. Definition: an assortment of intestinal anomalies of rotation and retroperitoneal fixation.
2. Etiology: hedgehog signaling abnormality leading to failure of the intestines to rotate and fixate appropriately during weeks 6 to 10 of gestation. Intestines may twist on themselves (midgut volvulus), occluding the intestinal lumen, or may twist around the superior mesenteric artery, occluding intestinal blood supply. Ischemia and bowel necrosis follow.
3. Incidence: 1 per 5000 live births. The incidence of malrotation without significant symptoms is much higher than cases with clinically significant symptoms. More males are affected than females.
4. Associated anomalies.
   a. Intestinal atresia.
   b. Diaphragmatic hernia.
   c. Duodenal obstruction due to peritoneal (Ladd's) bands encircling the duodenum.
   d. Omphalocele.
   e. Gastroschisis.
5. Diagnosis.
   a. Presence of symptoms.
      1) Eighty percent of patients who become symptomatic do so within the first month of life, with the majority presenting within the first week. Approximately 90% of clinical symptoms appear in children in the first year of life.
      2) Acute presentation.
         a) Bilious vomiting, suggestive of malrotation with volvulus formation; needs immediate attention.
         b) Abdominal distention.
         c) Abdominal pain.
         d) Signs of shock and sepsis.
         e) Rectal bleeding.
      3) Less acute presentation.
         a) Intermittent bilious vomiting.
         b) Abdominal tenderness.
         c) Failure to thrive.
   b. Imaging studies.
      1) Upper GI radiograph is the gold standard.
      2) Plain radiographs. May appear normal in 20% of cases.
      3) Ultrasound.
      4) Classic early studies show distended stomach and proximal duodenum and scanty gas distributed throughout remainder of bowel. An airless abdomen is an ominous sign.
6. Prognosis: excellent if uncomplicated by infarction or associated anomalies. Mortality increases with intestinal necrosis, prematurity, or other abnormalities. Amount of intestinal resection is an important predicting factor in outcome. Major postoperative complication is short-bowel syndrome.
7. Preoperative care.
   a. See A. "General considerations."
   b. Perform complete evaluation for associated anomalies.
   c. Assess general perfusion; consider volume resuscitation for shock state.

8. Surgical repair.
   a. Surgery is emergent and cannot be delayed. Degree of surgery is dependent on pathology and amount of intestinal involvement.
   b. Volvulus is detorsed, Ladd's bands are divided, incidental appendectomy, and nonrotational return of bowel to the abdomen with the small bowel to the right and large bowel to the left.
9. Postoperative care.
   a. Pain management (see Chapter 16).
   b. Prevent infection.
      1) Routine wound care.
      2) Continue antibiotics.
   c. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   d. Nutrition: initially NPO until motility returns. Initiate enteral feeding with human milk or elemental formula and progress slowly as tolerated. Expect possible intolerance due to delayed gastric emptying and microcolon distal to repair site. Continue TPN until adequate enteral nutrition is established.

G. **Meconium ileus** (Waldhausen and Richards, 2018; Wood, 2018).
1. Definition: mechanical obstruction of the distal ileum due to intraluminal accumulation of thick, inspissated meconium. Although meconium ileus has been reported in a few patients without cystic fibrosis (CF), it is the predominant cause of meconium ileus in infants.
   a. Types of meconium ileus.
      1) Simple meconium ileus.
         a) More common.
         b) Distal segment of the small bowel is obstructed with thick, tar-like, tenacious meconium, and the proximal segment of the small bowel is dilated.
         c) Clinical presentation is usually within 48 hours.
      2) Complicated meconium ileus.
         a) Volvulus.
         b) Intestinal necrosis and perforation.
         c) Meconium peritonitis or pseudocyst formation.
         d) Clinical presentation is usually within 24 hours.
2. Etiology: exact cause unknown. Two implicating factors are hyposecretion of pancreatic enzymes, which may play a part in some, but not all, cases of meconium ileus (as a result, meconium contains an abnormal amount of proteins and glycoproteins, making the meconium thick and viscid); or abnormal viscid secretions from the mucous glands of the small intestine.
3. Incidence: exact incidence unknown. CF occurs in 1 in 2000 live births of white infants; 10% to 15% of children with CF have meconium ileus.
4. Associated conditions.
   a. CF.
   b. Hepatobiliary disease.
5. Diagnosis.
   a. Abdominal distention at birth.
   b. Bilious vomiting.
   c. Failure to pass meconium within 12 to 24 hours.
   d. Palpable, rubbery loops of bowel. Small grapelike pellets of meconium may be palpated distally.
   e. Complicated form has earlier presentation, and these infants appear sicker, with signs of sepsis and respiratory distress.
   f. Family history of CF. Definitive diagnosis based on sweat chloride iontophoresis (sodium and chloride concentrations >60 mEq/L) or chromosome analysis (defect located on chromosome 7).
   g. Radiologic studies.
      1) Plain radiograph shows "soap bubble" or ground-glass appearance of distal intestine created by the mixture of air and meconium; distended bowel loops without air–fluid levels; scattered calcifications due to intrauterine intestinal perforations may be seen in complicated form.
      2) Contrast radiograph may show microcolon.
6. Prognosis: dependent on number and degree of organs affected by CF, as well as associated anomalies.
7. Pre–nonsurgical procedure and preoperatively.
   a. See A. "General considerations."
   b. Perform complete evaluation for associated conditions; volvulus, atresia, perforation, and peritonitis must be ruled out.
   c. Evaluation by pediatric surgeon who remains in attendance during nonsurgical procedure.
   d. Patient should be prepared for surgery should complications occur during nonsurgical procedure.
8. Nonsurgical procedure.
   a. A hypertonic contrast water-soluble enema may be successful in dislodging the meconium by drawing fluid into the intestine and allowing for normal intestinal activity. Successful in up to 60% of patients. Usually meconium pellets are passed quickly, followed by liquid meconium for 24 hours after the procedure. A second enema may be required.
9. Surgical repair: uncomplicated meconium ileus.
   a. Used when nonsurgical procedure has failed.
   b. A T-tube (Fig. 29.5) is inserted into the ileum, which is irrigated postoperatively with *N*-acetylcysteine pancreatic enzymes.

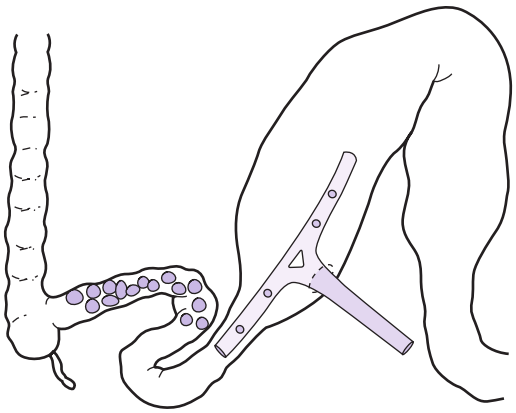

Fig. 29.5 T-tube. (From Mak, G. Z., Harberg, F. J., Hiatt, P., Deaton, A., Calhoon, R. & Brandt, M. L. [2000]. T-tube ileostomy for meconium ileus: Four decades of experience. *Journal of Pediatric Surgery*, 35[2], 349–352.)

10. Surgical repair: complicated meconium ileus.
    a. Always requires surgical intervention.
    b. Compromised intestine is resected.
    c. If the bowel is viable, end-to-end anastomosis is performed.
    d. In extreme cases in which bowel necrosis has occurred, all compromised intestine is resected and an ostomy is placed at the proximal and/or distal segments.
11. Postprocedural care.
    a. Fluids at one-and-one-half times maintenance. Hypovolemic shock can occur secondary to rapid fluid shift resulting from hypertonic solution used for enema. Careful monitoring of urine output, urine specific gravity or osmolality, blood urea nitrogen, creatinine, and serum osmolality.
    b. Physical assessment. Intestinal perforation may occur up to 48 hours after administration of enema. Risk of intestinal perforation increases with successive attempts at nonoperative techniques.
12. Postprocedural management and postoperative care.
    a. Pain management (see Chapter 16).
    b. Prevent infection: administer antibiotics; chest physiotherapy, aerosolized mucolytic agents (acetylcysteine sodium [Mucomyst]), and supplemental humidity to prevent atelectasis and pneumonia, which infants with CF are prone to develop.
    c. NPO.
    d. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
    e. Irrigation of distal stoma or T-tube with *N*-acetylcysteine or pancreatic enzymes around postoperative day 3.
    f. Nutrition.
        1) TPN is used until sufficient enteral intake is established.
        2) Enteral nutrition is initiated when the surgical site has healed.
        3) Begin feedings with elemental formula or human milk, supplemented with pancreatic enzymes.
    g. Parental education.
        1) Genetic counseling.
        2) Pulmonary hygiene, infection prevention, nutritional supplements.
    h. Observe for postoperative complications.
        1) Volvulus.
        2) Gangrene.
        3) Perforation.

H. **Meconium plug syndrome** (Cunnca et al., 2012).
1. Definition: a mechanical obstruction, usually of the distal segment of the colon and the rectum, that occurs from thick, inspissated meconium, usually in the absence of an abnormality of ganglion cells or enzymatic deficiency, although there are some reports of an association with Hirschsprung's disease. Because the meconium plug is formed primarily by mucus and intestinal secretions, the plug appears yellowish white and is gelatinous.
2. Etiology: unclear; results from diminished colonic motility and meconium clearance. More common with the following:
    a. Maternal diabetes, probably because of increased fetal glycogen production leading to decreased bowel motility.
    b. Neonatal hypermagnesemia: usually occurs after mother has been treated with magnesium sulfate for pregnancy-induced hypertension or preterm labor; the decreased bowel motility is secondary to myoneural depression.
    c. Prematurity.
    d. Hypotonia in infant with CNS disease.
    e. Sepsis.
3. Incidence: 1 in 100 newborns; 75% of newborns are able to expel the plug spontaneously, avoiding the complication of intestinal obstruction. The remaining 25% are cleared with a contrast enema.
4. Associated conditions.
    a. Hirschsprung's disease.
    b. CF.
5. Diagnosis.
    a. Clinical presentation.
        1) Abdominal distention. Multiple dilated loops of bowel.

2) Failure to pass meconium by 48 hours of life.
3) Hyperactive bowel sounds.
4) Bilious vomiting (late sign).

b. Plain radiograph showing multiple distended loops of bowel (see Chapter 14).
c. Water-soluble contrast enema often outlines an intraluminal plug. Such an enema will commonly dislodge the plug, and no further interventions will be required.

6. Prognosis: generally excellent if no associated conditions exist.
7. General care.
   a. See A. "General considerations."
   b. Medications: generally not required.
   c. Perform complete evaluation for associated conditions; volvulus, atresia, Hirschsprung's disease, perforation, and peritonitis must be ruled out.
8. Interventions.
   a. Rectal examination may expel plug in some circumstances.
   b. Enemas of warm saline, meglumine diatrizoate, or acetylcysteine.
      1) Meglumine diatrizoate is hyperosmolar, drawing fluid into the bowel from interstitial space. Careful assessment and management of fluid status are important.
   c. Surgery rarely necessary.

I. **Hirschsprung's disease (congenital megacolon, aganglionic megacolon)** (Pini Prato et al., 2019).
1. Definition: a non-mendelian congenital genetic absence of parasympathetic innervation to the colon with partial penetrance and variable expressivity. The affected intestine is unable to relax, resulting in a functional obstruction.
   a. Length of bowel involvement is dependent on the time during which migration of neuroblasts ceased.
   b. Agangliosis commonly involves rectum or rectosigmoid portion of colon only.
   c. Agangliosis may extend to proximal colon. Total colon agangliosis is rare.
2. Etiology: failure of ganglion cells to migrate cephalocaudally before week 12 of gestation, resulting in partial or complete agangliosis of the submucosal and mesenteric plexuses of the colon. Eight genomes have been associated with Hirschsprung's disease, as well as abnormal neural crest cell migration signaling pathways. The lack of intestinal ganglion cells prevents the inhibitory relaxation normally regulated by parasympathetic nerves. The affected segment is unable to relax, and functional obstruction ensues. The normally innervated proximal colon becomes hypertrophied from its attempts to overcome the functional obstruction. The oral, facial, and cranial ganglia arise from the same craniocervical neural crest as the ganglionic plexus of the bowel, explaining associated conditions (Rao and Gershon, 2018).
3. Incidence: 1 in 5000 live births. Males are affected 4 times more often than females. More than one third of affected patients have a relative with Hirschsprung's disease.
4. Associated conditions:
   a. Sensorineural deafness with central alveolar hypoventilation and Shah–Waardenburg syndromes (Chandra Mohan, 2018).
   b. Cardiovascular, skeletal, and limb anomalies seen with DiGeorge and X-linked aqueductal stenosis syndromes.
   c. Systemic anomalies seen with multiple endocrine neoplasia and Smith–Lemli–Opitz syndrome.
   d. Other: colonic atresia or imperforate anus; trisomy 21 is the most common chromosomal abnormality associated with Hirschsprung's disease and occurs in 3% to 10% of cases; ocular neuropathies.
5. Diagnosis.
   a. Clinical presentation.
      1) Early symptom: failure to pass meconium within 24 to 48 hours after birth.
      2) Bilious vomiting.
      3) Progressive abdominal distention.
      4) Poor feeding with failure to thrive.
      5) Late symptom: inability to stool normally. Abnormal stooling since birth is a common symptom of Hirschsprung's disease. As the obstruction continues, enterocolitis may develop with fever, abdominal distention, and diarrhea. The infant usually has symptoms in the first several weeks and then has diarrhea, abdominal distention, and/or vomiting. In advanced cases, urinary obstruction may occur secondary to mechanical compression of the ureters and bladder.
         a) Any neonate with trisomy 21 presenting with failure to stool should be evaluated for Hirschsprung's disease.
   b. Radiologic examination.
      1) Plain radiograph demonstrating proximal bowel dilation with an absence of air in the rectum is suggestive.
      2) Contrast studies showing a nondistensible rectal ampulla, with a dilated bowel above and a transition zone (an area between the normal and abnormal aganglionic intestine having a conical tapering appearance), are suggestive.
      3) Retained barium in the rectum for more than 24 hours after the procedure is suggestive.

c. Anal manometry is useful in very-short-segment agangliosis or in patients who have normal findings on contrast studies.
d. Confirmation: rectal biopsy demonstrating absence of ganglion cells. Punch or suction biopsy may be done in the nursery. Full-thickness biopsy under general anesthesia is rarely needed. Increased acetylcholinesterase content in rectal tissue is identified by histochemical staining.
e. A monoclonal antibody (anti-MAP2 antibody neuronal marker, Abcam, Cambridge, MA) has been developed with exceptional specificity and sensitivity to detect ganglionic cells in rectal biopsy specimens.

6. Prognosis: mortality rate increases when diagnosis is delayed and enterocolitis occurs as a result of bowel wall distention and ischemia, followed by bacterial translocation into circulation, resulting in sepsis. Enterocolitis is the leading cause of death. Approximately 10% of patients with Hirschsprung's disease will have subsequent elimination problems, such as constipation, incontinence, anal sphincter achalasia, and delayed toilet training. Mortality is affected by comorbidities.
7. Preoperative care.
   a. See A. "General considerations."
   b. Perform complete evaluation for associated conditions; volvulus, atresia, perforation, and peritonitis must be ruled out.
   c. Rectal irrigation is routinely performed to allow repeated emptying of colon and prevent enterocolitis.
8. Surgical repair. Goal: bring the normal ganglionated bowel down to the anus. The transanal procedure eliminates an abdominal incision and results in a primary pull-through repair.
9. Postoperative care.
   a. Pain management (see Chapter 16).
   b. NPO.
   c. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   d. Nutrition.
      1) TPN is used until sufficient enteral intake is established.
      2) Enteral nutrition is initiated when the anastomosis site has healed.
   e. Careful monitoring of fluid and electrolyte balance.
   f. Close observation for shock and recurrent enterocolitis.
   g. Routine ostomy care if applicable. Complications include ostomy prolapse, intestinal obstruction, skin dehiscence and excoriation, and stomal ulceration and bleeding.
   h. Routine rectal irrigations with normal saline to decrease risk of postoperative enterocolitis.
   i. If frequent and liquid stools cause perineal irritation, loperamide may be administered to reduce stool frequency, and kaolin–pectin suspension can solidify stools.
   j. Special diets may be necessary to improve stool consistency.
   k. Genetic counseling should be offered to the infant's family.
   l. A regimen of anal dilation begins approximately 2 weeks postoperatively in primary pull-through patients.
10. Complications.
   a. Fecal incontinence.
   b. Persistent constipation.
   c. Anastomotic leakage with subsequent stricture formation.
   d. Rectal stenosis.

J. **Imperforate anus (anorectal agenesis)** (Khanna et al., 2018; Wood and Levitt, 2018).
1. Definition: a broad spectrum of anorectal malformations characterized by a stenotic or atretic anal canal. A fistula between the rectum and the perineum, vagina in females or urethra in males, may also occur.
2. Classified dependent on level of defect (i.e., above [high] or below [low] a line drawn from the symphysis pubis to the coccyx [pubococcygeal line]).
   a. High imperforate anus.
      1) More common and generally more complex.
      2) Male predominance.
      3) Rectourinary and rectovaginal fistulas are common associations. Infants with a fistula are at risk for hyperchloremic acidosis as a result of colonic absorption of urine.
      4) High imperforate anus with sacral anomaly can be associated with lack of innervation of the bowel and/or bladder, resulting in incontinence.
   b. Low imperforate anus.
      1) Male/female ratio closer to 1:1.
      2) Perineal fistula is common.
3. Etiology: failure of differentiation of the urogenital sinus and cloaca during embryologic development (Blackburn, 2018).
4. Incidence: 1 in 5000 live births.
5. Common associations: anomalies, including vertebral, genitourinary, cardiovascular, and GI malformations, in 20% to 75% of infants. Specific anomalies include cryptorchidism, congenital heart defects, esophageal atresia, and spinal dysraphism.

6. Diagnosis.
   a. Physical examination. An infant with anal stenosis or imperforate anal membrane may have a normal-appearing rectum, with the condition detected only after the absence of stooling is noted.
   b. Imaging studies.
      1) Plain and contrast radiographs. An inverted lateral radiograph may be obtained to determine the level of the air-filled rectal pouch in relation to the pubococcygeal line.
      2) Ultrasonography.
7. Prognosis: level of defect significantly influences outcome regarding fecal continence. Continence is dependent on voluntary muscle structure, anorectal sensation, and bowel motility. The long-term outcome is affected by type of malformation, sacral development, and presence of spinal abnormalities.
8. Outcome is generally excellent with low imperforate anus, although there is an association with constipation. High imperforate anus is associated with bowel incontinence.
9. Preoperative care.
   a. See A. "General considerations."
10. Surgical repair.
   a. Surgical intervention is always necessary, with the procedure dependent on the level of the anorectal pouch. High and intermediate pouches are treated with a colostomy and a definitive pull-through procedure performed after the infant is approximately 8 months of age and weighs 18 pounds. A low pouch can usually be repaired by anorectoplasty with good results.
11. Postoperative care.
   a. Pain management (see Chapter 16).
   b. NPO.
   c. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   d. Nutrition.
      1) TPN is used until sufficient enteral intake is established.
      2) Enteral nutrition is initiated when the anastomosis site has healed.
   e. Routine ostomy care if applicable. Complications include ostomy prolapse, intestinal obstruction, skin dehiscence and excoriation, and stomal ulceration and bleeding.
   f. Anal dilation for approximately 2 weeks postoperatively in infants with anoplasty to prevent anal stenosis.

Necrotizing Enterocolitis

(Fidanza and Sables-Baus, 2019; Hagen and Skelley, 2019; Kim and Claud, 2019; Yanowitz et al., 2019)

A. **General considerations.**
   1. Definition: an acquired disease that affects the GI system, particularly that of premature infants. It is characterized by inflammation of the bowel wall followed by areas of necrosis, most commonly in the terminal ileum and proximal colon, but may affect any or all of both the small and large intestine.
   2. Etiology: unknown, thought to be multifactorial. Several mechanisms have been suggested.
      a. Intestinal ischemia (asphyxia/hypoxemia; redistribution of blood flow [hypotension, hypovolemia, polycythemia, patent ductus arteriosus, severe stress, hypothermia, umbilical arterial catheter, blood transfusion, exchange transfusion]). Tumor necrosis factor α and platelet-activating factors contribute to inflammation, intestinal mucosal injury, neutrophil activation, free radical release, and ischemia-reperfusion injury.
      b. Bacterial colonization of the initially sterile intestinal tract. The occurrence of NEC in clusters suggests a role for microorganism involvement. Organisms commonly associated with NEC include *Klebsiella*, *Escherichia coli*, and *Clostridium* species. A disruptive balance between normal and pathogenic flora initiates proinflammatory mediator release, promoting inflammation.
      c. Enteral feedings. Majority of NEC cases preceded by enteral feeding (90% to 95%). Increased occurrence when hyperosmolar formulas and medications (aminophylline, vitamin E) are administered enterally and when feeding volume increases exceed 20 mL/kg/day. Mechanism is unclear; formula may provide a substrate for bacterial proliferation; feeding and medications may increase intestinal oxygen demand during absorption, resulting in tissue hypoxia; fluid shifts into the intestine, resulting in decreased GI blood flow and intestinal ischemia. Human milk may have a protective effect against development of NEC. Protective ingredients include secretory immunoglobulin A, lactobacilli (antistaphylococcal agents), complement components, lysozymes, lactoferrins, macrophages, and lymphocytes. However, NEC can occur in infants who have received human milk.

d. Chorioamnionitis and prolonged rupture of membranes.
e. Genetic predisposition.

3. Prevention.
   a. Emphasis is on minimizing the factors contributing to NEC.
   b. Prevent/correct acid–base imbalance, hypoxemia, hypovolemia, hypotension.
   c. Correct hyperviscosity.
   d. Utilization of human milk, both maternal and donor.
   e. Cautious initiation of enteral feedings in small premature infants and in infants who have had perinatal asphyxia/hypoxemia.
   f. Careful monitoring of feeding tolerance.
   g. Oral administration of immunoglobulins and *Bifidobacterium* may be beneficial.
4. Focal intestinal perforation.
   a. Can occur in the absence of NEC.
   b. Factors distinguishing focal perforation from NEC.
      1) Less hemodynamic instability.
      2) Less metabolic acidosis.
      3) Improved survival rate.
      4) Use of umbilical artery catheter and administration of indomethacin or ibuprofen more common.
      5) Pathologic finding of coagulation necrosis found in NEC is absent in focal intestinal perforations.
5. Incidence: up to 10% of all admissions to the NICU; approximately 90% of cases occur in preterm infants. Occurs sporadically and in clusters. Occurs within first week of life to several weeks after birth.
   a. Factors contributing to the preterm infant's susceptibility to NEC.
      1) Decreased immunologic factors in the intestinal tract.
      2) Increased gastric pH.
      3) Immature intestinal barrier.
      4) Decreased intestinal motility.
6. Associated conditions.
   a. Prematurity.
   b. Patent ductus arteriosus.
   c. Infection.
7. Diagnosis.
   a. Physical examination.
      1) Positive abdominal signs: distention, visible bowel loops, diminishing peristalsis, tenderness, discoloration.
   b. Clinical presentation.
      1) Gastric residuals.
      2) Lethargy.
      3) Apnea and bradycardia.
      4) Blood in stools: occult or frank blood.
      5) Temperature instability.
      6) Diminished urinary output.
      7) Hypoperfusion.
      8) Hypotension due to third-space fluid loss from the intravascular space into the extracellular (third-space) compartment.
      9) Bilious vomiting.
   c. Radiologic examination (plain film).
      1) Diffuse gaseous distention of intestines is an early but nonspecific sign.
      2) Asymmetric bowel gas pattern and a relative lack of gas in a certain area with dilation in another area.
      3) Persistently dilated loop of bowel usually represents advanced disease.
      4) Pneumatosis intestinalis (air within the wall of the intestine) is pathognomonic of NEC (see Chapter 14).
      5) Air in the portal venous system (see Chapter 14).
      6) Pneumoperitoneum: represents intestinal perforation (see Chapter 14). Absence of free air does not rule out intestinal perforation.
   d. Laboratory studies.
      1) Abnormal CBC: leukocytosis or leukopenia, thrombocytopenia.
      2) Abnormal blood chemistry: metabolic acidosis, electrolyte imbalances.
      3) Abnormal blood gases: hypoxemia, hypercapnia.
      4) Abnormal clotting studies: disseminated intravascular coagulation (DIC).
      5) Presence of blood in stools.
      6) CHO malabsorption; may be an early sign of NEC.
7. Prognosis: survival rate varies between institutions and also depends on amount of bowel involvement and resection. Mortality is higher with a low pH before surgery and hypotension requiring vasopressors.

B. **Care of the infant with NEC.**

1. Medical management.
   a. See A. "General considerations."
   b. NPO.
   c. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   d. Medications: antibiotics (both penicillin-based β-lactam and an aminoglycoside), 3 to 14 days, depending on clinical status.
   e. Frequent CBCs and electrolytes to evaluate infant for thrombocytopenia and electrolyte imbalances.
   f. Serial plain radiographs (usually every 6 to 8 hours).

g. Respiratory and ventilatory support as needed.
h. Circulatory support as needed to prevent hypotension. Fresh frozen plasma, vasopressors should be considered.
i. Platelet transfusions for thrombocytopenia.
j. Fresh frozen plasma for DIC; consider use of vitamin K.
k. Careful monitoring of intake and output. "Third spacing" of fluids is common and may lead to hypovolemia and hypotension.
l. Frequent serial abdominal girth measurements.
m. Frequent blood glucose measurements.

2. Surgical management.
   a. Preoperative care: continue medical management.
   b. Surgery is used if medical management is not possible or fails. Indications for surgery include the following:
      1) Absolute indication.
         a) Pneumoperitoneum.
      2) Relative indications.
         a) Intestinal gangrene.
         b) Progressive clinical deterioration.
         c) Portal venous gas.
         d) Persistent fixed dilated loop of bowel.
         e) Abdominal wall edema or erythema.
         f) Progressive pneumatosis.
         g) Progressive acidosis.
         h) Progressive thrombocytopenia.
         i) Leukopenia or leukocytosis.
   c. Surgical repair.
      1) Principles of surgery for NEC are to decompress the bowel, resect necrotic bowel, and divert the proximal fecal stream. Actual procedures performed are dependent on condition and age of infant and amount of bowel necrosis.
      2) In an infant who has isolated necrosis with remaining bowel appearing viable and no intestinal perforation, resection of necrotic bowel and primary anastomosis is appropriate.
      3) When there is less than 25% viable bowel, options include simple closure of the abdomen (always fatal), resection of all necrotic bowel and creation of stomas (frequently results in short-bowel syndrome), and proximal diversion without bowel resection (may allow healing of part of bowel). Subsequent operations are usually required to resect gangrenous bowel, but there may be enough remaining bowel for survival.
      4) Placement of peritoneal drains without surgery has had some success with the initial management of critically ill, extremely low birth weight infants with perforated NEC or isolated intestinal perforation.
   d. Postoperative care.
      1) Pain management (see Chapter 16).
      2) NPO.
      3) Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
      4) Nutrition.
         a) TPN is used until sufficient enteral intake is established.
         b) Enteral nutrition is initiated when the operative site has healed. Initiate enteral feeding of human milk or elemental formula and progress slowly as tolerated.
      5) Routine ostomy care if applicable. Complications include ostomy prolapse, intestinal obstruction, skin dehiscence and excoriation, and stomal ulceration and bleeding.
      6) Maintenance of fluid and electrolyte balance.
      7) Medications: continue antibiotics.
      8) Observation of stomas for color and drainage.
      9) Observe for complications.
         a) Strictures occur in approximately a third of infants with resection. Signs of strictures include bloody stools, failure to thrive, feeding abnormalities, and diarrhea.
         b) Enteric fistulas and short-bowel syndrome (malabsorption and diarrhea).
         c) Recurrent NEC is not common but can occur.

Short-Bowel Syndrome (Chandra and Kesavan, 2018; Mayer and Kerner, 2017; Norsa et al., 2019)

A. **General considerations.**
   1. Definition: syndrome of chronic malabsorption and malnutrition as a result of bowel shortening. Pathophysiology depends on length of intestine, segment of remaining intestine, and whether the ileocecal valve is intact. Following bowel resection, the remaining bowel has the ability to adapt to increase its digestive and absorptive capabilities. Villi and crypts elongate, and epithelial hyperplasia occurs. Adaptive process is greater in the ileum than in the jejunum. Adaptation occurs over 1 to 2 years. Consequences of short-bowel syndrome are related to malabsorption due to decreased surface area and loss of specific functions of resected segments.

2. Etiology.
   a. Surgery requiring extensive resection of bowel.
      1) NEC (most common, as high as 50%).
      2) Jejunal or ileal atresia.
      3) Midgut volvulus.
      4) Extensive Hirschsprung's disease.
      5) Omphalocele or gastroschisis.
3. Incidence: 2 per million per year.
4. Associated conditions.
   a. GI tract defects: atresia, malrotation, gastroschisis, omphalocele, Hirschsprung's disease.
5. Diagnosis.
   a. Substantial small intestine is removed during surgery.
   b. Clinical presentation: in general, infants experience malabsorption and diarrhea; specific problems are dependent on length of small bowel remaining, presence of ileocecal valve, and site of intestinal loss.
6. Prognosis.
   a. Both the length of intestine and site of intestinal loss influence survival of infants receiving enteral nutrition. Increasing length alone permits longer contact between the product of digestion and the mucosa. If enteral feeding is inadequate, TPN is required. Long-term TPN carries the risk of cholestasis and hepatic damage. Cholelithiasis may occur, due to depletion of bile acids, resulting in a cholesterol–bile salt ratio abnormality.
   b. Loss of stomach is well tolerated if vitamin B_{12} is periodically given parenterally to prevent anemia.
   c. Jejunum is the primary site of digestion and absorption; however, these functions can be performed in other areas of the intestine after adaptation occurs. Infants with loss of jejunum tend to do much better than those whose ileum is removed. Loss of jejunum can result in nutritional deficiencies, steatorrhea, and cholestasis.
   d. Ileum is responsible for the absorption of fat-soluble vitamins, vitamin B_{12}, and bile salts. Loss of ileum has significant metabolic and nutritional consequences.
   e. Ileocecal valve delays intestinal transit time and prevents overgrowth of colonic bacteria in the small intestine. Loss of ileocecal valve results in less time for digestion and absorption of nutrients in the small intestine and small-bowel colonization with colonic bacteria.
   f. Loss of the colon may result in hypovolemia, dehydration, and electrolyte disturbances.
   g. Overall survival has improved with new therapies.
   h. With an intact ileocecal valve, infants with as little as 15 cm of small bowel can survive.
   i. Without an intact ileocecal valve, infants require approximately 30 to 45 cm of small bowel for survival.

B. **Care of the infant with short-bowel syndrome.**
1. Medical management.
   a. Stabilize fluid and electrolytes and maintain normal profile.
   b. Nutrition.
      1) TPN is used until sufficient enteral intake is established to sustain adequate growth. Cyclic administration of TPN is often used. Careful monitoring for associated complications is required.
      2) Intestinal rehabilitation to avoid nutritional failure requiring intestinal transplantation. Initiate enteral feeds with human milk or an elemental formula containing medium-chain triglycerides.
   c. Medications.
      1) Gastric acid blockade (50% have a temporary increase in gastric acid postoperatively).
      2) Cholestyramine for steatorrhea.
      3) Antiperistaltic agents for persistent diarrhea. Somatostatin is used to suppress intestinal hormones, decrease gastric and pancreatic secretions, and decrease GI motility. Octreotide is a somatostatin mimetic.
      4) Teduglutide (Gattex) is a glucagon-like peptide-2 analogue that increases intestinal absorption by promoting growth, proliferation, and maintenance of the GI tract lining (Kim and Keam, 2017).
      5) Trimethoprim–sulfamethoxazole, metronidazole, or other nonabsorbable antibiotics for bacterial overgrowth.
      6) Vitamin B_{12} is required if the stomach or ileum is lost.
      7) Vitamins A, D, E, and K are required if the ileum is lost.
   d. Provision of nonnutritive sucking.
   e. Prevention of skin breakdown due to diarrhea.
2. Surgical management.
   a. Any of a variety of surgical procedures to increase intestinal surface area or decrease intestinal motility: longitudinal intestinal-lengthening procedure, or transverse enteroplasty.
   b. Small-bowel transplant. Successful for only a small number of infants, ≈40% survival rate; reserved for infants in whom medical and other surgical management has been unsuccessful or who have life-threatening complications of TPN. Contraindications: profound neurologic disabilities, life-threatening and other noncorrectable

illnesses not directly related to the digestive system, severe congenital or acquired immunologic deficiencies, and insufficient vascular patency to guarantee easy central venous access for up to 6 months after transplantation.

Biliary Atresia (Bezerra et al., 2018; Siddiqui and Ahmad, 2019; Wehrman et al., 2019)

A. **General considerations.**
   1. Definition: obstruction of bile flow in the bile duct system due to fibrosis, bile duct obstruction, and cholestasis. Occurs exclusively in infants. Two types:
      a. Intrahepatic. An embryonic form with failure of ductal formation. Associated with other congenital anomalies.
      b. Extrahepatic. Perinatal fibro-obliteration of ducts, which has three forms: type I with atresia of the common bile duct with patent proximal ducts, type II with atresia of the common hepatic duct with patent proximal ducts, and type III with atresia of the right and left hepatic ducts at the porta hepatis.
      c. With both intrahepatic and extrahepatic forms of biliary atresia, bile fails to exit the liver, resulting in hepatic fibrosis and cirrhosis with progressive liver failure and portal hypertension. With liver failure, liver functions diminish (clotting factors, albumin, drug biotransformation, phagocytosis of foreign substances and bacteria, and excretion of waste material and toxins). Deficiencies of fat-soluble vitamins and vitamin K occur as a result of alterations in fat digestion and absorption.
   2. Etiology: exact mechanism unknown. Suggested theories: alteration in embryologic development, immune or autoimmune response, and association with viral infections. Research points to a genetic causation in some cases.
   3. Incidence: 1 in 8000 to 18,000 live births, with a slight preponderance in females; 20% intrahepatic and 80% extrahepatic.
   4. Associated anomalies: occurrence in 10% to 15% of infants; including cardiovascular disorders, polysplenia or asplenia with or without situs inversus, preduodenal or absent portal vein, malrotation, and intestinal atresias.
   5. Diagnosis.
      a. Clinical presentation.
         1) Normal appearance at birth, with gradual manifestation during first month of life.
         2) Jaundice: usually becomes apparent between second and sixth weeks of life. Skin is not yellow (unconjugated/indirect bilirubin), but rather a green-bronze color because of conjugated/direct hyperbilirubinemia, which is always pathologic.
         3) Acholic stools (meconium is normal in color). Dark urine secondary to bilirubin excretion.
         4) Portal hypertension. Seen in advanced liver disease when high pressure exists between portal vein and inferior vena cava.
            a) Engorged veins: periumbilical, esophageal, and rectal.
            b) Ascites: result of low albumin level and increased hydrostatic pressure in abdominal vessels.
      b. Physical examination.
         1) Abdominal distention.
         2) Distended, tortuous abdominal veins.
         3) Hepatosplenomegaly. Liver is hard.
      c. Imaging studies.
         1) Ultrasound.
         2) Hepatobiliary scintigraphy (hepatobiliary iminodiacetic acid [HIDA] scan).
         3) Intraoperative cholangiography.
         4) ERCP. Development of a side-view instrument makes ERCP now possible in infants.
      d. Laboratory studies.
         1) Elevated serum levels of aminotransferase, ALP, γ-glutamyl transpeptidase, and 5′-nucleotidase and hyaluronic acid.
         2) Late findings: abnormal clotting studies, hypoalbuminemia.
      e. Other.
         1) Liver biopsy.
   6. Prognosis.
      a. Without surgical treatment, most infants will die by 2 years of age.
      b. Surgical management with a hepatoportoenterostomy (Kasai procedure) relieves the obstruction in approximately 50% of infants. However, secondary to ongoing fibrosis and end-stage liver disease, a liver transplant is needed in childhood.
      c. Survival is improved for patients who initially undergo a hepatoportoenterostomy followed by liver transplantation. Less than 20% of patients who have a hepatoportoenterostomy survive to adulthood without a liver transplant.

B. **Care of the infant with biliary atresia.**
   1. Preoperative care.
      a. Evaluation for additional anomalies.
   2. Surgical procedures.
      a. Intrahepatic form requires liver transplantation. Lack of intrahepatic ducts precludes any drainage procedures.

b. Extrahepatic form. Goal: reestablishment of bile drainage. Treatment is dependent on the type.
   1) Resection of atretic segments and end-to-end anastomosis: possible in only a few cases.
   2) Hepatoportoenterostomy (Kasai procedure). Intestinal conduit is created between the liver surface and small intestine. Typically performed by laparotomy. May be performed using robotic laparoscopic technique but with less favorable results than with laparotomy (Madadi-Sanjani et al., 2017). This is most successful when performed by 2 months of age. The conduit is sometimes exteriorized temporarily to allow assessment of bile flow. Complications include the following:
      a) Cholangitis: most common complication; results from bile stasis and bacterial contamination of the intestinal conduit. Presents with fever, leukocytosis, increased serum bilirubin, and nonspecific signs of infection.
      b) Cessation of bile flow.
      c) Portal hypertension.
   3) Liver transplant.

3. Postoperative care.
   a. Pain management (see Chapter 16).
   b. NPO.
   c. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
   d. Medications.
      1) Antibiotics to decrease risk of cholangitis.
      2) Fat-soluble vitamins (A, D, E, K).
      3) Choleretic agents such as ursodiol (Actigall) may be given to increase bile flow.
      4) Steroids are commonly given for a month and then tapered. Used for their choleretic effect and to decrease scarring at the site of anastomosis.
   e. Nutrition.
      1) TPN is used until sufficient enteral intake is established.
      2) Enteral nutrition is initiated when the operative site has healed. Initiate enteral feeding containing human milk or medium-chain triglycerides and progress as tolerated.
   f. Assessment of bile flow and replacement as appropriate (if exteriorized).
   g. Monitor for hemorrhage secondary to portal hypertension and bleeding tendencies.

Cholestasis (Ananth, 2018; Moreira-Silva et al., 2019; Pandita et al., 2018)

A. **General considerations.**
   1. Definition: marked impairment of hepatic bilirubin secretion leading to conjugated hyperbilirubinemia and jaundice.
   2. Etiology: the main determinant of bile flow is the enterohepatic circulation, with the rate-limiting step being secretion of bile by the hepatocyte. The neonatal liver is prone to cholestasis because its bile acid pool size is diminished and hepatic uptake and excretion mechanisms are immature. Research also points to a genetic causation in some cases. Causes of cholestasis by anatomic location:
      a. Extrahepatic bile duct: biliary atresia, choledochal cyst, choledocholithiasis, and bile duct perforation.
      b. Intrahepatic bile duct: syndromic paucity of bile ducts (Alagille syndrome [70% with abnormal chromosome 20p12]), nonsyndromic paucity of bile ducts, bile duct dysgenesis, CF, Langerhans cell histiocytosis, and hyper-immunoglobulin M syndrome.
      c. Hepatocyte: bacterial and viral (cytomegalovirus [CMV], herpes simplex virus [HSV], hepatitis) infection, progressive familial intrahepatic cholestasis syndrome, neonatal hemochromatosis, and total parenteral nutrition–associated cholestasis (TPNAC).
      d. Genetic abnormalities: α_1-antitrypsin deficiency, tyrosinemia type I, classic galactosemia, mitochondrial DNA depletion syndrome, argininemia, mitochondrial cytopathy, congenital disorders of glycosylation type Ia, Zellweger syndrome, Niemann–Pick type C, and citrullinemia type II.
   3. Incidence: overall incidence is 1 in 2500. Incidence of cholestasis associated with TPN varies from 7% to 50%. Frequency increases with younger gestational age and longer duration of TPN. Most cases occur within 2 to 10 weeks after starting TPN; 90% of infants develop cholestasis within 13 weeks.
   4. Associated conditions: see 2. Etiology, earlier.
   5. Diagnosis: there is no single test for cholestasis. Once it is established that the infant has conjugated hyperbilirubinemia, the diagnostic evaluation should be individualized. For suspected genetic issues, consider DNA mutation analyses.
      a. History.
      b. Clinical presentation.
         1) Normal appearance at birth, with gradual manifestation during first month of life.

2) Jaundice; usually becomes apparent between second and sixth weeks of life. Skin is not yellow (unconjugated/indirect bilirubin), but rather a green-bronze color due to conjugated/direct hyperbilirubinemia.
3) Acholic stools, malabsorption of fat (steatorrhea) and lipid-soluble vitamins, mineral and trace mineral deficiency, growth failure. Dark urine secondary to bilirubin excretion.
4) Hepatomegaly due to hepatocellular damage. Portal hypertension if cholestasis is prolonged and liver failure occurs.
5) Pruritus, xanthomas due to retention of bile acids and cholesterol.

c. Imaging studies.
1) Ultrasound.
2) Hepatobiliary scintigraphy (HIDA scan).
3) Percutaneous or endoscopic cholangiography.
4) ERCP.
5) Radiographs of long bones and skull for congenital infections.

d. Laboratory studies.
1) Urinalysis.
2) Bacterial cultures of blood and urine.
3) Serology for vital hepatitides, human immunodeficiency virus, and TORCH (*t*oxoplasmosis, *o*ther [congenital syphilis and viruses], *r*ubella, *c*ytomegalovirus, *h*erpes simplex).
4) Bilirubin fractionation: direct bilirubin greater than 2 mg/dL. Direct-to-total bilirubin ratio greater than 15%.
5) Liver enzymes: elevated aminotransferase concentrations (hepatocellular damage). Elevated ALP, 5′-nucleotidase or γ-glutamyl transpeptidase (biliary injury or obstruction).
6) Assessment of synthetic liver function: serum albumin, glucose, ammonia, cholesterol, PT.
7) Test for inborn errors of metabolism.
8) Sweat chloride iontophoresis.

e. Other.
1) Ophthalmologic examination.
2) Liver biopsy.

6. Prognosis: related to underlying cause.

B. **Management of the infant with cholestasis: management is specific to the etiology.** No specific therapy reverses cholestasis or prevents its progression. In cases of outflow obstruction, eliminate the obstruction (see Biliary Atresia). Chromosomal abnormalities cannot be reversed but may be palliated. With an infectious etiology, treat underlying infection. For TPNAC, minimize TPN concentration and duration and provide enteral nutrition if possible. Goals of therapy are to improve nutritional status, maximize growth, and minimize discomfort.

1. TPN management.
a. Decrease parenteral protein to 1 to 2 g/kg/day.
b. Decrease parenteral dextrose concentration to 10%.
c. Eliminate hepatic trace elements.

2. Enteral feeding management.
a. Increase enteral feedings as tolerated. Caloric intake should be 125% to 150% of recommended dietary additives.
b. Administer formulas with medium-chain triglycerides (e.g., Pregestimil, Alimentum).
c. Encourage human milk feeding as long as infant grows appropriately.

3. Medications.
a. Supplemental fat-soluble vitamins. Tocopheryl polyethylene glycol succinate (TPGS)–tocopherol (Liqui-E or Nutr-E-Sol) is the preferred vitamin E preparation, to be given with a multivitamin supplement (e.g., Poly-Vi-Sol) and vitamin K. These preparations should all be mixed together for administration.
b. Cholestyramine to increase fecal excretion of bile acids. The decrease in bile acids returning to the liver stimulates the production of new bile acids from cholesterol, resulting in the reduction of toxic bile acids in the liver and a decrease in cholesterol. May help decrease pruritus.
c. Ursodeoxycholic acid for pruritus and to increase intestinal excretion of bile acids.
d. Phenobarbital to decrease bile acid pool size.

Gastroesophageal Reflux (Gulati and Jadcherla, 2019; Janek et al., 2019)

A. **General considerations.**
1. Definition: GER is the retrograde movement of gastric contents into the esophagus and above. With gastroesophageal reflux disease (GERD), there are symptoms of disease resulting from GER events. GERD has not been well defined in neonates. Regurgitation is a movement of gastric contents into the mouth. It may be a sign of GER, but GER can occur without regurgitation.
a. Spectrum of GER.
1) Reflux episodes occur to some extent in all individuals, especially after meals.
2) Reflux is considered physiologic as long as the individual continues to thrive and has no complications.
3) Complications generally do not occur as long as the frequency and duration of reflux are in the normal range.

4) Infants who have regurgitation as their only sign of reflux are considered to have physiologic GER and are referred to as "happy spitters."
5) Pathologic GER usually manifests as malnutrition, respiratory disorders, or esophagitis.

2. Etiology. Mechanisms for reflux in infants includes a transient relaxation of the lower esophageal segment (LES), delay in esophageal clearance of contents, air entry into stomach during swallowing, excessive swallowing, delayed gastric emptying, and decreased esophageal motility. A complete understanding of the pathophysiology of GER remains unclear.
3. Incidence: varied; 40% to 50% of infants regurgitate more than once a day. GER with symptoms has been noted in 3% to 10% of premature infants less than 1500 g.
4. Associated conditions.
   a. Prematurity.
   b. Birth asphyxia with neurodevelopmental delay. Infants treated with extracorporeal membrane oxygenation (ECMO) are at risk for GER because of the acute status requiring ECMO.
   c. GI tract anomalies/conditions: craniofacial anomalies, airway anomalies, EA/TEF, esophagitis, hiatal hernia, pyloric stenosis, gastroschisis/omphalocele, duodenal atresia, malrotation.
   d. Diaphragmatic hernia/paralysis.
   e. Chronic lung disease.
   f. Medications: xanthines, β-mimetics, prostaglandin E_1, dopamine.
5. Diagnosis.
   a. Clinical presentation.
      1) Feeding difficulties.
         a) Regurgitation; most common presentation in infants.
         b) Gagging.
         c) Feeding refusal.
         d) Aspiration.
         e) Failure to thrive.
      2) Fussiness, irritability, colic-like behavior, back arching with feeding.
      3) Respiratory difficulty.
         a) Apnea.
            (1) Protective airway reflexes may respond to refluxed pharyngeal material, causing laryngospasm and obstructive apnea.
            (2) Reflux-related apnea most commonly occurs after a meal, with the infant supine or seated. The infant may not cough, choke, or gag before the apneic episode.
         b) Stridor.
   b. Radiologic examination.
      1) Fluoroscopy or upper GI series (30% false positive).
      2) Scintigraphy.
   c. Other studies.
      1) Esophageal pH probe. Detects acid reflux only; does not detect nonacid (milk) or gas reflux.
      2) Intraesophageal electrical impedance (pH independent).
      3) Esophageal manometry.
      4) Endoscopy.
6. Prognosis. Resolves in almost all infants by 12 to 18 months of age; 10% to 15% require prolonged medical management; 10% to 15% also require surgery. Success after fundoplication varies. Prognosis depends on complications: respiratory (worsening of chronic lung disease; bronchospasm and pneumonia), esophageal (esophagitis [occurs in 61% to 83% of infants with clinically significant reflux], bleeding, strictures), and hematologic (anemia from chronic bleeding).

B. **Management of the infant with GER.**
1. Conservative measures.
   a. Interventions to minimize simple regurgitation.
      1) Thicken feedings with rice cereal or other commercially available thickeners. Thickening increases viscosity. It also increases caloric density, thus reducing the volume needed to supply adequate calories.
      2) Feed slowly.
      3) Frequent burping.
      4) Small frequent feedings.
      5) Position infant at a 45- to 60-degree angle during feeding.
      6) Avoid pressure on abdomen during and immediately after feeding.
      7) Avoid jiggling or bouncing the infant during feeding and for at least an hour afterward.
   b. Minimize/eliminate provoking and aggravating factors.
      1) Provoking factors: frequent suctioning, chest physical therapy.
      2) Aggravating factors: xanthine and β-mimetic agents (increase LES relaxation).
   c. Position.
      1) Upright for 30 minutes after feeding (infant held upright by caregiver). Upright position in a car seat can make reflux worse, as typically the infant's lower body slides forward, increasing intraabdominal pressure and possibly compromising the airway by a chin-on-chest position.
      2) Left side or supine position. Preterm delivery and GER do not exempt an infant from

supine position recommendations (American Academy of Pediatrics Task Force on Sudden Infant Death Syndrome, 2016).
3) The surface on which the infant is placed for sleep should be firm and without soft bedding or gas-trapping objects.

2. Pharmacologic measures.
   a. Prokinetics. Used to increase gastric motility. Commonly used agents include bethanechol, metoclopramide, and erythromycin. Some studies show no benefit to these agents.
   b. Histamine$_2$-receptor antagonists or proton pump inhibitors. Reduce gastric acid when complications such as esophagitis occur. Commonly used agents include ranitidine, famotidine, and omeprazole. Studies show use of these agents increases the risk for infection.
   c. Acid-neutralizing agents (e.g., calcium- and aluminum-containing antacids). Facilitate healing of esophagitis but are infrequently given to neonates because of the side effect of constipation.
3. Surgical measures: initiated when conservative and medical management has failed and the infant has developed or is anticipated to develop sequelae and complications. Frequently performed using laparoscopic technique.
   a. Nissen fundoplication (Fig. 29.6). Stomach fundus is wrapped 360 degrees around the LES. Procedure most commonly performed.
   b. Variations of Nissen technique, including the Thal (270-degree) procedure, the Mutaf gastric tube cardioplasty, posterior 180-degree procedure, anterior 180-degree procedure, and an anterior 90-degree procedure.

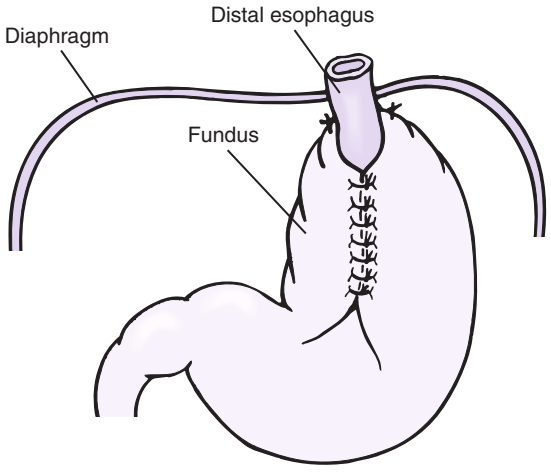

Fig. 29.6 Nissen fundoplication for repair of hiatal hernia. Fundus of stomach is wrapped around distal esophagus and sutured to itself. (From Lewis, S. L., Dirksen, S. R., Heitkemper, M. M., & Bucher, L. [2014]. *Medical-surgical nursing: Assessment and management of clinical problems* [9th ed.]. St. Louis, MO: Elsevier Mosby.)

Multisystem Disorders With Gastrointestinal Involvement (Achour et al., 2018)

A. Eagle–Barrett syndrome (prune-belly syndrome; prune-belly association).
   1. Definition: triad of congenital anomalies consisting of complete or partial absence of abdominal musculature, genitourinary tract abnormalities, and cryptorchidism (undescended testes). Most common genitourinary defects are as follows:
      a. Megaloureter.
      b. Cystic renal dysplasia.
      c. Urethral obstruction.
      d. Megacystitis.
   2. Etiology: unclear, but may be the result of a generalized developmental defect of abdominal parietes and mesenchyma. Recent cytogenic testing has elucidated a number of variations, inheritance from a phenotypically unaffected biological parent, and duplication of the *AGTR2* gene on the X chromosome. Affected genes influence mesodermal, muscle, and urinary tract development (Iqbal et al., 2018).
   3. Incidence: 1 in 35,000 to 50,000 live births. Approximately 97% of affected infants are male. With familial cases, the incidence of affected males decreases to 72%. The incidence is also higher in twin gestations, African American infants, and cases of trisomy 21.
   4. Associated conditions.
      a. Pulmonary conditions: hypoplasia.
      b. GI tract anomalies (30%): malrotation, volvulus, atresia or stenosis, imperforate anus, persistent cloaca.
      c. Cardiac anomalies (10%): patent ductus arteriosus, atrial and ventricular septal defects, tetralogy of Fallot.
      d. Genitourinary conditions: patent urachus, posterior urethral valves, bilateral hydroureter, and hydronephrosis.
      e. Musculoskeletal anomalies: limb abnormalities (clubfoot and other positional deformations), scoliosis, congenital hip dysplasia, contractures.
   5. Diagnosis.
      a. Prenatal ultrasonography, including high-resolution method. May show a dilated renal pelvis (>5 mm at 16 to 18 weeks of gestation), dilated ureters, and bladder distention.
      b. History of oligohydramnios: suggestive of renal pathologic changes.

c. Inspection at birth: shapeless, flat abdomen with wrinkled skin; respiratory distress, compression deformities.
d. Physical examination: Potter facies and skeletal deformities; bell-shaped chest, respiratory distress, cardiac murmur; wrinkled abdomen with visible bowel loops and possible margins of liver and spleen, enlarged kidneys, distended bladder (4 cm from symphysis by percussion), urinary drainage via the umbilicus; bilateral cryptorchidism, pseudohermaphroditism in females.

6. Imaging studies.
   a. Ultrasound: kidneys, ureters, bladder, urethra.
   b. Voiding cystourethrogram: controversial. Evaluates urethra, bladder, vesicoureteral reflux, and ureteral stenosis and detects patent urachus.
   c. Computed tomography scan.
   d. Nuclear scan: technetium (Tc-99 m) dimethylsuccinic acid (DMSA) renal scan.
7. Other: karyotyping if sex is indeterminate.
8. Prognosis: directly related to degree of urinary tract dysfunction, especially renal. Approximately 20% of infants die during the first month of life from renal dysplasia or hypoplasia. Renal failure develops in childhood in approximately 30% of those who survive infancy. Treatment required includes dialysis or transplantation. Long-term considerations include difficulty voiding and the need for nephrostomy or ureterostomy; constipation is common; long-term antibiotic therapy may be necessary to prevent infection.

B. **Management of the infant with Eagle–Barrett syndrome.**

1. Medical management.
   a. Respiratory: support as needed; alert for pulmonary air leak.
   b. Correct fluid, electrolyte, and acid–base status. Sodium reabsorption is diminished or deficient; hyponatremia may rapidly result. Blood urea nitrogen and serum creatinine: rising values may indicate renal insufficiency.
   c. Nutrition. Low protein intake reduces renal workload.
   d. Antibiotics to prevent urinary tract infection due to urinary stasis and reflux and invasive procedures.
2. Surgical procedures.
   a. Prenatal: shunting to preserve renal function by preventing bladder distention. Procedures include vesicoamniotic shunting, open fetal surgery, and fetoscopic surgery.
   b. Postnatal: urinary diversion is essential to sustain renal function. Procedures include urethrotomy for urethral obstruction; cutaneous vesicostomy with the bladder brought to the abdominal surface; repair of posterior urethral valves; closure of patent urachus, although many spontaneously close; orchiopexy to prevent testicular malignancy; and abdominal wall reconstruction.

CONGENITAL DIAPHRAGMATIC HERNIA (AYDIN ET AL., 2019; BASURTO ET AL., 2018)

1. Definition: herniation of abdominal organs into the thoracic cavity through a defect in the diaphragm. About 85% occur on the left. Approximately 95% occur posteriorly (Bochdalek type), whereas 5% occur anteriorly (Morgagni type). The defect can vary from a small slit to the complete absence of the diaphragm on the affected side. Severity is related to timing and degree of prenatal herniation. Early herniation through a large defect is associated with bilateral pulmonary hypoplasia, pulmonary hypertension, and intrapulmonary shunt (V/Q mismatch). A right-to-left shunt occurs through the ductus arteriosus and/or foramen ovale, further compromising pulmonary blood flow and sending deoxygenated blood to the body.
2. Etiology: unknown; retinoid signaling and transcription factors are considered. May occur as isolated defect or part of a syndrome. Numerous genetic abnormalities are associated with CDH. A genetic microarray rather than isolated karyotype is recommended for enhanced detection of genetic issues.
3. Incidence: 1 in 2200 to 3000 live births.
4. Associated conditions.
   a. Chromosomal abnormalities: most common are trisomies 13, 18, and 21 and 45,X.
   b. Associated anomalies are reported to be greater than 40% and include CNS, cardiovascular, skeletal, GI, and genitourinary defects. Intestinal malrotation is common.
5. Diagnosis.
   a. Prenatal ultrasonography, including the high-resolution method. Hallmark finding: fluid-filled stomach just behind the left atrium.
   b. History of polyhydramnios.
   c. Clinical presentation.
      1) Respiratory distress and cyanosis at birth or shortly after birth, typically followed by worsening presentation. Condition worsens rather than improves with bag-and-mask ventilation as intestines in the thorax distend with air and further compromise lung function.
      2) Hypoperfusion and decreased oxygen saturation due to right-to-left shunting through the ductus arteriosus, foramen ovale, and intrapulmonary shunts.
   d. Physical examination.
      1) Diminished breath sounds: decreased on ipsilateral side due to lung compression by abdominal organs; decreased on contralateral side due to mediastinal shift.

2) Heart tones may be shifted from their normal point of maximal intensity.
3) Barrel chest.
4) Scaphoid abdomen.

e. Radiologic examination.
1) Plain radiograph showing displaced gastric bubble and a bowel gas pattern in the thorax (see Chapter 14). A radiograph taken immediately after birth may not demonstrate bowel gas in the intestines, whereas later radiographs demonstrate it clearly.

f. Laboratory tests: blood gas analysis demonstrating hypoxemia, hypercapnia, and combined metabolic and respiratory acidosis.

6. Prognosis: survival varies depending on the size of the defect and amount of herniated viscera, early intervention (especially at a tertiary care center), pulmonary hypertension, and associated conditions. Presence of a hernia sac pointed to a better outcome, whereas presence of the liver herniation into the thorax pointed to a worse outcome. Both conditions affected pulmonary development. Despite current interventions and a shift from early surgical repair to supportive therapy and techniques to avoid lung injury, survival is approximately 70%. Although some institutions report higher survival rates, the reported survival rates do not include infants who expired before arriving at the respective institution. Structured follow-up care is required for infants with long-term sequelae (Wigen et al., 2019).

C. **Management of the infant with CDH.**

1. Prenatal treatment: the gravid mother must be transferred to a facility capable of management of the infant postnatally, including neonatal intensive care, inhaled nitric oxide (iNO), ECMO, pediatric surgery, and genetic evaluation. Additional services to consider are pediatric cardiology and pediatric thoracic surgery.
2. Preoperative care: CDH is no longer considered a surgical emergency. Concerns immediately after birth include pulmonary hypoplasia and pulmonary hypertension. In addition, not rushing to surgery allows stabilization of the infant and evaluation for associated conditions that may preclude ECMO or surgery.
a. Respiratory.
1) Intubate and support as needed. Avoid bag–mask ventilation to prevent GI distention. Remain alert for pulmonary air leak. Immediate treatment must be prompt and aggressive. Primary considerations are as follows:
a) Establishment of adequate perfusion. Use of inotropes to increase systemic blood pressure and decreased right-to-left shunting.
b) Correction of acid–base imbalances and provision of adequate oxygenation.
c) May require high-frequency ventilation, administration of iNO. Prophylactic surfactant treatment at birth has no benefit in either preterm or term infants because surfactant maturation is unaffected in infants with CDH. Hyperventilation and hyperalkalinization to force alkalinization are no longer recommended because they cause ventilation-induced lung injury, complicate electrolyte management, and decrease cerebral blood flow.

b. ECMO is instituted if ventilation does not effectively stabilize the pulmonary status. ECMO may be used preoperatively to stabilize the patient for surgery, intraoperatively, and/or postoperatively to rest the lungs.
c. NPO.
d. Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
e. Complete examination for other anomalies.

3. Surgical procedures.
a. Prenatal surgery.
1) Percutaneous fetoscopic endoluminal tracheal occlusion (FETO) promotes lung growth in severe cases. Airway obstruction prevents egress of lung fluid, increases airway pressure, activates stretch receptors, and induces proliferation.
2) In-utero repair of CDH does not improve survival over conventional postnatal care.

b. Postnatal surgery.
1) Primary closure of the diaphragmatic defect is usually possible. With large defects or a totally absent diaphragm, a synthetic patch can be used to close the diaphragmatic defect.

c. Postoperative care.
1) Pain management (see Chapter 16).
2) Continue preoperative care.
a) Respiratory support with oxygenation, ventilation, iNO, ECMO.
b) NPO.
c) Gastric decompression with a vented sump tube to low continuous suction until gastric output is minimal and peristalsis is normal. To prevent dehydration, measure amount every 4 hours and replace milliliter for milliliter with physiologic IV fluid.
d) Inotropes: decrease right-to-left shunting.
e) If placed during surgery, a chest tube for drainage should be placed on a water seal (without suction) to prevent acute mediastinal shift.

f) Coordinated long-term follow-up is required, as some survivors demonstrate neurologic issues: abnormal muscle tone and delayed neurocognitive and language skills.

D. **Hyperbilirubinemia** (Cayabyab and Ramanathan, 2019; Dani et al., 2019; Fidanza and Sables-Baus, 2019; Hamza, 2019).

1. Definitions.
   a. Hyperbilirubinemia: an elevated total serum bilirubin (TSB) level. Abnormal values differ by gestational age, days of life, and concomitant illness or conditions. A recognizable sign is jaundice. TSB is the combination of conjugated/direct and unconjugated/indirect serum bilirubin levels (Fig. 29.7).
   b. Jaundice (icterus): the yellowish coloration of the skin and sclera caused by the presence of bilirubin in elevated concentrations. Jaundice appears cephalad to caudal and regresses in the reverse order.
   c. Conjugated: direct serum hyperbilirubinemia.
   d. Unconjugated: indirect hyperbilirubinemia.
   e. Acute bilirubin encephalopathy: acute bilirubin toxicity manifested by a direct correlation between lethargy and unconjugated serum bilirubin concentration and abnormal brainstem auditory evoked response. Brain magnetic resonance images show focal changes. If not reversed, the process progresses to permanent neurologic impairment or death. Survivors demonstrate cerebral palsy and sensorineural hearing loss. Autopsy also reveals renal, intestinal, and pancreatic cell involvement. Calculation of a risk index score:
      1) Phase 1: poor sucking, hypotonia, depressed sensorium.
      2) Phase 2: fever, retrocollis, hypertonia of extensor muscles, opisthotonos, high-pitched cry.
      3) Phase 3: shrill cry, hearing and visual derangements, no feeding, athetosis, apnea, seizures, deep stupor to coma, death.
   f. Kernicterus: for consistency, the American Academy of Pediatrics (AAP) recommends this definition: irreversible, chronic sequelae of bilirubin toxicity (AAP Subcommittee on Hyperbilirubinemia, 2004).
      1) During the first year of life, characteristic findings are hypotonia, active deep tendon

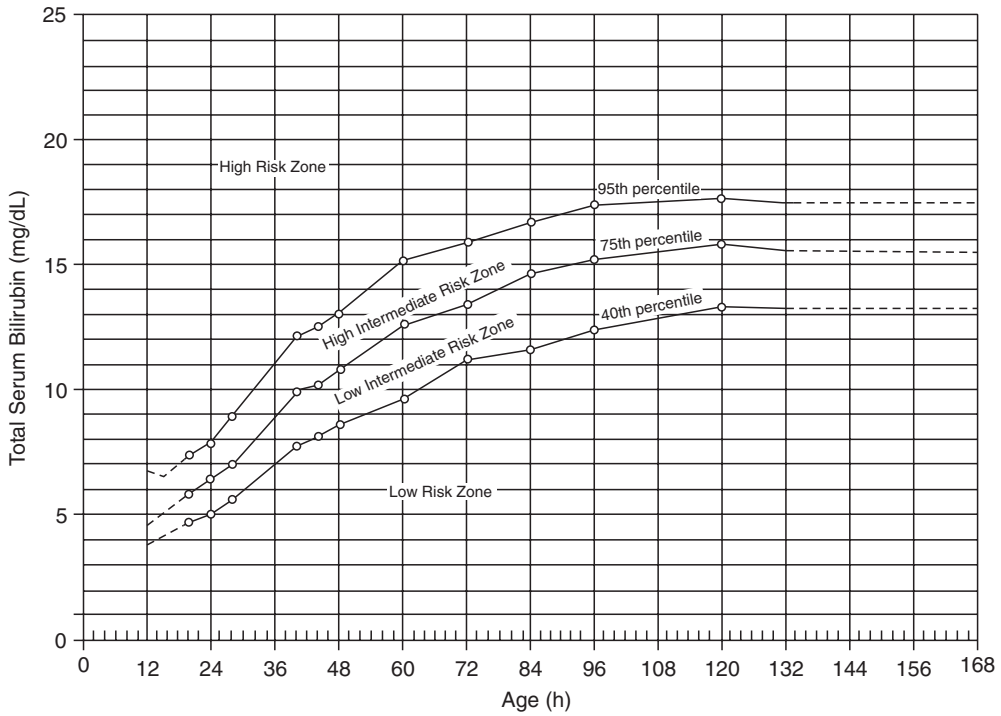

Fig. 29.7 Risk designation of term and near-term well newborns based on their hour-specific serum bilirubin values. The high-risk zone is designated by the 95th percentile track. The intermediate-risk zone is subdivided to upper- and lower-risk zones by the 75th percentile track. The low-risk zone has been electively and statistically defined by the 40th percentile track. (Dotted extensions are based on <300 total serum bilirubin [TSB] values/epoch.) (From Bhutani, V. K., & American Academy of Pediatrics, Committee on Fetus and Newborn. [2011]. Phototherapy to prevent severe neonatal hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*, 128[4], e1046–e1052.)

reflexes, persistent tonic neck reflex, and delayed acquisition of motor skills.

2) Characteristics of fully developed encephalopathy include hearing loss, choreoathetoid cerebral palsy, and gaze abnormalities, especially upward gaze. Intellectual deficits are common but usually not severe.

3) Treatment: none.

2. Etiology.

a. Bilirubin metabolism (Fig. 29.8).

1) Synthesis: bilirubin is primarily the metabolic end product of erythrocyte (red blood cell [RBC]) breakdown. One gram of heme produces 34 mg of bilirubin; normal neonates produce 8 to 10 mg/kg/day.

2) Transport: heme reversibly binds to albumin (1 g of albumin can bind with approximately 8 mg of bilirubin) and is transported via the bloodstream to the liver as an unconjugated, fat-soluble product with a propensity for fatty tissues such as subcutaneous and brain tissue.

3) Metabolism: glucuronyl transferase converts bilirubin and glucuronic acid into water-soluble glucuronide.

4) Excretion: glucuronide is excreted into bile and enters the intestine, where bacteria convert it to urobilinogen. Urobilinogen is converted to stercobilin and excreted in feces, giving feces a brownish color.

5) Enterohepatic reabsorption of bilirubin: in the small intestine, the high concentration of β-glucuronidase in the brush border in newborn infants can convert conjugated bilirubin into the unconjugated form, which is easily absorbed from the small intestine into the portal circulation. In fetal life, this permits bilirubin to be transported across the placenta for maternal excretion. Increased amounts of bilirubin in the amniotic fluid may indicate hemolytic disease or fetal intestinal obstruction below the bile ducts.

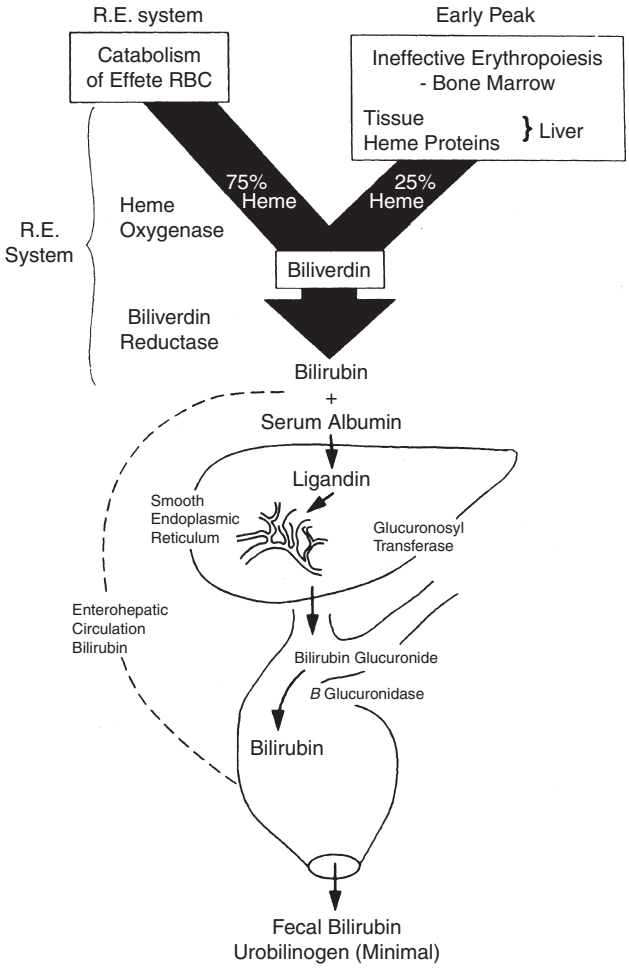

Fig. 29.8 Neonatal bile pigment metabolism. *RBC*, Red blood cells; *R.E.*, reticuloendothelial. (From Maisels, M. J. [1999]. Jaundice. In G. B. Avery, M. A. Fletcher, & M. G. MacDonald [Eds.], *Neonatology: Pathophysiology and management of the newborn* [5th ed., p. 767]. Philadelphia, PA: Lippincott, Williams & Wilkins.)

b. Nonpathologic unconjugated hyperbilirubinemia: a result of an elevated hematocrit level at birth, increased RBC destruction (neonatal RBCs have a 70- to 90-day life span), reduced hepatic uptake of unconjugated bilirubin, and enterohepatic reabsorption of bilirubin. TSB levels generally peak on day 3 of life in full-term infants and on days 5 to 6 in preterm infants. Factors that may further accentuate this normal process include the following:

1) Hemolysis.

a) ABO/Rh incompatibilities.

b) Bacterial and viral infection (especially TORCH infections).

c) Inherited disorders of RBC metabolism.

(1) RBC membrane defects: spherocytosis, elliptocytosis.

(2) RBC enzyme defects: glucose-6-phosphate dehydrogenase (G6PD) deficiency and pyruvate kinase deficiency.

d) Inherited disorders of bilirubin metabolism: Crigler–Najjar syndrome types I and II, Gilbert syndrome.

e) Medications that cause hemolysis or compete with albumin for binding sites, and free fatty acids from emulsified fats (Intralipid).

2) Extravasation of blood.

a) Cephalohematoma or bruising.

b) Pulmonary, cerebral, or retroperitoneal hemorrhage.

3) Increased enterohepatic circulation.
   a) Delayed feeding.
   b) Intestinal obstructions.
4) Decreased hepatic function and perfusion.
   a) Metabolic derangements: hypoxia, acidosis, hypothermia, hypoglycemia, starvation.
   b) Infection.
5) Endocrine disorders.
   a) Hypothyroidism.
   b) Hypopituitarism.
6) Inborn errors of metabolism (with both unconjugated and conjugated hyperbilirubinemia).
   a) Galactosemia.
   b) α_1-Antitrypsin deficiency.
   c) Tyrosinosis.
   d) Hypermethioninemia.
   e) CF.
7) Globin synthesis defect: α-thalassemia.

c. Pathologic unconjugated hyperbilirubinemia (for blood incompatibilities, see Chapter 31): when the nonpathologic unconjugated hyperbilirubinemia processes are exaggerated and when available albumin-binding sites are saturated, unconjugated bilirubin circulates as free bilirubin and can cross the blood–brain barrier (BBB). This BBB breach is accentuated with meningitis.
   1) Unconjugated hyperbilirubinemia is pathologic when:
      a) Jaundice appears in the first 24 hours of life.
      b) TSB level increases by more than 5 mg/dL/day.
      c) TSB level exceeds 12.9 mg/dL in a term infant or 15 mg/dL in a preterm infant.
      d) TSB level is in the 95th percentile for age in hours or is "jumping the tracks" (see Fig. 29.7).
      e) Jaundice lasts for more than 1 week in a term infant or 2 weeks in a preterm infant.

d. Conjugated hyperbilirubinemia.
   1) Hepatic cell injury: TPN, infection (TORCH and viral hepatitis and systemic bacterial), medications, metabolic derangements and inborn errors of metabolism.
   2) Biliary obstruction: see Biliary Atresia.
   3) Excessive bilirubin load.
   4) Maternal–fetal blood group incompatibility: ABO, Rh (see Chapter 31).

e. Human milk feeding jaundice: onset 2 to 4 days of life; related to low enteral intake. Self-limiting as milk supply increases.

f. Human milk jaundice: onset 4 to 7 days of life; exaggerated physiologic jaundice related to substances in human milk that cause glucuronyl transferase inhibition. Occurs in 10% to 30% of human milk–fed newborns; TSB levels may reach 12 to 20 mg/dL and persist for up to 2 months.

3. Incidence: dependent on etiology.
   a. Influenced by:
      1) Ethnicity (higher in infants of East Asian and Mediterranean descent).
      2) Elevated hematocrit level (delayed cord clamping, maternal diabetes).
      3) Extravasated blood (bruising, cephalohematoma, intracranial hemorrhage, swallowed blood).
      4) Maternal medications: oxytocin and bupivacaine. Mechanism is unclear but may involve hemolysis.
      5) Hepatic dysfunction: prematurity, asphyxia.
      6) Feeding: early enteral feeds promote peristalsis and passage of bilirubin-containing stool and introduce bacteria into the gut (contributes to the conversion of bilirubin to urobilin, a substance that cannot be reabsorbed).
   b. Nonpathologic unconjugated hyperbilirubinemia (physiologic jaundice): jaundice develops in more than 60% of term newborn infants and 80% of preterm infants; it is visible when the serum bilirubin concentration is greater than 6 to 7 mg/dL.
   c. Conjugated hyperbilirubinemia: dependent on etiology.
   d. Human milk feeding jaundice: 1 in 10 human milk–fed infants.
   e. Human milk jaundice: 1 in 200 human milk–fed infants.
4. Associated conditions.
   a. Prematurity.
   b. Infection.
   c. Dehydration.
5. Diagnosis.
   a. Nonpathologic unconjugated hyperbilirubinemia.
      1) Clinical presentation: onset of jaundice around day 2 to 3 of life. No hepatosplenomegaly.
      2) Laboratory tests: transcutaneous bilirubin meter helps establish a risk assessment but does not determine exact TSB levels. Usefulness in preterm infants, infants receiving phototherapy, and infants with TSB values above 15 mg/dL requires further study. Definitive bilirubin levels are obtained only by analysis of TSB levels.
   b. Pathologic unconjugated hyperbilirubinemia.
      1) See a. Nonpathologic unconjugated hyperbilirubinemia.

2) Clinical presentation: jaundice within 24 hours of birth. Signs of acute bilirubin encephalopathy.
3) Laboratory tests: TSB increase of 5 mg/dL or more in a 24-hour period or above the 95th percentile for age (hours).

c. Conjugated hyperbilirubinemia.
1) See Biliary Atresia.

d. Human milk feeding jaundice: peaks around day 3 as enteral intake increases, then resolves.

e. Human milk jaundice: prolonged appearance, no signs of bilirubin encephalopathy.

6. Prognosis: dependent on etiology and early detection and treatment, when necessary.

E. **Care of the infant with hyperbilirubinemia.**

1. **Management** of nonpathologic unconjugated hyperbilirubinemia.
a. Frequent enteral feeding, including promotion and support of human milk feeding. This promotes removal of meconium from the intestines. Meconium contains 1 mg of bilirubin per 1 g of meconium. Delayed stooling promotes enterohepatic recirculation of bilirubin.

b. Establish protocols to identify hyperbilirubinemia and measure bilirubin levels. Interpret results by infant's age—gestationally and hours of life. Follow-up care postdischarge is required for all infants discharged before 48 hours of age.

c. At discharge, provide caregivers with verbal and written information about hyperbilirubinemia, need for follow-up monitoring, and how monitoring will be accomplished.

2. **Management of pathologic unconjugated hyperbilirubinemia.**
a. Goal: prevent bilirubin toxic effects. Recognize that all infants are at risk. Risk is increased with decreasing gestational age, in infants less than 38 weeks of gestation who are receiving human milk feeding, and in the ill neonate.

b. Guidelines for treating hyperbilirubinemia in healthy term infants are listed in Table 29.4. Management of hyperbilirubinemia in low birth weight infants is determined by clinical status, age, weight, and history (Table 29.5).

Table 29.4

Management of Hyperbilirubinemia in Healthy Term Neonate*

	TSB LEVEL, mg/dL (mcmol/l)			
Age (Hours)	Consider Phototherapy*	Phototherapy	Exchange Transfusion if Intensive Phototherapy Fails†	Exchange Transfusion and Intensive Phototherapy
≤24‡				
25 to 48	≥12 (170)	≥15 (260)	≥20 (340)	≥25 (430)
49 to 72	≥15 (260)	≥18 (310)	≥25 (430)	≥30 (510)
>72	≥17 (290)	≥20 (340)	≥25 (430)	≥30 (510)

TSB, Total serum bilirubin.

*Phototherapy at these TSB levels is a clinical option, meaning that the intervention is available and may be used on the basis of individual clinical judgment.

†Intensive phototherapy should produce a decline of TSB of 1 to 2 mg/dL within 4 to 6 hours, and the TSB level should continue to fall and remain below the threshold level for exchange transfusion. If this does not occur, it is considered a failure of phototherapy.

‡Term infants who are clinically jaundiced at ≤24 hours of age are not considered healthy and require further evaluation.

From American Academy of Pediatrics, Provisional Committee for Quality Improvement and Subcommittee on Hyperbilirubinemia. (1994). Practice parameter: Management of hyperbilirubinemia in the healthy term newborn. *Pediatrics*, *94*(4 Pt. 1), 558–565.

Table 29.5

Management of Hyperbilirubinemia in the Low Birth Weight Infant

	TOTAL SERUM BILIRUBIN LEVEL, mg/dL			
	HEALTHY		SICK	
Gestational Age	Phototherapy	Exchange Transfusion	Phototherapy	Exchange Transfusion
Premature				
<1000 g	5 to 7	Variable	4 to 6	Variable
1001 to 1500 g	7 to 10	Variable	6 to 8	Variable
1501 to 2000 g	10 to 12	Variable	8 to 10	Variable
2001 to 2500 g	12 to 15	Variable	10 to 12	Variable

From Martin, R. J., Fanaroff, A. A., & Walsh, M. C. (2011). *Fanaroff and Martin's neonatal-perinatal medicine: Diseases of the fetus and infant* (9th ed.). Philadelphia, PA: Elsevier Mosby.

c. Jaundice before 24 hours of age and rising TSB levels exceeding 5 mg/dL per day require investigation.
d. Phototherapy: converts bilirubin to a water-soluble product at 0.5 to 1 mg% per hour and by 30% to 40% after 24 hours of treatment. Effectiveness influenced by:
   1) Energy output of phototherapy unit. Bulbs require changing as energy output decreases. Light irradiance meters are used to determine bulb output.
   2) Spectrum of light: special blue light labeled F20T12/BB (General Electric, Westinghouse, Sylvania) or TL52/20 W (Phillips, Eindhoven, The Netherlands) at 450 nm is most effective. Disadvantage: distortion of infant's color. White lamps, high-intensity gallium nitride light-emitting diodes, and fiberoptic blankets are effective alternatives.
   3) Amount of infant's body surface area exposed to light. Turn infant frequently to allow all areas of the skin to be exposed.
   4) Distance between light and infant. Follow equipment manufacturer's recommendations. Monitor infant's temperature. Fluorescent lights should be at a distance of 10 cm from the infant, who is placed naked in a bassinet. When bank lights are used, lamps should be covered with a clear acrylic shield to protect the infant from ultraviolet light.
e. Monitor fluid and electrolytes. Phototherapy increases insensible water loss and stooling. The AAP Subcommittee on Hyperbilirubinemia (2004) recommends milk-based enteral feeding that inhibits enterohepatic reabsorption of bilirubin.
f. Monitor TSB during and after therapy. A rebound of 1 to 2 mg/dL can be expected.
g. Side effects: bronze skin, if conjugated bilirubin is elevated; lethargy; skin rashes; risk of eye damage, if eye patches are not secure; abdominal distention; hypocalcemia; lactose intolerance; and thrombocytopenia.
h. Home phototherapy: an option that decreases hospitalization time for an otherwise healthy infant.
i. Intensive phototherapy uses multiple phototherapy units above and below the completely naked infant. In addition, aluminum foil or a white cloth on the bassinet side is employed to reflect light onto the infant. All facilities providing care to infants should be capable of providing intensive phototherapy.
j. Exchange transfusion.
   1) Used when intensive phototherapy has been unsuccessful in controlling TSB and at any time signs of acute bilirubin encephalopathy are present, regardless of TSB level; used more often in hemolytic conditions.
   2) Hemolyzed and antibody-coated RBCs are removed over approximately 2 hours in small aliquots (3 to 5 mL/kg in preterm infants, 10 mL/kg in term infants) and replaced with donor blood. Double volume exchange (160 mL/kg) will reduce the TSB by 50%. Expect a rebound TSB of 60% to 70% of the pre-exchange transfusion level.
   3) IV gamma globulin (0.5 to 1 mg/kg over 2 hours), if phototherapy fails to control bilirubin levels or the TSB is approaching exchange transfusion level decreases isoimmune hemolysis.
   4) The administration of albumin before the exchange transfusion is not recommended.
   5) Stabilize infant before the procedure: treat hypoglycemia, acid–base derangements, hypotension, and temperature abnormalities.
   6) CMV-negative blood less than 48 hours old should be used to minimize problems with elevated potassium that occurs in older blood.
   7) Procedure.
      a) Exchange transfusion is performed only by trained personnel in a NICU with monitoring and resuscitation capabilities.
      b) Secure infant on radiant warmer bed. Ensure oxygen, suction, and resuscitation equipment are immediately available. Observe neonate with a cardiorespiratory monitor and assess vital signs frequently.
      c) Ideally, an umbilical artery catheter and umbilical venous catheter are placed (see Chapter 15 for procedure).
      d) Laboratory studies.
         (1) On initial blood removed: CBC, bilirubin and calcium levels, and blood cultures.
         (2) During procedure: calcium level (if signs of hypocalcemia present).
         (3) On final aliquot removed: CBC, bilirubin, and calcium.
      e) Accurate recording of blood volumes exchanged is essential during the procedure.
      f) Observe for hypocalcemia. Anticoagulant citrates (acid–citrate–dextrose and citrate–phosphate–dextrose negative [CPD−] adenosine) bind to calcium. Symptoms of hypocalcemia include irritability, tachycardia, and prolonged Q–T interval.
      g) Calcium gluconate is used to treat hypocalcemia. Normal dose is 1 to 2 mL/kg

(100 to 200 mg/kg) per dose of 10% calcium solution.

h) Evaluate medications. Medications whose levels are known to decrease significantly during an exchange transfusion should be administered after the exchange: ampicillin, gentamicin, digoxin, phenobarbital, vancomycin.

8) Complications.
   a) Electrolyte and substrate abnormalities: hyperkalemia, hypocalcemia, hypomagnesemia, hypoglycemia, hyperglycemia.
   b) Clotting abnormalities: thrombocytopenia, embolization, thrombosis.
   c) Respiratory and cardiovascular events: apnea, bradycardia, cardiac dysrhythmias and arrest, cyanosis, vasospasm, heart failure, acidosis.
   d) NEC and infection.

9) Postexchange care.
   a) Continue phototherapy.
   b) Laboratory studies: TSB every 4 hours. Rebound usually occurs within 1 hour after the exchange.
   c) Monitor blood glucose levels frequently. Dextrose in the blood preservative is equivalent to 300 mg of glucose per liter of blood. Rebound hypoglycemia can occur after an insulin response to the glucose.
   d) Monitor for complications.

3. **Management of conjugated hyperbilirubinemia.**
   a. Management is related to etiology.
   b. Eliminate or reduce causative factors; treat the remainder as appropriate (see Biliary Atresia and Cholestasis sections).
   c. Evaluate liver function; evaluate for infection, including urinalysis and urine culture; check newborn screen for thyroid deficiency and galactosemia. Evaluate for G6PD deficiency.
4. **Management of human milk feeding jaundice.**
   a. Increase enteral intake by feeding 8 to 12 times per day. The AAP does not encourage the interruption of human milk feeding (AAP Subcommittee on Hyperbilirubinemia, 2004).
   b. No supplementation with water or glucose water in term, nondehydrated infants.
   c. Systematic assessment for hyperbilirubinemia risk, including maternal blood typing and neonatal direct antibody testing for incompatibility.
   d. Establish protocols for jaundice assessment and follow-up, including when the nurse can obtain a TSB if jaundiced before 24 hours of age; follow-up required.
5. **Management of human milk jaundice.**
   a. Obtain total and direct serum bilirubin to evaluate for cholestasis if jaundice is present at or beyond 3 weeks of age. Ensure normal thyroid and galactosemia screen.
6. **Alternative therapies.**
   a. Binding agents: agar and activated charcoal bind bilirubin in the gut and decrease the enterohepatic circulation.
   b. Phenobarbital: increases hepatic ligandin concentration and induces the cytochrome P-450 enzymatic system.
   c. Metalloporphyrins: inhibit heme oxygenase, the enzyme that catalyzes the conversion of heme to biliverdin, thereby decreasing bilirubin production. Tin mesoporphyrin and tin protoporphyrin are the two metalloporphyrins most commonly used; however, their use is not approved by the U.S. Food and Drug Administration and is still investigational.

F. **Hydrops** (Abbasi and Ryan, 2019; Carvalho, 2019; Gilby et al., 2018).
1. Definition: a prenatal form of heart failure almost always caused by fetal anemia; characterized by generalized subcutaneous edema and fluid in two compartmental spaces, including the peritoneum, pericardium, pleura, or skin.
2. Etiology: an imbalance of interstitial fluid production and lymphatic return.
   a. Immune hydrops (IH), also known as *alloimmune* or *isoimmune hydrops*: fetal RBCs enter maternal circulation, inducing maternal antibodies that cross the placenta and attack and destroy fetal RBCs. Seen in Rh and ABO disease.
   b. Nonimmune hydrops (NIH): disease or anomalies interfere with fetal fluid management. Most conditions associated with hydrops cause edema either through anemia with hypoxia and subsequent capillary leak or through cardiovascular anomalies with heart failure and subsequent tissue hypoxia, vascular permeability, and decreased lymphatic flow.

1) Cardiovascular (most frequent cause).
   a) Dysrhythmias: supraventricular tachycardia, atrial flutter, complete heart block.
   b) Cardiac malformation: left and right outflow tract obstructions; hypoplastic left heart syndrome, and endocardial cushion defects are the most common.
   c) Myocarditis.

2) Chromosomal: aneuploidy, including trisomies 13, 18, and 21; triploidy; and 45,X (Turner's syndrome); achondroplasia.
3) Infection: TORCH, parvovirus B19, and congenital hepatitis.
4) Hematologic.
   a) α-Thalassemia.
   b) G6PD deficiency.

c) Chronic fetal-to-maternal or twin-to-twin transfusion.
d) Hemorrhage, including fetomaternal hemorrhage.
e) Bone marrow failure.
f) RBC enzyme deficiency.
5) Renal.
a) Nephrosis.
b) Renal vein thrombosis.
c) Renal hypoplasia.
d) Urinary obstruction.
6) Pulmonary.
a) Pulmonary hypoplasia.
b) Cystic adenomatoid malformations.
c) Pulmonary lymphangiectasis.
d) CDH.
7) Gastrointestinal.
a) In-utero volvulus.
b) Meconium peritonitis.
c) Prune-belly syndrome.
8) Inborn errors of metabolism: lysosomal storage disease.
9) Maternal.
a) Toxemia.
b) Diabetes.
c) Systemic lupus erythematosus.
10) Placenta and cord (uncommon).
a) Chorioangioma.
b) Umbilical vein thrombosis.
c) Arteriovenous malformation.
11) Idiopathic: approximately 25% of cases have no identifiable cause. Incidence of idiopathic NIH is dependent on the thoroughness of the diagnostic workup of the populations studied.

3. Incidence: exact figure unknown, as some fetuses die or hydrops resolves in utero. Current estimates range from 1 in 600 to 1 in 4000 live births. Males affected more than females.
a. IH: incidence has significantly decreased to approximately 10% to 20% of hydrops cases with the wide use of anti-D antibody prophylaxis using Rh immunoglobulin for Rh-negative mothers at 28 weeks of gestation (after suspected fetomaternal hemorrhage) and postpartum (after the delivery of an Rh-positive infant). In addition, in-utero fetal transfusion has lessened the incidence.
b. NIH: approximately 80% to 90% of hydrops cases.
4. Associated conditions.
a. Chromosomal abnormalities.
b. Congenital malformations: heart defects, especially outflow tract obstruction (both left and right).
c. Prematurity.
d. Inborn errors of metabolism.
5. Diagnosis.
a. Prenatal.
1) Polyhydramnios.
2) High-resolution ultrasound and fetal echocardiography: hepatosplenomegaly, cardiomegaly, cardiac defects, pleural effusion, pericardial effusion, ascites, generalized edema.
3) Fetal blood sampling via cordocentesis.
4) Amniocentesis: chromosome analysis for associated defects, bilirubin level.
5) Serologic testing for isoimmunization and infection (TORCH; polymerase chain reaction for parvovirus B19).
6) Kleihauer–Betke test for fetomaternal hemorrhage.
b. Postnatal.
1) Clinical presentation.
a) Physical examination: generalized edema; respiratory distress; cardiovascular abnormalities, including dysrhythmia, murmur, diminished perfusion; abdominal findings, including hepatosplenomegaly, distention.
2) Imaging studies: skeletal radiographs, ultrasound for pleural and pericardial effusions, ascites.
3) Laboratory studies.
a) Hematology: CBC to evaluate anemia, thrombocytopenia, reticulocytosis; hemoglobin electrophoresis.
b) Other: serum albumin, metabolic panel, chemistries, karyotype if not already done.
6. Prognosis. IH is associated with a survival rate of approximately 75%. Prognosis in NIH is very poor and is related to the underlying cause. Multiple anomalies and chromosomal abnormalities carry an extremely high mortality. Neurologic outcome in survivors is concerning.

G. **Care of the infant with hydrops.**
1. Prenatal: depends on etiology. The gravid mother must be transferred to a facility capable of managing the infant postnatally, including neonatal intensive care, ventilatory and inotropic support, and genetic evaluation.
a. Intrauterine transfusion to ameliorate anemia.
b. Amniocentesis to determine karyotype, follow bilirubin level, and reduce uterine volume to prevent premature delivery.
c. Thoracentesis or thoracoamniotic shunt placement.
d. Maternal medication administration to control fetal dysrhythmias.
e. Fetal medication administration.
f. Delivery.

2. Postnatal.
   a. Resuscitation is frequently required, including intubation, bilateral thoracentesis (which may include bilateral tube thoracotomy), pericardiocentesis, and umbilical venous catheter placement (generalized edema prohibits successful peripheral IV placement). Umbilical artery catheter placement can be obtained once initial stabilization is accomplished.
   b. Respiratory support as needed with acid–base determination and management. Paracentesis and additional thoracentesis or tube thoracotomy drainage may be required to enhance ventilation efforts. Frequent monitoring of breath sounds and chest movement and radiographs are essential.
   c. Anticipate and treat metabolic abnormalities.
   d. Exchange transfusion or partial exchange transfusion for severe anemia.
   e. Cardiovascular support: inotropes to improve cardiac output; pericardiocentesis; diuretic therapy.
   f. Fresh frozen plasma may be given for hypoalbuminemia.
   g. Assess for associated anomalies, syndromes, or malformations. Determine etiology of hydrops if unknown.

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CHAPTER 30
Endocrine Disorders

Susan Tucker Blackburn

OBJECTIVES

1. Define the endocrine system.
2. Describe endocrine system regulation.
3. Identify and discuss endocrine disorders that manifest in the neonatal period, including disorders of the thyroid, pituitary, adrenal gland, pancreas, and genital development.
4. List effective ways to help parents cope with the birth of an infant with a disorder of sexual development.

The Endocrine System

Disorders of the endocrine system are relatively rare in neonates, but usually have lifelong consequences. The classic endocrine system is a group of nine ductless glands (Table 30.1), but in reality, it includes every organ and cell in the body that produces and responds to hormones and the system of communication between different cells of the body. The endocrine system is intricately linked with the neurologic, immune, and other systems in a vast, interacting control network. The endocrine system, and particularly the hypothalamic–pituitary–adrenal (HPA) and hypothalamic–pituitary–thyroid (HPT) axes, is critical for fetal and neonatal development and maturation. The HPA axis regulates fetal–placental homeostasis, as well as maturation of the lungs, liver, and central nervous system (CNS), and influences the timing of parturition and metabolic and cardiovascular programming (Blackburn, 2018). Coordination and regulation of metabolism and energy, the internal environment, growth and development, and sexual differentiation and reproduction are among the functions of the endocrine system.

A. **Hormones**.
   1. Hormones are the molecular messengers of the endocrine system, allowing communication between organs, tissues, and cells throughout the body. Hormones are steroids, proteins, glycoproteins, peptides, and amines.
   2. Hormones bind to specific receptors on the surface of or within the cytoplasm or nucleus of target cells to produce physiologic actions. Sensitivity of a target cell to its hormones is critical to normal function.
   3. Many hormones are secreted directly into the circulation for transport to various target tissues. Hormones can also act on cells in the immediate vicinity of their release (paracrine regulation) or on the cell that produced the hormone (autocrine or intracrine regulation).
   4. Some hormones circulate partly in free form and partly bound to transport proteins. It is the free form that is available for receptor binding and that dictates regulatory influences on hormone release. Clinical states of hormone excess and deficiency correlate best with free hormone levels.
   5. Most hormones are secreted in their biologically active form (such as insulin), but others (such as thyroxine) must be converted to their final active form in peripheral tissues.

B. **Endocrine system regulation** (Fig. 30.1).
   1. Many hormones are regulated by a negative-feedback loop involving the hypothalamic–pituitary (HP) axis and target endocrine glands. In response to hormonal or neural input, the hypothalamus produces either releasing hormones or inhibiting hormones. These are transported via the pituitary portal system to the anterior pituitary, the gland that controls the secretory activity of most target organs. The anterior pituitary releases trophic hormones that in turn stimulate release of target gland hormones. As blood concentrations of target hormones reach certain thresholds, a negative message to the anterior pituitary inhibits further release of trophic hormones. Examples of hormones regulated by negative feedback are thyroid hormone and cortisol. Negative feedback can be direct (at the level of the pituitary gland) or indirect (at the level of the hypothalamus).
   2. Other endocrine glands, such as the parathyroids and the pancreatic islets, are not part of the HP axis but have "freestanding" control mechanisms. These glands release hormones that stimulate a target

Table 30.1

Major Glands and Hormones of the Endocrine System

Endocrine Gland	Hormones Produced
Hypothalamus	Corticotropin-releasing hormone (CRH) Thyrotropin-releasing hormone (TRH) Gonadotropin-releasing hormone (GnRH) Somatostatin Growth hormone–releasing hormone (GHRH) Prolactin-releasing factor (PRF) Prolactin release–inhibiting hormone (PIH; dopamine)
Anterior pituitary	Adrenocorticotropic hormone (ACTH) Thyroid-stimulating hormone (TSH; thyrotropin) Follicle-stimulating hormone (FSH) Growth hormone (GH) Luteinizing hormone (LH) Prolactin (PRL)
Posterior pituitary	Arginine vasopressin (AVP) also called antidiuretic hormone (ADH) Oxytocin (OCT)
Thyroid gland	Thyroxine (T_4) Triiodothyronine (T_3) Calcitonin
Parathyroid gland	Parathyroid hormone (PTH)
Adrenal medulla	Epinephrine (adrenaline) Norepinephrine (noradrenaline)
Adrenal cortex	Cortisol (hydrocortisone) Aldosterone
Pancreas	Insulin Glucagon Somatostatin
Pineal gland	Melatonin

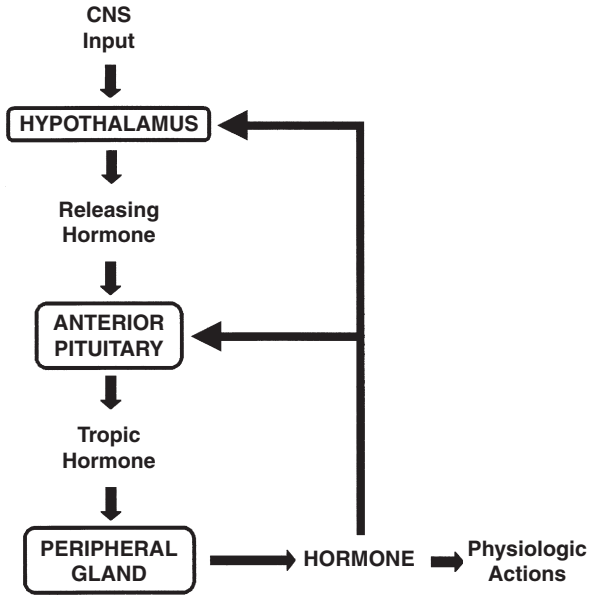

Fig. 30.1 Negative-feedback-loop control of endocrine gland function. Hypothalamic-releasing hormones stimulate pituitary trophic hormones, which in turn act on peripheral glands to release hormones. Levels of circulating hormones then exert feedback control on the pituitary and hypothalamus, modulating further output by these glands. *CNS*, Central nervous system.

tissue to produce an effect, which in turn directly modifies the output of the gland.

3. The neuroendocrine system plays a key role in body homeostasis. Hormones act as neurotransmitters, and neurotransmitters are involved in regulating endocrine function. The neuroendocrine system is important in the smooth adaptation of the neonate to the stresses of extrauterine life.

C. **Endocrine disruptors.**

1. Endocrine disruptors are synthetic or naturally occurring compounds that can mimic or block the body's endogenous hormones and disrupt endocrine function. Estrogens, androgens, and thyroid hormones are particularly vulnerable to interference by endocrine disruptors.
2. Exposure to an endocrine disruptor during embryonic gonadal sex differentiation can alter male germline epigenetics, a mechanism that can transmit adult-onset diseases, such as spermatogenic defects, prostate disease, kidney disease, and cancer, to both current and future generations (Xin et al., 2015).
3. Sources of these chemicals include pharmaceuticals, dioxin and dioxin-like compounds, polychlorinated biphenyls, dichlorodiphenyltrichloroethane (DDT) and other pesticides, and plasticizers such as bisphenol A.

D. **Developmental origins of health and disease** (Blackburn, 2018; DiVall and Merjaneh, 2018; Nuyt et al., 2017; Schwartz and Rose, 2017).

1. Developmental origin of adult disease refers to the effects of the perinatal environment on the growth and development that can persist into adult life, increasing the risk of later metabolic and cardiovascular disease. Events during the perinatal period may alter fetal programming, which is defined as "the process whereby early adaptation to adverse environment results in permanent physiologic changes that may be beneficial during fetal life but are less advantageous postnatally" (Schwartz and Rose, 2017, p. 1488).
2. Perinatal events may lead to morphologic and functional changes in organ systems via epigenetic changes in gene expression and hormonal effects, such as occur with stress or oxidative stress. For example, chronic stress may permanently alter the fetal HP axis. In response to stressors, the fetus generates glucocorticoids and catecholamines that

program the fetal endocrine system and may induce epigenetic changes that increase the risk of later endocrine, metabolic, and cardiovascular diseases, such as type 2 diabetes, coronary artery disease, hypertension, renal disease, and depression.

E. **Endocrine disorders in the neonate.**
   1. Most endocrine disorders are caused by hormone overproduction or underproduction, altered receptor function, or altered tissue response to hormones. In addition to specific neonatal endocrine disorders (e.g., hypothyroidism, congenital adrenal hyperplasia [CAH]), endocrine dysfunction can affect the preterm infant in a variety of ways as a function of the developmental physiology and level of maturation.

Pituitary Gland Disorders

A. **Anatomy and physiology.**
   1. The pituitary gland consists of the anterior and posterior glands. Although these two structures with different origins form a single gland, they are functionally separate.
   2. The anterior pituitary arises from the oral ectoderm and its cells to differentiate into specific hormone-producing cells. The release of trophic hormones—growth hormone (GH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), luteinizing hormone (LH), and prolactin (PRL)—is influenced by hypothalamic-releasing/-inhibiting hormones.
   3. The posterior pituitary develops from neuroectoderm evaginating ventrally from the brain. The posterior pituitary produces oxytocin and arginine vasopressin (AVP), also called antidiuretic hormone (ADH).

B. **Hypopituitarism** (Cavarzere et al., 2014; Devaskar and Garg, 2018).
   1. Although rare in the newborn, hypopituitarism can be congenital or acquired secondary to infection, hypovolemic shock, precipitous delivery, or anoxia. Congenital hypopituitarism can be caused by mutations in signaling molecules of transcription factors regulating pituitary gland development, or it may be part of a syndrome, such as optic nerve hypoplasia, and be associated with absent septum pellucidum. Congenital hypopituitarism can overlap with hypogonadotropic hypogonadal disorders.
   2. Types include absence of pituitary gland (pituitary agenesis), panhypopituitarism (deficiency of all pituitary hormones), and an isolated hormone defect, such as GH deficiency. A primary hypothalamic disorder can also result in hypopituitarism.
   3. Neonates with congenital hypopituitarism can initially be asymptomatic, with evidence of pituitary hormone deficiencies developing over time. Neonates with hypopituitary syndromes can present with midline craniofacial defects such as cleft lip, cleft palate, bifid uvula, or micropenis in boys. Hypoglycemia can be mild or severe and persistent.
   4. Later, neonates may present with prolonged jaundice and direct hyperbilirubinemia or evidence of other endocrinopathy, such as diabetes insipidus.
   5. Diagnosis is made by hormone testing (including GH, thyroid hormone, cortisol), ultrasound or magnetic resonance imaging (MRI) of anatomic structures, and genetic analyses. Tests of pituitary function include stimulation tests (ACTH, thyrotropin-releasing hormone [TRH], glucagon) to test the response of pituitary hormones. A pediatric endocrinologist usually coordinates the diagnostic testing and interpretation for these infants.
   6. Management involves correcting hypoglycemia and replacing deficient hormones.

C. **Diabetes insipidus** (Dabrowski et al., 2016).
   1. Diabetes insipidus (DI) is a deficiency of AVP or AVP resistance with polyuria. DI can be central (90%) or nephrogenic. It can be associated with midline facial defects, CNS injury, hypoxia, or neoplasm.
   2. Up to 90% of neonates with inherited nephrogenic DI are boys with an X-linked form caused by mutations in the arginine vasopressin receptor 2 gene (*AVP2R*).
   3. AVP secretion is normally triggered by changes in osmolality, increasing or decreasing to regulate urine output. In DI, AVP is deficient, resulting in free water loss.
   4. Clinical manifestations are vigorous sucking followed by vomiting, polyuria (high urine output with low specific gravity), irritability, fever, and evidence of dehydration. Polyuria in the neonate is greater than 150 mL/kg/day.
   5. Diagnosis is made by reviewing serum electrolytes, osmolality, plasma AVP levels, genetic analysis, urine output, and urinalysis. MRI may be done to visualize the posterior pituitary.
   6. DI is treated with cautious fluid management to correct dehydration without causing rapid shifts in serum sodium levels. Medications may be required to supplement AVP if the neonate is unable to concentrate urine.

D. **Syndrome of inappropriate ADH** (AVP).
   1. Impairment of free water clearance caused by an uncontrolled release of ADH.
   2. Causes include CNS infection, birth asphyxia, intracranial hemorrhage, and meningitis. The release of ADH is inappropriate to the level of osmolality in the serum, causing fluid retention, oliguria, hyponatremia, weight gain, and edema.

3. Diagnosis is made by finding an elevated circulating ADH level with low serum osmolality and hyponatremia.
4. Treatment involves fluid restriction and monitoring of electrolytes, glucose, intake, and output. If it is not possible to manage with fluids alone, desmopressin (DDAVP), a long-acting synthetic analogue of pituitary AVP, may be used.

Thyroid Gland Disorders

THE THYROID GLAND

A. **Anatomy**.
   1. The thyroid gland comprises two lateral lobes connected by a band of tissue (isthmus) and contains densely packed, colloid-rich follicular cells and parafollicular cells. Parafollicular cells (C cells) produce the calcium-lowering hormone calcitonin.

B. **Normal physiology.**
   1. Functions of the thyroid gland.
      a. Concentrates and stores iodide, a trace element required for thyroid hormone synthesis.
      b. Synthesizes thyroglobulin, a thyroid hormone precursor.
      c. Synthesizes and releases the thyroid hormones thyroxine (T_4) and triiodothyronine (T_3), catalyzed by the enzyme thyroid peroxidase (TPO).
   2. Thyroid hormone metabolism.
      a. The thyroid gland produces T_4 and a small amount of T_3. Most of the plasma T_3 (the more potent hormone) is derived from peripheral metabolism (deiodination) of T_4.
      b. T_4 enters the cell and is converted to T_3 by enzymes.
      c. Deiodination of the outer ring of T_4 produces T_3. Deiodination of the inner ring of T_4 produces reverse T_3 (rT_3), a biologically inactive product.
   3. Thyroid hormone transport.
      a. Thyroid hormones circulate in the blood bound to thyroid-binding globulin (TBG) and other globulins. Only a tiny fraction is in equilibrium as free hormone, but it is this free fraction that is responsible for hormonal action.
      b. TBG, synthesized in the liver, has a high affinity for T_3 and T_4, carrying 70% of circulating hormone. When TBG is deficient, total thyroid hormone concentrations may be lower but free hormone levels are normal.
   4. Mechanisms of thyroid gland regulation.
      a. HPT axis. Hypothalamic TRH is secreted in response to neural input, such as cooling of the skin. TRH stimulates synthesis and release of TSH (thyrotropin) by the anterior pituitary. TSH secretion is inhibited by dopamine, somatostatin, and high doses of corticosteroids. TSH binds to receptors on thyroid cell membranes and stimulates production of thyroid hormones. As thyroid hormone levels rise, TSH and TRH secretion is inhibited.
      b. Deiodinase enzymes in the anterior pituitary, brain, heart, liver, and other tissues regulate intracellular T_3 availability.
      c. Autoregulation of hormone synthesis occurs in relationship to its iodine supply.
      d. Stimulation or inhibition of thyroid function by TSH receptor antibodies.
   5. Physiologic effects of thyroid hormones.
      a. Metabolic processes such as oxygen consumption; thermogenesis; cardiac output; erythropoiesis; respiratory drive; gut motility; and metabolism of carbohydrates, proteins, and lipids.
      b. Growth and differentiation of organs and tissues, including the bones, lungs, and CNS. Thyroid hormones induce differentiation and maturation of neural circuits during critical periods of brain development.

C. **Fetal thyroid development** (Blackburn, 2018; Kim et al., 2018).
   1. The thyroid is the first endocrine gland to develop in the fetus, appearing as a thickening in the pharyngeal pouch at 20 to 22 days of gestation. The thyroid eventually migrates downward, reaching its final position by 45 to 50 days.
   2. At about 10 to 12 weeks of gestation, the hypothalamus begins synthesizing TRH, the pituitary gland begins secreting TSH, and TBG is detectable in fetal serum. T_4 can be detected by 12 to 14 weeks, but fetal function is minimal until midgestation.
   3. The HPT axis is functional by 18 to 20 weeks, perhaps earlier. At this time, iodide uptake increases and the fetal thyroid gland begins to increase T_4 release. Total and free T_4, TSH, and TBG increase steadily until term. The T_3 level remains low until 30 weeks of gestation, then increases as mechanisms for deiodination of T_4 mature.
   4. Before 20 weeks of gestation, transplacental passage of maternal T_4 largely provides for fetal thyroidal needs and is critical for normal development. Maternal hypothyroidism during early gestation can impair CNS development in the fetus. By the start of the second trimester, the fetal contribution to circulating thyroid hormones is significant. Maternal T_4 continues to be used for fetal development and neuroprotection.
   5. The fetus is dependent on the maternal–placental system for adequate supply of iodide, a critical substrate for fetal thyroid hormone synthesis. Iodide is actively transported across the placenta with greater uptake by the fetal thyroid. Autoregulation of iodide uptake is not yet mature, so the fetal

thyroid is susceptible to inhibitory effects of both iodide deficiency and exposures to maternal iodide excess.

6. Cord blood TSH and T_4 levels are directly proportional to birth weight and gestational age.

D. **Neonatal thyroid physiology** (Blackburn, 2018; Huang, 2017; Kim et al., 2018).

1. The birth process for term and late preterm neonates, stimulates TRH release, resulting in a sharp rise in the serum TSH level by the following mechanisms: stimulation of skin thermoreceptors via skin cooling, which increases production of T_3 in brown adipose tissue; umbilical cord cutting, which increases liver blood flow; and the stress of birth, which causes a surge of circulating catecholamines.
2. TSH peaks 2 to 4 hours of age and then falls to a normal (<20 mU/L) level during the first 3 days of life.
3. The TSH surge stimulates an abrupt rise in thyroid hormone levels. T_4 and T_3 both increase in response to TSH, peaking at 24 to 48 hours after birth, leading to a transient physiologic hyperthyroid state. T_4 and T_3 peak by 24 hours then gradually fall over the first 4 to 5 weeks. The rise in T_4 causes the TSH to decline to 20 mU/L or less (the cutoff used in most screening programs for congenital hypothyroidism) by 3 to 10 days because of feedback inhibition.
4. Postnatal changes in TSH, T_4, and T_3 occur in less mature infants as well but are quantitatively lower due to immaturity of the HPT axis with limited TSH response to low T_4 levels. The extremely preterm infant exhibits a dramatic fall in T_4 over the first 1 to 2 weeks of life.

HYPOTHYROIDISM (KIM ET AL., 2018; WASSNER, 2017; WASSNER AND BROWN, 2018)

Hypothyroidism in the neonate can be either permanent (lifelong therapy required) or transient (spontaneously resolving in weeks or months; treatment is temporary or not required at all). Hypothyroidism can also be termed *congenital* (existing at birth) or *acquired*. Other labels indicate the origin of the hypothyroidism.

1. Primary hypothyroidism. A disorder involving the thyroid gland or some aspect of thyroid hormone synthesis, metabolism, or transport.
2. Central (also called *secondary/tertiary*). Deficient thyroid hormone secretion due to a disorder affecting pituitary control (TSH production) or hypothalamic control (TRH production).

A. **Etiologies of permanent congenital hypothyroidism (CH).**

1. Thyroid abnormalities.
   a. Thyroid dysgenesis: absent (agenesis/athyreosis), hypoplastic, and/or ectopic (usually sublingual) gland. Ectopic gland is the most common etiology of CH. Familial thyroid dysgenesis is primarily caused by mutations in the thyrotropin receptor gene *TSHR* (Wassner and Brown, 2018).
   b. Familial dyshormonogenesis: inborn errors of thyroid hormone biosynthesis, transport, or metabolism. About 10% to 20% of infants with CH have inherited defects of thyroid hormone metabolism, the most common of which is a defect related to deficient activity of the TPO enzyme.
2. Extrathyroid abnormalities.
   a. Defects of the pituitary gland (e.g., hypopituitarism) or the hypothalamus.
   b. TBG deficiency: X-linked disorder; more common in males.
   c. Thyroid hormone resistance. Resistance to the actions of endogenous and exogenous T_4 and T_3, a form of "peripheral hypothyroidism," is becoming more common. All serum thyroid hormone levels are elevated, and many patients have goiter.

B. **Etiologies of transient hypothyroid states.**

1. Prenatally acquired.
   a. Maternal autoimmune thyroid disorders characterized by transplacental passage of TSH receptor–blocking antibodies, which inhibit the binding of TSH to the thyroid cell.
   b. Drugs given to the mother that cross the placenta and affect fetal thyroid production (propylthiouracil, methimazole, lithium, phenytoin, amiodarone, and radioiodine).
   c. Ingestion or absorption of excess iodine or severe maternal dietary iodine deficiency.
2. Postnatally acquired: transiently impaired thyroid hormone production from exposure to iodine-containing topical disinfectants, ointments, drugs such as amiodarone, or intravenously administered contrast media. Preterm infants can absorb and excrete large amounts of iodine; thus, exposure to iodinated products should be minimized.

C. **The preterm infant:** in addition to the same incidence of permanent CH as full-term infants, several transient hypothyroid states have been described in preterm infants. Because two or more transient conditions can coexist, it is not always possible to determine the precise cause of low thyroid hormone levels in preterm infants.

1. Transient hypothyroxinemia of prematurity. Serum levels of thyroid hormones in preterm neonates are significantly lower and more variable than those of term neonates and correlate with gestational age and birth weight (Fisher, 2007). T_4 levels of most

preterms reach a nadir at 7 to 14 days of age and then climb to normal within 4 to 8 weeks. Seen primarily in infants born at <30 to 32 weeks' gestation. These infants have low T_4 and fT_4 and normal to low TSH levels (Kim et al., 2018). Sicker preterm infants demonstrate more variability in T_4 values than healthy preterms of the same gestation.

2. Preterm infants have an initial TSH surge after birth, but it is blunted in comparison to more mature neonates. The TSH of preterm infants with hypothyroxinemia is not consistently elevated, suggesting a relative lack of hypothalamic response to the lower T_4 level. This condition is believed to be a developmental phenomenon caused by one or more of the following (Blackburn, 2018; Kim et al., 2018):
   a. Immaturity of thyroid hormone metabolism and the HPT axis.
   b. Loss of maternal contributions to the thyroid hormone pool at birth.
   c. Low TBG levels.
   d. Increased use of T_4 to meet the demands of extrauterine adaption.
   e. Insufficient enteral or parenteral iodine intake.
   f. Immaturity of iodinase enzymes with a decreased ability to convert T_4 to T_3.
3. Nonthyroidal illness syndrome. In some ill preterm infants, T_4 is preferentially converted to rT_3 instead of T_3, possibly as an adaptive response to lower the metabolic rate during times of severe illness. The outcome is low serum concentrations of both T_4 and T_3. rT_3 is elevated and decreased (in severe illness) or normal (in mild to moderate illness) TSH (Kim et al., 2018). This condition, also known as *low T_3* syndrome or *euthyroid sick syndrome*, occurs in infants who have immature lungs or infections. The low T_4 from nonthyroidal illness reverses spontaneously when the infant's condition improves without treatment. Similar effects are seen in infants who are receiving dopamine or glucocorticoids, both of which can lower serum T_4 concentrations.

D. **Clinical presentation and assessment.**
1. Few neonates are diagnosed with CH solely on clinical grounds. Signs and symptoms of CH can be slow to develop due to the persistence of maternal thyroid hormone and are subtle and nonspecific. Early diagnosis is critical to ensure prompt treatment that will reduce the risk for cognitive impairment because by the time clear signs appear, significant impairment may have already occurred.
2. The signs and symptoms of hypothyroidism in the neonate reflect the wide-ranging actions of thyroid hormones on metabolism, intestinal motility, cardiac function, temperature regulation, neurologic function, and skeletal maturation. The possibility of CH must be considered in infants presenting with birth weight in excess of the 90th percentile, prolonged jaundice, hypothermia and cold mottled skin, an enlarged (>1 cm) posterior fontanelle, umbilical hernia, and failure to feed well (Rastogi and LaFranchi, 2010).
3. Other features traditionally associated with hypothyroidism (macroglossia, dry skin, lethargy, hypotonia, hoarse cry, coarse hair, edema, and constipation) evolve over the first weeks of life. A palpable, enlarged thyroid gland (also called a *goiter*) can be associated with impaired thyroid hormone synthesis and hypothyroidism. Hyperplasia of the thyroid gland results from hypersecretion of TSH in response to low T_3 and T_4 levels. Infants with suspected central hypothyroidism may present with midline or cranial defects or other signs of pituitary deficiency. Central hypothyroidism should be suspected in infants presenting with optic nerve hypoplasia, hypoglycemia, micropenis, or cleft lip/palate.

E. **Diagnostic studies in hypothyroidism (Table 30.2):** unless the infant is born to a mother with a history of thyroid dysfunction or has obvious clinical signs of hypothyroidism at birth, the diagnosis is usually made after the infant is identified by neonatal screening.
1. Newborn screening for hypothyroidism.
   a. Screening for CH uses either a two-tiered T_4-TSH testing approach or, more commonly, primary TSH testing. In the two-tiered system, TSH is measured only if the T_4 level is low.
   b. Due to the physiologic surge in TSH in the first hours of life, the specimen must be collected when the infant is at least 24 hours of age, and preferably between 2 and 4 days of age. If collected earlier, particularly in the first 3 hours of life, a false-positive result can occur. In those instances, a repeat specimen must be collected within the first 7 days of life, regardless of the first test results.
   c. The incidence of CH is approximately 1:2000 births, an increase in recent years that is likely due to more stringent newborn screening with identification of milder forms of CH (Wassner, 2017). An elevated TSH level (>40 mU/L) is presumed to be CH until further testing proves otherwise. Rapid confirmation is essential. TSH is elevated because the low T_4 does not provide the usual negative feedback to inhibit the anterior pituitary gland.
   d. Screening errors caused by improper specimen collection, storage, or transport can result in a false-negative test. Thyroid medications taken by the mother during pregnancy can also produce false-negative results.
   e. Approximately 5% to 8% of infants with CH are missed on initial screening (Kim et al., 2018);

Table 30.2

Summary of Low Thyroid States in the Newborn Infant

Screening Results	Possible Conditions	Further Diagnostic Tests	Treatment
T_4 low[a], TSH elevated[b]	Congenital hypothyroidism (thyroid agenesis, ectopia dyshormonogenesis)	Serum TFTs[c], Tg[d] level; thyroid scan; ultrasonography; bone age radiography	Thyroid replacement
	Transient hypothyroidism	TSI, TBA	Monitoring
	Maternal (autoimmune, drugs) iodine exposure	Urinary iodine level	Monitoring
T_4 low, TSH normal or low-normal, TSH slightly elevated (borderline)	Congenital hypothyroidism	Repeat screen, other tests as for congenital hypothyroidism (above)	Thyroid replacement
	Early specimen collection (<24 hours) or false-positive	Repeat screen	
T_4 low, TSH normal	Hypothyroxinemia of prematurity	Serum TFTs or repeat screen to detect delayed TSH rise	Monitoring
	TBG deficiency	Serum TFTs; TBG level; T_3, resin uptake level[e]	None
	Early specimen collection (<24 hours) or false-positive	Repeat screen	
T_4 low, delayed TSH rise	Atypical hypothyroidism Some VLBW infants (nonthyroidal illness?)	Serum TFTs	Close monitoring; possible treatment
	Congenital hypothyroidism (some functional thyroid; ectopic or hypoplastic)	Serum TFTs and other tests as for congenital hypothyroidism (see earlier)	Thyroid replacement
T_4 low, TSH low	Central hypothyroidism (hypothalamic–pituitary)	Serum TFTs; TRH stimulation test[f]; other tests of pituitary function (cortisol, growth hormone)	Thyroid replacement; other hormonal therapy

T_3, Triiodothyronine; *T_4*, thyroxine; *TBA*, thyroid-blocking antibodies; *TBG*, thyroid-binding globulin; *TFTs*, thyroid function tests; *TSH*, thyroid-stimulating hormone; *TSI*, thyroid-stimulating immunoglobulins; *VLBW*, very low birth weight.

[a]T_4 low: <6 mcg/dL.

[b]TSH elevated: greater than 40 mU/L; TSH normal: <10 mU/L; TSH borderline: 20 to 40 mU/L. Note that a slightly elevated TSH level may be normal in the first 2 days of life.

[c]TFTs: May include assays of total and free T_4 and T_3 along with TSH.

[d]Tg: Thyroglobulin, a thyroid hormone precursor produced by the thyroid gland. A low level suggests thyroid agenesis.

[e]T_3, resin uptake level: an indirect measure of protein binding. A high level suggests low binding capacity, as in TBG deficiency.

[f]TRH stimulation is a test of hypothalamic or pituitary control of thyroid function. A dose of TRH is administered and TSH is measured serially. A subnormal TSH response suggests a deficient pituitary gland, and a delayed response suggests hypothalamic congenital hypothyroidism.

they are detected only through routine second screening in states where this is required or on clinical grounds. Some of these infants have compensated hypothyroidism or delayed rise in the TSH level; most seem to have milder forms of hypothyroidism but still require treatment.

f. Infants at risk of a missed or delayed diagnosis are those born at home, those who were extremely ill in the neonatal period, and those who were transferred to another hospital at an early age.

2. Thyroid function tests.
   a. A low serum T_4 and a serum TSH greater than 40 mU/L suggests CH. A normal T_4 with elevated TSH suggests enough functional thyroid tissue to respond to excess TSH stimulation (seen in compensated or subclinical hypothyroidism). Free T_4 and T_3 levels may also be measured, along with other tests, as needed, to determine the cause of abnormal screening results (see Table 30.2).
   b. Age-related reference norms, for both gestational age and hours of age, should be used when interpreting all thyroid test results.
   c. If maternal antibody–mediated hypothyroidism is suspected, maternal antithyroid antibody (TRBAb) testing is done. Other thyroid autoantibodies that can produce hypothyroidism include thyroglobulin antibodies (TGAb) and thyroid peroxidase antibodies (TPOAb).
   d. TBG levels can be measured to rule out TBG deficiency. Thyroglobulin levels in infants with

possible CH can help differentiate between thyroid agenesis and dyshormonogenesis as an adjunct to thyroid imaging.

3. Imaging studies: further evaluation for the cause of a CH blood profile includes Doppler ultrasonography of the neck, thyroid radionuclide imaging (to identify normal or ectopic thyroid tissue), and bone age radiography of the knee or foot (delayed bone ossification suggests long-standing thyroid deprivation).

F. **Management**.

1. CH.
   a. Early (within the first 3 weeks or sooner) adequate treatment of CH is critical for optimal neurologic development. The goal of hormone replacement therapy is to rapidly normalize and maintain the infant's serum T_4 level in the upper half of the normal range, which should result in a TSH of 0.5 to 2 mU/L (Kim et al., 2018). The agent of choice is sodium levothyroxine because it is substantially converted to T_3 within the brain.
   b. Infants receiving thyroid replacement therapy must be monitored closely for adequacy of treatment and evidence of thyrotoxicosis (irritability, tachycardia, poor weight gain). Serum T_4 should normalize in 1 to 2 weeks; serum TSH can take longer to normalize.
      1) Overtreatment can lead to advanced bone age, craniosynostosis, and thyrotoxicosis (tachycardia, irritability, hyperactivity, poor weight gain, and loose stools).
      2) Undertreatment leads to clinical hypothyroidism, delayed bone maturation, and neurologic damage.
2. Transient hypothyroidism (Chuang et al., 2015; Huang, 2017; Kim et al., 2018; Wassner and Brown, 2018).
   a. Transient hypothyroxinemia of prematurity is associated with higher mortality and neurodevelopmental deficits, yet cumulative evidence to date has not demonstrated clear benefits of routinely supplementing these infants with thyroxine during early life; there are also concerns about the risks of overtreating hypothyroidism in these infants. A Cochrane review did not support the use of prophylactic thyroid hormones in preterm infants to reduce neonatal mortality or morbidity or to improve neurodevelopmental outcomes (Osborn and Hunt, 2007). However, infants with a low T_4 and elevated TSH level do require treatment. Thyroid function tests should be followed carefully in preterm infants at risk for hypothyroxinemia, and treatment should be instituted promptly if indicated by elevated TSH.
   b. Transient hypothyroidism caused by maternal antithyroid medication will resolve spontaneously when the drug is cleared from the infant's circulation, usually within a day or two after birth. The infant's serum T_4 and TSH should be monitored to ensure that they return to normal. Supplementation with levothyroxine is not usually necessary.
   c. Transplacentally acquired TRBAb can be slow to degrade completely; therefore, most infants will require supplementation for several months.
   d. TRBAb levels in the infant can be monitored to determine when to discontinue therapy. Breastfeeding is not contraindicated in neonates whose mothers continue their antithyroid medication in the postpartum period, as very little passes into the breast milk.

G. **Outcome**.

1. CH.
   a. CH is one of the most preventable causes of mental retardation. Most infants with early diagnosis and early and adequate treatment will have normal IQs. A delay in treatment after birth can lower IQ by several points per week (Fisher, 2000). Children with severe hypothyroidism are at risk for mild deficits in motor development, verbal skills, attention, and memory (Wassner, 2017).
   b. Lifelong thyroid replacement therapy is necessary for normal growth and development.
   c. Infants who are taking levothyroxine should not ingest soy-based products, including soy formula, because soy interferes with the absorption of levothyroxine and the infant can remain hypothyroid (Wassner, 2017).
2. Transient hypothyroidism.
   a. Hypothyroxinemia of prematurity is transient, correcting spontaneously over 6 to 10 weeks as the infant matures.
   b. More research is needed to determine whether hypothyroxinemia of prematurity is a benign physiologic phenomenon or a cause of psychomotor and neurodevelopmental sequelae in the preterm population.

HYPERTHYROIDISM (KIM ET AL., 2018; LÉGER, 2017)

A. **Etiologies**.

1. Maternal Graves' disease (either active or inactive) causes transient neonatal Graves' disease in approximately 2% of infants (Léger, 2017). Thus, most babies born to mothers with Graves' disease have normal thyroid function.
2. Rare causes of neonatal hyperthyroidism include McCune–Albright syndrome and mutations in the TSH receptor.

B. **Pathophysiology of Graves' disease.**

1. Transient neonatal Graves' disease occurs in infants born to mothers with the condition, to those who

have undergone thyroidectomy or radioiodine ablation of the thyroid gland, and to women taking antithyroid drugs.
2. Maternal TRSAbs cross the placenta readily and stimulate the fetal thyroid gland, causing an overproduction of thyroid hormone and, in some cases, development of a goiter. Usually, the higher the TRSAb level in the mother, the more severely affected the infant.
3. Hyperthyroidism in the neonate is typically transient, lasting approximately 3 to 12 weeks (until the maternal antibodies are catabolized). The clinical course varies depending on the characteristics of the mother's disease and treatment. The onset of hyperthyroidism may be delayed for 8 to 14 days in neonates whose mothers produce not only TRSAb but TRBAb as well.
4. Similarly, if the mother took antithyroid medication during pregnancy, the neonate might not exhibit evidence of hyperthyroidism for several days until the drugs are metabolized (and might even be hypothyroid during that time).
5. Occasionally, the hyperthyroidism persists beyond the expected recovery period and becomes true, permanent Graves' disease.

C. **Clinical presentation and assessment.**
1. Neonates may be born preterm, often with evidence of intrauterine growth restriction (IUGR). Common clinical signs of thyrotoxicosis include tachycardia, arrhythmias, hypertension, tachypnea, poor feeding and weight gain, thyroid enlargement, vomiting, sweating, hyperthermia, flushing, diarrhea, restlessness, tremors, irritability, and hyperalertness. An elevated fetal heart rate (>160 beats per minutes) and evidence of fetal goiter may be noted on history. Signs in the neonate generally develop within 2 to 5 days after birth.
2. More severe manifestations of thyrotoxicosis, such as congestive heart failure, hepatosplenomegaly, thrombocytopenia, and hyperviscosity syndrome, may occur.
3. In severe cases of untreated maternal Graves' disease, advanced bone age, craniosynostosis, and microcephaly are evident in both the fetus and newborn.
4. The infant should be examined for a goiter, which can be very small or large enough to compress the trachea and cause respiratory distress in the newborn. A goiter is a symmetrical, smooth enlargement of the gland and can be recognized as a swelling in the anterior neck of the neonate.

D. **Diagnostic studies.**
1. Serum T_4, free T_4, and T_3 are elevated, and serum TSH is low, all relative to age-appropriate norms.
2. A TRSAb titer in the neonate will give an indication of the expected severity of the disease course. Infants at risk (e.g., high maternal titer of TRSAb) for severe thyrotoxicosis require frequent monitoring of free T_4 and TSH.
3. A thorough maternal history is essential (e.g., history of radioablation therapy, antithyroid drugs taken during pregnancy and when taken, and any maternal symptoms.

E. **Management**.
1. The mainstays of treatment of hyperthyroidism in the neonate are iodine, antithyroid medication, sedation, and β-adrenergic blockers, if needed. Treatment is tailored to the severity of the infant's symptoms. Lugol's iodine solution (potassium iodide), given in a single drop 3 times daily, acutely inhibits the release of thyroxine from the thyroid gland. The agents of choice are usually methimazole or carbimazole. Propylthiouracil is generally not recommended for use in infants due to a risk of liver failure (Kim et al., 2018).
2. Propranolol can be used to manage tachycardia and other cardiovascular symptoms. The infant's serum T_4 must be followed closely during treatment for possible iatrogenic hypothyroidism. TRSAb levels are also followed to monitor the infant's recovery and aid in determining the appropriate time for weaning antithyroid medication.
3. In cases of maternal thyrotoxicosis, thyrotoxicosis should be anticipated in the neonate so diagnosis and treatment can be instituted without delay.

F. **Outcome**.
1. Neonatal hyperthyroidism is almost always transient, usually lasting 2 to 3 months, but can last longer in some infants.
2. Mortality is related to cardiovascular compromise, arrhythmia, tachycardia, and heart failure.
3. Survivors of severe, prolonged thyrotoxicosis often have permanent neurologic impairment from premature craniosynostosis and the direct effects of excess thyroid hormones on the brain.

Adrenal Gland Disorders

THE ADRENAL GLAND

A. **Anatomy and physiology.**
1. The adrenal glands are located at the superior poles of the kidneys. Each highly vascular gland is composed of two endocrine organs: the inner adrenal medulla and the outer adrenal cortex.
2. The adrenal medulla produces and stores catecholamines (epinephrine, norepinephrine, dopamine) and is linked to the sympathetic nervous system.
3. All adrenocortical hormones (steroids) are synthesized from cholesterol. Three classes of steroids are produced by the adrenal cortex: glucocorticoids, mineralocorticoids, and androgens.

B. **Adrenocortical hormones.**
   1. Cortisol, the primary glucocorticoid, has a major role in glucose homeostasis and key regulatory roles in development, growth, inflammatory responses, cardiovascular function, and response to stress.
   2. Cortisol is closely regulated by ACTH and the HPA axis via an acute or chronic negative-feedback loop. Increased plasma cortisol inhibits secretion of corticotropin-releasing hormone and ACTH, whereas decreased plasma cortisol permits their release. Cortisol is also released in response to stress, hypoglycemia, surgery, extreme heat or cold, decreased oxygen concentration, infection, or injury.
   3. Aldosterone, the most important mineralocorticoid, regulates renal sodium (Na^+) and water retention and potassium (K^+) excretion, thus affecting not only electrolyte balance but also blood pressure and intravascular volume. Aldosterone is regulated by the plasma renin–angiotensin system and by plasma K^+ concentrations. A drop in intravascular volume or the Na^+ concentration or a rise in the K^+ level stimulates the renin–angiotensin system, which in turn stimulates production of aldosterone.
   4. Adrenal androgens include dehydroepiandrosterone (DHEA), DHEA sulfate, and androstenedione and are regulated by ACTH. These steroids have minimal androgenic activity but are converted in the peripheral tissues to two more potent androgens: testosterone and dihydrotestosterone.

C. **Fetal adrenocortical development** (Blackburn, 2018; DiVall and Merjaneh, 2018).
   1. Early in gestation, the fetal adrenal cortex begins to differentiate into distinct zones: a large, unique fetal zone and an outer definitive ("adult") zone, which produces aldosterone. Between 22 and 24 weeks, the transitional zone develops; this zone becomes the site of glucocorticoid production after birth. The fetal zone is responsible for most of the steroids produced during fetal life. Fetal adrenal growth is rapid; at term, the gland is twice the size of the adult gland, but undergoes extensive remodeling and shrinks in size after birth as the fetal zone involutes.
   2. The fetal adrenal gland and the placenta (fetoplacental unit) are an integrated endocrine organ. The fetal zone, deficient in a critical enzyme for cortisol synthesis, produces mostly DHEA and DHEA sulfate. These are the precursors for placental estrogens, which are essential for maintenance of the pregnancy and fetal well-being. In turn, the placenta provides substrates for fetal cortisol production.
   3. The fetal HPT axis and fetoplacental unit are critical for maintaining the pregnancy; for initiation of labor and birth; for maturation of the lungs, liver, renal system, gastrointestinal tract, and CNS; and for glycogen storage in the liver.
   4. Until about 30 weeks of gestation, fetal cortisol comes from both the fetal gland and placental transfer. In the placenta, 85% of maternal cortisol is rapidly metabolized to inactive cortisone to protect the fetus from very high cortisol levels. Fetal adrenal cortisol production begins to increase 7 to 10 weeks before birth and is important for increasing conversion of T_4 to T_3, epinephrine release from the adrenal medulla, and enhanced secretion and synthesis of liver and gut enzymes. Near term, maturation of fetal enzyme systems allows greater conversion of cortisone back to cortisol and synthesis of cortisol from cholesterol. Increases in circulating cortisol during the last 10 weeks of gestation induce critical physiologic changes that prepare the fetus for extrauterine life, including maturation of pulmonary surfactant.
   5. Aldosterone production increases throughout pregnancy, preparing the fetus to assume control of salt and water balance after birth.

D. **Neonatal adrenocortical function.**
   1. Plasma cortisol levels are high at the time of birth but begin to fall in the first few days of life. In term infants, a nadir is seen on day 4. Likewise, levels of a cortisol precursor, 17-hydroxyprogesterone (17-OHP), are high at birth but decline to normal neonatal levels by 12 to 24 hours of age. The cortisol surge is blunted in very low birth weight infants.
   2. A diurnal pattern of cortisol secretion is evident at about 2 to 3 months of age in most infants, influenced more by environmental factors than genetic factors (Custodio et al., 2007). Cortisol in the newborn plays a key role in response to stress and illness and is important in the maintenance of blood pressure (Ng, 2011).
   3. Aldosterone concentration and plasma renin activity (PRA) are elevated compared with values for older infants, allowing for positive Na^+ balance until the kidneys fully mature. The hyponatremia and urinary Na^+ loss often seen in preterm infants during the early postnatal weeks are due to a relative mineralocorticoid deficiency as a consequence of immaturity of both the kidneys and the adrenal glands.

ADRENAL DISORDERS IN THE NEONATE

A. **Transient adrenocortical insufficiency of prematurity** (Finken et al., 2017; Ng, 2011, 2016; Watterberg and Muglia, 2017).
   1. A limited ability of the adrenal glands to maintain cortisol homeostasis in the early days of life has been observed in some preterm newborns, particularly those born at less than 30 weeks. This is related to an immature HPA axis and an inadequate pituitary response to CRH by the immature endocrine system leading to decreased cortisol production.

2. Manifestations are a low serum cortisol, normal or exaggerated pituitary response, and good recovery of adrenal function by day 14 of life.
3. Some very low birth weight infants with inotrope and volume-resistant hypotension show an inadequate adrenal response to stress in the immediate postnatal period that responds to intravenous corticosteroids.
4. The exact role of a relative adrenal insufficiency in hemodynamic instability and hypotension in critically ill infants is still unclear.

B. **Adrenal hemorrhage** (Fechner, 2018; Mutlu et al., 2011).
1. Adrenal hemorrhage in the neonate can be precipitated by traumatic delivery, breech presentation, macrosomia, sepsis, ischemic disorders, or disseminated intravascular coagulation. The large size and vascularity of the fetal adrenal gland predispose the gland to injury and rupture during the birth process.
2. Although often asymptomatic, classic findings include jaundice, pallor, and a flank mass on either side (although hemorrhage is more common on the right) with discoloration and purpura of the overlying skin and discoloration of the scrotum. In severe cases, the infant may exhibit signs of adrenal insufficiency. Infants with small hemorrhages may eventually develop anemia and persistent jaundice.
3. Adrenal hemorrhage can be visualized on ultrasound and usually resolves in 4 to 16 weeks.

CONGENITAL ADRENAL HYPERPLASIA (FECHNER, 2018; MCCANN-CROSBY AND SUTTON, 2015; SHNORHAVORIAN AND FECHNER, 2018; STOKOWSKI, 2014; WITCHEL, 2017)

A. **Definition:** a group of autosomal-recessive genetic disorders resulting from deficient activity of one of the enzymes required to synthesize cortisol from cholesterol in the adrenal cortex. Each enzyme is encoded by its own gene. Mutation of the 21-hydroxylase (21-OHD) gene, *CYP21*, accounts for 90% to 95% of disorders, and is the most common cause of ambiguous genitalia in the neonate. Currently there are more than 200 known different mutations of *CYP2A12* that range from having absolutely no enzyme activity to partial enzyme function (Witchel, 2017). The worldwide incidence of classic 21-OHD is approximately 1 in 5000 to 1 in 15,000 live births (Stokowski, 2014).

B. **Pathophysiology (Fig. 30.2).**
1. Because the overwhelming majority of CAH cases are the result of 21-OHD deficiency, the remainder of the discussion will pertain to this form of CAH.

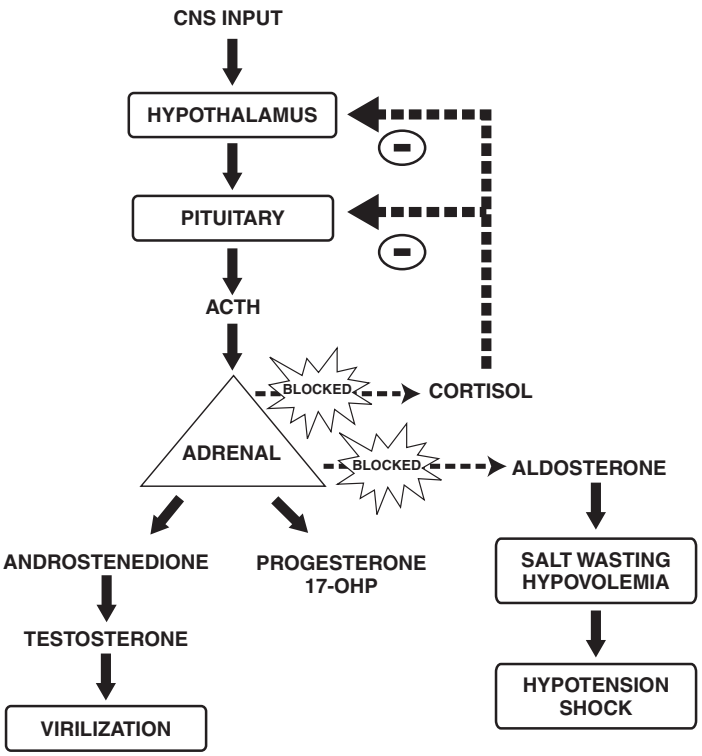

Fig. 30.2 Pathophysiology of congenital adrenal hyperplasia caused by 21-hydroxylase deficiency. In the absence of cortisol, adrenocorticotropic hormone (ACTH) stimulates the adrenal cortex to produce virilizing androgens. Diminished production of aldosterone leads to salt wasting and hypovolemia. *CNS*, Central nervous system; *17-OHP*, 17-hydroxyprogesterone. (Adapted from Martin, R. J., Fanaroff, A. A., & Walsh, M. C. [2011]. *Fanaroff and Martin's neonatal-perinatal medicine: Diseases of the fetus and infant* [9th ed.]. Philadelphia, PA: Elsevier Mosby.)

2. Lack of fetal 21-OHD prevents conversion of progesterone to its two end products: cortisol and aldosterone.
3. By reduced negative-feedback regulation, the absence of cortisol causes oversecretion of ACTH, which chronically stimulates the adrenal cortex, resulting in hyperplasia.
4. The cortisol precursor 17-OHP accumulates in the blood because its conversion to cortisol is blocked.
5. The excess 17-OHP enters the unblocked androgen metabolic pathway, which results in an overproduction of androgens. At a critical stage in fetal development, androgens cause virilization of the external genitalia in female fetuses. Also important may be the effects of this androgen exposure on the developing CNS.

C. **Clinical presentation.**
1. The two classic forms of CAH are (1) simple virilization and (2) salt wasting, which involves a deficiency of aldosterone. Approximately 75% of infants with CAH have the salt-wasting form (Shnorhavorian and Fechner, 2018).
2. Female infants with CAH are usually identified at birth by their abnormal genitalia, a key feature in CAH (Stokowski, 2014).
3. Neonates with CAH may present with a range of findings, including clitoromegaly and posterior fusion of the labia majora with rugae. A single urogenital orifice, where the vagina joins the urethra above the perineum, may also be noted instead of separate urethral and vaginal openings (Stokowski, 2014; Witchel, 2017).
4. In severe cases, clitoral hypertrophy is so marked that it resembles a penile urethra. These infants can be mistaken for boys with bilateral cryptorchidism and hypospadias.
5. There may also be hyperpigmentation of the genital skin resulting from excessive pituitary ACTH secretion.
6. Male infants with 21-OHD are phenotypically normal at birth and may not be identified immediately after birth, because the onset of adrenal symptoms is delayed until 7 to 14 days of life.
7. Undetected infants with the salt-wasting form may present to the emergency room with signs and symptoms of impending adrenal collapse: vomiting, weight loss, lethargy, dehydration, hyponatremia, hyperkalemia, hypoglycemia, hypovolemia, and shock. This often occurs at 5 to 15 days.
8. Infants of either gender who are untreated will undergo rapid postnatal growth and sexual precocity; those with severe enzyme deficiencies can develop a fatal salt-losing crisis (Speiser et al., 2010).

D. **Diagnosis.**
1. Genital ambiguity can be lifesaving in females because it alerts the health care team to the possible diagnosis of CAH before a salt-losing crisis ensues. With neonatal screening, diagnosis of CAH before the advent of a salt-losing state has become more common.
2. Diagnostic tests and findings in 21-OHD CAH are as follows:
   a. 17-OHP level is markedly elevated and is hyperresponsive to ACTH stimulation; levels of testosterone and its precursors are also increased. Random 17-OHP levels in affected infants can reach 10,000 ng/dL (normal is $<$100 ng/dL). However, such high 17-OHP levels may not be reached until the second or third day of life, so a specimen drawn too early could lead to false reassurance that the infant does not have CAH. Prenatal or postnatal steroids can suppress the 17-OHP level and produce a false-negative result as well. Blood for 17-OHP level must be drawn before any hormone replacement is administered. Cutoff values for positive screens vary between laboratories and countries.
   b. Biochemical support for CAH diagnosis also includes elevated serum DHEA and androstenedione levels in males and females, and elevated serum testosterone in females.
   c. Serum aldosterone and PRA are measured to detect salt-losing states. The aldosterone level is low and PRA is high.
   d. Serum and urine electrolytes and steroid profiles are determined. Positive findings are hyponatremia, hyperkalemia, and high urine Na^+ excretion. Other metabolic disturbances include hypoglycemia and metabolic acidosis.
   e. Karyotype testing. It may be difficult for parents to accept that their severely virilized newborn is a genetic female without this testing. If genetic testing for *CYP21B* (gene for 21-OHD) is to be done, blood samples are taken from both the infant and the parents to determine heterozygosity.
   f. Ultrasonography and/or MRI of the pelvis and abdomen are done to visualize the uterus and adrenal glands.
3. Neonatal screening for CAH is currently required in all 50 states and the District of Columbia (National Newborn Screening and Genetics Resource Center, 2014).
   a. The goals of screening are the presymptomatic identification of infants at risk for life-threatening adrenal crisis and prevention of incorrect sex assignment of affected females.
   b. The basis of screening for CAH is measurement of 17-OHP, which is markedly elevated in neonates with the disorder. False-positives occur in about

1% of all tests, but higher rates are seen in preterm infants or sick infants, both of whom have higher levels of 17-OHP (Mitchell et al., 2014).

E. **Management of CAH.**
   1. Restore physiologic level of cortisol, suppress ACTH and androgen overproduction, and correct and maintain fluid and electrolyte homeostasis.
   2. Administer hydrocortisone (glucocorticoid) and, for the salt-wasting form, administer 9-α-fludrocortisone (mineralocorticoid). Further clinical management is guided by daily weights, adrenal steroid concentrations, PRA, electrolytes, blood glucose, and other data. PRA should be compared with age-specific norms, because basal PRA is higher in the newborn than in older infants.
   3. Dietary sodium supplementation to prevent hyponatremia, if needed. Fludrocortisone is not effective without salt supplementation.
   4. In a salt-losing state/adrenal crisis, management may include intravenous administration of fluids (glucose and sodium to correct dehydration and metabolic imbalances), treatment of shock, and correction of acidosis.
   5. Genetic counseling.
      a. Prenatal diagnosis for subsequent pregnancies using direct molecular genetic analysis of the fetal DNA (Shnorhavorian and Fechner, 2018).
      b. Intrauterine treatment may prevent or reduce some or all of the virilization of female fetuses. Dexamethasone given to the mother crosses the placenta and suppresses fetal ACTH. Treatment must begin by 6 to 7 weeks after conception and continue to term in affected female fetuses. Treatment is controversial because it must be started before genetic diagnosis so all fetuses are exposed to the therapy, not just the females with CAH who will benefit. This may change with newer technologies, such as analysis of fetal cell free DNA from maternal serum, which can identify fetal sex as early as 7 weeks, so male fetuses would not be treated (McNamara et al., 2017). There are also concerns about the risks of long-term steroid therapy. If the fetus is later determined to be male or a female without CAH, therapy is discontinued (Miller, 2015; Shnorhavorian and Fechner, 2018).
   6. Parent education. Parents need to understand that there is no cure for CAH, but it can be managed with medications and close monitoring. Their baby should receive care from a pediatric endocrinologist. Advise parents about immediate and long-term management of the disorder, the importance of compliance with therapy, and the need for follow-up of growth and development. Parents need to be aware of the requirement for double or even triple doses of steroids during illness and fever. Avoid using the term *ambiguous genitalia* in discussions with parents (Ono and Harley, 2013). Talking with parents is discussed further in the section "Disorders of Sexual Development."

F. **Management of virilized female neonates with CAH.** Issues that might be raised regarding the neonate with virilizing CAH are gender of rearing and the type and timing of surgery needed, if any.
   1. Gender of rearing. Most 46,XX individuals with CAH develop a female gender identity, regardless of the degree of genital virilization present at birth (McCann-Crosby and Sutton, 2015). Therefore, even in cases in which babies are initially "misassigned" as boys, it is still generally recommended that these genetic females with CAH be raised as females, although some experts maintain that, in extensively virilized infants, a male sex assignment should be considered (Shnorhavorian and Fechner, 2018). Hypertrophy of the clitoris will gradually abate with medical therapy; however, severe virilization will not be reversed.
   2. Surgery. Parents of virilized female infants may have many questions about possible genital surgery. Although such surgery is not usually performed immediately, it is helpful for the parents to meet with the pediatric endocrinologist and pediatric urologic surgeon to discuss available options, one of which is to delay surgery performed for cosmetic purposes until the child is old enough to participate in the decision (Ahmed et al., 2015; Lee et al., 2006; McCann-Crosby and Sutton, 2015). Decisions regarding surgery are influenced by the degree of virilization and the presence of a urogenital sinus. The goals of genital surgery for virilized girls with CAH are to achieve genital appearance compatible with gender, unobstructed urinary emptying without incontinence or infections, and good adult sexual and reproductive function.
   3. After discharge, infants with CAH must be closely followed by a pediatric endocrinologist for assessments of hormone levels, blood sugar, blood pressure, growth, skeletal maturation, and other parameters necessary to guard against overtreatment or undertreatment.

G. **Complications of CAH.**
   1. Adrenal crisis can occur with sudden signs of cortisol insufficiency (shock, hypotension, acidosis, hypoglycemia, seizures) plus sodium depletion. This can be triggered by episodes of illness or stress (such as systemic infection or surgery) in the neonatal period. Stress therapy to prevent this complication requires 2 or 3 times the usual dosage of hydrocortisone.
   2. Consequences of poorly controlled CAH.
      a. Failure to suppress ACTH and androgen production can result in signs of virilization and accelerated growth or bone maturation.

b. Overtreatment, resulting in hypertension, pulmonary edema, congestive heart failure, growth failure, adrenal atrophy, and lowered resistance to infection.

H. **Outcome**.
1. Lifelong hormonal replacement is usually necessary to improve chances for normal growth, pubertal development, and fertility.
2. Missed or delayed diagnosis can result in sudden deterioration or death in infants with undiagnosed salt-wasting CAH.

Sexual Development

Sexual development before birth is a sequential process with three stages: (1) fertilization (determination of chromosomal sex by the sex chromosome of the fertilizing sperm), (2) gonadal determination with establishment of sex by 7 weeks, and (3) differentiation of phenotypic or somatic sex (internal ductal system and external genitalia) (McNamara et al., 2017).

Further development is directed by genes. All embryos have bipotential gonads and structures for both male and female internal and external genitalia. Male-specific development requires the expression of the testis-determining gene (*SRY*) located on the Y chromosome. *SYR* alone is not sufficient for establishment of the testes; genes on the X chromosome and autosomes are also required. Genes (such as *SYR, SOX9, SF1,* and *WT1*) direct the gonad to differentiate into a testis, the key event in sex determination, by downstream regulation of sex-determining factors (McCann-Crosby and Sutton, 2015). In the female, the absence of the testes-organizing genes on the Y chromosome and the influence of other genes such as *WNT4 RSPO1,* and *FOXL2* lead to development of the ovary (McNamara et al., 2017). Thus, a large number of regulatory genes acting in networks drives the process of embryonic gonadal development. Single mutations in some of these genes are known to cause disorders of sexual development (DSDs). Because most genes related to gonadal development are expressed in other organs as well, mutations can cause syndromes of gonadal dysgenesis, such as Denys–Drash syndrome and camptomelic dysplasia.

A. **Internal genitalia:** the next events in sexual development are hormonally mediated, based on the gonadal gender (i.e., ovary or testes).
1. By 7 weeks of gestation, the fetus has two sets of primitive ducts that will become the internal reproductive tracts: the müllerian (female) and wolffian (male). In the XY fetus, the testis differentiates by the end of week 7.
2. The embryonic testis develops two types of hormone-producing cells: the Sertoli and the Leydig cells. The Sertoli cells begin secreting anti-müllerian hormone (AMH), causing the müllerian ducts to regress. By the ninth week, testicular Leydig cells are secreting the androgens necessary for further virilization of the male fetus.
3. Testosterone, the major androgen produced by the testes, acts locally in high concentrations to induce development of the wolffian ducts into the epididymis, vas deferens, and seminal vesicles.
4. In the absence of testosterone, the wolffian ducts in the female regress at 11 weeks of gestation. Müllerian ducts require no ovarian hormonal inducement to develop into fallopian tubes, uterus, and upper vagina.

B. **External genitalia.**
1. The primitive external genitalia are identical in both sexes (Fig. 30.3). At this indifferent stage, a genital tubercle forms and elongates to form a phallus and urogenital sinus, surrounded by inner urogenital folds and labioscrotal swellings.
2. Between the 8th and 14th weeks of gestation, male differentiation of the external genitalia takes place. Central to this development is availability of dihydrotestosterone (DHT), a potent metabolite produced from testosterone by the enzyme 5-α-reductase-2 (5-ARD-2). With 10 times the binding affinity of testosterone, DHT binds to androgen receptors in the genital tissues, stimulating fusion of the urethral folds to form the penile shaft and the labioscrotal swellings to form the scrotum. The urogenital sinus becomes the urethra.
3. Penile growth continues throughout gestation, and migration of the testes from the abdominal cavity to the scrotum is a late event, at 25 to 35 weeks of gestation. Androgen exposure after about 14 weeks contributes to further phallic enlargement (Shnorhavorian and Fechner, 2018).
4. In the absence of DHT, feminization of the external genitalia occurs. The phallus becomes a clitoris, and the labioscrotal swellings remain unfused to form the labia majora and minora. The urogenital sinus develops into the lower vagina and urethra. Feminine external genital development is complete by 11 weeks of gestation. Androgen exposure after this critical period can promote growth of the clitoris but does not cause labial fusion or the development of a penile urethra (Shnorhavorian and Fechner, 2018).

Disorders of Sexual Development (McCann-Crosby and Sutton, 2015; McNamara et al., 2017; Shnorhavorian and Fechner, 2018; Stokowski, 2014)

A DSD is an incongruence between molecular, gonadal, and phenotypic sex (McCann-Crosby and Sutton, 2015).

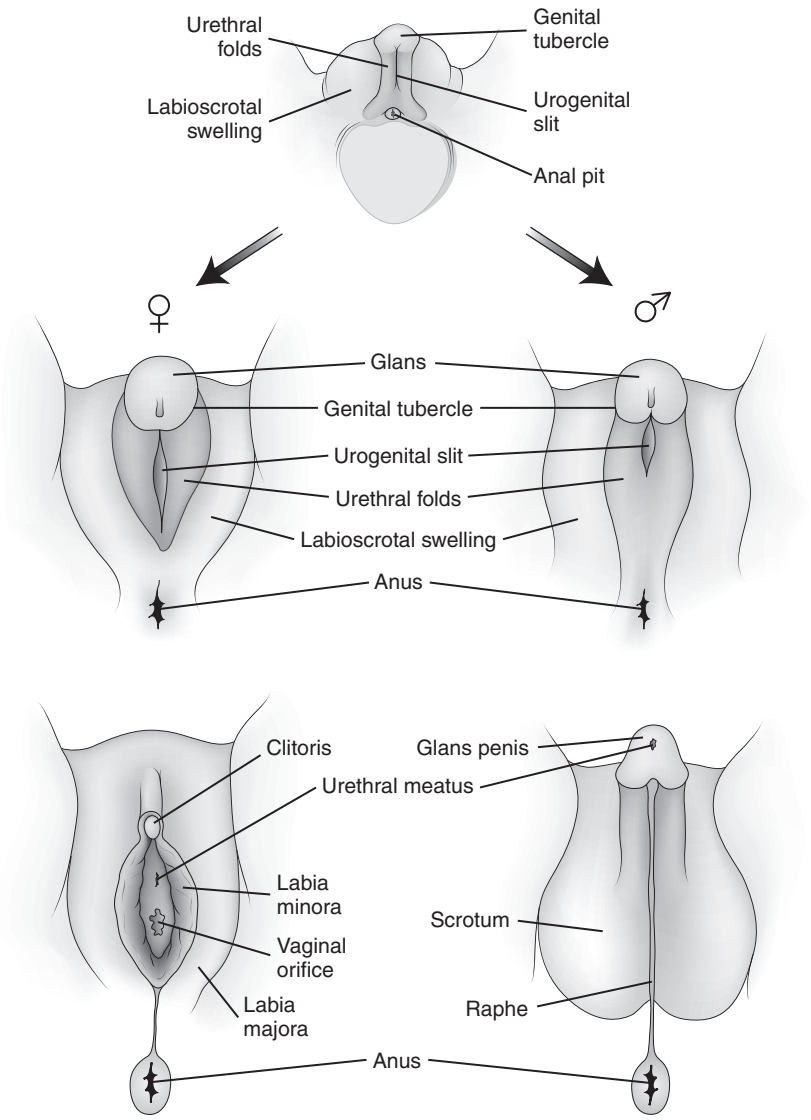

Fig. 30.3 Development and differentiation of male and female external genitalia. (Adapted from Spaulding, M. H. [1921]. The development of the external genitalia in the human embryo. *Contributions to Embryology of the Carnegie Institute*, *13*, 69–88, 1921; Kronenberg, H. M., Melmed, S., Polonsky, K. S., & Larsen, P. R. [Eds.]. [2008]. *Williams' textbook of endocrinology* [11th ed.]. Philadelphia, PA: Elsevier Saunders.)

Many people still refer to DSDs as "ambiguous genitalia," but this is a feature of some DSDs, rather than a diagnosis. Most DSDs result from either a failure in one of the steps of the male sexual developmental pathway or the exposure of an XX fetus to androgens during a sensitive period of development. Less frequent are DSDs resulting from gonadal differentiation, chromosomal disorders, and syndromes associated with ambiguous genitalia (Shnorhavorian and Fechner, 2018).

Sex chromosome DSD involves deletion or addition of sex chromosomes or sex chromosome mosaicism. Examples include Turner syndrome (45,X) and Klinefelter's syndrome (47,XXY). These disorders are discussed in Chapter 35.

46,XX DSD

These disorders include disorders of ovarian development and androgen excess. The most frequently encountered DSD in the neonate is the virilized female, or the 46,XX infant with virilized external genitalia and normal female internal structures. By far, the most common etiology is 21-OHD deficiency CAH (Fig. 30.4). This enzyme deficiency results in an overproduction of androgens at a critical stage of development, causing masculinization of the external, but not the internal (ovaries, uterus, fallopian tubes), genitalia. In severe cases, the excess androgens also prevent the vagina from fully descending into the perineum, leaving a common urogenital canal. Rarer causes of virilization of external genitalia in the 46,XX infant are

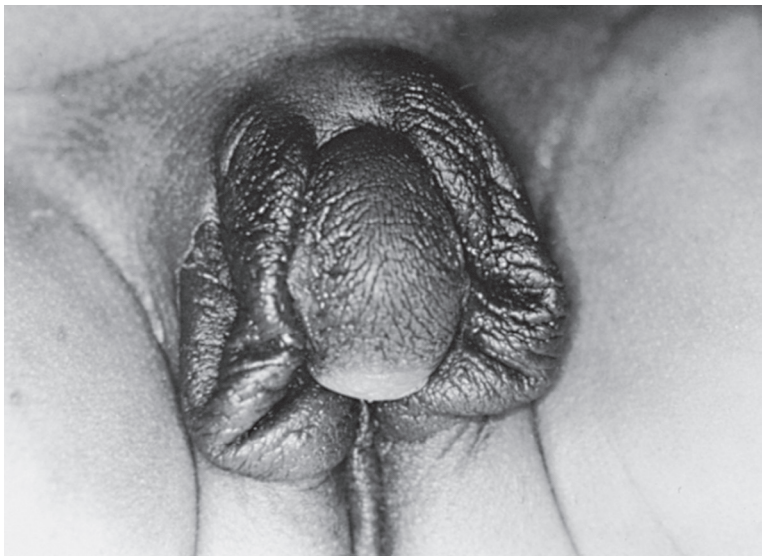

Fig. 30.4 Virilization in a 46,XX infant with 21-hydroxylase deficiency. Note clitoral hypertrophy and hyperpigmented and rugated labiosacral folds, resembling an empty scrotum. (Courtesy Michael S. Kappy, MD, PhD.)

placental aromatase deficiency, maternal androgen-producing or adrenal tumors, and maternal medications with androgenic action taken during pregnancy. CAH is discussed further under "Adrenal Gland Disorders."

46,XY DSD

These disorders include disorders of testicular development and disorders of androgen synthesis or action, such as androgen insensitivity syndrome, testicular biosynthesis defects, and 5-α-reductase-2 deficiency. The combination of a 46,XY karyotype with ambiguous genitalia results from a failure in one of the steps involved in the synthesis of or response to testosterone during sexual differentiation and penile growth. These infants have bilateral testicular development but have incomplete virilization of the internal or external genitalia. This results in an external phenotype ranging from completely female to isolated hypospadias or cryptorchidism. Another condition associated with incomplete virilization in the XY male is cloacal exstrophy, a defect of embryogenesis involving exstrophy of the bladder. Although not a DSD, significant ambiguity of external genitalia may be present.

ANDROGEN INSENSITIVITY SYNDROME (AIS)

A. **Pathophysiology**.
   1. AIS is caused by a complete or partial loss-of-function mutation in the androgen receptor gene located on the long arm of the X chromosome. Over 400 different mutations have been found (Shnorhavorian and Fechner, 2018).
   2. Both testosterone and its target tissue metabolite, DHT, must bind to androgen receptors to masculinize the genital tissues. When androgen receptor activity is impaired, androgen binding is insufficient.
   3. AIS variants include receptor negative (cytosol receptors are incapable of binding DHT) and receptor positive (receptors are able to bind DHT, but this does not result in normal differentiation). Both internal wolffian structures and external genitalia fail to respond to high levels of testosterone and DHT.
   4. The partial and complete forms of the disorder result in different degrees of undervirilization. In partial androgen insensitivity syndrome (PAIS), the clinical phenotype varies considerably and often parallels the severity of androgen resistance. Mild AI is not detected in the newborn because genitals are those of a typical male.

B. **Clinical manifestations.**
   1. Infants with PAIS have undervirilization ranging from simple hypospadias to microphallus with a labia majora–like bifid scrotum, undescended testes, and a urogenital sinus. No visible features distinguish PAIS from other causes of incomplete masculinization.
   2. Infants with complete androgen insensitivity syndrome (CAIS) are born with apparently female genitalia. However, these neonates may have palpable inguinal or labial masses, which further testing will reveal to be testes. Some may also have a short, blind-ending vagina.

C. **Diagnosis**.
   1. The diagnosis of CAIS is missed in the newborn period unless the infant presents with bilateral masses in the labia or inguinal canals or a boy was

expected based on a prenatal karyotype. CAIS might also be discovered at the time of inguinal hernia repair, or there may be a history of similarly affected family members.

2. Investigations include a karyotype and levels of testosterone, DHT, and LH. In PAIS, the ratio of androstenedione to testosterone is normal. Testosterone, estradiol, and LH are normal or high; FSH is usually normal.
3. Molecular genetic testing for mutations in the *AR* gene and/or androgen-binding assays. In approximately 50% of infants with PAIS a mutation has been found in the androgen receptor (McNamara et al., 2017).
4. Imaging studies reveal the absence of female internal reproductive structures (uterus, fallopian tubes). Two normal testes are present.

D. **Management**.

1. Infants with CAIS have unambiguously female external anatomy and are raised as girls. These children may not be diagnosed until puberty, when they have amenorrhea. Testes are removed (usually after puberty) to prevent later malignancy.
2. The gender assignment of infants with PAIS can be more complex and is often based on the severity of the phenotype. When the phenotype is predominantly male, a male sex of rearing is recommended. However, no consensus exists for the management of infants with severe perineoscrotal hypospadias and microphallus. The detection of somatic mutations in AIS is of importance for correct gender assignment because the presence of a functional wild-type *AR* receptor can induce virilization at puberty (Batista et al., 2018).
3. When a male sex of rearing is contemplated, a therapeutic trial with pharmacologic doses of androgen is often used to predict potential androgen responsiveness at puberty. If the phallus does not grow in response to testosterone, some experts recommend consideration of a female gender assignment. However, many others believe that, given the influence of prenatal androgen exposure on the developing CNS and the possibility that the child will develop a male gender identity, it is more prudent to raise these infants as boys.

TESTOSTERONE BIOSYNTHETIC DEFECTS

A. **Pathophysiology**.

1. Defects in the chain of steroidogenic enzymes involved in the testosterone biosynthesis pathway result in insufficient androgen concentrations during fetal development.
2. Disorders include congenital lipoid adrenal hyperplasia (CLAH), 3β-hydroxysteroid dehydrogenase (3β-HSD) deficiency, 17α-hydroxylase/17,20-lyase deficiency, and 17β-hydroxysteroid dehydrogenase (17β-HSD) deficiency. CLAH is caused by a defect in the steroidogenic acute regulatory (StAR) protein, responsible for transporting cholesterol to the inner membrane of the mitochondria.
3. Insufficient testosterone in affected males leads to underdeveloped wolffian duct structures and external male anatomy. Müllerian structures are absent because there is normal testicular AMH production.

B. **Clinical manifestations.**

1. Male infants with CLAH present with complete adrenal insufficiency: vomiting, weight loss, and hypotension. Genital appearance is primarily female.
2. Infants with 3β-HSD can present with varying degrees of genital ambiguity and evidence of salt-losing crisis.
3. Infants with 17α-hydroxylase/17,20-lyase deficiency have genital ambiguity.
4. Patients with primary 17α-hydroxylase deficiency also have hypertension.
5. Infants with 17β-HSD present with what appear to be external female genitalia that may include mild clitoral enlargement; an inguinal hernia may be present.

C. **Diagnosis**.

1. Laboratory investigations in suspected testosterone biosynthetic defects include chromosomes; baseline levels of testosterone, androgen precursors, and DHT; and levels of steroids and steroid precursors.
2. A human chorionic gonadotropin (hCG) stimulation test measures the ratio of androstenedione to testosterone; an elevated ratio suggests 17β-HSD deficiency.
3. In CLAH, ultrasound, computed tomography, or MRI may show enlarged, lipid-laden adrenal glands (Shnorhavorian and Fechner, 2018).

D. **Management**.

1. Acute management of these disorders requires full steroid replacement with both glucocorticoids and mineralocorticoids.
2. In CLAH and 3β-HSD, general supportive measures may be necessary, because severe adrenal insufficiency can cause rapid metabolic decompensation if the disorder is not recognized at birth.
3. Genetic XY infants with CLAH are raised as girls. Children with 17β-HSD often virilize significantly at puberty due to increased peripheral conversion of androstenedione to testosterone by 17β-HSD isoenzymes, making gender assignment of those diagnosed as neonates less straightforward.

5-α-REDUCTASE-2 DEFICIENCY

A. **Pathophysiology**.

1. An autosomal-recessive disorder caused by more than 20 different mutations of the *5-ARD* gene.

5-ARD-2 is an enzyme found in the genital skin and fibroblasts of the developing fetus, without which testosterone is not converted to DHT and fetal external genitalia do not virilize.
2. Development of the internal structures is unaffected because DHT is not required, so the wolffian ducts differentiate normally in response to testosterone and the müllerian ducts regress. At puberty, the external genitalia become virilized and fertility is possible.

B. **Clinical manifestations (Fig. 30.5) and diagnosis.**
1. Findings range from mild (isolated micropenis or hypospadias) to severe (a female phenotype with clitoromegaly, mild rugation, or pigmentation) undervirilization.
2. Testes are intact and are found in the inguinal canals, labioscrotal folds, or abdomen. The uterus and fallopian tubes regress because of normal secretion of AMH.
3. Wolffian duct differentiation is not affected because DHT is not required. Male internal ducts terminate either in a blind pseudovaginal pouch or on the perineum.
4. Diagnosis is made by assessing the ratio of testosterone to DHT after an hCG stimulation test. The hCG stimulation test also rules out other causes of undervirilization, such as Leydig cell hypoplasia and testosterone biosynthetic defects.
5. Analysis of 5-ARD-2 activity in genital skin fibroblasts provides a definitive diagnosis.

C. **Management**.
1. Boys respond to endogenous testosterone and undergo virilization and penile growth at puberty. This may be from extraglandular DHT formation due to peripheral conversion of testicular testosterone by unaffected isoenzymes.
2. For this reason, it is recommended that when the diagnosis is made in the newborn period, a male gender assignment is made.

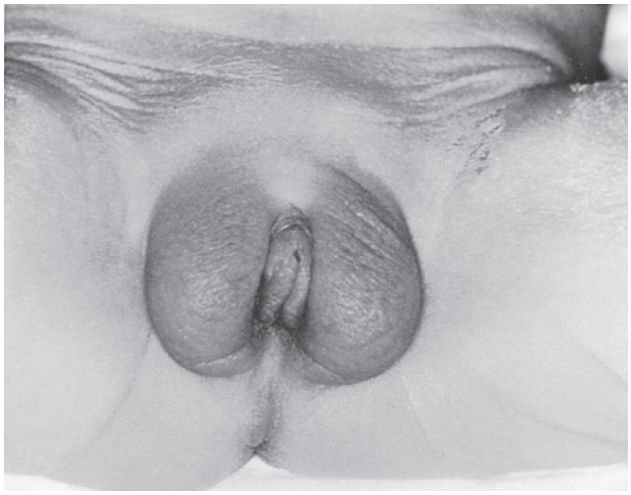

Fig. 30.5 Infant with 46,XY karyotype and ambiguous genitalia caused by 5-α-reductase deficiency. Note absence of a penis and lack of fusion of labiosacral folds, indicating incomplete virilization. (Courtesy Michael S. Kappy, MD, PhD.)

GONADAL DYSGENESIS

This group of disorders is usually associated with chromosomal anomalies or mutations, or deletions of genes responsible for sexual differentiation. Karyotypes producing gonadal dysgenesis include 46,XY, 46,XX, 46,XY/46,X, and other mosaic forms. Gonadal dysgenesis can occur as an isolated condition or as part of a complex syndrome such as Fraser syndrome, Denys–Drash syndrome, or camptomelic dysplasia.

A. **Pathophysiology**.
1. A dysgenetic testis either fails to produce testosterone or produces insufficient levels, resulting in varying degrees of undervirilization of the fetus.
2. Gonadal dysgenesis is considered partial or incomplete when the testes are dysgenetic or incompletely formed, and complete when the gonads are streaks containing only stromal tissue.
3. Mixed gonadal dysgenesis occurs when one gonad is a streak and the other is a well-formed testis. The internal ducts correlate with the ipsilateral gonad. On the side of a streak gonad, a fallopian tube and a hemiuterus will develop, and on the side of a normal testis, the vas deferens and epididymis will form.

B. **Clinical manifestations and diagnosis.**
1. The external genitalia are highly variable depending on how much testosterone is produced. In mixed gonadal dysgenesis, the external genitalia are asymmetrical, appearing male on one side and female on the other. A vagina and uterine cavity may be present.
2. Complete (or pure) gonadal dysgenesis is a form of sex reversal that results in unambiguously female genitalia with features of Turner's syndrome. These infants might not be identified in the newborn period unless a discrepancy is noted between a prenatal karyotype (46,XY) and appearance of the genitals.
3. Diagnosis includes karyotyping imaging studies to define the internal anatomy, and gonadal histologic analysis is necessary to differentiate gonadal dysgenesis from ovotesticular DSD in which elements of both testes and ovary are present.

C. **Management**.
1. Determining the gender of rearing for the infant with partial or mixed gonadal dysgenesis can be a difficult decision, one that is typically based on the degree of virilization and details of the internal anatomy.
2. When a uterus is present, the female gender assignment may be preferred. Most infants with complete gonadal dysgenesis are raised as females.

OVOTESTICULAR DSD

In ovotesticular DSDs, both ovarian and testicular components are present in the same individual. Possible combinations include an ovary on one side and a testis on the other, an ovary or testis with an ovotestis, or two ovotestes. More than half of affected babies will have an XX karyotype. This condition was formerly known as *true hermaphroditism*.

A. **Pathophysiology**.
   1. The amount of testosterone produced by the testicular tissue determines the degree of differentiation of wolffian ducts, regression of müllerian ducts, and virilization of external genitalia.
   2. The internal ducts usually parallel the ipsilateral gonadal histology. Ovarian tissue can be normal.

B. **Clinical manifestations and diagnosis.**
   1. Asymmetry of the external genitalia is a hallmark of ovotesticular DSD. Genital ambiguity ranges from a female phenotype with slight clitoromegaly to a mildly undervirilized male phenotype.
   2. The most common presentation is marked genital ambiguity: microphallus with penoscrotal or perineoscrotal hypospadias, fusion of labioscrotal folds, and cryptorchidism.
   3. Diagnosis involves karyotyping, and imaging studies are used to define the internal anatomy. Laparoscopy with gonadal biopsy is necessary at some point to confirm the diagnosis.

C. **Management.** Principles of management for infants with true ovotesticular DSD are similar to those for gonadal dysgenesis.

GENERAL PRINCIPLES OF MANAGEMENT OF DSDS

A. **Delivery room management.**
   1. Not being told immediately whether the newborn baby is a boy or a girl is one of the most incomprehensible things that can happen to parents at delivery. This situation requires a high degree of sensitivity and tact.
   2. Infants may be identified prenatally after ultrasound recognition of genital ambiguity or a karyotype/phenotype discordance, and these families will be prepared, to some degree, for the experience of having a baby of uncertain sex. Others will be taken completely by surprise.
   3. In spite of the family's desire for a quick answer, no attempt should be made by the health care team at the time of birth to guess the gender of the baby. The extreme phenotypic heterogeneity seen in DSDs makes it impossible to accurately predict either the diagnosis or the karyotype from a brief genital examination (McCann-Crosby and Sutton, 2015).
   4. Neonates who do not have health concerns requiring intensive care monitoring or treatment should not be transferred to the neonatal intensive care unit, because this only heightens the parents' anxiety unnecessarily and impairs parent–infant bonding.
   5. The Lawson Wilkins Pediatric Society and the European Society for Paediatric Endocrinology published a consensus statement on management of DSDs (Lee et al., 2006). That document represents the first agreed-upon set of guiding principles for approaching and managing the newborn with a DSD. More recently guidelines on initial management of an infant or adolescent with a DSD have been published by the Society for Endocrinology UK (Ahmed et al., 2015).

B. **Clinical manifestations** (Auchus et al., 2010; McCann-Crosby and Sutton, 2015; McNamara et al., 2017; Shnorhavorian and Fechner, 2018; Stokowski, 2014).
   1. Obtain a detailed family history. Any of the following might suggest a congenital or inherited DSD: maternal virilization or ingestion of hormones or oral contraceptives during pregnancy; consanguinity; history of urologic abnormalities, infertility, or genital ambiguity in other family members; or previous neonatal deaths that might suggest an undiagnosed adrenal crisis.
   2. Complete a full physical assessment. Dysmorphic features suggest the possibility of a syndrome. Alterations in hydration and blood pressure may indicate CAH.
   3. Conduct a detailed assessment of the genitalia. All examinations should respect the privacy of the infant and the family as much as possible, avoiding overexposure of the infant even for educational purposes (Auchus et al., 2010). Because of considerable overlap in the genital anatomy among DSDs, the physical assessment alone is insufficient for a definitive diagnosis. However, some assessment findings can provide clues to the underlying pathophysiology and guide the diagnostic process.
   4. A precise description of the anatomy is more useful than simple staging classifications. However, the degree of virilization can also be documented by Prader staging (Fig. 30.6) from a phenotypic female with mild clitoromegaly (Prader stage II) to a phenotypic male with glandular hypospadias (Prader stage III).
      a. Gonads. Determine whether gonads are palpable. The presence or absence of palpable gonads helps differentiate the major categories of DSDs. An apparent male infant with bilateral or a single impalpable testis with hypospadias should be considered as having a potential DSD until proven otherwise. A palpable gonad excludes the diagnosis of virilized genetic female (46,XX) with CAH. A gonad palpated below the external

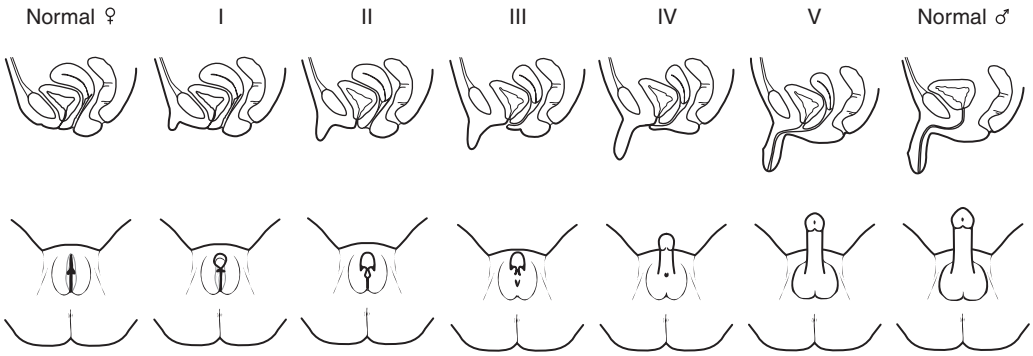

Fig. 30.6 Degrees of genital virilization based on the stages of Prader. The upper panel illustrates the sagittal view; the lower panel illustrates the perineal view. (From Scriver, C. R. [1995]. *The metabolic and molecular basis of inherited diseases* [7th ed.]. New York, NY: McGraw-Hill Companies.)

inguinal ring is presumed to contain testicular tissue. Because ovaries are rarely palpable, a unilateral gonad is usually a testis or occasionally an ovotestis. To palpate testes, place finger flat from internal ring, and milk down into the labioscrotal folds. Gonads may be situated high in the inguinal canal, requiring a careful examination. Unilateral or bilateral absence of the testes is known as *cryptorchidism*.

b. Phallus. Phallic size should be measured with a straight-edge ruler, depressing the fat pad and measuring the stretched length from pubic tubercle to tip of penis, not including the foreskin. Both length and midshaft diameter of the penis should be noted. A stretched penile length of 2.5 standard deviations below the mean is considered micropenis in a male with normal genitalia (Merguerian and Rowe, 2018). Chordee, ventral curvature of the penis caused by residual urethral tissue that tethers the phallus to the perineum, should be noted because it can reduce the apparent length of the penis (Shnorhavorian and Fechner, 2018). The actual position of the urethral meatus and the severity of hypospadias, if present, should be determined.

c. Clitoral size should be measured when clitoromegaly is present. Clitoral length longer than 9 mm in term infants is considered excessive. Clitoral size often appears large in preterm infants because breadth remains constant from 27 weeks onward. A prominent, but not truly enlarged, clitoris, or a normally sized penis concealed by an abundance of prepubic fat is a normal assessment finding.

d. Labioscrotal folds. Labial fullness, a benign finding, is another feature occasionally mistaken for genital ambiguity. The labioscrotal folds are examined for fusion, which starts posteriorly and moves anteriorly, increasing the anogenital distance. The perineum is inspected by gently separating the labia and using an examination light to confirm the presence of separate urethral and vaginal openings or a single urogenital orifice (an opening connected to both urinary and genital systems). Visualization of voiding is helpful. If skin tags with a slightly bluish hue are seen, a hymen and vagina are present. Note rugosity or hyperpigmentation of the labioscrotal fold, signifying hypersecretion of ACTH associated with CAH. Other variations include a bifid scrotum (a deep midline cleft) or a shawl scrotum (scrotum surrounds the penis like a shawl).

C. **Diagnostic studies.**

1. Diagnosis is made by analysis of results of biochemical, hormonal, imaging, and molecular testing.
2. The aim of the initial investigation is to rule out a life-threatening illness such as salt-wasting CAH, which can precipitate an adrenal crisis. Such testing includes serum 17-OHP level (after 24 to 48 hours of age), electrolytes, glucose, and a hormonal profile with baseline levels of testosterone, DHT, and other steroid precursors (progesterone, DHEA, 4-androstenedione, and 17α-hydroxypregnenolone). A karyotype with X- and Y-specific probe detection is obtained from all infants, even if a prenatal karyotype is available (Shnorhavorian and Fechner, 2018).
3. A urinary steroid profile is helpful in the diagnosis of disorders of steroid biosynthesis. Other investigations that may be warranted include ACTH stimulation test, PRA, and serum AMH, LH, and FSH. An hCG stimulation test is undertaken to delineate a block in testosterone biosynthesis from androstenedione (17β-HSD deficiency) or conversion of testosterone to DHT (5-α-reductase deficiency). An hCG test measures baseline levels of testosterone

and its precursors DHEA or DHEA sulfate and androstenedione and its metabolite, DHT.

4. Imaging studies include abdomino-pelvic ultrasound (to determine presence or absence of a uterus, to visualize the presence or absence of gonads in the inguinal region, and to assess the müllerian anatomy), genitourethrogram (to delineate the anatomy of the vagina and urethra and where the vagina opens into the urogenital sinus), and pelvic MRI. Laparoscopic exploration with gonadal biopsy may be necessary to evaluate gonadal histology. Finally, molecular analysis may be required to arrive at a definitive diagnosis for some disorders.

D. **Interpretation of findings:** it can be difficult even for health care professionals to understand that only a minority of patients will receive a definitive diagnosis and prognosis in the neonatal period (Ono and Harley, 2013).
   1. The most common cause of genital ambiguity in the newborn is 21-OHD CAH, responsible for more than 90% of cases of ambiguous genitalia. It presents with a virilized XX (female) infant and should be suspected in the presence of a virilized infant with a uterus and no palpable gonads (McCann-Crosby and Sutton, 2015).
   2. Among the remainder of infants with genital ambiguity, the most common diagnoses are gonadal dysgenesis, PAIS, and testosterone biosynthetic disorders. Symmetrical external genitalia, with or without palpable gonads, and no uterus suggest an undervirilized male (McCann-Crosby and Sutton, 2015). A micropenis should prompt investigation for hypopituitarism or GH deficiency, particularly in the presence of hypoglycemia (Shnorhavorian and Fechner, 2018).
   3. It is not always possible to reach a diagnosis in the undervirilized male infant.

E. **Talking with families.**
   1. Optimal care of the infant with a DSD involves a well-coordinated team (neonatologist, neonatal nurse, pediatric endocrinologist, pediatric surgeon/pediatric urologic surgeon, social worker, and psychologist or other mental health professional, and often a geneticist) experienced in the management of DSDs (Ono and Harley, 2013; Shnorhavorian and Fechner, 2018).
   2. The initial contact with parents of a newborn with a DSD is extremely important. This interaction should emphasize that a DSD is not a shameful condition and does not preclude the child from becoming a well-adjusted, functional adult who can be expected to lead a fulfilling life (Houk and Lee, 2012).
   3. A single person should communicate diagnostic findings and plans with the family. When discussing possible diagnoses with the family, language must be carefully chosen. Words such as "hermaphrodite," "pseudohermaphrodite," "ambiguous genitalia," "intersex," and "sex reversal" are outdated, confusing, and perceived as distasteful by many (Ono and Harley, 2013). Use accurate, informative terms that describe the infant's diagnosis.
   4. A clear explanation of sexual development in the fetus will help parents understand how an infant can be born with atypical genitalia, an important component of parental coping (Houk and Lee, 2012). Parents may find comfort in knowing that the appearance of the external genitalia is the result of prenatal androgen exposure and not caused by the molecular sex (Stokowski, 2014; Witchel, 2017).
   5. The parents have the responsibility to make or defer decisions about care for their infant with a DSD, including gender of rearing. The role of the health care team is to provide information, to share and explain all diagnostic findings, to inform parents of all available options, and to support the parents in the decision-making process.
   6. The approach should be family-centered as well as culturally sensitive. Family concerns must be respected and addressed in strict confidence. A relationship of trust requires open and honest communication and full disclosure of available information, including candid discussion of the controversies and dilemmas concerning gender assignment and early genital surgery.
   7. Parental acceptance of the child with a DSD is a key determinant of a favorable outcome (Houk and Lee, 2012). Health care professionals must also recognize and respect the cultural and psychosocial influences on parents' decisions about care for their infant.

F. **Gender assignment.**
   1. Parents are naturally anxious to find out their baby's gender so that they can name the baby and announce the birth to family and friends. Nevertheless, it must be sensitively communicated that, although their distress is acknowledged, when gender is in doubt, a gender-of-rearing decision is one with lifelong implications and cannot be made in haste. Gender assignment must be deferred until expert evaluation of the newborn takes place and sufficient data are available for a fully informed decision by the parents (McCann-Crosby and Sutton, 2015; Shnorhavorian and Fechner, 2018).
   2. If gender is undetermined, use gender-neutral terms such as *baby* (vs. "he" or "she"), *genital tubercle* (vs. "penis" or "clitoris"), and *gonads* (vs. "ovary" or "testes") (McCann-Crosby and Sutton, 2015).
   3. Unfortunately, some tests required for evaluation of a DSD must be sent out to referral laboratories, and the long wait for results can be frustrating for the

parents. It is helpful if an experienced mental health professional can meet very early with the parents to help them decide what to tell family and friends while awaiting a final diagnosis. One suggested approach is to tell family and friends that the infant's genital development is incomplete and that more tests are needed (McCann-Crosby and Sutton, 2015).

Pancreas

A. **The pancreas is both an exocrine and endocrine gland.** The endocrine pancreas is responsible for hormonal regulation of blood glucose levels. The endocrine functions are performed by clusters of cells called *islets of Langerhans* that include alpha, beta, and delta cells. Hormones secreted by the endocrine pancreas include glucagon, insulin, amylin, and somatostatin.

B. **Fetal insulin, present by 8 to 10 weeks of gestation, is secreted in response to both glucose and amino acids.** The fetus is dependent on its own supply of insulin, which does not cross the placenta. Insulin stimulates uptake of glucose by muscle and adipose tissue. The fetal pancreas becomes progressively more responsive to glucose late in gestation, and beta cell mass increases markedly.

C. **At birth, when maternal glucose supply ceases, the neonate's blood glucose and insulin levels decline.** A concomitant surge in counterregulatory hormones epinephrine and glucagon sets in motion the production of glucose that will sustain the neonate until milk feeding is established.

D. **The exocrine portion of the pancreas constitutes 80% of the total gland.** Acinar cells secrete digestive enzymes, including trypsin, lipase, and amylase, into the duodenum.

DISORDERS OF THE PANCREAS

Rare pancreatic disorders in the newborn include congenital conditions such as pancreatic agenesis, pancreatic hypoplasia, and annular pancreas. Disorders of the endocrine pancreas include neonatal diabetes mellitus and hyperinsulinism, as well as the developmental disorder of the pancreas seen in the infant of the diabetic mother. The most common newborn disorder of the exocrine pancreas is cystic fibrosis (CF).

INFANT OF A DIABETIC MOTHER (SEE CHAPTER 9). Diabetes in pregnancy has increased in recent years due to the increases in people with type 2 diabetes and prediabetes. This has led to more newborns being at risk for the problems associated with glucose intolerance and abnormal glucose regulation during pregnancy.

NEONATAL DIABETES MELLITUS (NDM) (SEE CHAPTER 9). NDM is a rare disorder manifested by persistent, insulin-sensitive hyperglycemia occurring as early as the first week of life and lasting longer than 2 weeks. About half of all cases of NDM are of the transient form (these infants are usually IUGR) that resolves by 18 months.

CONGENITAL HYPERINSULINISM (ARNOUX ET AL., 2011; DEVASKAR AND GARG, 2018). Congenital hyperinsulinism is a group of disorders with the common feature of hyperinsulinemic hypoglycemia secondary to inappropriate secretion of insulin (Arnoux et al., 2011). Although this is the most common cause of severe, persistent hypoglycemia in the newborn, the incidence is approximately 1:50,000 in the general population (Devaskar and Garg, 2018). Multiple genetic mutations in transporter proteins, enzymes, and potassium channels have been identified that can lead to different variants of this disorder. Between 10% and 15% of congenital hyperinsulinism is transient and will spontaneously resolve at 1 month of age. Beckwith–Wiedemann syndrome is a congenital overgrowth syndrome with hyperinsulinism caused by beta cell hyperplasia.

A. **Pathophysiology**.
   1. Hyperinsulinism is due to unregulated insulin release either from the entire pancreas (diffuse beta cell hyperfunction) or from confined areas of the pancreas (focal adenomatous islet-cell hyperplasia).
   2. Insulin lowers circulating glucose, suppressing lipolysis and ketogenesis and decreasing the availability of free fatty acids and ketone bodies. Because these are alternative energy substrates for the brain during hypoglycemia, hyperinsulinemia places the infant at risk for severe neurologic dysfunction and seizures as consequences of neuroglycopenia.

B. **Clinical manifestations.**
   1. Most infants with congenital hyperinsulinism are term and present shortly after birth. They may be appropriate or large for gestational age.
   2. Many present initially with repeated hypoglycemic episodes, then after a few days with severe recurrent hypoglycemia. Some infants may also present with seizures, hypothermia, apnea, and cyanosis (Devaskar and Garg, 2018).
   3. Many are macrosomic with a characteristic facial appearance.
   4. Neonates with Beckwith–Wiedemann syndrome present with a constellation of findings, including macroglossia, abdominal wall defects, Wilms' tumors, renal abnormalities, and facial nevus.

C. **Diagnosis**.
   1. Prompt diagnosis and management are critical to prevent neurologic damage.
   2. Severe hypoglycemia with an insulin level that is inappropriate to the level of blood glucose (e.g.,

an insulin level >5 mU/mL with a plasma glucose level <50 mg/dL) suggests the diagnosis.
3. Other diagnostic criteria are a high glucose requirement (>6 to 8 mg/kg/min) needed to maintain normoglycemia, low serum blood glucose by laboratory analysis, measurable insulin, elevated C-peptide, low free fatty acids, and low ketone body concentrations.
4. Blood sampling must take place during hypoglycemia to be of diagnostic value.

D. **Management**.
1. Management involves a high caloric intake and pharmacologic therapy to inhibit insulin secretion by the pancreas. A central venous catheter is required for reliable and safe administration of high glucose infusates. Glucose infusion rates of 10 to 15 mg/kg/min or higher may be required, and the rate of glucose necessary to maintain normoglycemia) is an indicator of the severity of the disease (Arnoux et al., 2011).
2. Drugs include diazoxide, which inhibits insulin secretion by blocking the sulfonylurea receptor of the beta cell, and octreotide, a somatostatin analogue. Diazoxide must be used with caution in the presence of hyperbilirubinemia because it displaces bilirubin from albumin-binding sites. Glucagon to mobilize hepatic glucose can be added if needed as a short-term adjunct to therapy (Arnoux et al., 2011).
3. The response to these agents is inconsistent and variable. Infants who do not show an adequate and immediate response may require pancreatectomy to prevent recurrent neuroglycopenia. Preoperative localization procedures and intraoperative biopsies will determine the exact nature of the lesion and how much of the pancreas must be removed. Focal disease may require only a partial pancreatectomy, but a near-total (>95%) removal of the pancreas is indicated for diffuse congenital hyperinsulinism. Loss of the pancreas can pose additional risks such as pancreatic insufficiency and diabetes mellitus.

Cystic Fibrosis

CF is an autosomal-recessive multisystem disorder caused by mutations in the gene encoding for the cystic fibrosis transmembrane conductance regulator (CFTR) protein, of which more than 2000 mutations have been identified (Elborn, 2016). In the United States CF occurs in 1 in 2500 to 3000 whites, 1 in 15,000 blacks, 1 in 31,000 Asian Americans, and 1 in 9200 Hispanics (Filbrun et al., 2016).

A. **Pathophysiology**.
1. Mutations in the *CFTR* gene affect the cyclic adenosine-5′-monophosphate (AMP)–mediated signals that stimulate chloride conductance in the epithelial cells of the exocrine ducts. Deficient chloride transport and the associated water-transport abnormalities result in the production of abnormally viscid mucus.
2. Nearly all organs and systems of the body are affected, including the lungs and upper respiratory tract, gastrointestinal tract, pancreas, liver, sweat glands, and genitourinary tract. Hyperviscous secretions in the intestines and a deficiency of pancreatic enzymes combine to create a sticky plug of meconium, a condition known as *meconium ileus* (see Chapter 29). The meconium has a higher protein and lower carbohydrate concentration, making it more viscid than normal meconium.

B. **Clinical manifestations.**
1. Without a family history or parental screening (now routine in many prenatal practices), CF is not recognized at the time of birth in most affected neonates unless a meconium ileus is present, typically identified by 24 to 48 hours of age.
2. Although not always present in the neonate, most patients with CF have pancreatic enzyme insufficiency and present with digestive symptoms or failure to thrive early in life.
3. Other neonatal signs and symptoms include intestinal atresia, prolonged jaundice, and abdominal or scrotal calcifications.

C. **Diagnosis**.
1. The possibility of CF is raised in the neonate with meconium ileus and can be confirmed with DNA testing. A sweat test can also be performed after the first 48 hours of life. A sweat test uses electrical–chemical stimulation of the skin to induce sweat, which is collected and analyzed for chloride content. Because the neonate may not produce enough sweat, the test may need to be repeated.
2. Newborn screening for CF is accomplished by measuring immunoreactive trypsinogen in dried blood samples. Screening for CF is conducted in all 50 states and the District of Columbia and in most countries with a high prevalence of CF (Elborn, 2016).

D. **Management**.
1. Meconium ileus requires prompt attention to prevent complications such as volvulus, sepsis, bowel necrosis, or intestinal perforation (see Chapter 29).
2. CF is managed with a diet high in energy and fat to compensate for malabsorption and the increased energy demand of chronic inflammation. In addition to vitamin and mineral supplementation, a hydrolyzed protein formula containing medium-chain triglycerides is used, because they do not require digestion by pancreatic enzymes for absorption.

3. Pancreatic enzyme supplements are also needed to improve fat absorption. Meticulous care of the perianal area must be taken because these enzymes can cause severe perianal dermatitis.
4. Breastfeeding has been shown to be beneficial for infants with CF; although growth might be slightly slower, breastfeeding should be encouraged (Lawrence and Lawrence, 2016).
5. Infants can also develop early pulmonary infections with *Staphylococcus aureus* followed often by *Pseudomonas aeruginosa* (Wiencek and Lo, 2018).
6. Newer therapies target the basic defects in CF and have reduced later pulmonary complications. Average life expectancy is currently more than 40 years (Elborn, 2016).

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CHAPTER 31
Hematologic Disorders

William Diehl-Jones and Debbie Fraser

OBJECTIVES

1. Understand the processes of hematopoiesis and erythropoiesis.
2. Recall erythrocyte and leukocyte development from pluripotent stem cells.
3. Relate the consequences of anemia to the management of the infant.
4. Evaluate the clinical presentation of disseminated intravascular coagulation in relation to coagulation consumption and fibrinolysis.
5. Describe the etiologic factors of hemorrhagic disease of the newborn.
6. Describe key indicators for nursing assessment of the thrombocytopenic infant.
7. Evaluate the neonatal consequences of maternal immune thrombocytopenic purpura.
8. Discuss the role of partial exchange transfusion in the treatment of neonatal polycythemia.
9. Describe current recommendations for the use of blood components.
10. Analyze the components of the complete blood cell count, and describe the usefulness of each in the determination of neonatal sepsis.

To meet the objectives, this chapter presents an overview of blood cell development and coagulation factors, including normal birth values and common diagnostic tests. Blood products and transfusion therapies are discussed, with current recommendations for use. Common hematologic problems and therapies affecting the newborn infant are outlined. An evaluation of the red blood cell (RBC) indices, useful for diagnosis of hematologic disorders, is included.

Development of Blood Cells

A. **Hematopoiesis:** formation, production, and maintenance of blood cells (Blackburn, 2013; Dror et al., 2016; Gallagher, 2015; Ohls, 2017).
B. **Fetal hematopoiesis:** occurs in three distinct phases: mesoblastic, hepatic, and myeloid.
   1. RBCs arising from embryonic connective tissues or mesenchyme can be seen by the 14th day of gestation.
   2. Primitive erythroblasts arising from megaloblasts are detectable in circulating blood between 21 and 35 days of gestation.
   3. Extravascular liver hematopoiesis begins with migration of pluripotent stem cells from the yolk sac; well established by week 5 or 6 of gestation.
   4. Liver hematopoiesis peaks at 3 to 6 months of gestation and then slowly regresses as medullary (bone marrow) hematopoiesis predominates from 22 weeks of gestation.
   5. Sites of extramedullary hematopoiesis (spleen, lymph nodes, thymus, kidneys) aid production of cells during fetal life when long bones are small.
   6. Pluripotent cells develop into either colony-forming unit–granulocyte, erythrocyte, monocyte, macrophage (CFU-GEMM); colony-forming unit–erythroid (CFU-E); or colony-forming unit–granulocyte-macrophage (CFU-GM) cell lines, which evolve into specific cell lines (Fig. 31.1).
   7. Hypoxia, oxidative stress, bacterial infection, and other forms of physiologic stress can influence the rate of differentiation of pluripotent cells.
   8. Hematopoietic factors include interleukins (ILs; e.g., IL-1 through IL-4, IL-6 through IL-8, and IL-10 through IL-12), growth and differentiation factors such as granulocyte colony-stimulating factor (G-CSF), macrophage colony-stimulating factor (M-CSF), granulocyte–macrophage colony-stimulating factor (GM-CSF), thrombopoietin, and erythropoietin.
C. **Erythropoiesis:** production of erythrocytes (RBCs).
   1. The erythrocyte precursor or burst-forming unit, erythroid (BFU-E), develops from a myeloid stem cell (CFU-GEMM), which also differentiates to produce a megakaryocyte precursor (CFU-Meg).
   2. Erythropoiesis and synthesis of hemoglobin are regulated by a hormone, erythropoietin, which is in turn regulated by hypoxia-sensing mechanisms in the fetal liver and kidney.

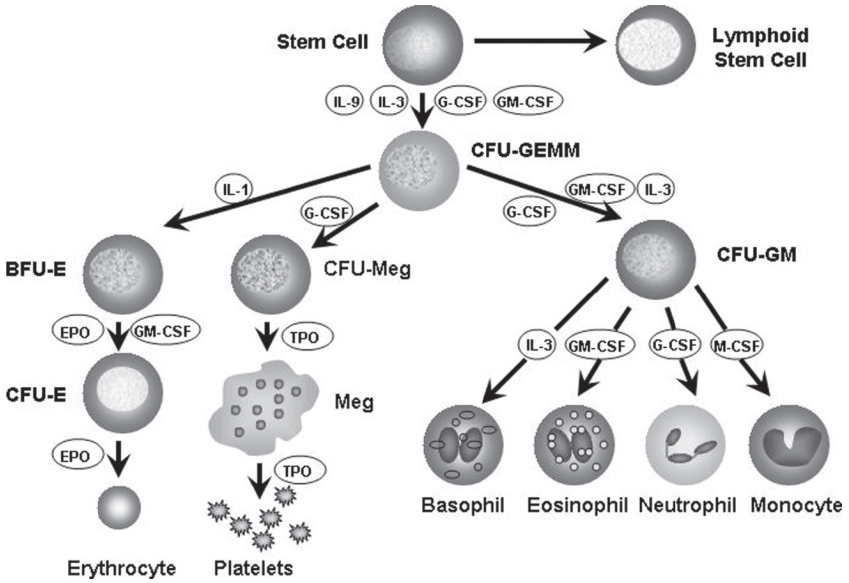

Fig. 31.1 Hematopoiesis and selected growth factors. *BFU-E*, Burst-forming unit, erythroid; *CFU-E*, colony-forming unit–erythroid; *CFU-GEMM*, colony-forming unit–granulocyte, erythrocyte, monocyte, macrophage; *CFU-GM*, colony-forming unit–granulocyte-macrophage; *CFU-Meg*, colony-forming unit–megakaryocyte; *EPO*, erythropoietin; *G-CSF*, granulocyte colony-stimulating factor; *GM-CSF*, granulocyte–macrophage colony-stimulating factor; *IL-1*, interleukin-1; *IL-3*, interleukin-3; *IL-9*, interleukin-9; *M-CSF*, macrophage colony-stimulating factor; *Meg*, megakaryocyte; *TPO*, thrombopoietin. (Adapted from Israels, L.G., & Israels, S. J. [2002]. *Mechanisms in hematology* [3rd ed., p. 402]. Toronto, Canada: Core Health Sciences.)

3. Erythropoietin is produced postnatally in the kidneys, but during fetal life, extrarenal sites (liver, submandibular glands) predominate.
4. Erythropoietin levels are increased in response to anemia and low oxygen availability to tissues and are decreased in response to hypertransfusion.
5. Erythropoietin levels are also elevated in infants with Down syndrome or intrauterine growth restriction and those born to women with diabetes or pregnancy-induced hypertension.

D. **Hemoglobin:** major iron-containing component of the RBCs.
1. Hemoglobin carries oxygen from the lungs to the tissue cells through the circulation.
2. Hemoglobin synthesis begins around 14 days of embryonic life.
3. Transition from predominant production of fetal hemoglobin (HbF) to production of adult hemoglobin (HbA) begins at the end of fetal life. RBCs contain 70% to 90% HbF at birth. The switch to production of HbA is delayed in cases of maternal hypoxia or fetal growth restriction and in infants of diabetic mothers.
4. Hemoglobin binds with 2,3-diphosphoglycerate (2,3-DPG), releasing an oxygen molecule.
   a. HbF has far less affinity for 2,3-DPG than does HbA, resulting in a greater affinity for oxygen.
   b. Levels of 2,3-DPG are directly proportional to gestational age.
5. Normal birth values (Table 31.1).
   a. Values depend on gestational age, volume of placental transfusion (timing of cord clamping, infant position), and blood sampling site; hemoglobin in capillary samples may be significantly higher than in venous samples.
   b. Peripheral vasoconstriction and stasis yield higher values from capillary samples.
   c. Hemoglobin levels are higher in newborns and decrease by the end of the first week of life to values similar to cord blood.
   d. Increased Pao_2 after delivery and increase in HbA causes a decrease in erythropoietin, leading to a gradual decline in hemoglobin (Diab and Luchtman-Jones, 2015).

E. **Hematocrit:** percentage of RBCs in a unit volume of blood.
1. Values rise immediately after birth and then decline to cord levels in the first week.
2. Normal birth values (see Table 31.1).
   a. Values depend on gestational age and volume of placental transfusion (timing of cord clamping, infant position).
   b. Peripheral vasoconstriction and stasis yield higher values from capillary samples.

F. **RBCs.**
1. The erythrocyte BFU-E differentiates under hormonal control to form a CFU-E, which loses its nucleus as it forms erythrocytes (see Fig. 31.1).

Table 31.1

Normal Blood Values in Premature and Term Infants

Value	GESTATIONAL AGE (WEEKS) 28	34	Term Cord Blood	Day 1	Day 3	Day 7	Day 14
Hb (g/dL)	14.5	15	16.8	18.4	17.8	17	16.8
Hematocrit (%)	45	47	53	58	55	54	52
Red cells (mm^3)	4	4.4	5.25	5.8	5.6	5.2	5.1
MCV (μ^3)	120	118	107	108	99	98	96
MCH (pg)	40	38	34	35	33	32.5	31.5
MCHC (%)	31	32	31.7	32.5	33	33	33
Reticulocytes (%)	5 to 10	3 to 10	3 to 7	3 to 7	1 to 3	0 to 1	0 to 1
Platelets (1000 s/mm^3)			290	192	213	248	252

Hb, Hemoglobin; *MCH*, mean corpuscular hemoglobin; *MCHC*, mean corpuscular hemoglobin concentration; *MCV*, mean corpuscular volume.
From Klaus, M. H., & Fanaroff, A. A. (2001). *Care of the high-risk neonate* (5th ed.). Philadelphia, PA: W. B. Saunders.

2. The CFU-Es (or reticulocytes), in the absence of physiologic stress, mature 1 to 2 days in the bone marrow and then another day in the circulation before maturing to erythrocytes.
   a. Reticulocyte count is inversely proportional to gestational age at birth (see Table 31.1) but falls rapidly to less than 2% by 7 days.
   b. Persistent reticulocytosis may indicate chronic blood loss or hemolysis.
3. RBC function.
   a. Oxygen transport via oxyhemoglobin.
   b. Carbon dioxide transport via carboxyhemoglobin.
   c. Carbon dioxide reacts with water to form carbonic acid; reaction catalyzed by carbonic anhydrase in the cytoplasm of RBCs.
   d. Carbonic acid dissociation to form bicarbonate ions.
   e. Buffering of protons via binding with hemoglobin to form acid hemoglobin and by reaction with bicarbonate ions.
4. RBC count.
   a. Number of circulating mature RBCs per cubic millimeter (see Table 31.1).
   b. Count equals production versus destruction or loss.
   c. RBC life span proportional to gestational age.
      1) Adult: 100 to 120 days.
      2) Term infant: 60 to 70 days.
      3) Premature infant: 35 to 50 days.
   d. Nucleated RBCs are circulating immature (pre-reticulocyte) RBCs.
      1) Number is inversely proportional to gestational age and declines rapidly in the first week.
      2) Increase may indicate hemolysis, acute blood loss, hypoxemia, congenital heart disease, or infection.
5. RBC indices: measure of RBC size and hemoglobin content used for designation of anemias (see Table 31.1).
   a. Mean corpuscular volume (MCV): average size and volume of a single RBC.
      1) MCV decreases as gestation progresses and continues to decrease after birth to adult size by 4 to 5 years.
      2) Increased MCV: RBCs referred to as macrocytes.
      3) Decreased MCV: RBCs referred to as microcytes.
   b. Mean corpuscular hemoglobin (MCH): average amount (by weight) of hemoglobin in each RBC.
      1) A decrease in MCH parallels a decrease in MCV.
      2) Increased MCH: RBCs appear hyperchromic.
      3) Decreased MCH: RBCs appear hypochromic.
   c. Mean corpuscular hemoglobin concentration (MCHC): average concentration of hemoglobin per single RBC, calculated from the amount of hemoglobin per deciliter of cells.
      1) Adult values for MCHC reached by 6 months.
      2) Increased MCHC: RBCs appear hyperchromic.
      3) Decreased MCHC: RBCs appear hypochromic.
   d. Erythrocyte mass: total mass of erythrocytes.
      1) Best measure of anemia.
      2) Direct correlation between erythrocyte mass and hemoglobin concentration.
      3) Gold standard is use of chromium-labeled erythrocytes.

G. **White blood cells (WBCs).**
1. Leukocyte precursors mature in the bone marrow and lymphatic tissues, in the absence of physiologic stress, through the CFU-GEMM and CFU-GM stages (see Fig. 31.1).
2. WBCs can leave the circulation to enter the extravascular tissues, where they function as an important part of the immunologic system in reaction to foreign protein.

3. Granulocytes, lymphocytes, and monocytes are types of WBCs.
   a. Granulocytes: include basophils, eosinophils, and neutrophils.
      1) Basophils.
         a) Important in allergic and inflammatory responses.
         b) Least numerous of the granulocytes: 0.5% to 1% of total WBC count.
      2) Eosinophils.
         a) Perform similar functions as neutrophils but are less effective in response.
         b) Unlike neutrophils, can survive for prolonged periods in extravascular space.
         c) Important in allergic and anaphylactic responses and most effective granulocyte for parasitic destruction.
         d) Benign eosinophilia of prematurity, inversely proportional to gestational age, may reflect immaturity of barrier mechanisms in the gastrointestinal and/or respiratory tract (Dror et al., 2016).
         e) Normally comprise 1% to 3% of total WBC count.
      3) Neutrophils.
         a) Neutrophils function as phagocytes that ingest and destroy small particles such as bacteria, protozoa, cells and cellular debris, and colloids.
         b) Physiologic stress can increase production and bone marrow release of immature forms.
         c) Neutrophils are increased at birth but decrease during the first week to reach percentages approximately equal to those of lymphocytes.
   b. Lymphocytes.
      1) Thymus-derived (T) lymphocytes: important in graft-versus-host disease and delayed hypersensitivity reactions.
      2) Bone marrow–derived (B) lymphocytes: important in the production and secretion of immunoglobulins and antibodies.
   c. Monocytes.
      1) Circulating immature macrophages.
      2) Transformed into macrophages in tissues (i.e., lung—alveolar macrophages; liver—Kupffer cell macrophages).
      3) Responsible for clearance of old blood cells, cellular debris, opsonized bacteria, antigen–antibody complexes, and activated clotting factors from the circulation.
4. WBC count.
   a. WBC count is the number of circulating WBCs per cubic millimeter (Table 31.2).
   b. WBC count is proportional to gestational age, with the total counts of premature infants approximately 30% to 50% lower than those of term infants.

H. **Platelets**.
1. Small, nonnucleated, disk-shaped cells aid in hemostasis, coagulation, and thrombus formation.
   a. Platelets are derived from megakaryocytes in the bone marrow.
   b. Disrupted endothelium stimulates platelet plug formation and initiates hemostasis.
2. After release into the bloodstream, platelets will circulate 7 to 10 days before removal by the spleen. In the absence of injury, they circulate freely without wall adhesion or aggregation with other platelets.
3. Normal range is 150,000 to 400,000/mm^3 in the term infant. Premature infants have a lower

Table 31.2

Normal Leukocyte Values in Premature and Term Infants

Age (hours)	Total White Cell Count	Neutrophils	Bands/Metas	Lymphocytes	Monocytes	Eosinophils
Term Infants						
0	10.0 to 26.0	5.0 to 13.0	0.4 to 1.8	3.5 to 8.5	0.7 to 1.5	0.2 to 2.0
12	13.5 to 31.0	9.0 to 18.0	0.4 to 2.0	3.0 to 7.0	1.0 to 2.0	0.2 to 2.0
72	5.0 to 14.5	2.0 to 7.0	0.2 to 0.4	2.0 to 5.0	0.5 to 1.0	0.2 to 1.0
144	6.0 to 14.5	2.0 to 6.0	0.2 to 0.5	3.0 to 6.0	0.7 to 1.2	0.2 to 0.8
Premature Infants						
0	5.0 to 19.0	2.0 to 9.0	0.2 to 2.4	2.5 to 6.0	0.3 to 1.0	0.1 to 0.7
12	5.0 to 21.0	3.0 to 11.0	0.2 to 2.4	1.5 to 5.0	0.3 to 1.3	0.1 to 1.1
72	5.0 to 14.0	3.0 to 7.0	0.2 to 0.6	1.5 to 4.0	0.3 to 1.2	0.2 to 1.1
144	5.5 to 17.5	2.0 to 7.0	0.2 to 0.5	2.5 to 7.5	0.5 to 1.5	0.3 to 1.2

From Oski, F. A., & Naiman, J. L. (1982). *Hematologic problems in the newborn* (3rd ed.). Philadelphia, PA: W. B. Saunders.

platelet count with a broader range of normal (Deschmann and Sola-Visner, 2018). Counts are 20% to 25% lower in infants who are small for gestational age.

4. Neonatal platelets are hypoactive in the first few days after birth; this property protects against thrombosis but may increase risk of bleeding and coagulopathy.

I. **Blood volume.**
   1. Volume of blood is measured in milliliters per kilogram of body weight.
   2. Factors affecting blood volume.
      a. Gestational age.
         1) Term infant: approximately 80 to 100 mL/kg.
         2) Preterm infant: approximately 90 to 105 mL/kg.
      b. Placental transfusion.
         1) Timing of cord clamping.
         2) Position of infant relative to placenta (above or below) before cord clamping.
         3) Timing and strength of uterine contractions.
         4) Onset of respiration and decrease in pulmonary vascular resistance.
         5) Cord compression.
      c. Maternal–fetal or fetal–maternal transfusion.
      d. Twin-to-twin transfusion.
      e. Placenta previa or abruptio placentae.
      f. Nuchal cord.
      g. Iatrogenic loss.

Coagulation

Hemostasis is accomplished by biochemical and physiologic events initiated to stop the flow of blood when vessel injury occurs (Saxonhouse, 2018).

A. **Deficiencies in newborn clotting mechanisms.**
   1. Transient diminished platelet function.
   2. Transient deficiency of clotting factors II, VII, IX, X, XI, and XII. Neonatal levels are approximately 50% of adult levels in the early weeks after birth (Blackburn, 2013).
      a. Immaturity of hepatic enzymes responsible for production.
      b. Transient deficiency of vitamin K, needed for synthesis of factors II, VII, IX, and X.
      c. Factor concentrations: proportional to gestational age.

B. **Hemostatic mechanisms.**
   1. Vascular: damaged vessel contracts, minimizing blood loss.
   2. Intravascular: platelet plug formation. Platelet function is stimulated by exposure to damaged endothelial lining. Platelets:
      a. Swell and develop thornlike projections.
      b. Adhere to subendothelial fibers.
      c. Secrete adenosine diphosphate to trigger swelling and adhesiveness in nearby platelets.
      d. Aggregate and form platelet plug.
   3. Extravascular.
      a. Compression by surrounding tissue.
      b. Release of tissue thromboplastin by injured tissue.

C. **Coagulation process.**
   1. Cascade of events, requiring both cellular and plasma components (Fig. 31.2).
   2. Culminates in the formation of fibrin-based clots and requires serial activation of precursor zymogens.
   3. Calcium, iron, and phospholipids are key components of the coagulation cascade.
      a. Extrinsic system triggered by tissue injury and exposure of cell membrane tissue factor.
      b. Intrinsic system triggered by vascular endothelial injury; amplifies factor X activation, which is a cofactor common to intrinsic and extrinsic pathways.
      c. Factor X activation begins the process of prothrombin-to-thrombin conversion. Conversion hydrolyzes fibrinogen (soluble protein in plasma) to fibrin (insoluble, threadlike polymer) and activates factor XIII, stabilizing fibrin threads into a meshwork to trap platelets and other cells to form the clot.
   4. Intravascular clotting is balanced by concurrent fibrinolysis.
      a. Inactive plasminogen synthesized by the liver is converted to plasmin, an active enzyme, when a fibrin clot is present.
      b. Plasmin begins fibrin clot dissolution, releasing fibrin degradation products (FDPs), also called *fibrin split products (FSPs),* into the circulation.
      c. FDPs exert an anticoagulant effect by interfering with clot formation and the function of platelets, thrombin, and fibrinogen.

D. **Coagulation tests** (Pal et al., 2015) (Table 31.3).
   1. Platelet count is used to assess platelet number.
   2. Prothrombin time (PT) is used to assess extrinsic and common portions of the coagulation cascade. In neonates, a prolonged PT reflects decreased vitamin K–dependent clotting factors.
   3. Partial thromboplastin time (PTT) is used to assess intrinsic and common portions of the coagulation cascade. A prolonged PTT in a neonate reflects a decrease in both vitamin K–dependent factors and contact factors (XI, XII, prekallikrein).
   4. Fibrinogen level is used to assess the circulating level of this protein substrate, required for clot formation. The presence of fetal fibrinogen may result in falsely elevated fibrinogen levels in the newborn.
   5. Individual clotting factors may be assayed, depending on results of the tests cited earlier.

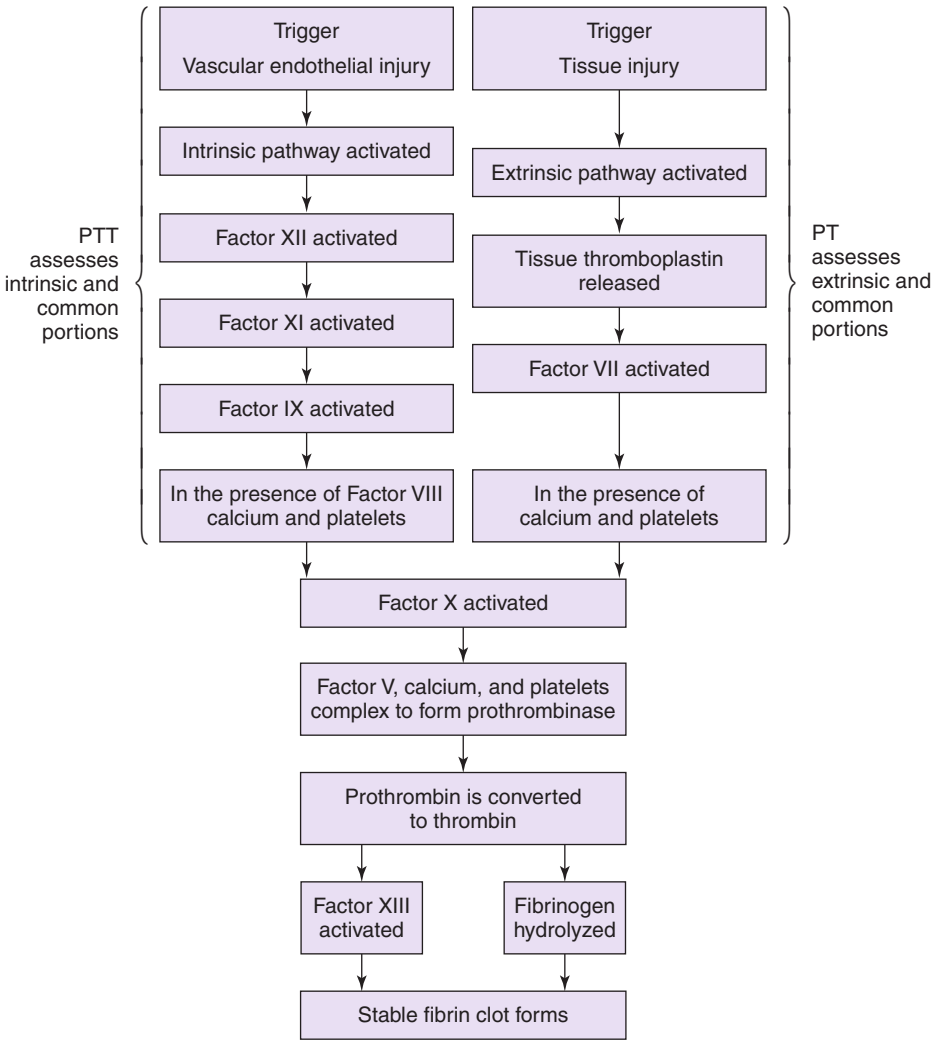

Fig. 31.2 Fibrin clot formation through activation of intrinsic or extrinsic pathways of coagulation process. *PT,* Prothrombin time; *PTT,* partial thromboplastin time.

Part 3

Table 31.3

Normal Values for Tests of Hemostasis

Parameter	FETUSES (WEEKS OF GESTATION) 19 to 23 (*n* = 20)	24 to 29 (*n* = 22)	30 to 38 (*n* = 22)	Newborns (*n* = 60)	Adults (*n* = 40)
PT (s)	32.5 (19 to 45)	32.2 (19 to 44)†	22.6 (16 to 30)†	16.7 (12.0 to 23.5)*	13.5 (11.4 to 14)
PT (INR)	6.4 (1.7 to 11.1)	6.2 (2.1 to 10.6)†	3 (1.5 to 5)*	1.7 (0.9 to 2.7)*	1.1 (0.8 to 1.2)
APTT (s)	168.8 (83 to 250)	154 (87 to 210)†	104.8 (76 to 128)†	44.3 (35 to 52)*	33 (25 to 39)
TCT (s)	34.2 (24 to 44)*	26.2 (24 to 28)*	21.4 (17 to 23.3)	20.4 (15.2 to 25)†	14 (12 to 16)
Factor					
I (g/l, Von Clauss)	0.85 (0.57 to 1.50)	1.12 (0.65 to 1.65)	1.35 (1.25 to 1.65)	1.68 (0.95 to 2.45)†	3 (1.78 to 4.50)
I Ag (g/l)	1.08 (0.75 to 1.50)	1.93 (1.56 to 2.40)	1.94 (1.30 to 2.40)	2.65 (1.68 to 3.60)†	3.5 (2.50 to 5.20)
IIc (%)	16.9 (10 to 24)	19.9 (11 to 30)*	27.9 (15 to 50)†	43.5 (27 to 64)†	98.7 (70 to 125)
VIIc (%)	27.4 (17 to 37)	33.8 (18 to 48)*	45.9 (31 to 62)	52.5 (28 to 78)†	101.3 (68 to 130)
IXc (%)	10.1 (6 to 14)	9.9 (5 to 15)	12.3 (5 to 24)†	31.8 (15 to 50)†	104.8 (70 to 142)
Xc (%)	20.5 (14 to 29)	24.9 (16 to 35)	28 (16 to 36)†	39.6 (21 to 65)†	99.2 (75 to 125)
Vc (%)	32.1 (21 to 44)	36.8 (25 to 50)	48.9 (23 to 70)†	89.9 (50 to 140)	99.8 (65 to 140)
VIIIc (%)	34.5 (18 to 50)	35.5 (20 to 52)	50.1 (27 to 78)†	94.3 (38 to 150)	101.8 (55 to 170)

Continued

Table 31.3

Normal Values for Tests of Hemostasis—cont'd

Parameter	FETUSES (WEEKS OF GESTATION) 19 to 23 (*n* = 20)	24 to 29 (*n* = 22)	30 to 38 (*n* = 22)	Newborns (*n* = 60)	Adults (*n* = 40)
XIc (%)	13.2 (8 to 19)	12.1 (6 to 22)	14.8 (6 to 26)†	37.2 (13 to 62)†	100.2 (70 to 135)
XIIc (%)	14.9 (6 to 25)	22.7 (6 to 40)	25.8 (11 to 50)†	69.8 (25 to 105)†	101.4 (65 to 144)
PK (%)	12.8 (8 to 19)	15.4 (8 to 26)	18.1 (8 to 28)†	35.4 (21 to 53)†	99.8 (65 to 135)
HMWK (%)	15.4 (10 to 22)	19.3 (10 to 26)	23.6 (12 to 34)†	38.9 (28 to 53)†	98.8 (68 to 135)

From Nathan, D. G., Orkin, S. H., Ginsberg D., & Look, A. T. (Eds.). (2003). *Nathan and Oski's hematology of infancy and childhood* (6th ed., p. 1855). Philadelphia, PA: W. B. Saunders.

Ag, Antigenic value; *APTT*, activated partial thromboplastin time; *c*, coagulant activity; *HMWK*, high-molecular-weight kininogen; *INR*, International Normalized Ratio; *PK*, protein kinase; *PT*, prothrombin time; *TCT*, thrombin clotting time. Values are the mean, followed in parentheses by the lower and upper boundaries including 95% of the population.

* $P = 0.05$.

† $P = 0.01$.

E. **Physiologic anemia of infancy** (Gallagher, 2015).
   1. Hemoglobin levels decline after birth, reaching a physiologic nadir at 8 to 12 weeks. Hemoglobin levels at this time are typically around 11 g/dL (110 g/L).

Anemia

Low hemoglobin concentration and/or decreased number of RBCs diminishes the oxygen-carrying capacity of the blood and the level of oxygen available to the tissues. Anemia at birth can be classified into three major causes: (1) the result of blood loss (hemorrhage); (2) shortened RBC survival, including hemolysis; or (3) underproduction of erythrocytes (Gallagher, 2015).

A. **Etiologic factors.**
   1. Hemorrhage.
      a. Fetal–maternal. Occurs in 50% to 75% of all pregnancies. May be acute or chronic. In 1% of pregnancies, the exchange of blood exceeds 15 mL (Gallagher, 2015).
         1) Spontaneous.
         2) Traumatic amniocentesis.
         3) External cephalic version.
      b. Twin-to-twin: 8% to 15% of monochorionic twins (Gallagher, 2015).
         1) Monozygotic, monochorionic (single) placenta.
         2) Hemoglobin difference between twins greater than 5 g/dL (50 g/L).
      c. Placental/cord.
         1) Umbilical cord rupture.
         2) Cord or placental hematoma.
         3) Anomalous cord insertion.
         4) Rupture of anomalous vessels of cord or placenta.
         5) Accidental incision of cord or placenta.
         6) Placenta previa or abruptio placentae.
      d. Internal.
         1) Intracranial (subdural, subarachnoid, intraventricular), subgaleal.
         2) Organ rupture (liver, spleen, adrenal, kidney).
         3) Pulmonary.
      e. External.
         1) Phlebotomy.
         2) Iatrogenic (e.g., catheter losses).
   2. Hemolysis.
      a. Blood group incompatibilities.
         1) Rh incompatibility: erythroblastosis fetalis (Liley et al., 2015).
            a) Sequence of events: fetal blood cells containing Rh antigen (Rh positive) enter the maternal circulation; maternal RBCs have no antigen (Rh negative); maternal immune system produces antibodies against the foreign fetal antigens; in subsequent pregnancies, maternal antibodies enter fetal circulation and destroy fetal RBCs.
            b) Predisposing factors.
               (1) Previous pregnancy or abortion.
               (2) Fetal–maternal hemorrhage during pregnancy.
               (3) Delivery (vaginal, breech, cesarean).
               (4) Amniocentesis, chorionic villus sampling.
               (5) External version.
               (6) Manual removal of placenta.
            c) Infant presentation.
               (1) Anemia (caused by hemolysis, resulting in increased production of very immature RBCs).
               (2) Tissue hypoxia, acidosis (decreased RBC count and decreased oxygen-carrying capacity of immature cells).
               (3) Congestive heart failure and hydrops fetalis (fetus attempts to expand

blood volume and cardiac output, resulting in generalized edema).
(4) Ascites, pleural effusion (fluid collecting in large cavities).
(5) Hepatosplenomegaly (increased extramedullary hematopoiesis).
(6) Petechiae (thrombocytopenia accompanying severe anemia).
(7) Hypoglycemia (increased RBC destruction stimulates insulin secretion, resulting in hyperplasia of pancreatic islets and hyperinsulinemia).
(8) Positive direct Coombs' test result.

d) Prophylactic therapy: anti-D immune globulin.
(1) Anti-D antibodies injected into maternal circulation (one dose accommodates approximately 15 mL of fetal whole blood or approximately 30 mL of RBCs).
(2) Destruction of fetal RBCs in maternal circulation, blocking maternal antibody production.
(3) Ninety percent effective in prevention of sensitization.
(4) Recommended administration at 28 weeks of gestation; within 72 hours after delivery; and after amniocentesis, chorionic villus sampling, percutaneous umbilical blood sampling, or evidence or possibility of fetal–maternal hemorrhage.

2) ABO incompatibility (Christensen, 2018; Manco-Johnson et al., 2016).
a) More frequently occurring but less severe hemolytic disease than with Rh incompatibility.
b) Most often seen in mothers with O blood type (absence of antigen) carrying fetus with A or B blood type (see Table 31.4 for other potential incompatibilities).
c) Maternal exposure to naturally occurring A and B antigens in food, bacteria, and pollen initiates maternal production of anti-A and anti-B antibodies and accounts for occurrence of disease with first pregnancy.
d) ABO incompatibility protects against fetal Rh disease because of rapid destruction of fetal A/B cells, preventing Rh antigen exposure and maternal antibody production.
e) Infant presentation includes the following:
(1) Mild hemolysis, anemia, reticulocytosis.
(2) Hyperbilirubinemia (occasionally requiring exchange).

b. Enzymatic defect: glucose-6-phosphate dehydrogenase (G6PD) deficiency (see also Chapter 29).
1) Most common inherited disorder of RBCs (sex-linked disease affecting mainly male offspring, occasionally female carriers).
2) Interaction of intracellular abnormality (deficiency of RBC enzyme) and extracellular factor (exposure to oxidant stress: drugs, infection), causing hemolysis and shortened erythrocyte life.
3) Most common occurrence in African American infants (10% to 15%) and in infants of Mediterranean, African, and Asian descent.

c. Hemoglobin disorders (Christensen, 2018; Sankaran et al., 2015).
1) α-Thalassemia.
a) Deletion of one or more of the four α-globin genes.
b) Severity of expression is related to the number of globin genes missing.
(1) Silent carrier—single gene deletion, asymptomatic.
(2) α-Thalassemia trait—deletion or dysfunction of two genes resulting in mild microcytic anemia.
(3) Hemoglobin H disease—absence or nonfunction of three globin genes. Mild to moderate hemolytic anemia exacerbated by oxidant stresses.
(4) α-Thalassemia (homozygous)—deletion of all four globin genes results in hydrops fetalis and, often, fetal death as a result of severe intrauterine hemolytic anemia.
c) Most common in infants of Southeast Asian, Middle Eastern, and Mediterranean descent.
2) β-Thalassemia.
a) Occurs as a result of deletion of β-globin gene.
b) Most common in infants of Southeast Asian, African, or Mediterranean descent.
c) Neonates occasionally present with hemolytic anemia.

Table 31.4
Potential Maternal–Fetal ABO Incompatibilities

Maternal Blood Group	Incompatible Fetal Blood Group
O	A or B
B	A or AB
A	B or AB

d) Does not usually present before 2 months of age because of the presence of HbF.

d. Infection. Intrauterine (viral, protozoan, spirochetal) and postnatal (bacterial) infection may cause neonatal hemolysis, anemia, thrombocytopenia, and disseminated intravascular coagulation (DIC).

3. Anemia of prematurity.
   a. Hemoglobin concentration at birth varies only slightly in relation to gestational age.
   b. During the first 2 to 3 months, hemoglobin concentration falls to the lowest value that occurs at any developmental period.
   c. Anemia of prematurity is considered physiologic because it is characteristic of healthy infants.
   d. Associated factors.
      1) Rates of decline and nadir are inversely proportional to gestational age.
      2) Iron concentration is low because of decreased blood volume and decreased concentration of circulating hemoglobin iron.
      3) Improved extrauterine oxygen delivery causes a temporarily inactive stage of erythropoiesis.
      4) Erythropoietin production in response to anemia is diminished.
      5) Shortened RBC life span decreases RBC mass.
      6) Growth causes dilutional anemia as a result of decreased hemoglobin concentration with expanding blood volume.
      7) Despite rapid hemoglobin fall, tissue oxygenation is maintained by events responsible for right shift of the hemoglobin–oxygen dissociation curve.
   e. Some infants do manifest symptoms of hypoxemia (poor feeding and weight gain, dyspnea, tachypnea, tachycardia, diminished activity, pallor) in the absence of other problems and require transfusion.
4. Iatrogenic postnatal phlebotomy. Critically ill infants who require frequent monitoring may have excessive amounts of blood removed for diagnostic studies, thereby inducing anemia. Removal of more than 20% of the blood volume over 24 to 48 hours can produce anemia; in a 1500-g infant this represents approximately 25 mL (Dror et al., 2016).

B. **Clinical presentation: varies with the volume of hemorrhage and the time period over which the blood is lost.**
   1. Acute blood loss.
      a. Pallor initially and then cyanosis and desaturation.
      b. Shallow, rapid, irregular respirations.
      c. Tachycardia.
      d. Weak or absent peripheral pulses.
      e. Low or absent blood pressure, low venous pressure.
      f. Hemoglobin concentration may be normal initially, with rapid decline over 4 to 12 hours with hemodilution.
   2. Chronic blood loss.
      a. Pallor without signs of acute distress.
      b. Possible signs of congestive heart failure with hepatomegaly.
      c. Normal blood pressure, normal or elevated venous pressure.
      d. Low hemoglobin concentration.

C. **Clinical assessment.**
   1. Family history.
      a. Bleeding, anemia, splenectomy.
      b. Consanguinity.
      c. Ethnic and geographic origins.
      d. Blood group incompatibilities.
      e. Previous child with anemia or jaundice.
   2. Maternal history.
      a. Blood type.
      b. Late third-trimester bleeding.
      c. Infection.

D. **Physical examination.**
   1. Signs of acute or chronic blood loss, as noted earlier.
   2. Jaundice.
   3. Cephalohematoma.
   4. Abdominal distention or mass: liver, spleen, adrenal, kidney rupture.
   5. Petechiae, purpura.
   6. Cardiovascular abnormalities: tachycardia, murmur, gallop rhythm.
   7. Hydropic changes.

E. **Diagnostic studies.**
   1. Hemoglobin concentration: normal hemoglobin values are dependent on gestational age, site of sampling, and timing of cord clamping (Gallagher, 2015). Values vary according to birth weight and postnatal age (Table 31.5).
   2. Reticulocyte count: this reflects new erythroid activity and is persistently elevated with ongoing RBC destruction.
   3. Peripheral blood smear.
      a. Test evaluates alterations in size, shape, and structure of RBCs that might enhance destruction because of decreased deformability.
      b. Fragmentation of RBCs can be identified.
   4. Blood type to identify common blood group antigens: A, B, O, and Rh.
   5. Direct antiglobulin test (DAT).
      a. Positive DAT indicates presence of maternal immunoglobulin G (IgG) antibodies on the surface of infant's RBCs.
      b. Positive result on indirect antiglobulin test means that antibodies against the infant's RBCs are present in the maternal serum.

Table 31.5

Serial Hemoglobin Values in Low Birth Weight Infants

	HEMOGLOBIN CONCENTRATION (g/dL) BY AGE				
Birth Weight (g)	**2 weeks**	**4 weeks**	**6 weeks**	**8 weeks**	**10 weeks**
800 to 1000	16 ± 0.6	10.2 ± 3.2	8.7 ± 1.5	8 ± 0.9	8 ± 1.1
1001 to 1200	16.4 ± 2.3	12.8 ± 2.5	10.5 ± 1.8	9.1 ± 1.3	8.5 ± 1.5
1201 to 1400	16.2 ± 1.3	13.4 ± 2.8	10.9 ± 1.2	9.9 ± 1.9	—
1401 to 1500	15.6 ± 2.2	11.7 ± 1	10.5 ± 0.7	9.8 ± 1.4	—

From Oski, F. A. (1994). Hematologic problems. In G. B. Avery (Ed.): *Neonatology: Pathophysiology and management of the newborn* (4th ed.). Philadelphia, PA: Lippincott.

6. Kleihauer–Betke test.
   a. Test identifies fetal hemoglobin in maternal blood.
   b. Calculations indicate volume of fetal–maternal hemorrhage and dose of anti-D immune globulin (Rhogam) required to prevent sensitization.

F. **Differential diagnosis:** diseases that diminish oxygen delivery to the tissues (e.g., pulmonary, cardiac).

G. **Complications**.
   1. Inadequate tissue oxygenation, poor growth.
   2. Transfusion.
      a. Transfusion reaction.
      b. Overhydration with pulmonary congestion.

H. **Patient care management** (see "Transfusion Therapies").
   1. Emergency treatment for acute blood loss resulting in hypovolemia.
      a. Whole blood or packed RBCs (PRBCs).
         1) Type: group O, Rh negative.
         2) Amount: 10 to 20 mL/kg.
      b. Saline solution if blood is unavailable.
         1) Amount: 10 to 15 mL/kg.
   2. Nonemergency replacement transfusion: clinical decision based on adequacy of tissue oxygenation in the individual infant.
      a. Advantages of transfusion must be weighed against risks, including infection, graft-versus-host disease, and other complications.
      b. Consider gestational and postnatal age; intravascular volume; and coexisting cardiac, pulmonary, or vascular conditions.
   3. Exchange transfusion.
      a. Treatment of jaundice caused by blood group incompatibility.
      b. Partial exchange if necessary to treat severe anemia of hydrops without increasing intravascular volume.

I. **Outcome**.
   1. Improved tissue oxygenation and resolution of symptoms with replacement transfusion.
   2. Long-term outcome varies with degree of anemia and underlying cause.

Hemorrhagic Disease of the Newborn

Hemorrhagic disease of the newborn (HDN) is caused by vitamin K deficiency and decreased activity of factors II, VII, IX, and X. Previously referred to as "hemorrhagic disease of the newborn," the newer term, *vitamin K–dependent bleeding (VKDB)* is thought to describe more accurately the link between vitamin K deficiency and spontaneous hemorrhage and to exclude newborn infants with bleeding from other causes (Blackburn, 2013; Johnson, 2013; Pipe and Goldenberg, 2015).

A. **Etiologic factors: primary vitamin K deficiency.**
   1. Required for activation of clotting factors II, VII, IX, and X and of proteins C and S after liver synthesis.
      a. Vitamin K is important in the formation of calcium binding sites, which are necessary for functional activation of clotting factors.
      b. In the absence of vitamin K, circulating proteins are decarboxylated; levels of protein induced by vitamin K absence (PIVKA) can be used as an indirect measure of bleeding risk.
   2. Limited vitamin K availability.
      a. Inadequate placental transfer.
      b. Deficient hepatic stores.
      c. Limited postnatal dietary intake.
         1) Human milk contains 1 to 5 mcg/L of vitamin K. The use of one dose of oral vitamin K at birth, in conjunction with exclusive breastfeeding, has been implicated in some cases of late-onset VKDB (McMillan, 1997/2016).
   3. Three forms of vitamin K deficiency are recognized:
      a. Early—within 24 hours in neonates born to women taking certain anticonvulsants, antitubercular medications, and vitamin K antagonists such as warfarin (Coumadin).
      b. Classic or VKDB—seen at 2 to 6 days.
         1) Incidence is 0.25 to 1.7 per 100 live births if no vitamin K is given (Johnson, 2013).
      c. Late onset—occurs at 2 to 12 weeks in infants not receiving vitamin K at birth or receiving an inadequate oral dose and breastfeeding or in

infants with hepatobiliary disease. Intracranial bleeding is more common in late-onset disease.

B. **Clinical presentation of VKDB**: bleeding.
   1. Begins at 24 to 72 hours of age.
   2. May be localized or diffuse.
   3. Rarely life threatening.
   4. Late-onset bleeding possible at approximately 2 to 3 weeks of age.

C. **Clinical assessment:** oozing.
   1. Localized: frequently gastrointestinal (hematemesis, melena).
   2. Diffuse: umbilical cord, circumcision, puncture sites.

D. **Physical examination.**
   1. Diffuse ecchymosis, petechiae.
   2. Oozing puncture sites.
   3. Abdominal distention.
   4. Jaundice.

E. **Diagnostic studies.**
   1. Response to vitamin K administration establishes the diagnosis.
   2. PT and PTT are prolonged.
   3. Levels of vitamin K–dependent clotting factors are low.
   4. PIVKA levels are elevated.

F. **Differential diagnosis.**
   1. Decreased absorption of vitamin K.
      a. Biliary atresia.
      b. Cystic fibrosis.
      c. Cholestasis.
   2. Pharmacologic antagonism of vitamin K (Saxonhouse, 2018).
      a. Anticonvulsants (hydantoin, phenobarbital, carbamazepine, diazepam), anticoagulants (coumarin, warfarin), and antibiotics (cephalosporins, isoniazid, quinolones, and rifampin).
      b. Coumarol derivatives: replace with heparin during pregnancy.
      c. Maternal supplementation with oral vitamin K from 36 weeks of gestation to delivery might prevent neonatal hemorrhage associated with anticonvulsant therapy; extra vitamin K given to the mother to increase vitamin K available to the fetus.

G. **Complications**.
   1. Anemia.
   2. Intraventricular/intracranial hemorrhage.

H. **Patient care management.**
   1. Prophylactic vitamin K at the time of delivery.
      a. Phytonadione (naturally occurring vitamin K), 1 mg intramuscular (IM) administration for term infant, 0.5 mg for premature infants (American Academy of Pediatrics [AAP], 2015).
      b. The Canadian Paediatric Society (Canadian Paediatric Society, Fetus and Newborn Committee, 2012) and the AAP (2015) recommend the use of only IM vitamin K at birth because of the history of prevention of life-threatening HDN with the parenteral preparation and the need for further research on the efficacy, safety, and bioavailability of oral preparations.
      c. Late HDN occurs primarily in breastfed infants who have not received adequate vitamin K prophylaxis.
         1) Parental concern with IM administration of vitamin K might stem from the following:
            a) Need for injection.
            b) Exposure to preservatives.
            c) Reports linking IM vitamin K to childhood cancer (Weddle et al., 2015).
      d. Commercial formulas contain vitamin K supplement.
      e. Intestinal flora of breastfed infant may produce less vitamin K than that of formula-fed infant.
   2. Significant bleeding (hemoglobin concentration <12 g/dL). PRBC infusion may be indicated.
   3. Persistent bleeding in premature infant.
      a. Fresh frozen plasma (FFP) infusion may be indicated to replace clotting factors.
      b. Repeated doses of vitamin K are needed.

I. **Outcome.** Prophylactic treatment has virtually eliminated the disease.

Disseminated Intravascular Coagulation

DIC is an acquired hemorrhagic disorder associated with an underlying disease manifested as uncontrolled activation of coagulation and fibrinolysis. Consumption of clotting factors is thought to be initiated by release of thromboplastic material from damaged or diseased tissue into the circulation. In DIC, fibrinogen converts to fibrin to form microthrombi. Neonates are at increased risk of DIC because of inherent imbalances between fibrinolytic, anticoagulant, and procoagulant factors, particularly decreased levels of antithrombin and protein C (Blackburn, 2013; Manco-Johnson et al., 2016; Pipe and Goldenberg, 2015).

A. **Common precipitating factors.**
   1. Maternal.
      a. Preeclampsia, eclampsia, and placental abruption.
      b. Placental abnormalities.
   2. Intrapartal.
      a. Fetal distress with hypoxia and acidosis.
      b. Dead twin fetus.
      c. Traumatic delivery.
   3. Neonatal.
      a. Infection (bacterial, viral, fungal).
      b. Conditions causing hypoxia, acidosis, and shock.
      c. Severe Rh incompatibility.

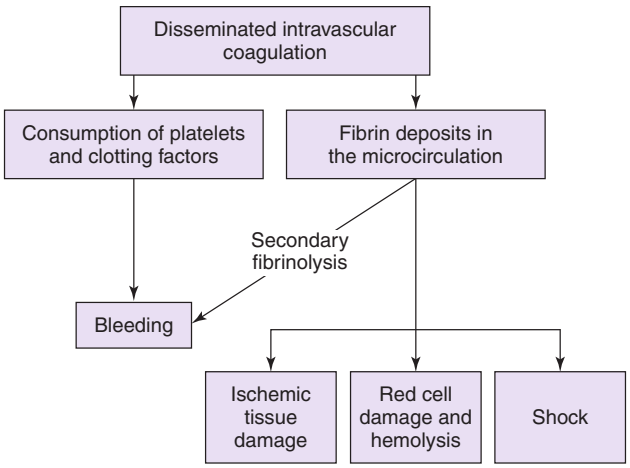

Fig. 31.3 Sequence of events in pathologic changes of disseminated intravascular coagulation.

d. Thrombocytopenia.
e. Tissue injury (birth trauma, breech crush injury, necrotizing enterocolitis [NEC]).

B. **Clinical presentation** (Fig. 31.3).
1. Hemorrhage: predominant symptom.
a. Clotting factors and platelets are depleted.
b. Fibrinolysis is stimulated.
c. Endogenous thrombin and plasmin are formed.
2. Organ and tissue ischemia. Microvascular thrombosis (occlusion) by fibrin thrombi causes potential ischemia and necrosis of any organ, particularly the kidneys.
3. Anemia.
a. Blood loss.
b. RBC fragmentation by fibrin strands.

C. **Clinical assessment.**
1. Review the history for precipitating factors.
2. Concurrent evidence of coagulation and fibrinolysis.

D. **Physical examination.**
1. Variable signs, depending on underlying disease process.
2. Prolonged oozing from puncture sites or umbilicus.
3. Petechiae, purpura, ecchymosis.
4. Hemorrhage (pulmonary, gastrointestinal, cerebral).
5. Localized necrosis and gangrene resulting from microvascular thrombosis of peripheral vessels.

E. **Diagnostic studies.**
1. Variable diagnostic studies are performed for delineation of the underlying disease process.
2. Platelet count is low.
3. PT and PTT are prolonged in 50% to 60% of patients (Pipe and Goldenberg, 2015).
4. Peripheral blood smear identifies microangiopathic hemolytic anemia, abnormalities of RBC shape, cell fragmentation, and decreased number of platelets.
5. Fibrinogen level is low.
6. Fibrinogen degradation products are significantly increased but are not specific markers of DIC.
7. D-Dimer is a sensitive marker for endogenous thrombin/plasmin production and can detect much milder forms of DIC.
8. Additional factors and levels might be evaluated: factors VIII and II are decreased, as well as protein C, protein S, and antithrombin III.

F. **Differential diagnosis.**
1. Parenchymal liver disease.
2. Vitamin K deficiency.
3. Microangiopathic disease.
4. Primary fibrinogenolysis.

G. **Complications**.
1. Microvascular thrombosis.
2. Organ failure resulting from ischemia and necrosis, especially renal.
3. Intraventricular and parenchymal hemorrhage.

H. **Patient care management.**
1. Aggressive treatment of the underlying disease.
2. Supportive care.
a. Replacement transfusion with significant bleeding.
1) Whole blood for hypovolemia and shock.
2) PRBCs for isovolemic anemia.
3) Platelets for consumption.
b. Maintenance of blood pressure.
3. Measures to control DIC.
a. Replacement of clotting factors.
1) FFP (replaces all factors, coagulation proteins, and coagulation inhibitors; small amount of fibrinogen).
2) Platelet concentrates.
3) Cryoprecipitate (replaces fibrinogen, factor VIII).
4) Antithrombin III (inhibits coagulation, controls fibrinolysis). High doses (120 to 250 units/kg/day) might attenuate organ failure and reverse coagulopathy in DIC without heparin therapy.
b. Heparin therapy remains controversial; use if treatment of underlying disease and replacement of clotting factors fail to reverse the process or with evidence of significant large-vessel thrombosis.
1) Goals are to interrupt fibrin deposition and to achieve normal fibrinogen levels and platelet counts.
2) Continuous infusion is more physiologic and is safer because intermittent doses may aggravate existing hemorrhage.
3) Dosage is adjusted to maintain PTT within 60 to 70 seconds (once achieved, lower-dose heparin therapy may control ongoing consumption).

I. **Outcome: related to the prognosis of the underlying disease and the severity of the DIC.**

Thrombocytopenia

Thrombocytopenia is an acquired disease in which there is a significant decrease in the platelet count (<150,000/mm^3) of the term or premature infant (Blickstein and Friedman, 2015; Dror et al., 2016). Severe thrombocytopenia is estimated to occur in 1 in 700 neonates (Kamphuis et al., 2014).

A. **Etiologic factors.**
   1. Platelet destruction.
      a. Maternal autoantibodies (autoimmune): idiopathic thrombocytopenic purpura, systemic lupus erythematosus.
         1) Maternal autoantibodies bind to platelet surface antigens, making them susceptible to premature destruction.
         2) IgG antibodies cross the placenta and destroy fetal platelets.
            a) Approximately 10% to 15% have cord platelet counts of less than 100,000/mm^3 (half of these have counts <50,000/mm^3).
            b) Nadir usually occurs on the second day.
            c) Counts can be depressed for 2 to 4 months (as long as maternal IgG antibodies remain in circulation).
         3) Maternal platelet count is low.
      b. Neonatal conditions.
         1) Neonatal alloimmune thrombocytopenia—major cause of significant thrombocytopenia in a healthy neonate (Kamphuis et al., 2014).
            a) Analogous to Rh incompatibility.
               (1) Fetal platelets contain an antigen lacking in the mother.
               (2) Fetal platelets enter maternal circulation, resulting in maternal production of antibodies against foreign platelets.
               (3) Maternal antibodies cross into fetal circulation and coat fetal platelets, which are then destroyed.
            b) Fetal thrombocytopenia can occur as early as 20 weeks of gestation.
            c) Nadir occurs in the first few days; counts normalize by the end of the first month.
            d) About 15% to 25% have intracranial hemorrhage (approximately 10% occur in utero).
            e) Maternal platelet count remains normal.
            f) Workup includes both neonatal and parental blood screening for human platelet antigens (HPAs).
            g) Treatment includes platelet transfusion, preferably with matched platelets, steroids, and intravenous immunoglobulin (IVIG) (Mella and Eddelman, 2014).
         2) Infection: bacterial (especially gram-negative sepsis) or congenitally acquired (rubella, cytomegalovirus, herpes, enterovirus, or human immunodeficiency virus).
            a) Megakaryocyte degeneration in bone marrow.
            b) Can cause DIC (platelet consumption).
            c) Activates reticuloendothelial system (increased platelet sequestration).
            d) Platelets may form antigen–antibody complexes with infectious agent.
         3) Thrombotic disorders.
            a) Large-vessel disease (renal vein thrombosis).
            b) Microvascular disease (NEC, respiratory distress syndrome, persistent pulmonary hypertension of the newborn).
            c) DIC (platelet consumption).
         4) Birth asphyxia. Fetal megakaryocytes may have increased sensitivity to hypoxic injury.
         5) Giant hemangiomas.
            a) Kasabach–Merritt syndrome. Vascular malformation results in platelet and fibrinogen consumption.
            b) Mechanical destruction and sequestration.
         6) Exchange transfusion: shortened survival of transfused platelets.
   2. Impaired platelet production (rare, <5%) associated with congenital malformations.
      a. Trisomy syndromes (13, 18). Bone marrow hypoplasia affects megakaryocyte production.
      b. Thrombocytopenia with absent radii syndrome.
         1) Defective megakaryocyte progenitor cell.
         2) Presentation at birth, improvement thereafter.
         3) Anomalies of the radius but not the thumb.
      c. Fanconi's anemia.
         1) Thumb, skeletal, renal, and central nervous system (CNS) anomalies; café-au-lait spots.
         2) Thrombocytopenia: presentation rare in the neonatal period; worsens with time.
      d. Other rare syndromes associated with unusually small or giant platelets.
   3. Platelet interference: maternal drug ingestion.
      a. Interference with platelet aggregation.
      b. Meperidine (Demerol), promethazine (Phenergan), acetylsalicylic acid, sulfonamides, quinidine, quinine, thiazides.

B. **Clinical presentation:** platelet-type bleeding.
   1. Petechiae, purpura, epistaxis.
   2. Ecchymosis over presenting part.
   3. Cephalohematoma.

4. Bleeding (mucous membranes, gastrointestinal tract, genitourinary system, umbilical cord, puncture sites, superficial cuts, or abrasions).

C. **Clinical assessment.**
1. Family history: bleeding complications in previous children, other family members.
2. Maternal history.
   a. History of bruising or bleeding, infections, collagen vascular disease, splenectomy.
   b. Platelet count (low or normal).
   c. Peripheral blood smear (may show low platelet count, increased immature forms).
   d. Medication history.
3. Birth history.
   a. Hypoxia.
   b. Infection risk.

D. **Physical examination.**
1. Signs of clinical presentation.
2. Jaundice.
3. Intrauterine growth restriction, microcephaly, hepatosplenomegaly with infectious cause (absent with immune etiology).
4. Congenital anomalies consistent with syndromes.

E. **Diagnostic studies.**
1. Platelet count is low.
2. Peripheral blood smear shows low platelet count and increased immature forms; may show abnormal size.
3. PT and PTT are normal for age.
4. Bleeding time is prolonged.
5. Maternal blood can be tested for HPA type and for the presence of platelet-specific antibody (up to 2 weeks postpartum).
6. In severe cases, platelet typing of mother, father, and infant might be indicated.

F. **Differential diagnosis: DIC, vitamin K deficiency.**

G. **Complications**.
1. Cranial hemorrhage with neurologic sequelae in alloimmune disease.
   a. Associated with approximately 12% mortality rate.
   b. Increased incidence in infants weighing less than 1500 g.
2. Entrapped hemorrhage.
3. Anemia.
4. Hyperbilirubinemia.

H. **Infant management** (see Table 31.5).
1. Supportive care and treatment of underlying disease. Majority of neonatal thrombocytopenia is secondary to other disease processes.
2. Cesarean delivery.
   a. Autoimmune.
      1) Rarely of benefit for infant.
      2) Consider if:
         a) Maternal disease is severe, with high antibody levels.
         b) Prior infant was severely affected.
   b. Alloimmune: maternal HPA typing not routinely done; infants identified postnatally.
3. Platelet transfusion.
   a. Recommended goal: keep platelet count greater than 30,000/mm^3 in the first 48 hours, and greater than 50,000/mm^3 if surgery is necessary or infant is premature and at risk for intraventricular hemorrhage.
   b. Autoimmune.
      1) Rarely needed; platelet counts greater than 20,000/mm^3, usually benign course.
      2) Consider transfusion if platelet counts less than 50,000/mm^3 for clinically unstable or very low birth weight (VLBW) infants.
      3) Consider transfusion if platelet counts less than 20,000/mm^3 for other stable preterm infants (Sparger et al., 2015).
   c. Alloimmune.
      1) Serial transfusions may be necessary.
      2) Obtain HPA type for infant before transfusion.
      3) Transfusion of random donor platelets rarely results in sustained increase because of antibody destruction.
      4) Transfuse maternal platelets (in absence of HPA) that have been washed and resuspended in AB-negative plasma.
   d. Production defects: repeated transfusions usually necessary.
4. Steroids.
   a. May be used in infants with platelet counts less than 25,000/mm^3 and clinical bleeding.
   b. May be used for initial treatment of thrombocytopenia resulting from hemangioma.

I. **Outcome**.
1. Varies with underlying disease, presence of congenital malformations.
2. Autoimmune etiology: usually causes only mild, transient problems, with full recovery of platelet count in 8 to 12 weeks.
3. Isoimmune etiology: causes mild to moderate problems with full recovery of platelet count in 6 to 8 weeks.

Polycythemia

Polycythemia is a condition in which infants demonstrate an excess in circulating RBC mass. Blood viscosity increases with hematocrits greater than 65% or when venous hemoglobin is greater than 22 g/dL (220 g/L) and leads to a reduction of blood flow to the organs. Occurs in 1% to 2% of live births, increasing to 5% at high altitudes (Gallagher, 2015).

A. **Etiologic factors** (Gallagher, 2015).
1. Intrauterine hypoxia, placental insufficiency. Hypoxia stimulates erythropoiesis, increasing the fetal RBC mass.

a. Maternal preeclampsia/eclampsia.
b. Postmaturity syndrome, intrauterine growth restriction.
c. Maternal smoking.
2. Maternal–fetal and twin-to-twin transfusion.
3. Maternal diabetes: possibly resulting from abnormal fetal erythrocyte deformability.
4. Congenital syndrome resulting in increased RBC mass.
5. Perinatal hypoxia.

B. **Clinical presentation.**
1. Many infants are asymptomatic.
2. Plethora.
3. Cyanosis.
4. CNS abnormalities (lethargy, jitteriness, seizures).
5. Respiratory distress (tachypnea, pulmonary edema, pulmonary hemorrhage).
6. Tachycardia, congestive heart failure.
7. Hypoglycemia.
8. Poor feeding behaviors (poor nippling, regurgitation).

C. **Clinical assessment: history and physical examination usually identify cause.**

D. **Physical examination.**
1. Findings may be normal except for plethora and occasionally cyanosis.
2. Symptoms of clinical presentation cannot be attributed to other disease.

E. **Diagnostic studies.** Venous hemoglobin concentration and hematocrit are elevated. Computed tomography scan if stroke suspected.

F. **Complications.**
1. Hyperbilirubinemia.
2. Hypoglycemia—mechanism unknown.
3. Hyperviscosity syndrome: elevated whole blood viscosity associated with reduced blood flow, organ damage, seizures, NEC, and possible poor developmental and neurologic outcomes (Gallagher, 2015).

G. **Patient care management.**
1. Administration of a normal saline bolus. For asymptomatic infants with a hematocrit greater than 70% or those with symptoms and a hematocrit between 65% and 70%, a bolus of 10 mL/kg of normal saline may be adequate.
2. Partial exchange transfusion.
a. Controversial in asymptomatic infants. Has not been shown to decrease neurologic morbidity (Gallagher, 2015).
b. Desired reduction of hematocrit to less than 60% (blood viscosity is thought to be relatively normal at this level).
c. Gastrointestinal symptoms: 11-fold increased risk of NEC after partial exchange transfusion (New et al., 2016).
3. Supportive treatment of persistent symptoms.

H. **Outcome** (Gallagher, 2015; New et al., 2016).
1. Neonates with proven hyperviscosity are at risk of an adverse neurologic outcome.

Inherited Bleeding Disorders

Although inherited bleeding disorders were recognized as early as AD 600, the specific clotting abnormalities have been delineated only in this century, with the last (deficiency of factor XIII) documented in 1963. Although the overall incidence of these genetic disorders is rare and phenotypic expression is extremely variable, it is estimated that 15% to 33% of infants with an inherited bleeding disorder will present with symptoms in the newborn period (Chalmers, 2004).

A. **Etiologic factors.**
1. Hemophilia.
a. Ninety percent of infants with hemophilia will have either classic hemophilia (hemophilia A, factor VIII deficiency) or Christmas disease (hemophilia B, factor IX deficiency).
1) Incidence of hemophilia A is 1 per 5000 male births (Diab and Luchtman-Jones, 2015).
2) Incidence of hemophilia B is 1 per 30,000 male births (Diab and Luchtman-Jones, 2015).
b. X-linked recessive inheritance.
1) Gene is located on the X chromosome.
2) Females are carriers; disease is present in male infants because they have only one X chromosome, which carries the abnormal gene (no normal X chromosome as counterbalance).
3) Each pregnancy carries a 25% chance of occurrence (50% of the male offspring will be affected).
4) Up to 70% percent have a family history of a male with a bleeding disorder (Kumar and Carcao, 2013).
2. von Willebrand's disease.
a. Autosomal dominant inheritance.
1) Males and females are equally affected.
2) Each pregnancy carries a 50% chance of occurrence.
3) Transmission is vertical (disease is seen in successive generations).
b. Gene expression markedly variable (family history may be absent despite dominant inheritance).
3. Factor XIII deficiency: autosomal recessive inheritance.
a. Both parents are phenotypically normal carriers.
b. Males and females are equally affected.
c. In each pregnancy, 25% of the offspring will be affected, 50% will be carriers, and 25% will be normal.

d. Expression is horizontal (deficiency is seen in siblings; skips a generation).

B. Clinical presentation (Saxonhouse, 2018).
1. Rare newborn presentation except for factor XIII deficiency.
2. Usually well infant with delayed bleeding.
3. Clotting screening results usually normal.

C. **Clinical assessment.**
1. Late bleeding.
a. Delayed umbilical cord bleeding (>80% with factor XIII).
b. Circumcision oozing: most common site of bleeding (45%) (significant hemorrhage is rare).
c. Intracranial hemorrhage (17%).
2. Family history.

D. **Diagnostic studies.**
1. PT, PTT, platelet count, fibrinogen level (usually normal).
2. Specific factor assays (identification by factor levels and DNA analysis).
a. Factor VIII levels should be comparable to normal adult levels in the newborn period.
b. Factor IX levels are normally low in the neonatal period; however, infants with bleeding presentation will be severely affected, with less than 2% activity (clearly abnormal level).

E. **Patient care management.**
1. Optimal mode of delivery for infants at risk of hemophilia is controversial (Bravo et al., 2016).
2. Initial correction is with FFP (contains adequate amounts of all clotting factors except factor VIII).
3. Cryoprecipitate can be used if bleeding persists after use of FFP (enriched with approximately 20 units of factor VIII per milliliter).
4. Diagnosis allows replacement of specific factor.
a. Recombinant factor VIII is available for classic hemophilia.
b. Purified (monoclonal antibody) factor IX is available for Christmas disease.
c. Prothrombin concentrates are not recommended for neonatal use because of thrombogenicity.
5. Use precautions to prevent bleeding.
a. Immunizations should be given subcutaneously, with an ice pack applied to the site post injection.

F. **Outcome: episodic bleeding requiring lifelong replacement.**

Transfusion Therapies

A. **Recommendations for use of blood components** (Canadian Paediatric Society, Fetus and Newborn Committee, 2012; Dror et al., 2016; Patel and Josephson, 2018).
1. Develop and document criteria indicating need.
2. Use only the blood components required for therapy.
3. Use crystalloid or nonblood colloid whenever possible.
4. Use universal precautions when handling blood products.

B. **Written, informed consent has been recommended since 1986 to ensure that families understand risks and explore alternatives.**
1. Ethical or religious basis: autonomy—the right of choice.
2. Legal basis: failure to inform adequately and to obtain consent constitutes negligence.
3. Time-consuming: start a few days in advance of need (i.e., include in discussion on the first day of life of sick preterm infants).

C. **Informed consent includes discussion of the following:**
1. Risks (American Red Cross, 2013; Fasano et al., 2015; Keir et al., 2016).
a. Infection.
1) Blood is screened for human immunodeficiency viruses types 1 and 2 (HIV-1, HIV-2), hepatitis B virus (HBV), hepatitis C virus (HCV), Chagas' disease (*Trypanosoma cruzi*), human T-lymphotropic virus, West Nile virus, and *Treponema pallidum* (syphilis).
2) Cytomegalovirus transmission can be prevented by using cytomegalovirus-seronegative blood or leukocyte-depleted, irradiated products.
3) Major risks for transmission via transfusion (Fasano et al., 2015).
a) HIV infection incidence is 1 per 2.3 million using nucleic acid testing.
b) HBV (hepatitis B surface antigen) infection incidence is 1:300,000.
c) HCV infection incidence is 1 in 1.8 million.
4) Predonation questions foster self-elimination of prospective donors with high-risk behaviors.
5) Confidential unit exclusion allows donors to designate the elimination of their donation if they recognize risk but want to avoid the embarrassment of refusing to donate.
b. Transfusion reactions (rare in neonates).
1) Febrile reactions (Fasano et al., 2015).
a) Probably caused by transfused (passenger) WBCs and/or their cytokine products (RBC and platelet transfusions).
b) Leukocyte reduction might prevent reaction.
(1) Expensive and time-consuming.
(2) One unit of PRBCs can contain 1 billion WBCs.

(3) WBCs can be removed by centrifugation or by filtering at donation (pre-storage leukocyte depletion) or at transfusion (bedside filtration).

2) Allergic reactions.
   a) Urticaria, angioedema, asthma.
   b) Higher incidence with multiple transfusions.
3) Hemolytic reactions.
   a) Usually ABO incompatibilities.
   b) Possible acute or delayed hemolysis.
   c) Most reactions can be eliminated by typing, screening, and cross-matching.
4) Transfusion-related acute lung injury (TRALI) (Fasano et al., 2015).
   a) Pulmonary edema occurring within 4 hours after a transfusion.
   b) Probably under-recognized in preterm infants because of preexisting lung disease.

c. Graft-versus-host disease (Fasano et al., 2015).
   1) Risk factors include neonates with congenital immunodeficiency syndromes, those receiving intrauterine or exchange transfusions, and extremely premature infants.
   2) Immature immune system may not reject foreign lymphocytes (present in erythrocyte and platelet products); donor lymphocytes proliferate and damage the host (infection and neutropenia).
   3) Clinical symptoms (within 100 days of transfusion) include rash, diarrhea, hepatic dysfunction, and bone marrow suppression with generalized reduction in all cell lines (pancytopenia).
   4) Gamma irradiation of blood products will prevent lymphocyte proliferation.
      a) Mature erythrocytes and platelets are resistant to radiation damage.
      b) Enhances efflux of potassium ion from RBCs (store <28 days, wash to remove excess potassium before transfusion).
d. Hemodynamic complications.
   1) Fluid overload: volumes should not exceed 20 mL/kg.
   2) Hypoglycemia, metabolic acidosis, hyperkalemia, and hypocalcemia.
e. NEC, also referred to as *transfusion-related acute gut injury (TRAGI)* (Fasano et al., 2015).
   1) Some evidence has been presented that suggested a relationship between RBC transfusions and late-onset NEC in low birth weight infants (Amin et al., 2012). More recent research now suggests that the presence of significant anemia is responsible for NEC that presents after a blood transfusion rather than the transfusion itself (Patel et al., 2016).

2. Expected benefits.
   a. Whole blood (increases hematocrit approximately 35%).
      1) Replacement of blood volume.
      2) Treatment (massive hemorrhage, exchange transfusion).
   b. PRBCs: typically 10 to 15 mL (Fasano et al., 2015).
      1) Improved oxygen-carrying capacity and tissue oxygenation.
      2) Relief of symptoms of anemia (tachypnea, apnea, periodic breathing, tachycardia, poor weight gain).
      3) Treatment (active bleeding, hemolytic disease, extracorporeal membrane oxygenation).
   c. Platelets.
      1) Improved coagulation.
      2) Treatment (hemorrhage caused by thrombocytopenia or platelet dysfunction).
   d. FFP: replacement of clotting factor deficiency.
   e. Albumin.
      1) Volume expansion; improved oncotic pressure.
      2) Treatment (for hypovolemia, third-space losses).
3. Alternatives.
   a. Directed donation.
      1) Family and friends with compatible blood type can donate for infant.
      2) Blood must be irradiated to prevent graft-versus-host disease.
      3) There is no evidence of overall increased safety in comparison with anonymous volunteer donations.
         a) Donors might be more truthful (i.e., regarding acceptability for donation) because they know the recipient.
         b) Donors might be less truthful because they feel pressure to donate.
      4) Parental donation.
         a) Maternal plasma is unacceptable for transfusion to neonates because of the possible presence of antibodies directed against inherited paternal antigens on infant's cells.
         b) Maternal platelets and RBCs can be used if washed before transfusion.
         c) Paternal donation might be problematic if infant has circulating maternal antibodies produced by stimulation of inherited paternal antigens.
      5) All blood products from directed donors should be irradiated. Potential antigen similarities between close family members may impede recognition and destruction of foreign lymphocytes.

b. Delayed cord clamping has been shown to decrease the need for transfusions among VLBW infants (Fasano et al., 2015).
c. Erythropoietin (EPO) (Fasano et al., 2015; Lopez et al., 2015).
   1) Recombinant human EPO (r-HuEPO) might be used to treat symptomatic anemia caused by physiologic decline in hematocrit or by blood loss from phlebotomy, or it might be used as a prophylactic therapy to minimize blood product exposure in preterm or sick neonates.
   2) Plasma EPO levels are lower in anemic preterm infants, suggesting responsibility for hematocrit decline.
      a) The liver, the initial site of EPO production at early gestation, is less responsive than the kidneys to tissue hypoxia caused by anemia.
      b) EPO pharmacokinetics differ in preterm infants as follows: faster rate of clearance, larger volume of distribution, shorter elimination and mean residence times.
      c) Clearance increases with duration of r-HuEPO therapy, suggesting the need for progressively higher doses.
   3) Variable results and small sample sizes hamper clinical trials testing different doses and treatment schedules.
      a) Therapy with r-HuEPO and iron stimulates erythropoiesis and increases reticulocyte counts.
      b) Increase in reticulocyte count is dose dependent.
      c) Oral iron supplement, adequate to support enhanced erythropoiesis, may not be tolerated. Intravenous iron therapy has not yet been adequately studied to ensure absence of oxidant injury and toxic metabolites; however, preterm infants appear to need a supplement of 4 to 4.5 mg/kg of dietary iron to prevent late anemia (Canadian Paediatric Society, Fetus and Newborn Committee, 2012).
      d) The combination of r-HuEPO and iron stimulates erythropoiesis in infants of ≤1250 g birth weight; however, support for the use of EPO in neonates has been mixed. In a Cochrane review done in 2017, Ohlsson and Aher concluded that the erythropoietin resulted in a small reduction in the need for transfusions, but the reduction was not likely to be clinically significant (Ohlsson and Aher, 2017).
d. Thrombopoietin. Recombinant human thrombopoietin is currently under development and testing for use as a megakaryocyte enhancer.
e. G-CSF: currently under investigation; stimulates growth of neutrophil colonies and induces maturation of promyelocytes to mature neutrophils.

D. **Transfusion volumes.**
   1. Transfusions with PRBCs: for prevention of overhydration, replacement is usually given in increments of 15 mL/kg.
   2. Partial exchange transfusions.
      a. With normal saline solution: treatment of polycythemia (to reduce hematocrit without reducing blood volume).
      b. With PRBCs: treatment of hydrops fetalis (to correct anemia without increasing blood volume).
      c. Calculations for total exchange volume:
         1)

$$\text{Volume of normal saline solution to exchange} = \frac{\text{Blood volume} \times (\text{Measured hematocrit} - \text{Desired hematocrit})}{\text{Measured hematocrit}}$$

         2)

$$\text{PRBC volume to exchange} = \frac{\text{Blood volume} \times (\text{Desired hematocrit} - \text{Measured hematocrit})}{\text{PRBC hematocrit} - \text{Measured hematocrit}}$$

   3. Exchange transfusions.
      a. Single unit of blood (approximately 250 mL) will usually exchange twice the blood volume and remove 85% of the initial RBCs and 25% to 45% of the available intravascular bilirubin (Fasano et al., 2015).
      b. For treatment of hyperbilirubinemia.
      c. Because preservatives provide a significant glucose load, rebound hypoglycemia may occur.
      d. Preservatives contain citrate, which binds calcium and magnesium; hypocalcemia and hypomagnesemia may occur.
      e. Potassium level rises as blood ages; blood should be less than 5 days old.
   4. Platelets.
      a. One unit (approximately 40 mL) provides approximately 5×10^{10} platelets; transfusion of 10 to 15 mL/kg of platelets should increase the platelet count by 50,000 to 100,000/mm^3 (Fasano et al., 2015).
      b. Routine volume reduction (platelet concentration) before transfusion is not indicated in infants.
      c. Platelets are separated from single units of whole blood within 6 hours of collection and suspended in small amounts of plasma, or they are obtained by apheresis (single-donor platelets).
   5. FFP.
      a. FFP is usually transfused in increments of 10 mL/kg to minimize overhydration.

b. Transfusion of 15 to 20 mL/kg replaces all coagulation proteins present in adult concentrations.
c. Plasma is obtained from a unit of whole blood and frozen within 6 hours of collection.

6. Cryoprecipitate.
   a. Transfusion volume is usually 1 unit/kg (approximate volume, 15 mL).
   b. One unit contains approximately 100 to 250 mg of factor I (fibrinogen), approximately 80 to 100 units of factor VIII (von Willebrand's factor), and 50 to 75 units of factor XIII.
7. Albumin.
   a. For volume expansion, 5% albumin is usually administered in increments of 10 mL/kg; for improvement of oncotic pressure, 25% albumin might be used in increments of 1 g/kg (4 mL/kg).
   b. Albumin is a major contributor to oncotic pressure because of molecular size and weight.
8. Granulocytes.
   a. Collected by leukapheresis and selectively harvested from whole blood.
   b. Granulocyte transfusions are rarely used due to the difficulty in isolation and the lack of evidentiary support (Dror et al., 2016).

Evaluation by Complete Blood Cell Count

The complete blood cell count is used in evaluating RBCs, WBCs, and platelets. The WBC indices are reviewed in Chapter 32.

A. **Evaluation of RBC indices.**
   1. Identification of diseases affecting synthesis of hemoglobin.
   2. RBC morphology.
      a. Anisocytosis: abnormal variation in size of erythrocytes (severe anemia).
      b. Macrocytosis: diameter greater than 9 mcm (increased cell volume: vitamin B_{12} and folic acid deficiencies).
      c. Microcytosis: diameter less than 9 mcm (decreased cell volume: iron deficiency, spherocytic and hemolytic anemias).
      d. Poikilocytosis: variation in shape (severe anemia).
      e. Spherocytosis: increased thickness and rounding (decreased deformability and greater susceptibility to destruction; seen in congenital spherocytosis, hemolytic anemias, after transfusion of stored blood).
      f. Target cells: thin, with large diameter, dark center and periphery, and a clear ring between the periphery and the center (hemoglobinopathies, sickle cell/thalassemia, liver disease).
      g. Burr cells: crenations; long spinous processes (hemolytic anemias, DIC, liver disease).
      h. Howell–Jolly bodies: spherical blue bodies in or on erythrocytes; nuclear debris (in asplenia, pernicious anemia).
      i. Nucleated RBCs: immature RBCs with nuclei still present (in chronic blood loss, significant hemolysis, chronic hypoxia, infection).

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CHAPTER 32

Infectious Diseases in the Neonate

Kathryn M. Rudd

OBJECTIVES

1. Differentiate the methods of acquisition of neonatal infection.
2. Identify risk factors for infection associated with term and preterm infants.
3. Describe clinical signs and symptoms of infection and septic shock.
4. Calculate the absolute neutrophil count and immature/total neutrophil ratio from a complete blood cell count and differential cell count.
5. Identify the common gram-positive and gram-negative organisms responsible for bacterial infections in the neonatal period.
6. Name common broad-spectrum antimicrobial agents used to treat neonatal sepsis and discuss indications for and risks of their use.
7. Differentiate between mucocutaneous, systemic, and cutaneous candidiasis.
8. Identify clinical symptoms and therapies associated with ToRCHES CLAP spectrum infections.
9. List prevention strategies for hospital-acquired infections.

Neonatal sepsis is defined as a systemic bacterial, viral, or fungal infection that occurs in the first 28 days of life with hemodynamic changes that result in significant morbidity and mortality (Barnden et al., 2016; Shane et al., 2017). The immature immune system of a neonate is characterized by immature activation and function of immune responses that make newborns more susceptible to infections with a frequency and intensity greater than at any other period of life. Neonatal sepsis is the highest within the first 28 days of life and is the third leading cause of neonatal deaths behind prematurity and intrauterine complications (Zea-Vera and Ochoa, 2015). Precise estimates of the incidence of neonatal sepsis vary throughout the world with significant economic determinants (Shane et al., 2017). Up to 40% of the survivors will have some neurologic sequelae (Wynn, 2016). Data collected from 2000 to 2010 estimate that 15% of neonatal deaths worldwide are due to sepsis (Barnden et al., 2016; Lui et al., 2012). Altered pharmacokinetics in neonates is complicated by slower drug absorption, higher volume of distribution, and a less efficient metabolism and elimination of medications (Rivera-Chaparro et al., 2017).

More than 1 million newborns globally die each year from sepsis. In the United States, as many as 1 to 4 infants per 1000 live births will have early-onset sepsis (EOS), and as many as 250 infants per 1000 live births will acquire late-onset sepsis (LOS) (Bulkowstein et al., 2016). The incidence of septicemia increases substantially in very low birth weight (VLBW) and extremely low birth weight (ELBW) premature infants and results in 50% mortality (Wynn, 2016). *Neonatal sepsis* is a general term used to define actual or potential infection in the neonatal and newborn period and is defined on a continuum. The diagnosis of sepsis remains one of the most difficult diagnostic tasks. Early detection and implementation of therapy are critical. Failure to identify early signs of sepsis contributes to morbidity, mortality, and increased health care costs. This chapter provides a comprehensive review of common neonatal infections, treatment modalities, and the latest recommendations for reducing hospital-acquired infections.

Transmission of Infectious Organisms in the Neonate

Neonatal sepsis can be divided into EOS that occurs within the first week of life and LOS that occurs after 7 days of life (Bulkowstein et al., 2016). EOS often presents in the first 24 hours, with the leading causative organisms being group B streptococcus (GBS) in developed countries followed by *Escherichia coli* (Barnden et al., 2016). EOS are thought to be acquired through vertical transmission, whereas LOS can be a result of the environment in the hospital or the community (Barnden et al., 2016). LOS can occur up to 90 days after birth and result from GBS, coagulase-negative Staphylococci, *Staphylococcus aureus, E. coli,* and *Haemophilus influenzae* (Bulkowstein et al., 2016).

A. Vertical transmission: mother to infant.
   1. Intrauterine acquisition with intact membranes—organism most commonly crosses transplacentally from maternal bloodstream through the placenta to the fetus, but may be a direct extension of an infected uterus, ascend from the genital tract, or descend through the fallopian tubes.
      a. May result in death and embryo reabsorption, abortion, stillbirth, premature delivery, low birth weight (LBW), congenital anomalies, sepsis, or congenital disease.
   2. Intrapartum acquisition after rupture of membranes: organism may ascend through genital tract with prolonged rupture of membranes. Infection may also result from aspiration of infected amniotic fluid or occur by colonization during passage of the fetus through the birth canal. Infection has also been demonstrated to occur through skin abrasions, such as scalp electrodes during labor.
   3. Postpartum acquisition: transmission through maternal breast milk to infant of several viruses, including human immunodeficiency virus (HIV), hepatitis B virus, and cytomegalovirus (CMV).

B. **Horizontal transmission:** transmission to the infant from nursery personnel, family members and visitors, contaminated hospital equipment, invasive procedures and devices, and blood products; also known as a *nosocomial infection* or *hospital-acquired infection (HAI).*

Risk Factors

IDENTIFICATION OF PREDISPOSING RISK FACTORS FOR NEONATAL INFECTION

A. **Maternal**.
   1. Antepartum risk factors include inadequate prenatal care, inadequate nutrition, low socioeconomic status, recurrent abortion, substance abuse, history of maternal sexually transmitted infections (STIs), maternal urinary tract infection (UTI), and premature rupture of membranes (PROM).
   2. Intrapartum risk factors include prolonged rupture of membranes (>12 to 18 hours), vaginal GBS colonization, chorioamnionitis, uterine tenderness, purulent amniotic fluid, foul-smelling amniotic fluid, maternal fever greater than 101° F (38° C), prolonged or difficult labor, premature labor, maternal UTI, invasive intrapartum procedures (i.e., internal fetal monitoring), elevated maternal heart rate (>100 beats per minute [bpm]), and elevated fetal heart rate (>180 bpm).

B. **Neonatal**.
   1. Neonatal risk factors include prematurity, LBW, difficult delivery, birth asphyxia, meconium staining, resuscitation, low Apgar score (<6 at 5 minutes), congenital anomalies (i.e., abdominal wall and spinal defects), breach of skin integrity, and multiple-order births.

C. **Environmental**.
   1. Environmental risk factors include hospital admission, length of stay, invasive procedures (i.e., peripheral intravenous [IV] punctures, endotracheal tubes, umbilical catheters, central and peripherally inserted venous lines, thoracotomy tubes, and other surgical interventions), common use of broad-spectrum antibiotics, use of humidification systems in ventilation, and incubator care.

Diagnosis and Treatment

RECOGNITION OF CLINICAL MANIFESTATIONS OF NEONATAL INFECTION

A. **Variable nonspecific presentation of sepsis:** appearance of infant "just not right," accompanied by subtle changes in feeding and activity. Culture-proven sepsis is difficult in the newborn infant; most are symptomatic without correlation of positive cultures.

B. **Specific manifestations of sepsis by systems.**
   1. Thermoregulatory instability: temperature instability, fever, or hypothermia.
   2. Neurologic: lethargy, jitteriness, irritability, seizures, hypotonia or hypertonia, bulging fontanelles, high-pitched or abnormal cry.
   3. Respiratory distress (most common clinical sign): tachypnea, grunting, nasal flaring, retractions, cyanosis, apnea, respiratory acidosis, respiratory insufficiency, and radiologic evidence of pneumonia or pleural effusion.
   4. Cardiovascular: tachycardia or bradycardia; arrhythmias; hypotension or hypertension; cold, clammy, or mottled skin; decreased peripheral perfusion or vasoconstriction; poor peripheral pulses; delayed capillary refill (>3 seconds); cardiomegaly; and poor cardiac function.
   5. Gastrointestinal: poor feeding; vomiting; diarrhea; abdominal distention; feeding intolerance; hypoactive bowel sounds; and radiologic evidence of ileus, portal venous gas, pneumatosis, or free air.
   6. Integumentary: rash, pustules or vesicles, jaundice, pallor, gray undertones, and petechiae.
   7. Internal organ: hepatomegaly and splenomegaly.
   8. Metabolic: hyperglycemia, hypoglycemia, or glucose instability and metabolic acidosis.

C. **Septic/distributive shock:** profound sepsis resulting in insufficient perfusion, oxygenation, and delivery of nutrients to satisfy tissue requirements, resulting in cellular dysfunction and ultimately cell destruction. Lactic acid is one of the end products of anaerobic metabolism, so it is used as an indicator for decreased

perfusion (Friedman and Bone, 2014). Rapid identification and treatment is paramount to preventing impending death (Friedman and Bone, 2014) (see also Chapter 28).

1. Clinical presentation of septic shock.
   a. Tachycardia or bradycardia.
   b. Increased work of breathing, tachypnea, retractions, apnea, progressing to respiratory insufficiency and failure.
   c. Persistent pulmonary hypertension with resulting decreased oxygenation.
   d. Poor perfusion with pallor, mottling, delayed capillary refill (>3 seconds), weak pulses, cool extremities, wide pulse pressures.
   e. Hypotension, decreased urinary output, organ dysfunction, and ileus.
   f. Metabolic acidosis and other electrolyte disorders.
   g. Coagulopathy, oozing, or bleeding; may progress to disseminated intravascular coagulation.
   h. Edema from capillary leak.
   i. Myocardial dysfunction, arrhythmias, impending cardiac arrest.

HEMATOLOGIC EVALUATION

A. Complete blood cell count (CBC).
   1. White blood cell (WBC) count: interpretation is often difficult because of the wide range of normal values in the neonate (5000 to 30,000 cells/mm^3) (Gera et al., 2016; Mischler et al., 2017). WBC count is an unreliable indicator of infection, as leukocyte counts are normal in greater than 30% of infants with proven bacteremia, and leukopenia (<5000 cells/mm^3) or leukocytosis (>20,000 cells/mm^3) may be present when greater than 50% of culture results are negative (Fuchs et al., 2016). This suggests leukocytosis can be a normal finding in the newborn infant. Leukopenia less than 1750 cells/mm^3 is generally considered an abnormal finding and may be due to sepsis, but may also be associated with maternal hypertension, asphyxia, or hemolytic disease.
   2. Differential cell count (Fig. 32.1).
      a. Neutrophil count.
         1) Absolute neutrophil count (ANC) is calculated as:

$$\text{ANC} = \text{WBCs} \times (\%\,\text{Immature neutrophils} + \%\,\text{Mature neutrophils}) \times 0.01.$$

            a) Manroe and colleagues (1979) developed a reference range for the ANC in term infants (Fig. 32.2).
         2) Neutropenia: less than or equal to 1800 cells/mm^3. Affects 6% to 8% of all neonatal intensive care unit (NICU) patients, or as many as 48,000 infants in the United States annually (Gupta et al., 2016; Maheshwari, 2014). Incidence is highest in premature infants and LBW infants, with 6% to 58% occurrence.
            a) Relationship between neutropenia and risk of infection is not well established in neonates, and infants with more than 1000 cells/mm^3 may not be at increased risk (Maheshwari, 2014).
            b) Decision to treat should not be based upon neutropenia alone.
         3) Neutrophilia.
            a) Inconsistent response to infection, often normal with serious infection.
            b) May be elevated at birth (as high as 26,000 cells/mm^3) because of birth stress, maternal fever, ≥6 hours of oxytocin, asphyxia, meconium aspiration, pneumothorax with uncomplicated hyaline membrane disease, seizures, prolonged crying (≥4 minutes), hypoglycemia less than

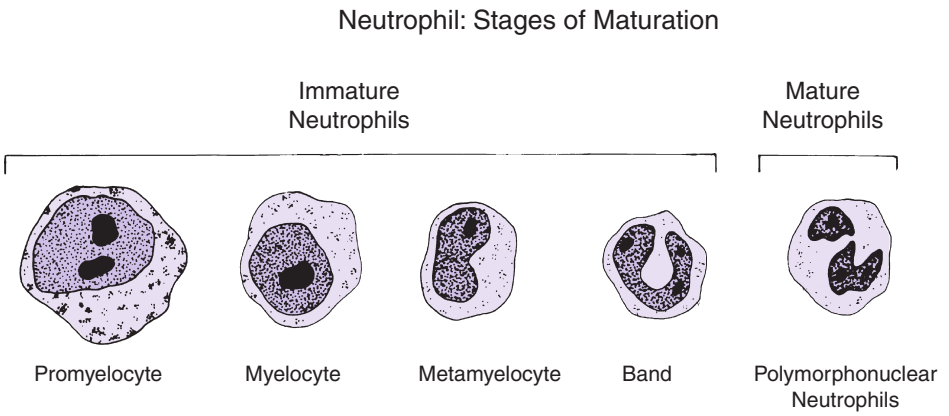

Fig. 32.1 Neutrophils represent a percentage of the total white blood cell count and are reported as the differential on a complete blood cell count.

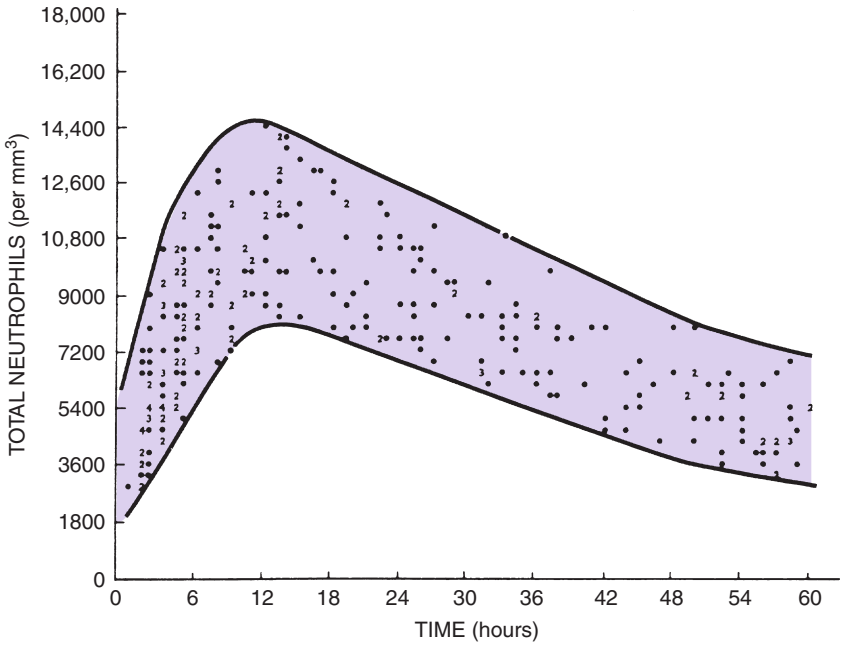

Fig. 32.2 Absolute neutrophil count reference range in the first 60 hours of life. (From Manroe, B. L., Weinberg, A. G., Rosenfeld, C. R., & Browne, R. [1979]. The neonatal blood count in health and disease. *Journal of Pediatrics*, 95[1]:89–98.)

30 mg/dL, hemolytic disease, surgery, and high altitude (Ognean et al., 2017).

b. Immature/total neutrophil (I/T) ratio.
   1) Increase in the I/T ratio is known as a *left shift*; reflects an increase in immature neutrophils.
   2) Not a consistent correlation with presence of serious infection. Low immature band counts may be due to depleted bone marrow reserves producing misleading low I/T ratios.
   3) Best used for negative predictor value. If I/T ratio is normal, likelihood of infection is absent with 99% predictive value (Ognean et al., 2017).
   4) I/T ratio greater than 0.2 to 0.25 is suggestive of infection (Fig. 32.3).
   5) Calculation of I/T ratio:

$$\frac{\%\,\text{Bands} + \%\,\text{Immature } \textit{forms}}{\%\,\text{Mature} + \%\,\text{Bands} + \%\,\text{Immature forms}}$$

3. Platelet count.
   a. Normal count: 100,000 to 400,000/mm^3 in the first 10 days of life, greater than 150,000/mm^3 during the next 3 weeks of life (Anderson-Berry et al., 2015).
   b. Thrombocytopenia (<100,000/mm^3): possible association with bacterial sepsis or viral infection, but usual onset does not occur until 1 to 3 days after infection onset (late indicator) (Ognean et al., 2017). One percent to 5% of neonates and up to 35% in neonates admitted to the NICU experience thrombocytopenia (Fustolo-Gunnink et al., 2016). May also occur with maternal HELLP syndrome (*h*emolysis, *e*levated *l*iver function test results, and *l*ow *p*latelet count), pregnancy-induced hypertension, and intrauterine growth restriction, as well as some syndromes such as trisomies 13, 18, and 21; Turner's syndrome; and hemolytic disease.
   c. Severe and early-onset thrombocytopenia (<50,000/mm^3) is often an indicator of bacterial infection (Fustolo-Gunnink et al., 2016; Gera et al., 2016). With a clinically well infant without proven infection, neonatal alloimmune thrombocytopenia must be considered.

B. **C-Reactive protein (CRP).**
   1. Nonspecific acute-phase reactant globulin synthesized by the liver that appears in the blood during an acute inflammatory process and is closely associated with tissue injury.
   2. May act as a carrier protein facilitating removal of foreign or altered materials from invading microorganisms or damaged tissues. Role remains unclear in activation of immune system pathways (Cortese et al., 2016; Hisamuddin et al., 2015).
   3. Elevated cord blood CRP levels are associated with chorioamnionitis with prolonged rupture of membranes.

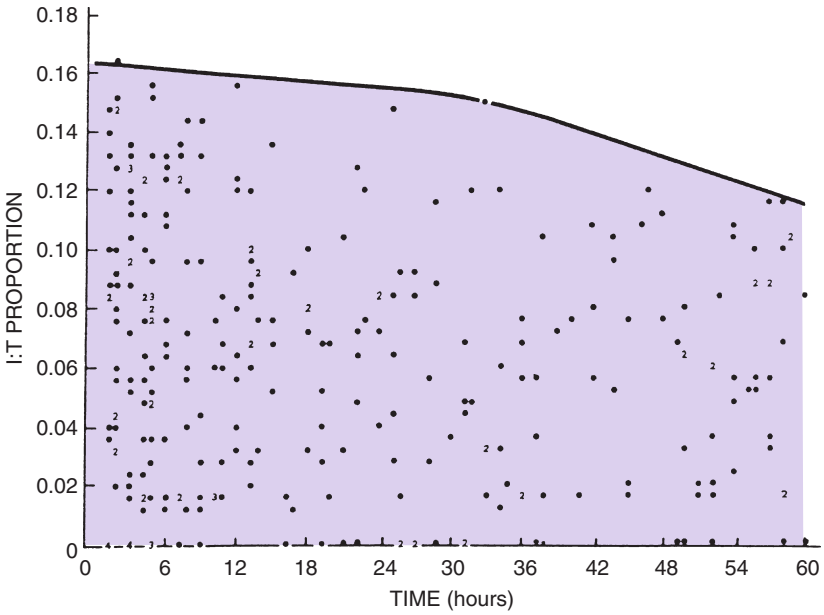

Fig. 32.3 I/T ratio. Reference range for the proportion of immature to total neutrophils in the first 60 hours of life. (From Manroe, B. L., Weinberg, A. G., Rosenfeld, C. R., & Browne, R. [1979]. The neonatal blood count in health and disease. *Journal of Pediatrics*, 95[1]:89–98.)

4. Elevated CRP is also associated with noninfectious conditions that cause tissue damage or inflammation, including asphyxia, respiratory distress syndrome (RDS), intracerebral hemorrhage, surgery, gastroschisis, meconium aspiration, and recent immunizations. This reduces the positive predictive value of the CRP level and its usefulness as a diagnostic tool.
5. Serial CRP levels are helpful in exclusion of serious infection. CRP is 40% sensitive at birth with a delay in 24 hours between onset of symptoms of infection and a rise in CRP (Xu et al., 2016). CRP levels then increase rapidly and peak at 2 to 3 days and remain elevated until infection and associated inflammatory process are resolved. CRP sensitivity in premature infants is 62% on day 1 of life (Hisamuddin et al., 2015). CRP levels then return to normal within 5 to 10 days in most infants. For infants undergoing sepsis evaluation, normal CRP levels 1 to 3 days after initiation of evaluation may have a negative predictive value of 99%, allowing the discontinuation of antibiotic therapy in light of negative cultures (Arunachalam and Pammi, 2015).

C. **Procalcitonin levels:** biomarker levels increase faster than CRP levels but are dependent on day of life and gestational age (Zea-Vera and Ochoa, 2015). Procalcitonin is a propeptide of calcitonin that is produced in the liver and is more specific in bacterial infections as opposed to viral infections (Anderson-Berry et al., 2015; Cortese et al., 2016). Elevated procalcitonin is more definitive than CRP assessments in LOS (Zea-Vera and Ochoa, 2015). Procalcitonin levels are predictive in neonates for bacterial infections after the first 24 hours (Anderson-Berry et al., 2015). Procalcitonin increases in neonatal infections after 4 hours as a result of the inflammatory action of bacterial endotoxins reaching their peak at 6 to 8 hours (Cortese et al., 2016). Procalcitonin levels increase in neonates with RDS, infants who received neonatal resuscitation, infants of mothers who are colonized with GBS, and infants of diabetic mothers (Anderson-Berry et al., 2015).

D. **CD64** is a nonculture neutrophil cell-surface antigen marker that has a high sensitivity for organisms and requires a small amount of blood (Zea-Vera and Ochoa, 2015). This marker is especially useful for premature infants when the amount of blood drawn is difficult to achieve (Zea-Vera and Ochoa, 2015).

E. Future studies in the area of genomics may display the host responses to infection (Arunachalam and Pammi, 2015). Proteomics analyzes the structure, function, and activities of proteins that are elevated in the blood in the presence of infection (Arunachalam and Pammi, 2015). Proteomics has also been used in the analysis of amniotic fluid that provides information on the inflammatory response (Arunachalam and Pammi, 2015).

F. Neonatal sepsis is described as occurring if two of the following criteria are present:
   1. ANC less than 1800 mm^3.
   2. CRP greater than 1 mg/dL.
   3. IT ratio $\geq$0.2.

4. Micro-erythrocyte sedimentation rate (ESR) ≥15 mm at the end of the first hour.
5. Serum direct bilirubin ≥2 meq/dL.
6. Total leukocyte count (TLC) ≤5000/Cumm (Hale et al., 2016).

ADDITIONAL DIAGNOSTIC EVALUATION

A. **Culture:** isolation of a pathogen in a blood culture obtained by using aseptic technique is the "gold standard" for diagnosing infection. Aerobic and anaerobic cultures are utilized to rule out bacterial pathogens; however, they are prone to false-negative and false-positive results (Verstraete et al., 2015).
   1. A minimum of 1 mL of blood should be obtained to improve chances for detection of bacteremia. Collection of only 0.5 mL has been shown to be unreliable in detection of pathogens and may be responsible for false-negative results (Verstraete et al., 2015). Many clinicians suggest cultures from two sites are preferable to substantiate a positive culture; however, single-site blood cultures are effective in isolating bacterial pathogens in neonates (Anderson-Berry et al., 2015). Adequate blood sample volume is associated with 90% sensitivity for bacterial detection and is twice as likely to yield a noncontaminant positive result (Zea-Vera and Ochoa, 2015).
      a. May be falsely negative if mother received antibiotics in labor or if the infant has been exposed to multiple courses of antibiotics.
      b. Bacterial growth is evident within 48 hours for most cultures. Culture results are followed at 24-hour intervals, with a final report at 5 to 7 days.
      c. About 92% of positive blood cultures will be positive by 24 hours (Biondi et al., 2014).
      d. False-positives can occur with contaminated specimens. Differentiating true sepsis from contamination can be challenging. Indicators of possible contamination include increased time (>2 to 3 days) until culture became positive, only a single culture is positive, infant is clinically well, organism is part of normal skin flora, multiple organisms grow in one culture bottle, or different organisms grow in separate cultures. If the infant has clinical deterioration, bacteremia must be presumed rather than a contaminant.
      e. In light of positive cultures, appropriate therapy should be continued and daily cultures drawn until a minimum of two consecutive cultures are negative.

B. **Cerebrospinal fluid (CSF) culture and polymerase chain reaction (PCR).**
   1. Routine use of lumbar puncture remains controversial in early sepsis evaluation. Up to 15% of infants with sepsis develop meningitis and may not have any accompanying clinical symptoms to indicate the disease. Bacterial meningitis occurs in fewer than 1 case per 1000 infants, but risk increases with LBW and prematurity (Simonsen et al., 2014). Lumbar puncture may be reserved for infants with clinical symptoms of central nervous system (CNS) involvement or proven bacteremia, or may be delayed for several days in an unstable infant until stabilization is achieved. The CSF culture results may be sterile after several days on antibiotic therapy, but abnormal CSF assays will still identify the presence of pleocytosis and an inflammatory reaction.
   2. Interpreting CSF findings.
      a. Cell counts vary widely in the first few weeks of life, making interpretation difficult. Additionally, blood in the CSF complicates interpretation.
      b. Polymorphonuclear leukocytes are often present in newborns.
      c. Elevated protein concentration occurs in newborns and is higher in premature and VLBW than term infants. By the third month of life, protein levels reach the normal values for older infants in term babies (<40 mg/dL), but may take longer in premature infants.
      d. CSF glucose concentrations are lower in neonates than in older infants and may be as low as 30 mg/dL in term infants or 20 mg/dL in premature infants (Thomson et al., 2018).
      e. Gram stain smear of CSF can detect organisms in up to 78% of gram-negative meningitis and up to 83% of GBS meningitis. Gram-positive bacteria can be detected for up to 36 hours on antimicrobial therapy, and some gram-negative organisms can be seen for several days (Thomson et al., 2018).
      f. CSF culture.
         1) Positive culture may reflect bacteremia from a bloody tap.
         2) Repeat the CSF tap every 24 to 36 hours until culture is sterile.
         3) Duration of antibiotic therapy is based on when the first negative culture is documented.
         4) There is a direct correlation between adverse neonatal outcomes and persistence of bacteria in the CSF.

C. **Urine culture.**
   1. Incidence of UTI is low in EOS (1% to 2%); yield is significantly higher in LOS (7% to 8%) (Bonadio and Maida, 2014).
   2. Contamination with urine obtained by an external collection bag is high. Urine sample should be obtained by sterile catheterization to avoid contamination and false-positive results.
      a. If urine is obtained by urethral catheterization, a bacterial count greater than 50,000 to 100,000 organisms per milliliter suggests infection.

D. **Repeat studies.**
   1. If a positive culture result has been obtained from blood, CSF, or urine specimen, a follow-up culture specimen should be obtained to document sterilization.
   2. Persistent bacteremia may be caused by resistance to antibiotics, incorrect administration of antibiotics, an occult site of infection that may require surgical intervention (e.g., abscess), or presence of invasive devices left in place during treatment for bacteremia.

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS)

A. Neonatal SIRS is considered a state of physiologic dysregulation that is associated with deviations in laboratory values and vital signs, and despite scientific advances, remains poorly understood. In the neonatal population, SIRS is generally *presumed* to be caused by infection. However, SIRS has many more noninfectious etiologies that produce symptoms mimicking sepsis, and prolonged treatment of presumed occult infection with negative cultures may cloud the timely identification and treatment of the causes of SIRS.

B. Definitions of and guidelines for SIRS have been modified from the adult literature to fit the neonatal population by the International Pediatric Sepsis Consensus Conference, published in 2005 (Goldstein et al., 2005). Based on the guidelines, a neonate must have the presence of two of the following criteria, one of which must be an abnormal temperature or leukocyte count.
   1. Core temperature of greater than 101.3° F (38.5° C) or less than 96.8° F (36° C) measured by axilla or central catheter.
   2. Tachycardia, defined as a mean heart rate greater than 2 standard deviations above normal for age in the absence of external stimulus, painful stimulus, or chronic medications. Otherwise, persistent unexplained elevation over a half-hour to 4-hour time frame.
   3. Bradycardia with heart rate less than 10th percentile for age in the absence of external vagal stimulus, β-blocker medications, or heart disease. Otherwise, persistent unexplained bradycardia over a half-hour to 4-hour time frame.
   4. Mean respiratory rate greater than 2 standard deviations above normal for age, mechanical ventilation related to acute deterioration, not due to neuromuscular disease or general anesthesia.
   5. Elevated or depressed leukocyte count for gestation or greater than 10% immature neutrophils.
   6. Proven or suspected sepsis caused by any pathogen or a clinical syndrome associated with high likelihood of infection. Positive evidence of infection, including derangements in examination, imaging, or laboratory tests, such as WBCs in normally sterile body fluid, perforated viscus, chest x-ray with pneumonia, petechial or purpuric rash, gray undertones, or purpura fulminans.
   7. SIRS in the presence of or as a result of proven or suspected infection (Goldstein et al., 2005).

C. Practitioners have the difficult task of deciding to discontinue empirical antibiotics with negative cultures.
   1. Differential etiologies for SIRS with negative cultures include viral infections, cardiopulmonary diseases (structural heart lesions, patent ductus arteriosus, pulmonary hypertension, pulmonary hypoplasia, surfactant protein deficiency, and bronchopulmonary dysplasia), intraventricular hemorrhage, seizures, subgaleal and intracranial hemorrhage, opiate withdrawal, necrotizing enterocolitis (NEC), malrotation, bowel obstruction (meconium plug syndrome, meconium ileus, Hirschsprung's disease), metabolic disorders, and inborn errors (galactosemia, urea cycle disorders, organic acidemias, adrenal hyperplasia, hypoglycemia, autoinflammatory diseases) (Davis et al., 2017).

THERAPY

A. **Antimicrobial therapy.**
   1. Appropriate antibiotic choice depends on prevalent organisms, age of onset of symptoms, and environmental setting. Additional factors include pharmacokinetics, efficacy, and potential toxicity of antimicrobial agents used.
      a. Treatment for suspected EOS must include antibiotics effective against gram-positive cocci (especially GBS), streptococci species, *Listeria monocytogenes*, and gram-negative enteric bacilli.
      b. Treatment for suspected LOS must include coverage for prevalent HAIs, such as coagulase-negative staphylococci (CoNS) and *S. aureus*, or organisms with increased incidences specific to the individual nursery.
   2. Ampicillin is commonly used in combination with an aminoglycoside, such as gentamicin or tobramycin, for synergy for initial broad-spectrum treatment of suspected or confirmed bacterial EOS.
      a. If GBS is identified in EOS, antibiotic coverage is changed to penicillin for the remainder of therapy. Additional aminoglycoside coverage is not necessary for synergy.
   3. If meningitis is suspected with EOS, ampicillin and cefotaxime are the antibiotics of choice until a specific organism has been identified.
      a. Third-generation cephalosporins, including cefotaxime and ceftazidime, have increased antimicrobial activity against gram-negative bacilli and enhanced penetration across the blood–brain barrier over gentamicin.
      b. Third-generation cephalosporins may lead to rapid emergence of drug-resistant bacteria

when used extensively for presumptive therapy and therefore should be limited to infants with evidence of meningitis or gram-negative sepsis.

4. Vancomycin and an aminoglycoside for synergy are used for initial treatment of suspected bacterial LOS due to penicillin G and ampicillin resistance of the majority of *S. aureus* organisms.
   a. Currently all staphylococcal strains in neonates have been susceptible to vancomycin, but vancomycin-resistant *S. aureus* has been identified in older populations (Clock et al., 2017). Judicious use of vancomycin may help prevent further development of resistance in neonates.
5. Duration of antibiotic therapy is a minimum of 10 to 14 days for proven sepsis with minimal or absent focal infection and a minimum of 21 days for meningitis.
6. If culture results are negative, antimicrobial agents may be discontinued after 48 to 72 hours, though antibiotics are often continued for 5 to 7 days of treatment in symptomatic infants or infants with deteriorating clinical condition despite negative culture results.
7. If the mother was treated before delivery, the antimicrobial course may be extended in the face of negative culture results or if multiple courses of antibiotics have presumably induced low bacterial load (i.e., recent course within 4 days of new-onset infection).

TREATMENT OF SEPTIC SHOCK

A. **Treatment goals of septic shock** include timely management of airway, breathing, and circulation to rapidly restore adequate tissue perfusion and improve patient outcomes (Pomerantz and Weiss, 2016).
   1. Provide adequate ventilatory support and secure appropriate airway.
   2. Treat hypovolemia with isotonic crystalloid (normal saline, lactated Ringer's solution) for acute volume expansion.
   3. Transfuse with packed red blood cells (RBCs), platelets, fresh frozen plasma, or cryoprecipitate for anemia, blood loss for disseminated intravascular coagulation.
   4. Correct metabolic and electrolyte derangements, provide adequate nutrition, and avoid hypoglycemia due to increased energy demands and to avoid catabolism.
   5. Treat hypotension with inotropic agents and consider cortisol.
      a. Dopamine—positive inotropic and chronotropic effects that increase myocardial contractility, dependent on myocardial norepinephrine stores.
      b. Epinephrine—potent inotropic and chronotropic effects, frequently used in infants nonresponsive to dopamine.
      c. Hydrocortisone—cortisol therapy in premature neonates is often used as a third-line treatment of refractory hypotension due to suspected adrenal insufficiency and may result in improved myocardial contractility, stroke volume, and cardiac output. It has been shown to increase blood pressure, decrease heart rate, and reduce the need for other vasoactive medications in neonates (Batton, 2017).
   6. Treat underlying infection.
   7. Evaluate cardiac function and arrhythmias with echocardiogram and electrocardiogram.
   8. Extracorporeal membrane oxygenation for infants greater than 34 weeks of gestation if nonresponsive to other interventions.

TREATMENT GOALS AND PREVENTION STRATEGIES

A. **Differential diagnosis.** Because the findings are so nonspecific, it is often difficult to differentiate neonatal sepsis from other disease. The differential diagnosis for neonatal sepsis in the term or near-term infant generally includes the following systemic infections. Appropriate culture and/or serology distinguishes these infections from neonatal sepsis.
   1. Viral infections such as enteroviruses, herpes simplex virus (HSV), CMV, influenza viruses, respiratory syncytial virus.
   2. Spirochete infections—syphilis.
   3. Parasitic infections—congenital malaria, toxoplasmosis.
   4. Fungal infection—candidiasis.
   5. Other bacterial infections include UTIs, osteomyelitis or septic arthritis, pneumonia, and tuberculosis.
   6. Other diagnoses that may present with similar nonspecific findings include neonatal hypoxia, inborn errors of metabolism, cyanotic congenital heart disease, and neonatal respiratory distress.

Neonatal Septicemia

A. **Neonatal sepsis and incidence.** Neonatal sepsis is a clinical syndrome in an infant 28 days of life or younger. It is manifested by systemic signs of infection and/or isolation of a bacterial pathogen from the bloodstream. Most commonly presents as bacteremia and/or meningitis.
   1. The overall incidence of neonatal sepsis in the United States in the last 10 years is between 1 and 5 per 1000 live births. Term infants have a reported rate of 1 to 2 per 1000 live births. The late preterm rate was 4 to 6 per 1000 live births (Zea-Vera and Ochoa, 2015). Worldwide neonatal sepsis results in 8% of all neonatal deaths (The Global Maternal and Neonatal Sepsis Initiative, 2017).

2. Defined by the age at which onset occurs.
   a. EOS is infection presenting at less than 72 hours (although 85% of EOS begin within 24 hours of age) is caused by maternal intrapartum transmission of invasive organism (Jefferies, 2017; Zea-Vera and Ochoa, 2015).
   b. LOS is infection presenting at greater than 72 hours and is attributed to pathogens acquired postnatally.
   c. Late-late-onset sepsis is defined as occurring in infants born at ≤28 weeks and infection presenting after 3 months of age.
3. The overall incidence of EOS is approximately 1 to 2 per 1000 live births, with increasing rates in premature infants. Mortality was 7% (Cortese et al., 2016).
   a. In VLBW infants (<1500 g birth weight), the incidence was 11 in 1000 live births. Mortality was 18% (Cortese et al., 2016).
   b. Rates of LOS are more common in preterm LBW infants, with rates from 1.87% to 5.42%, with decreasing rates as birth weight increases. LBW neonates are susceptible to the development of sepsis, with prematures especially at risk due to physiologic immaturity (Shane et al., 2017). Premature infants have up to 10 times the risk of developing sepsis than full-term neonates (Shane et al., 2017). The lack of transplacental transfer of maternal IgG antibodies and immune dysfunction increase the preterm infant to developing sepsis (Shane et al., 2017).
   c. African American preterm neonates account for 5.14 cases per 1000 births, with a case fatality rate of 24.4% (Shane et al., 2017).

B. **Responsible organisms.**
1. Currently, *Streptococcus agalactiae* (GBS) accounts for 43%, followed by *E. coli* with 29% (Shane et al., 2017). Combined they account for 70% of EOS and LOS cases (Cortese et al., 2016).
2. In VLBW infants with birth weights of less than 2500 g, rates of GBS were 2.1 in 1000 births and *E. coli* infection rates were 5.1 in 1000 births (Cortese et al., 2016).
   a. Other bacterial agents associated with early onset are *Listeria monocytogenes, H. influenzae, Enterobacter spp., Streptococcus pyogenes,* and *S. pneumoniae.*
3. According to the NICHD Neonatal Research Network Data, cases of LOS are most commonly associated with CoNS (rate of 48%), *S. aureus* (rate of 8%), *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterobacter* spp., *Citrobacter* spp., and *Candida* (Cortese et al., 2016). Gram-negative LOS is less common but has the greater mortality of 19% to 36% (Coretese et al., 2016). Fungal infections account for roughly 12% of LOS in VLBW infants, although the incidence among centers varies widely (Cortese et al., 2016).

COMMON FOCAL SITES AND PATHOGENS

Following are brief descriptions of common focal sites and pathogens that contribute to the overall septicemia seen in neonates.

A. **Meningitis.** Any isolation of a pathogen from CSF culture is generally considered evidence of meningitis, regardless of the CSF cell count or chemistries.
1. Incidence of meningitis has remained stable since the 1970s. Depending on the inclusion criteria, the incidence is between 0.25 and 0.32 per 1000 live births. Occurs in as many as 15% of neonates with bacteremia. In the United States, 72% of infants who had sepsis or meningitis and who presented within 72 hours of birth had infections caused by GBS or *E. coli* (Edwards and Baker, 2017).
2. EOS infections acquired in the first 2 to 6 days after birth reflect vertical transmission from maternal genital tract flora. Those infections acquired after the first week of life suggest vertical transmission with neonatal colonization from maternal flora or horizontal transmission through contact with colonized household or community caregivers.
3. Of neonates who present with early-onset GBS bacteremia, 5% to 10% will develop meningitis. Of those with late-onset GBS infection, 25% will have meningitis (Edwards and Baker, 2017).
   a. Other gram-positive organisms that contribute to 4% of cases overall are *Enterococcus*, coagulase-negative staphylococci, *S. aureus*, *L. monocytogenes*, and α-hemolytic streptococci. Mortality with gram-positive meningitis is approximately 10%.
4. Gram-negative bacillus is responsible for 3.6% of cases in which neonates present with meningitis (Ku et al., 2015). It is the fifth most common cause of meningitis in infants. Gram-negative bacilli seed the CSF secondary to bacteremia, trauma, and surgery. Subsequent meningitis can develop as a result of bacterial multiplication and induction of inflammation in the subarachnoid and ventricular space; this is followed by a progression of inflammation and development of neuronal damage.
   a. *E. coli* and *K. pneumoniae* account for the majority of cases; other less frequent pathogens include *P. aeruginosa*, *Acinetobacter*, *Enterobacter*, and *Serratia*. Gram-negative bacillary meningitis is commonly accompanied by bacteremia. *E. coli* has become the most common cause of EOS and meningitis in VLBW since the 1990s, surpassing GBS (Ku et al., 2015).

5. Chronic complications of neonatal meningitis include (Edwards and Baker, 2017):
   a. Hydrocephalus, multicystic encephalomalacia, porencephaly, and white matter atrophy. The clinical manifestations of these complications include:
      1) Developmental delay in approximately 25%.
      2) Late-onset seizures in approximately 25%.
      3) Cerebral palsy in approximately 19%.
      4) Hearing loss in approximately 10%.
      5) Cortical blindness in less than 10%.
   b. Term infants, after GBS meningitis, had mild to moderate neurologic impairment in 25% of cases, and 19% had severe neurologic impairment (Edwards and Baker, 2017).
6. The clinical presentation of neonatal meningitis typically is indistinguishable from that of neonatal sepsis without meningitis. The most commonly reported clinical signs are:
   a. Temperature instability: presents in approximately 60% of neonates with bacterial meningitis. Term infants are more likely to have fever, whereas preterm infants are more likely to have hypothermia.
   b. Neurologic signs of neonatal meningitis (Friedman and Sexton, 2017).
      1) Irritability is present in up to 60% of infants.
      2) Seizures have been reported as a presenting feature in 20% to 50%. Meningitis resulting from gram-negative pathogens presents with seizures, usually focal rather than generalized, more often than gram-positive pathogens.
      3) Bulging fontanelle is present in approximately 25% of infants and nuchal rigidity in approximately 15%. Findings of a full, but not bulging, fontanelle and normal neck flexion at the time of initial presentation are more the rule than the exception (Friedman and Sexton, 2017).
   c. Other findings reported are:
      1) Poor feeding/vomiting in approximately 50%.
      2) Respiratory distress in 33% to 50%.
      3) Apnea in 10% to 30%.
      4) Diarrhea in 20%.
7. Diagnostic features that are characteristic of neonatal bacterial meningitis include:
   a. Isolation of a bacterial pathogen from the CSF by culture and/or by visualization by Gram stain. CSF result may be positive even though blood culture result is negative.
      1) When the CSF culture is positive, a repeat culture should be done in 24 to 36 hours after initiation of treatment to ensure adequate therapy and document sterilization of the CSF.
      2) Neonates in whom a traumatic lumbar puncture occurred should be treated for presumed sepsis and meningitis, pending results of CSF culture.
   b. Increased WBC counts in CSF of greater than 1000 WBCs/mcl with predominately neutrophils.
   c. Decreased CSF glucose of less than 30 mg/dL in term and less than 20 mg/dL in preterm infants (Edwards and Baker, 2017).
   d. Elevated CSF protein of greater than 100 mg/dL in term and greater than 150 mg/dL in preterm infants.
   e. PCR assay is a tool to determine identification of GBS in the urine or CSF and HSV or enterovirus in the CSF (Gupta and Roychowdhury, 2018).
   f. Neuroimaging is indicated to assist in defining the potential complications of neonatal meningitis. It is suggested that a neuroimaging study be done 48 to 72 hours before the anticipated end of therapy.
      1) Cranial ultrasound can be performed at the bedside, and when completed early in the course of infection is most helpful for assessing ventricular size and the presence of intraventricular hemorrhage. It can also demonstrate ventriculitis and extracerebral fluid collections.
      2) Computed tomography or magnetic resonance imaging can demonstrate the degree of cerebral edema, obstruction of CSF flow, infarction, abscess, and subdural fluid collections.
8. Antibiotic therapy. Prompt initiation is crucial for optimal outcome, and antibiotics may be administered before results of CSF specimen are obtained.
   a. In EOS, appropriate broad-spectrum antimicrobial therapy for suspected bacterial meningitis within the first 3 to 6 days of age is ampicillin and an aminoglycoside, usually gentamicin.
   b. When meningitis resulting from a gram-negative organism is strongly suspected or CSF Gram stain reveals gram-negative bacilli, the empirical regimen of ampicillin and an aminoglycoside should be expanded to include cefotaxime for CSF penetration.
      1) Duration of therapy is dependent on recovered pathogens and clinical response, generally 14 to 21 days.
   c. Antibiotic choice in the neonate who presents with LOS bacterial meningitis depends on the preliminary CSF findings.
      1) LOS without meningitis in neonates needs to be treated with vancomycin and an aminoglycoside if the lumbar puncture suggests meningitis. Cefotaxime should be added to provide an extended spectrum for gram-negative enterics and for optimal activity in the CSF against pneumococci.
      2) Once the causative pathogen and susceptibility pattern are known, the antimicrobial therapy should be altered accordingly.

d. GBS is uniformly susceptible to penicillin and ampicillin, and a combination of either with an aminoglycoside is recommended. The aminoglycoside is to improve synergy.
e. Gram-negative enteric bacteria: *E. coli*—ampicillin is the antimicrobial of choice.
f. Ampicillin-resistant *E. coli* and other gram-negative organisms usually are treated with cefotaxime in combination with gentamicin.
   1) Once sterility of the CSF is documented, the combination is continued for 7 to 14 days.
g. Coagulase-negative staphylococci—vancomycin is the antibiotic of choice.

9. Management.
   a. Lumbar puncture should be repeated routinely at 24 to 48 hours after initiation of antimicrobial therapy to document CSF sterilization.
   b. Gram-positive bacteria usually clear from the CSF within 24 to 48 hours after initiation of appropriate therapy. Gram-negative pathogens may persist for several days in severe cases.
   c. Failure to respond to clinically and bacteriologically appropriate antimicrobial therapy can lead to significant neurologic sequelae such as hydrocephalus, multicystic encephalomalacia, porencephaly, and cerebral cortical and/or white matter atrophy.
   d. Infants with suspected bacterial meningitis need to be in the NICU setting and monitored for signs of increased intracranial pressure, such as bradycardia, hypertension, respiratory distress, bulging fontanelle, accelerated head growth, separation of the cranial sutures, hemiparesis, and focal seizures and/or new-onset seizures.
      1) Development of these complications may necessitate additional evaluation and neurologic consultation.
      2) Evaluation and management with infectious disease experts to ensure adequate duration of antimicrobial therapy.
   e. Long-term follow-up for survivors of neonatal meningitis includes monitoring of hearing, visual acuity, and development status.
      1) Hearing should be evaluated by evoked-response audiometry within 4 to 6 weeks of completion of therapy (Edwards and Baker, 2017).
   f. Survivors are also at risk for developmental delay and may be eligible to receive early intervention services in the United States (eligibility criteria vary by state).
   g. Appropriate referrals should be made as indicated, and developmental surveillance should continue throughout childhood.

B. **Pneumonia**

1. In developed countries, the estimated incidence of pneumonia in full-term infants is less than 1% and increases to 10% in preterm infants. Early-onset pneumonia is generally within 3 days of birth and is acquired by vertical transmission from the mother to the infant by one of three routes:
   a. Transplacental transmission of organisms from the mother to the fetus through the placental circulation.
   b. Intrauterine aspiration of contaminated amniotic fluid.
   c. Aspiration of infected amniotic fluid during or after birth. The neonate can aspirate vaginal organisms that are colonizing the maternal genital area, leading to respiratory colonization.
2. Late-onset pneumonia usually occurs after 3 days of life and generally arises from colonized organisms present in the hospitalized newborn. Horizontal transmission, or nosocomial infection, is acquired from infected caregivers, family members, or contaminated equipment. Microorganisms can invade through injured tracheal or bronchial mucosa or through the bloodstream.
3. The pathologic changes vary with the type of organism, either bacterial or viral.
   a. Bacterial pneumonia is characterized by inflammation of the pleura, infiltration or destruction of bronchopulmonary tissue, and leukocyte and fibrinous exudate within alveoli and the bronchi/bronchioles. Bacteria often reside within the interstitial spaces, alveoli, and bronchi.
   b. Viruses typically cause an interstitial pneumonia. The extensive inflammation occasionally occurs with hyaline membrane formation, followed by varying degrees of interstitial fibrosis and scarring.
   c. In the United States, GBS is the most common early-onset pathogen. Injury from GBS in the lungs increases the permeability that contributes to the development of alveolar edema and hemorrhage and possibly the mechanism that is responsible for bloodstream extension.
4. Pathogens responsible for EOS with pneumonia include *E. coli* > GBS > *Klebsiella* > *S. aureus* > *S. pneumoniae* (Friedman and Sexton, 2017).
   a. Other less common bacterial pathogens include *L. monocytogenes* and *Mycobacterium tuberculosis*, both of which can be transmitted transplacentally.
   b. Viral—of the viral infections, HSV is the most common viral agent to cause early-onset pneumonia. HSV pneumonia occurs in 33% to 54% of disseminated HSV infections and usually is fatal in spite of treatment (Pentima, 2016). Influenza A and B viruses neurologic syndrome, including aseptic meningitis, seasonal variations peak in the United States in January and February (Pentima, 2016). Influenza A affects the CNS with the development of encephalitis (Pentima, 2016).

c. Fungal—approximately 25% of VLBW infants are colonized by *Candida* in the gastrointestinal and respiratory tracts, presumably during labor and delivery.
   1) Pneumonia occurs in 70% of infants with systemic candidiasis (Pammi, 2015).

5. Late-onset pneumonia occurs usually in those infants who have prolonged hospitalization that results in deviations to normal flora. There is a predominance of gram-positive organisms, including *S. pyogenes*, *S. aureus*, and *S. pneumoniae*.
   a. *S. aureus* and *K. pneumoniae* cause extensive tissue damage, abscess formation, and empyema.
   b. *E. coli*, *Serratia marcescens*, *Enterobacter cloacae*, *S. pneumoniae*, and *P. aeruginosa* may cause pneumatoceles.
   c. *Citrobacter diversus* is frequently associated with brain abscess and can also cause lung abscess.
   d. *Chlamydia trachomatis* has a long incubation period and typically is associated with pneumonia occurring between 2 and 4 weeks of age. Occurs where untreated sexually transmitted disease is present.
6. Risks: patients who require assisted ventilation are at highest risk for late-onset pneumonia.
7. Clinical manifestations.
   a. Early-onset pneumonia commonly presents with respiratory distress beginning at or soon after birth. Infants may have associated lethargy, apnea, tachycardia, and poor perfusion. It can progress to septic shock.
   b. Some infants develop pulmonary hypertension.
   c. Ventilatory-dependent infants may have increased oxygen and ventilator requirements or purulent tracheal secretions.
8. Diagnosis: because signs of pneumonia are nonspecific, any newborn infant with sudden onset of respiratory distress or other signs of illness should be evaluated for pneumonia and/or sepsis.
   a. Cultures of blood and CSF should be obtained.
   b. If viral or other nonbacterial infection is suspected, specific studies should be obtained, including PCR.
   c. Gram stain and culture of tracheal aspirates may identify the causative organism.
   d. Chest x-ray examination.
      1) Bilateral alveolar densities with air bronchograms are characteristic, but irregular patchy infiltrates can occur.
         a) Pneumonia caused by GBS or other pathogens is difficult to distinguish from RDS in premature infants.
         b) Pleural effusions occur in up to 67% of infants with pneumonia, but are rarely found in RDS. However, pleural effusions can also be seen in infants with transient tachypnea of the newborn, congenital heart disease, and hydrops fetalis.
9. Therapy: the choice of empirical regimens is based upon whether the infection is early or late onset.
   a. In early-onset pneumonia, a frequently used initial regimen for empirical coverage is ampicillin and gentamicin. Ampicillin is effective against GBS and most other strains of streptococci.
      1) Third-generation cephalosporins should not be used for suspected sepsis or pneumonia.
      2) Gram-negative bacilli can rapidly develop resistance to cephalosporins.
   b. For late-onset pneumonia, antibiotic choice depends on the prevalence sensitivity of bacteria in both the community and the hospital. The choice for term infants is vancomycin plus gentamicin.
   c. The usual treatment course for uncomplicated pneumonia is 10 to 14 days.

C. **Urinary tract infections.** UTIs in newborns frequently are associated with bacteremia and may result in long-term complications. Newborns with UTI should be evaluated for associated systemic infection and anatomic or functional abnormalities of the urinary tract.
1. Incidence: in term newborns, the incidence of bacteriuria was 0.1% to 1%, and in preterm infants, the incidence is 2% to 6%. UTI occurs in males 1.5 to 5 times more than females. The incidence decreases in boys and increases in girls during the first 6 months after birth (Nafday, 2016). Approximately one third of newborns with UTI have an accompanying bacteremia, and 1% will have meningitis.
2. *E. coli* is the most common organism found, accounting for 80% of cases responsible for UTIs (Nafday, 2016).
   a. Other organisms found were *Klebsiella* > *Enterobacter* > *Citrobacter*.
   b. Most common gram-positive organisms were *Staphylococcus* and *Enterococcus* species, but they occur less frequently than do gram-negative pathogens.
3. Most UTIs in newborns represent upper tract infection (pyelonephritis). Pathogenesis includes either hematogenous spread secondary to bacteremia or ascending infections, especially in infants with urinary tract abnormalities. Approximately 30% to 50% of term newborns with a UTI have urinary tract abnormalities, of which vesicoureteric reflux is the most common (Nafday, 2016). Other lesions found in infants with UTI include obstructive abnormalities, such as posterior urethral valves, malformations such as ectopic ureter, and renal conditions such as polycystic diseases.

4. Clinical manifestations: general signs are often nonspecific and may include temperature instability, poor weight gain, poor feeding, cyanosis, abdominal distention, hyperglycemia, hematuria, and proteinuria. Localized signs consist of a weak urinary stream and/or bladder distention.
5. Diagnosis: a urine specimen should be obtained by sterile catheterization.
   a. Diagnosis of UTI is based on a culture of an organism from the urine.
   b. Because of the associated risk of bacteremia, blood cultures should be obtained.
6. Therapy: antimicrobial agents. Treatment with parenteral IV broad-spectrum antibiotics as soon as cultures of urine, blood, and CSF (if indicated) have been obtained.
   a. Ampicillin and gentamicin provide coverage for the most common bacterial pathogens. Changes in antibiotic therapy are based on culture results, including antimicrobial susceptibilities. Usual duration for therapy is 10 to 14 days.
7. Management: repeat urine culture should be sterile within 36 to 48 hours after initiation of antimicrobial therapy.
   a. If a UTI has been documented in an infant, voiding cystourethrogram should be performed to evaluate the possibility of any congenital abnormalities of the urinary tract.

Infection With Specific Pathogens

GROUP B STREPTOCOCCUS

A. *S. agalactiae* is a gram-positive diplococcus encapsulated bacterium that has been the principal GBS pathogen in the neonate for over 50 years. GBS accounts for more than 95% of EOS and more than 90% of LOS in neonates in the United States today. The reported fatality rate among preterm neonates with birth weights greater than 1500 g was 20%, nearly an eightfold increase compared with term infants (Puopolo and Baker, 2018).
   1. There are 10 GBS serotypes, with serotypes Ia, Ib, II, III, and V recognized as the most common organisms colonizing the gastrointestinal and genital tracts of 15% to 40% of pregnant women and as the primary risk factor for GBS infection in neonates from 0 to 90 days of age.
   2. GBS infection in neonates is classified by age at onset into early-onset GBS, occurring within 24 hours of birth up to day 7 of life; late-onset GBS, which has a broader range from 7 to 89 days; and late, late-onset GBS, which occurs in infants older than 3 months of age.
      a. Nearly 50% of infants who pass through a colonized birth canal become colonized. However, only 1% to 2% will develop invasive disease, dependent on the presence or absence of additional risk factors.
   3. Risk factors include:
      a. Delivery at less than 37 weeks of gestation.
      b. PROM.
      c. Rupture of membranes ≥18 hours before delivery.
      d. Clinical signs of chorioamnionitis, maternal temperature ≥100.4° F (38° C) during labor.
      e. Maternal GBS bacteriuria during the current pregnancy.
      f. Prior delivery of an infant with GBS disease.
      g. Heavy maternal colonization inoculum ($>10^5$ colony-forming units/mL) vaginally.
   4. Since the implementation of universal screening of pregnant women at 35 to 37 weeks of gestation and recommendations for providing intrauterine antibiotic prophylaxis (IAP) in 2002, surveillance data by the Centers for Disease Control and Prevention (CDC, 2015) demonstrate a decline from 1.8 cases per 1000 live births (1990) to 0.23 cases per 1000 live births (2015) in the United States.
      a. Racial disparities remain, with approximately twice the incidence occurring among African Americans than non–African Americans for all age groups.
      b. Despite highly effective prevention efforts, an estimated 1100 infants still become infected each year in the United States. Early-onset GBS accounts for 80% to 85% of cases. Late-onset GBS accounts for 50% of cases that present usually at 5 to 6 weeks after birth (Edwards, 2017).
      c. Late-onset GBS usually occurs at 4 or 5 weeks of age. Up to 50% of LOS is thought to be attributable to vertical transmission at birth and horizontally in household and community settings.
      d. Late, late-onset GBS occurs in infants older than 3 months of age. The infants who most commonly develop late, late-onset GBS are infants who were born before 28 weeks of gestation or those with a history of immunodeficiency (Edwards, 2017).
   5. Early-onset GBS infection most commonly manifests as:
      a. Generalized sepsis.
      b. Pneumonia.
      c. Meningitis.
      d. Infants whose mothers receive IAP are less likely to have sepsis, need assisted ventilation, or have documented GBS bacteremia (Edwards, 2017).
   6. Sepsis without a focus of infection occurs in 80% to 85% of cases of early-onset GBS. The signs and symptoms are nonspecific. Late-onset GBS disease most often presents as bacteremia without a focus in about 65% of cases. Meningitis remains the most

common presentation of late-onset GBS and occurs in approximately 25% to 30% of cases.
   a. Refer to sections on neonatal sepsis, pneumonia, and meningitis discussed earlier for clinical manifestations, diagnostics, therapy, management, and prevention.
   b. Penicillin remains the preferred agent, with ampicillin an acceptable alternative.
7. Other less common (2% to 3%) but well-described late-onset GBS focal infections are:
   a. Bacteremic cellulitis.
   b. Osteoarthritis.
8. Guidance with empirical therapy for early- or late-onset GBS can be reviewed online at https://www.cdc.gov/groupbstrep/guidelines/guidelines.html. In the 2010 guidelines:
   a. There are expanded options for laboratory detection of GBS, including use of pigmented media and PCR assays.
   b. There is a revised colony count threshold for laboratories to report GBS in the urine of pregnant women.
   c. There are revised algorithms for GBS screening and use of IAP for women with threatened preterm delivery, including one algorithm for preterm labor and one for preterm PROM.
   d. Recommendations for IAP agents are presented in an algorithm format to promote use of the most appropriate antibiotic for penicillin-allergic women.
   e. Penicillin dosing is geared to facilitate implementation in facilities with different prepackaged penicillin products.
   f. The neonatal management algorithm's scope applies to all newborns.
   g. Management recommendations depend on clinical appearance of the neonate and other risk factors, such as maternal chorioamnionitis, adequacy of IAP if indicated for the mother, gestational age, and duration of membrane rupture.
   h. The algorithm is used to reduce unnecessary evaluations in well-appearing newborns at relatively low risk for early-onset GBS disease.

FUNGAL INFECTION: CANDIDIASIS

A. Candidiasis is caused by *Candida*, budding yeasts that form long chains called *pseudohyphae*.
   1. The species causing most infections is *Candida albicans*, though *C. parapsilosis* and *C. glabrata* are also responsible for candidiasis in increasing numbers over the last 10 years in VLBW neonates who have prolonged hospital stays and central venous access (Pappas et al., 2016; Shane et al., 2017).
   2. *Candida* species are found on the skin and in the mouth, intestinal tract, and vagina. Transmission to the neonate can occur in utero, intrapartum, or postnatally through breastfeeding. Risk factors include infants less than 1500 g, intubation, abdominal or cardiac surgery, NEC, spontaneous intestinal perforation, neutropenia, use of corticosteroids and histamine$_2$ (H_2) blockers, long-term use of broad-spectrum antibiotics, use of total parenteral nutrition and lipids, hyperglycemia, and invasive central catheters. Of VLBW infants less than 1000 grams, 5% to 20% develop disseminated or invasive candidiasis, and approximately 75% have prolonged hospitalization, neurodevelopmental impairment (Pappas et al., 2016), and up to 30% mortality even with appropriate therapy (Pappas et al., 2016).
   3. Mucocutaneous candidiasis results in oral–pharyngeal (thrush) or vaginal and cervical candidiasis (lesions of gluteal folds, buttocks, groin, neck, and axillae).
      a. Most common form of candidiasis in the newborn infant.
      b. Mucosal lesions appear as white plaques on oral mucosa.
      c. Diaper dermatitis presents with intense erythema and satellite lesions.
   4. Congenital candidiasis presents with widespread erythematous maculopapular rash, and preterm infants may present with pneumonia.
   5. Disseminated candidiasis may involve any organ or anatomic site and may present with acute respiratory deterioration, acidosis, feeding intolerance, hypotension, skin abscesses, temperature instability, and/or erythematous rash.
      a. Common sites of lesions include the brain, kidneys, liver, spleen, lungs, and retinas, but lesions typically do not appear until late during the disease (Johnson, 2017).
   6. Mucocutaneous candidiasis is usually diagnosed clinically with the visualization of lesions. Disseminated candidiasis is confirmed through isolation of the organism from blood, CSF, or urine cultures. Focal lesions are diagnosed with ophthalmologic examination, ultrasonography, computed tomography, and magnetic resonance imaging.
   7. Treatment: guidelines for management were updated in 2016 by the Infectious Diseases Society of America and contain recommendations for neonates (available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4725385/) (Pappas et al., 2016).
      a. Mucocutaneous candidiasis is treated with oral nystatin suspension and topical nystatin cream or powder. Fluconazole is also used for oral therapy and may be more effective than nystatin. IV fluconazole or amphotericin B can be used for chronic, severe, or refractory cases.
      b. Invasive disease is treated by prompt removal of infected invasive catheters, and IV amphotericin B remains the drug of first choice for neonates.
         1) Fluconazole has limited data for treatment of meningitis and can be considered if UTI and meningitis are excluded.

2) Echinocandins are reserved for drug-resistant species and should be used with caution, as safety and dosing have not been established in neonates.
3) Most *Candida* species are susceptible to amphotericin B, though lipid preparations may not penetrate into the kidney parenchyma.

c. Fungal prophylaxis of VLBW infants less than 1000 or less than 1500 g has demonstrated significant reduction in *Candida* colonization, invasive disease, and related mortality in four prospective randomized controlled trials and 10 retrospective cohort studies. Based on these studies, fluconazole has been shown to be safe and effective as prophylaxis in this population and is recommended for NICUs with moderate (5% to 10%) or high (≥10%) incidence of invasive disease (CDC, 2016). Routine prophylaxis is not recommended for all NICUs due to the potential development of drug resistance, which has been documented in adult populations.

8. Isolation procedures: Standard Precautions.

ToRCHES CLAP INFECTIONS

A. Classification of ToRCHES CLAP organisms.
1. Common congenital infections were traditionally classified as TORCH infections for ease of identification and management. Some professionals have expanded the "O" (other infections) category beyond the original syphilis to include other well-described pathogens (Johnson, 2017). A new acronym—ToRCHES CLAP—has been suggested to be more inclusive of other well-described pathogens acquired congenitally and in the neonatal period (Johnson, 2017) and is utilized here, with the addition of respiratory syncytial virus (RSV) under the "R" and hepatitis B virus (HBV) under the "H" due to their prevalence as causes of neonatal infection. Viral sepsis may be difficult to differentiate clinically in the neonate from bacterial sepsis.
   a. To—*To*xoplasmosis (*Toxoplasma gondii*)
   b. R—*R*ubella virus and *R*espiratory syncytial virus
   c. C—*C*ytomegalovirus
   d. H—*H*erpes simplex virus and *H*epatitis B virus
   e. E—*E*nteroviruses
   f. S—Syphilis (*Treponema pallidum*)
   g. C—Chickenpox (varicella-zoster virus)
   h. L—*L*yme disease (*Borrelia burgdorferi*)
   i. A—*A*cquired immunodeficiency syndrome/human immunodeficiency virus
   j. P—*P*arvovirus B19

B. **ToRCHES CLAP Organisms**

To—*To*xoplasmosis.

a. Caused by an intracellular protozoan parasite, *Toxoplasma gondii*.
b. Maternally acquired from consumption of poorly cooked meat or by exposure to infected cat feces. Highest risk to fetus is primary acute maternal infection during pregnancy, but can occur with subsequent infections in immunocompromised women (Pomares and Montoya, 2016). Risk of transmission increases with increasing gestational age, but severity of the disease decreases. Estimated incidence of congenital toxoplasmosis ranges from 1 in 1000 live births in some areas of Latin America to 0.1 in 1000 live births in the United States. The overall transmission rate to neonates of mothers who have been treated is 30% (Pomares and Montoya, 2016).
c. Most infants are asymptomatic and without apparent abnormalities at birth. Some may present with fever, maculopapular rash, petechiae, purpura, hepatosplenomegaly, jaundice, pneumonitis, microcephaly, meningoencephalitis, hydrocephalus, intracranial calcifications, seizures, thrombocytopenia, lymphadenopathy, myocarditis, chorioretinitis, cataracts, optic atrophy, and bone lesions (Guerina and Marquez, 2017).
   1) Classic triad of associated morbidities includes chorioretinitis, hydrocephalus, and intracranial calcifications, but triad occurs in less than 10% of cases (Guerina and Marquez, 2017).
   2) The most common late finding is chorioretinitis, which can result in vision loss, retinal detachment, cataracts, glaucoma, and blindness. Additional sequelae include mental intellectual disability, seizures, deafness, spasticity, and learning disabilities.
d. Diagnosis may be made by a number of methods: isolation or histologic demonstration of the organism by PCR of amniotic fluid, CSF, urine, blood, or cord blood; observation of parasites (detection of *Toxoplasma* cysts) in tissues and body fluids or placenta; detection of parasites from blood or body fluids by mouse inoculation or tissue culture; and other serologic tests. The diagnosis of congenital toxoplasmosis IgG is through a dye test or the enzyme-linked immunosorbent assay (ELISA) assay (Pomares and Montoya, 2016). The diagnosis of congenital toxoplasmosis IgE is by the ELISA assay (Pomares and Montoya, 2016).
e. Treatment consists of an antiparasitic regimen for a year, including pyrimethamine plus sulfadiazine, and folinic acid to aid in prevention of bone marrow suppression. Glucocorticoids (prednisone) are added when chorioretinitis threatens vision. Clindamycin may be used for infants who develop an allergy to sulfadiazine (CDC, 2017).
f. Isolation procedures: Standard Precautions.

R—*R*ubella virus and *R*espiratory syncytial virus.

a. Congenital rubella syndrome (CRS).
   1) *Rubivirus*: enveloped, positive-stranded ribonucleic acid (RNA) virus from the family Togaviridae.
   2) Virus is found in nasopharyngeal secretions and is transmitted through direct or droplet contact. Most prevalent in winter and early spring. About 25% to 50% of infected individuals are asymptomatic. Outbreaks now occur in those born outside the United States or underimmunized people (Ezike, 2017). The Americas have achieved rubella and CRS elimination as of 2015 (Grant et al., 2017). To achieve global rubella elimination goals by 2020 as outlined by the Global Vaccine Action Plan (GVAP), a comprehensive vaccination program is being pursued (Allerberger, 2017). Acquiring rubella during pregnancy can result in a wide range of complications, including miscarriage, fetal death, and a group of anomalies described as CRS. Up to 85% of infants will have congenital defects if maternal infection occurs in the first trimester and 25% to 50% with second-trimester infection (Grant et al., 2017).
   3) Mild forms of CRS may have few or no apparent clinical symptoms at birth. Associated symptoms of CRS include cataracts, glaucoma, retinopathy, microphthalmos, myocarditis, patent ductus arteriosus, peripheral pulmonary artery stenosis, hearing impairment, meningoencephalitis, microcephaly, hydrocephalus, behavioral disorders, intellectual disability, intrauterine growth restriction, pneumonitis, hepatosplenomegaly, jaundice, thrombocytopenia, bone disease, "blueberry muffin" purpura, and petechiae.
   4) Diagnosis is made by detection of specific rubella immunoglobulin M (IgM) antibody. Most congenital cases are IgM positive at birth to 3 months of age, and postnatal cases are positive by 5 days after symptom onset. Congenital infection is also confirmed by stable or rising rubella immunoglobulin G (IgG) titers in serial sera obtained for the first 7 to 11 months. Virus is isolated primarily from throat or nasal secretions, and less consistently from urine, blood, and cataract specimens, with inoculation of appropriate cell culture. Special cell cultures are required for cultivation of rubella virus.
   5) Treatment is supportive, and prevention measures are as follows:
      a) Pregnant women should be screened for immunity whether or not they have received prior rubella immunization. Susceptible pregnant women should avoid exposure to infected persons. Pregnant women are not given the vaccine because of the small risk of transmission of virus to the fetus (1.3%, of whom 2% had subclinical infection and none had congenital defects) (Allerberger, 2017).
      b) Seronegative women should be vaccinated postpartum before discharge from the hospital. Vaccine virus is excreted in breast milk, but breastfeeding is not a contraindication to vaccination (CDC, 2018).
      c) Vaccination in the United States is a live-virus subcutaneous injection combined with measles and mumps vaccines (MMR) or MMR plus varicella (MMRV), recommended at 12 to 15 months of age, and repeated at 4 to 6 years of age. Routine vaccination should be administered to all infants, with a few exceptions for immunocompromised children and those who have recently received immune globulin (American Academy of Pediatrics (AAP) Committee on Infectious Diseases, 2012; CDC, 2018).
   6) Isolation procedures: droplet precautions for 7 days after onset of rash, and Contact Precautions in addition to Standard Precautions. Contact isolation is recommended from birth until ≥1 year of age for proven or suspected congenital rubella unless two separate negative cultures 1 month apart after 3 months of age are obtained.

b. **RSV.**
   1) Enveloped, nonsegmented, negative-stranded RNA virus of the Paramyxoviridae family. Only one identified serotype, but multiple strain variations may affect virulence and susceptibility to infection.
   2) Virus is found in oral, nasal, and respiratory secretions. Transmission is by exposure to large-particle droplets or contaminated surfaces. RSV can survive for several hours on environmental surfaces. The incubation period is most commonly 4 to 6 days, but ranges from 2 to 8, and may last as long as 3 to 4 weeks in immunosuppressed people. RSV is one of the most common diseases of early childhood. Most infants are infected in the first year of life, and almost all children

have had RSV by age 2. Approximately 20% to 30% of infants develop lower respiratory tract disease, and 0.7% of infants under 6 months of age require hospitalization for bronchiolitis and pneumonia (Brüggmann et al., 2017). One in 1000 infants die because of RSV infection (Rose et al., 2018).

a) Infection is most prevalent during winter and early spring (mid-October to early May, but varies year to year) in temperate climates (Rose et al., 2018).
b) Severe and often fatal in high-risk populations, including premature infants, infants with chronic lung disease or congenital heart disease, or immunocompromised infants.

3) Symptoms may be nonspecific and include poor feeding, lethargy, apnea, and irritability. Symptoms of bronchiolitis may include cough, wheezing, tachypnea, rales, rhonchi, increased work of breathing (retractions, nasal flaring, and use of accessory muscles), pneumonia, cyanosis, and pulmonary infiltrates.
   a) May result in respiratory failure.
4) Diagnosis is most commonly made by rapid viral antigen detection isolated from nasopharyngeal aspirate. Molecular testing using reverse transcriptase PCR assays is now commercially available and detects RSV at significantly higher rates than antigen or viral culture, but will detect viral RNA for weeks after the infectious period.
5) Treatment of infants with RSV is primarily supportive care and includes oxygen, clearing airway secretions as indicated, hydration, and isolation. High-risk infants may progress to assisted ventilation because of hypoxemia and hypercapnia.
   a) Aerosolized ribavirin has been associated with increased oxygen saturation during the acute phase of infection, but is not recommended for routine use due to the potential toxic effects of exposed health care personnel and clinical trials with conflicting efficacy results. May be considered for select cases of potentially life-threatening RSV (Krilov, 2017).
   b) Prophylaxis of RSV is indicated for high-risk infants less than 24 months old with a history of preterm birth (<35 weeks of gestation) and infants with chronic lung disease or significant congenital heart disease (Krilov, 2017). Number of doses to be received is determined by clinical status and associated risk factors, such as attending day care or having one or more siblings under 5 years of age.
   c) Palivizumab (Synagis) is a Food and Drug Administration (FDA)–approved biologic for RSV prophylaxis (Goldstein et al., 2017). Palivizumab, a humanized mouse monoclonal antibody, is administered intramuscularly once every 30 days during RSV season and reduces associated hospitalization rates by 39% to 82% (Krilov, 2017). In 2014 and again in 2018, guidelines and policies have been issued by the AAP and the Committee on Infectious Diseases concluding there is limited clinical benefit for otherwise healthy infants born at more than 29 weeks' gestation to receive palivizumab, as well as the high cost of immunoprophylaxis (Blake et al., 2017; Munoz et al., 2017). However, these guidelines have not agreed with the FDA (Goldstein et al., 2017). Guidelines and policies have to consider individual legal and medical considerations (Goldstein et al., 2017).
6) Isolation procedures: Contact Precautions in addition to Standard Precautions. Cohort infected infants to prevent widespread nursery infection.

C—Cytomegalovirus (CMV).

a. Viral genome double-stranded DNA of the herpesvirus family Herpesviridae.
b. Virus is found in saliva, urine, blood, breast milk, and seminal and cervical fluids. Transmission occurs horizontally from person to person with contaminated secretions, vertically from mother to infant in utero, perinatally or postnatally, and via transfusion or transplantation from infected donors. CMV is the most common congenital viral infection, with approximately 1% of all live-born infants infected in utero and excreting CMV at birth (Rawlinson et al., 2017). Severe sequelae are most commonly associated with primary maternal infection in the first trimester, though sequelae can occur regardless of trimester or reinfection. Intrapartum or postpartum infection in term infants is not usually associated with clinical illness, but in preterm or immunocompromised infants, infection after delivery can cause systemic infections.
c. Asymptomatic infections are most common in children, but vary with age and immunocompetence of the individual. Congenital infection is usually not evident at birth, with approximately 10% of infected newborn infants presenting

with clinical manifestations of the disease (Rawlinson et al., 2017). Symptoms of congenital infection include intrauterine growth restriction, hepatosplenomegaly, jaundice, purpura, pneumonitis, microcephaly, hydrocephalus, intracerebral calcifications, hearing loss, chorioretinitis, and optic atrophy. Prognosis is poor, with one third dying in infancy and up to 90% of survivors having severe neurologic sequelae. Progressive and late-onset sensorineural hearing loss is the most common sequela of congenital CMV. Twenty-one percent of all hearing loss at birth and 25% of all hearing loss at 4 years of age is attributable to CMV (Rawlinson et al., 2017). Perinatal and postnatal infections of preterm or immunocompromised infants include lower respiratory tract disease, interstitial pneumonia, prolonged fever, thrombocytopenia, and hepatitis.

d. Diagnosis of congenital CMV is made by viral isolation in cell culture from the infant's urine or saliva, or by a high anti-CMV IgM titer in the first 2 to 4 weeks of life.

e. Infants with symptomatic congenital CMV involving the CNS may benefit from treatment with antiviral ganciclovir IV or oral valganciclovir for 6 weeks. Data suggest that extending valganciclovir treatment to 6 months is protective against hearing deterioration and possibly decreases developmental delays (Rawlinson et al., 2017). Due to possible toxicities, including neutropenia, antiviral therapies are not recommended for all neonates, just those with CNS involvement who are able to start therapy within the first month of life. Current clinical trials involving these antivirals and investigative vaccines are ongoing.

f. CMV transmission from blood products can be eliminated by use of CMV antibody–negative donors, by freezing RBCs in glycerol before administration, or by filtration processes. Breastfeeding is not contraindicated due to the low incidence of developing clinical illness and transfer of maternal antibodies. Donor breast milk should be pasteurized, and freezing may also decrease the likelihood of transmission.

g. Isolation procedures: Standard Precautions.

H—*H*erpes simplex virus and *H*epatitis B virus.

a. **HSV**.

1) Enveloped, double-strand DNA viruses; two distinct types: HSV-1 and HSV-2.
   a) HSV-1 usually involves the face and skin above the waist, but can cause genital HSV.
   b) HSV-2 usually involves the genital area and skin below the waist in the sexually active, but also can be found above the waist. Causes approximately 75% of neonatal disease (Wang et al., 2017).
   c) Both viruses establish latency after primary infection and have periodic reactivation that causes recurrent symptomatic disease or viral shedding without symptoms.
2) Transmission to fetus may be by ascending infection through ruptured membranes, but is more common during birth through an infected genital tract and occurs occasionally postnatally through a nongenital infection, such as hands or mouth of a care provider, or from breast lesions during breastfeeding. Causes serious disease in fetus and neonate, with incidence estimated at 1 in 3000 to 1 in 20,000 births (Kimberlin et al., 2015). Primary maternal genital infection during pregnancy near the time of delivery accounts for as much as 25% to 60% of neonatal infection. Risk to the neonate of reinfection during the first half of pregnancy is less than 2%. More than 75% of infants who acquire neonatal HSV infection have been born to women who had no history or clinical findings suggestive of active HSV infection during pregnancy (Kimberlin et al., 2015).
3) Symptoms of HSV infection include skin vesicles or scarring, microcephaly, meningoencephalitis, keratoconjunctivitis, and liver failure.
   a) Disseminated disease (25% of cases) involving multiple organs, with up to 75% having CNS involvement, and approximately 67% have lesions that may not be initially present.
      (1) Typically presents at 7 to 14 days of life.
      (2) Severe liver dysfunction, abnormal CSF findings, seizures, profound sepsis, septic shock, high morbidity and mortality.
   b) Localized CNS disease (30% of cases), may have skin involvement.
      (1) Typically presents at 14 to 21 days of life.
   c) Localized skin, eyes, and mouth (SEM) disease (45% of cases); 80% of SEM cases have skin lesions; remainder are localized to eyes and oral mucosal lesions only.
      (1) Typically presents at 7 to 14 days of life.
4) Diagnosis: positive culture result with specimen obtained from vesicular fluid, blood, or CSF results in a diagnosis. The diagnostic yield of CSF culture for neonates with CNS

disease is less than 50%. The PCR test has a much higher yield in CSF and should be performed if available. Other rapid identification tests include direct fluorescent antibody staining of vesicle scrapings and enzyme immunoassay antigen detection in vesicles or body fluids.

a) Surface cultures from mouth, nasopharynx, conjunctivae, and anus greater than 12 to 24 hours after delivery and initial bath (to ascertain viral replication versus intrapartum exposure).
b) Skin swabs of vesicles.
c) Blood and CSF for HSV culture and HSV PCR, serum alanine aminotransferase (ALT).

5) Treatment of choice is acyclovir intravenously for 10 days for asymptomatic infants born to mothers with suspected or proven primary infection with active lesions at delivery, 14 days for SEM infection, or 21 days minimum for disseminated infection or CNS infections (Harris and Holmes, 2017).
   a) Repeat CSF HSV PCR near end of 21-day course and continue for additional 7 days or more if CSF remains positive.
   b) Acyclovir suppressive therapy for 6 months after acute phase improves neurodevelopmental outcomes and helps suppress skin recurrences.
   c) For infants with ocular involvement, a topical ophthalmic drug such as 3% vidarabine, 1% trifluridine, or 0.1% iododeoxyuridine is used in addition to parenteral antiviral therapy. An ophthalmology consultation should be obtained.
6) **Active maternal lesions at birth:** if neonate is ≤37 weeks gestation or born after PROM (>4 to 6 hours), immediate initiation of treatment should be considered (Harris and Holmes, 2017). For asymptomatic infants born to women with *recurrent* HSV genital lesions at birth, surface cultures and HSV blood PCR should be obtained at approximately 24 hours of life. If infant remains asymptomatic, acyclovir is not indicated at this time. Parents should be educated on signs and symptoms and the infant followed closely. Full evaluation and treatment should occur if any culture results become positive or infant becomes symptomatic. If active *primary* maternal HSV infection is proven or suspected, CSF for cell count, chemistries, HSV PCR, and a serum ALT should be sent in addition to surface cultures and HSV blood PCR. Acyclovir is then initiated. If infant remains asymptomatic with negative cultures and nonindicative CSF and normal ALT, treatment is continued for 10 days. If maternal type-specific serology for HSV-1 and HSV-2 antibodies testing is available and infection proves to be recurrent, treatment can be discontinued at 48 to 72 hours (Wang et al., 2017).
7) Isolation procedures: Contact Precautions in addition to Standard Precautions.
   a) Mothers with HSV infections need to use strict handwashing techniques before touching their infant.
   b) Mothers with active lesions may wear clean covering gown to provide care, and a surgical mask should be worn for oral/cold sore lesions. Breastfeeding is permissible if there are no breast lesions and other lesions are covered.

b. **HBV.**
1) DNA double-shelled virus.
2) Virus is found in any bodily secretion, including human milk. Transmission to fetus is vertical. There is no added risk to the infant of acquiring HBV infection while breastfeeding if appropriate immunoprophylaxis recommendations are followed. Two billion people worldwide are estimated to have acquired HBV, and more than 350 million are chronically infected (Schillie et al., 2018). In the United States, over 1 million people have HBV (CDC, 2018).
3) Infants are usually asymptomatic at birth. Elevated liver enzymes or acute fulminating hepatitis is occasionally present. Infants infected at delivery or after birth may become hepatitis B surface antigen (HBsAg) positive 4 to 12 weeks after birth and are lifelong carriers; the time of onset of symptoms after exposure ranges from 6 weeks to 6 months. Infants who become chronically infected are at risk of having chronic hepatitis, cirrhosis, or hepatocellular carcinoma later in life (Schillie et al., 2018). Mortality rate of fulminating hepatitis is around 67%, and many survivors require liver transplantation (Schillie et al., 2018).
4) Routine screening is used for all pregnant women with each pregnancy, and universal screening for all exposed infants should occur at 9 to 18 months of age or 1 to 2 months after primary immunization series. Routine neonatal immunization is with hepatitis B vaccine.
   a) Term infant is immunized at discharge and again at 1 to 2 months and at 6 to

18 months of age (AAP, Committee on Infectious Diseases and Committee on Fetus and Newborn, 2017; CDC, 2018).
   b) Preterm infant is immunized at discharge if weight is ≥2 kg or at 2 months of age.
5) Treatment of the infant born to an HBsAg-positive mother is 85% to 90% effective in preventing the development of the hepatitis B carrier state and should include:
   a) Administration of hepatitis B immune globulin, in addition to a hepatitis B vaccine ≤12 hours after birth (AAP, 2018; AAP, Committee on Infectious Diseases and Committee on Fetus and Newborn, 2017).
6) Isolation procedures: Standard Precautions.

E—*Enteroviruses.*

a. RNA virus of the family Picornaviridae; grouped together with Parechoviruses due to shared physical properties and symptoms that they cause.
   1) More than 100 serotypes identified as pathogenic in neonates, including polioviruses, coxsackieviruses, and echoviruses.
b. *Enterovirus* infections occur worldwide and are a common cause of neonatal infection, but clear data are unavailable regarding the incidence of symptomatic congenital and neonatal infections. Infections are most prevalent in the summer and fall in temperate climates, but occur all year in tropical settings. The virus is spread by fecal–oral and respiratory routes and from mother to infant in utero and peripartum, and may also be transmitted by breastfeeding. Polio vaccines have virtually eliminated poliomyelitis in the United States, but it remains endemic in parts of the world.
c. Clinical manifestations of *Enterovirus* infection include but are not limited to nonspecific febrile illness, respiratory symptoms (including bronchiolitis and pneumonia), pulmonary edema and hemorrhage, hand-foot-and-mouth disease, meningitis, encephalitis, paralysis, vomiting, diarrhea, hepatitis, acute hemorrhagic conjunctivitis, myocarditis, sepsis, and coagulopathy. Neonates present with more severe clinical disease and have increased incidence of long-term morbidities than do older children (Bennett, 2017).
d. Diagnosis of *Enterovirus* infection is made by PCR assay and cultures from stool, rectal, throat, and conjunctival swabs, as well as tracheal aspirates, urine, blood, CSF, and tissue biopsy.
e. No specific treatment other than supportive care, including antibiotics and corticosteroids (Bennett, 2017).
f. Isolation procedures: Standard Precautions, Contact Precautions, and cohorting are used for controlling nursery outbreaks.

S—Syphilis.

a. Caused by *Treponema pallidum*, a thin, motile spirochete.
b. Maternally acquired through sexual contact. Vertical transmission across placenta or via direct contact with active lesion at birth. Congenital infection can occur at any gestation, but frequency increases with advancing gestation. Maternal untreated primary or secondary syphilis causes highest risk to fetus, with 60% to 100% transmission (Willeford and Bachmann, 2016) and up to 30% to 40% spontaneous abortion occurring with early untreated syphilis (CDC, 2017). The incidence of congenital syphilis was about 2.1 per 1000 live births in the United States in 2001, which was the lowest rate since 1941 and then spiked in 2014 to 11.6 per 1000 live births, with a 28% increase in congenital syphilis in newborns from 2015 to 2016 (CDC, 2017; Hoppin et al., 2018; Willeford and Bachmann, 2016).
c. Presentation at birth varies with timing of intrauterine infection. Up to two thirds of infected neonates are asymptomatic at birth. Manifestations may include an edematous "barber's pole" umbilical cord with stripes of red, light blue, and chalky white; hepatomegaly; splenomegaly; jaundice; nasal rhinitis ("snuffles"); lymphadenopathy; fever; edema; rash; fissures and condylomata lata (wartlike lesions) around mucous membranes of mouth, nares, and anus; long-bone abnormalities; pneumonia alba; anemia; thrombocytopenia; and CNS involvement (CDC, 2017).
   1) Skin lesions: initially red or pink-colored maculopapular rash that is most prominent on the back, buttocks, posterior thighs, and soles; usually appears 1 to 2 weeks after rhinitis. Subsequent desquamation and crusting; lesions become copper-colored. Lesions present at birth may be bullous, ulcerative, and widely disseminated.
   2) CNS involvement may be asymptomatic but occurs in approximately 40% of symptomatic infants. Symptoms include progressive hydrocephalus, cranial nerve palsies, optic atrophy, seizures, and neurodevelopmental delay.
   3) Periostitis of long bones, with guarding of extremities, or "pseudoparalysis of Parrot" (lack of movement associated with pain from bone lesion).
d. Diagnosis is made by serologic testing of maternal blood with Venereal Disease Research

Laboratory (VDRL) or rapid plasma reagin (RPR) test early in pregnancy and at the time of delivery.

1) Diagnosis of active disease in the neonate includes:
   a) High VDRL titer (≥4 times higher than maternal titer).
   b) Reactive RPR.
   c) Serum IgM level greater than 20 mg/dL.
   d) Confirmation with a positive result on darkfield microscopic examination or direct fluorescent antibody staining of suspicious lesions, body fluids, placenta, or umbilical cord.
2) Uninfected infants possess maternally acquired antibodies at concentrations similar to those of infected infants. It may be difficult to interpret neonatal laboratory data; therefore, it is important to determine adequacy of maternal treatment, possibility of reexposure, and family compliance with follow-up.

e. Treatment.
   1) Treatment recommendation for infants with proven or highly probable congenital syphilis is 10 to 14 days of parenteral penicillin (aqueous penicillin G intravenously or procaine penicillin G intramuscularly).
   2) Treatment of at-risk neonates who are asymptomatic and have nonreactive VDRL or RPR or values less than four-fold the maternal titer varies depending on maternal history and treatment (Rawlinson et al., 2017).
      a) Treat with full 10- to 14-day course if mother was not treated, was inadequately treated, or has evidence of reinfection (≥four-fold increase in titers after treatment).
      b) May treat with single dose of benzathine penicillin G intramuscularly if mother had adequate treatment.
   3) No treatment necessary if all of the following are true: mother adequately treated with appropriate response in titers (decrease four-fold after therapy; VDRL ≤1:2 or RPR ≤1:4) and levels remained stable and low, maternal treatment occurred more than 4 weeks before delivery, and mother has no evidence of relapse or infection.

f. Isolation procedures: Standard Precautions.

C—Chickenpox.

a. Varicella-zoster virus (*Varicellovirus*) is a member of the Herpesviridae family that also includes HSV-1 and HSV-2, CMV, Epstein–Barr virus, and other herpesviruses.
b. Remains one of the most communicable human diseases. Transmission occurs through person-to-person contact of individuals with vesicular lesions, and may occur through infected respiratory tract secretions. Transplacental transmission occurs with maternal infection. Congenital varicella syndrome occurs in approximately 1% to 2% of infants with maternal infection before 20 weeks of gestation. Incubation period may be as short as 2 to 16 days after birth for infants born to actively infected mothers at the time of delivery (Bechtel, 2017). Infected individuals are contagious 1 to 2 days before onset of lesions and until all lesions are crusted.
c. Infection during the first or second trimester can result in fetal death, limb hypoplasia, cutaneous scarring, eye abnormalities, and CNS derangements. If maternal infection occurs 5 days before to 2 days after delivery, subsequent infant mortality is higher due to the immature immune system of the infant and insufficient maternal antibody transfer (Spear, 2018). Additional symptoms of chickenpox are a generalized pruritic, vesicular rash; low-grade fever; potential superinfection of skin lesions; pneumonia; thrombocytopenia; and, rarely, glomerulonephritis, hepatitis, and arthritis. Latent infection can occur, as well as infection after vaccination.
d. Diagnosis is made by PCR assay of vesicular fluid or scab; or saliva and buccal swabs; or by tissue culture of vesicles, CSF, or biopsy.
e. Acyclovir is commonly used to treat neonatal HSV, but limited data are available for its use in treating progressive varicella, and it is not recommended unless the infant has active zoster (Bechtel, 2017). Passive immunization using varicella-zoster immune globulin (VZIG or VariZIG) is recommended for infants born to women who developed active infection 5 days or less before delivery to 2 days after delivery, given as soon as possible after birth. Additional therapy of the neonate is supportive.
f. Isolation procedures: Standard, airborne, and Contact Precautions for hospitalized neonates, continued 21 to 28 days if treated with VZIG. Infants with embryopathy without active lesions do not require isolation.

L—*Lyme disease.*

a. Spirochete of the species *Borrelia burgdorferi*; common vector-borne illness transmitted by ticks.
b. Lyme disease occurs throughout the world, and in the United States most cases occur in endemic areas, including New York, New Jersey, Pennsylvania, Minnesota, and Wisconsin. Disease progression can cause severe sequelae, including meningitis and encephalitis and carditis. Concern regarding transplacental transmission

in humans exists due to known transmission and congenital infection of other spirochetes of the *Borrelia* genus, but documentation of congenital disease or complications of pregnancy due to Lyme disease have not been reported (Meyerhoff, 2019). *B. burgdorferi* has not been isolated in breast milk. Studies have isolated transplacental transmission in animals with reproductive failure and severe fetal infection (Meyerhoff, 2019), but studies in humans have shown no adverse effect to the fetus from maternal Lyme disease.

c. No diagnostic studies or treatment of the neonate is indicated with confirmed maternal Lyme disease. Parents should be assured there is no evidence suggesting increased risk to the infant.

A—*Acquired immunodeficiency syndrome/human immunodeficiency virus.*

a. HIV is a cytopathic lentivirus of the family Retroviridae; human RNA retrovirus.
   1) HIV type 1 (HIV-1) prevalent in the United States; HIV type 2 (HIV-2) predominantly found in West Africa; few cases have been reported in the United States.
      a) HIV-2 has a milder disease course with longer time to develop.
   2) HIV-1 requires reverse transcriptase enzyme to convert RNA to DNA, then becomes integrated in the host cell genome as a provirus.
   3) Suppression of T-helper lymphocytes. This results in B-cell and suppressor T-cell dysfunction, with subsequent defects in cell-mediated immunity and development of opportunistic infections.

b. Virus is found in blood, semen, cervicovaginal secretions, and breast milk. Most infants are infected perinatally, accounting for 91% of cases (Rivera, 2017), though intrauterine transmission may occur. Infants with a positive HIV peripheral blood test within the first 48 hours of life are considered to be infected in utero and tend to have early onset of symptoms. Intrapartum transmission during exposure to maternal blood or genital tract secretions is presumed. The risk of mother-to-child transmission without interventions is 12% to 40%, with an average of 25% to 30% in the United States. The CDC estimates 215 to 370 infants with HIV infection are born each year in the United States (Rivera, 2017).

c. Infants are asymptomatic at birth and are classified as exposed, infected, or seroreverted according to their immunologic status. Disease progression is more rapid in children than in adults, and infected infants may become seriously ill within 2 to 4 weeks of life. Ten percent to 20% of untreated infants die before 4 years of age, with a median age at death of 11 months. Symptoms of infection include (Rivera, 2017):
   1) Failure to thrive.
   2) Generalized lymphadenopathy, hepatomegaly, and splenomegaly.
   3) Recurrent oral and diaper candidiasis.
   4) Systemic bacterial infections.
   5) Lymphoid interstitial pneumonitis.
   6) Hyperreflexia, hypertonia, floppiness, and developmental delay.
   7) Parotitis, hepatitis, nephropathy, and cardiomyopathy.
   8) Recurrent diarrhea.
   9) Opportunistic infections (viral and bacterial).
   10) Unexplained fevers.
   11) Malignancies.

d. The preferred diagnostic test for neonatal HIV-1 is DNA PCR. HIV nucleic acid tests (NAT) tests results are available within a few days, and a neonate can now be diagnosed as likely to have an HIV infection within a few days (U.S. Department of Health and Human Services, 2017).
   1) May detect proviral DNA before 48 hours of life with a sensitivity of 55% (U.S. Department of Health and Human Services, 2017); considered in-utero transmission if positive.
   2) Test is 93% positive by 2 weeks of life, 96% to 99% by 1 month of age, with 97% specificity (U.S. Department of Health and Human Services, 2017).
      a) Western blot; confirmatory test, but unreliable for HIV-2.
   3) Plasma viral RNA assesses viral load and can aid in monitoring disease progression and therapy efficacy, but is unreliable for diagnosis in the first 2 weeks of life.
   4) Viral culture; expensive and long time for results, not recommended.
   5) Timing of initial testing varies from less than 48 hours of life to 14 days, and should be repeated at 1 to 2 months of age and again at 4 to 6 months of age. An infant is considered infected with two positive test samples by DNA or RNA PCR (Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children, 2017).

e. Initiation of early antiretroviral (ARV) therapy reduces maternal–child transmission, morbidity, and mortality. Maternal therapy should include a combination ARV therapy that includes oral zidovudine (ZDU) beginning at 14 to 34 weeks of gestation and continuing throughout pregnancy. During labor, IV ZDU is recommended, and delivery via cesarean section before rupture of membranes is recommended for women with unknown plasma viral loads or more than 1000 copies/mL

(https://aidsinfo.nih.gov/contentfiles/lvguidelines/PediatricGuidelines.pdf). Infants should receive ARV therapy from birth, regardless of clinical symptoms, viral load, or immune status.

1) Bathe as soon as possible after birth.
2) Low risk of perinatal HIV transmission due to mother receiving standard antiretroviral therapy (ART) during pregnancy then 4 weeks of ZDV (U.S. Department of Health and Human Services, 2017).
3) From birth in term and preterm neonates: ZDV, lamivudine, nevirapine (U.S. Department of Health and Human Services, 2017).
4) From birth in term infants: emtricitabine, raltegravir (U.S. Department of Health and Human Services, 2017).
5) From 2 weeks of age in term neonates: lopinavir, ritonavir (U.S. Department of Health and Human Services, 2017).
6) An additional one- to two-drug regimen is used for infants born to HIV-infected mothers who did not receive any ARVs before onset of labor or for infants proven to be infected while on ZDU prophylaxis. Additional medications include lamivudine, nelfinavir, didanosine, stavudine, nevirapine, or lopinavir–ritonavir, but not all may be paired due to adverse reactions. Standards are still evolving, and collaboration with an HIV treatment center is recommended.
7) In the United States, where formula is readily available and safe, breastfeeding is not recommended (U.S. Department of Health and Human Services, 2017).
8) Follow-up at 2 to 4 weeks is recommended to assure drug regimen compliance and to monitor for ZDU-associated anemia.
9) Newborns should be tested for HIV before beginning treatment and then again at 4 to 6 weeks, 3 months, and 6 months (U.S. Department of Health and Human Services, 2017).
10) Long-term follow-up and prompt intervention during bacterial and treatable opportunistic infections.
11) Routine immunization schedule and doses for all inactivated vaccines, with MMR considered for children not severely immunosuppressed, as they are at high risk for complications associated with varicella-zoster and measles (Rivera, 2017; U.S. Department of Health and Human Services, 2017).

f. Isolation procedures: Standard Precautions should be strictly followed.

***Parvovirus B19* (Erythrovirus**; commonly known as *fifth disease*).

a. Single-stranded, nonenveloped DNA virus of the family Parvoviridae.
b. Common cause of infection worldwide. Transmitted through respiratory secretions and blood, and vertical transmission from mother to fetus. Intrauterine transmission rates range from 15% to 70%, depending on the gestational age, with adverse fetal outcomes less than 10%; highest risk associated with initial infection before 20 weeks of gestation, though may cause fetal demise in all trimesters (Cennimo, 2018).
c. Neonatal morbidities associated with primary maternal infection during pregnancy include nonimmune hydrops fetalis, myocarditis, pericardial effusions, meconium ileus, peritonitis, hyperechoic bowel, anemia, and fetal demise, but also has been associated with asymptomatic neonatal infections and normal deliveries. Maternal symptoms include malaise, arthralgia, rash, coryza, or fever (Riley and Fernendes, 2018).
d. Mothers and fetuses with symptoms should be considered high risk and tested for serum IgG and IgM antibodies to parvovirus B19. Presence of IgG but not IgM indicates prior infection, as IgG is present for life. ELISA is also sensitive for B19 infections (Riley and Fernendes, 2018). Serum PCR assay also can detect low levels of the virus up to 9 months after acute infection.
e. Some cases of associated hydrops fetalis have successfully been treated with intrauterine blood transfusions. Other therapy is supportive.
f. Isolation precautions: Standard Precautions and droplet precautions for infants with unresolved hydrops fetalis associated with parvovirus B19 at the time of delivery.

Zika Virus.

a. Arthropod-borne flavivirus transmitted by *Aedes aegypti* mosquitoes first detected in humans in 1952 (LaBeaud, 2017).
b. Mortality rates are 4.6% with no specific treatment beyond supportive (LaBeaud, 2017).
c. The disease is associated with neurologic complications, including microcephaly; myelitis; low-grade fever; pruritic rash on face, trunk, palms, and soles; or arthralgia (LaBeaud, 2017).
d. Transmission to humans occurs through the bite of a mosquito; maternal–fetal transmission; vaginal, oral, or anal sex; blood product transfusion; organ transplantation; and laboratory exposure (LaBeaud, 2017).
e. Close monitoring, including ophthalmic examination, laboratory tests, and consultation with specialists such as neurologists (Nielsen-Saines, 2018).
f. Onset after contamination is 2 to 14 days with a mild illness that lasts 2 to 7 days (LaBeaud, 2017).
g. Complications are congenital microcephaly, encephalitis, brain ischemia, or fetal loss. Zika virus has been shown in semen and female genital secretions (LaBeaud, 2017).

h. A normal head circumference does not exclude the diagnosis of the Zika virus (Baley and Gonzalez, 2020).
i. Diagnosis should be suspected in pregnant woman who demonstrate clinical symptoms and have resided in or traveled to an area affected or had unprotected sexual contact with a person who also meets this criteria (LaBeaud, 2017).
j. Prevention: wear long sleeves and long pants, stay indoors, and avoid sexual contact with an individual who has traveled to an area with Zika virus for 3 weeks.
k. Additional measures include avoid standing water in areas such as flowerpots or discarded tires.
l. The presence of Zika virus RNA in serum, urine, or CSF within the first 24 hours of life (Nielsen-Saines, 2018). Maternal–fetal transference can occur during labor or delivery. Zika is identified also in breast milk.
m. The greatest risk of transmission is during the first or second trimester (Nielsen-Saines, 2018). Negative real-time reverse (rRT)-PCR with a positive Zika virus IgM indicates probable Zika infection (Nielsen-Saines, 2018). Infection is unlikely if both rRT-PCR and IgM are negative (Baley and Gonzalez, 2020).
n. Infants who acquire Zika postnatally have a milder course of the disease.

Chlamydia.

a. Most common notifiable disease caused by an intracellular gram-negative parasite, *C. trachomatis.*
b. Incubation period is 5 to 14 days after birth.
c. Infects the mucous membranes of the eye and develops conjunctivitis 5 to 12 days after birth or subacute, afebrile pneumonia that may occur 1 to 3 months after birth (CDC, 2015).
d. From 2010 to 2014, the rate of chlamydial conjunctivitis in infants decreased by 40.7%, or 2.7 to 1.6 cases per 100,000 live births, with an increase of 31.2% during 2014 to 2015 to 2.1 cases per 100,000 live births (CDC, 2017).
e. No agent can prevent the transmission of *C. trachomatis* from the mother to the baby (McCourt, 2017).
f. Prevention is only in the prenatal treatment of the pregnant mother.
g. Direct fluorescence antibody (DFA) tests and nucleic acid amplification tests (NAATs) are used to diagnose. NAAT is not currently approved by the FDA.
h. Neonates suspected of having chlamydial conjunctivitis should also be tested for *Neisseria gonorrheae* (CDC, 2015).
i. Symptoms include cough, nasal congestion, tachypnea, normal WBC count, and remaining afebrile.
j. Neonatal chlamydial conjunctivitis can be treated with an IV third-generation cephalosporin. Neonatal conjunctivitis is also treated with oral erythromycin for 14 days, which is 80% to 90% effective (McCourt, 2017).
k. Erythromycin use has been shown to increase infantile hypertrophic pyloric stenosis. Follow-up is required.
l. Alternative regimen is azithromycin daily for 3 days.
m. Additional complications can result in chlamydial pneumonia in the newborn.

Gonorrhea.

a. Second most commonly reported disease caused by *N. gonorrhoeae.*
b. Develops during the first month of life.
c. Purulent infection of the mucous membranes as infant passes through the vaginal canal of an infected mother or ascending infection through fetal monitoring devices of the scalp (Wong, 2017).
d. Incidence as much as 1% to 2% of all deliveries (McCourt, 2017).
e. Neonates are susceptible to ophthalmic neonatorum due to the lack of immunity, the absence of lymphoid tissue around the eyes, and the lack of tears (McCourt, 2017).
f. Vertical transmission can result in conjunctivitis, known as *ophthalmia neonatorum,* and can result in permanent damage and blindness (Wong, 2017).
g. Additional damage can result in systemic arthritis or meningitis.
h. Prevention is through the use of silver nitrate or erythromycin ointment.
   1) Two drops of 1% silver nitrate or a 1-cm ribbon of erythromycin placed in lower conjunctival sac.
   2) Erythromycin ointment is the drug of choice, as it has a lower incidence in the development of chemical conjunctivitis (McCourt, 2017).
i. Diagnosis through cultures of the eye, blood, CSF, or other potential sites of infection
j. Consult infectious disease specialist.
k. Initial treatment: ophthalmic irrigation, ceftriaxone 25 to 50 mg/kg IV or IM once (maximum 125 mg). Followed by ceftriaxone once a day for 7 days or every 12 hours for 7 days for neonates with hyperbilirubinemia (McCourt, 2017).
l. Ophthalmology clinic referral is needed.

Infection Control

A. **HAIs** are a major cause of morbidity and mortality in infants and children. The CDC estimates approximately 5%

to 10% of hospitalized patients in the United States develop HAIs, and the estimated cost for each central line–associated infection is $46,000 (CDC, 2016; Haddadin and Regunath, 2017). In the NICU, HAIs are primarily acquired from the neonate's own flora, but in the NICU environment the hands of health care workers also play an important role in transmission. Risk factors are confounded by multiple factors, including birth weight and the immature immune system. LBW remains one of the strongest risk factors, although the presence of indwelling intravascular or transmucosal medical devices has also been identified as one of the greatest risk factors of HAIs. Hand hygiene remains the single most important prevention of HAIs (CDC, 2016; Ramasethu, 2017).

1. The CDC has published guidelines and recommendations for the prevention of HAIs, including isolation precautions, guidelines for protecting health care workers, and guidelines for the prevention of postoperative and device-related infections. These guidelines can be found on the CDC website (https://www.cdc.gov/hai/prevent/prevention.html). Additional resources are available through the Society for Healthcare Epidemiology, the Association for Professionals in Infection Control and Epidemiology, and The Joint Commission.
2. Standard Precautions should be strictly adhered to for all patients, regardless of diagnosis, gestational age, or presence of infection. Transmission-based precautions should be utilized in addition to Standard Precautions for patients who are infected or colonized with pathogens that are transmitted by airborne, droplet, or direct contact. All health care providers are responsible for following infection control practices and staying informed and educated on the latest guidelines and practices to help prevent HAIs.
3. Central line–associated bloodstream infections (CLABSIs) remain a prominent concern in NICU settings. As a subset of nosocomial infections, CLABSI is defined as a bloodstream infection with an initial positive blood culture that occurs at least 2 days after placement or less than 2 days before a central line is placed or removed with the infection not attributable to another site (Marschall et al., 2014; Ramasethu, 2017). VLBW, infants less than 750 g, are at highest risk with significant neurodevelopmental impairment and prolonged hospitalizations occurring with one or more episodes of HAI in these LBW infants (Ramasethu, 2017). From 2008 to 2013, there was a 46% decrease in CLABSI in the United States as a result of adherence to CLABSI guidelines as outlined by the CDC (Ramasethu, 2017). CDC guidelines for prevention of CLABSIs were established in 2011 and updated in 2017 (available at https://www.cdc.gov/hai/prevent/prevention.html) and include:
   a. Prompt removal of unnecessary central lines with daily audits of necessity.
   b. Proper insertion practices.
      1) Proper hand hygiene, with palpation of insertion sites, before and after inserting, replacing, or dressing an intravascular catheter (Ramasethu, 2017).
      2) Strict aseptic technique with maximal sterile barrier precautions, including gown, mask, cap, sterile gloves, and full-body drape.
      3) Appropriate skin cleansing.
      4) Choose best insertion site to minimize infection and complications.
      5) Maintain intact sterile, transparent, semipermeable dressings.
   c. Maintain central lines appropriately.
      1) Proper hand hygiene.
      2) Scrub access port or hub immediately before use with antiseptic (e.g., chlorhexidine) (no claims can be made about the safety of chlorhexidine in infants <2 days) (Ramasethu, 2017), povidone–iodine, an iodophor, or 70% alcohol.
      3) Access with sterile devices only.
      4) Replace soiled, nonocclusive dressings.
      5) Dressing changes under aseptic technique using clean or sterile gloves.
   d. Empower staff to monitor proper procedures.
   e. Bundle supplies for ease of accessibility.
   f. Provide checklists for providers to ensure compliance with proper practices.
   g. Provide adequate access to hand hygiene and monitor adherence to procedure.
   h. Provide education to all staff regarding insertion, usage, and maintenance.
4. Prevention of ventilator-associated pneumonia (VAP). VAP is the second most common HAI in NICU patients. VAP is associated with increased hospitalization and health care costs. Rates of VAP ranging from 2.7 to 16.9 episodes per 1000 ventilator days have been reported in some neonatal and surgical populations (Al-Alaiyan and Binmanee, 2017).
   a. Associated with aspiration of secretions, colonization, or use of contaminated equipment.
   b. Risk factors include prematurity, LBW, sedation, paralytic agents, intubation, mechanical ventilation, orogastric/nasogastric tube placement, and use of medications that increase bacterial colonization (e.g., broad-spectrum antibiotics, antacids, or H_2 blockers) (Ramasethu, 2017).

c. Prevention strategies are based upon adult studies (Ramasethu, 2017) and include:
   1) Active surveillance for VAP.
   2) Minimize use of mechanical ventilation using weaning protocols, and promote use of noninvasive ventilation when possible.
   3) Educate providers who work with ventilated patients regarding VAP.
   4) Disinfect, sterilize, and maintain respiratory equipment; remove condensation from circuit; and change circuit when visibly soiled.
   5) Perform regular oral care.
   6) Maintain semirecumbent position (30- to 45-degree head-of-bed elevation) unless medically contraindicated.
   7) Avoid unplanned extubations.
   8) Avoid gastric overdistention.
   9) Avoid H_2 blockers.
   10) Use in-line suctioning devices.

5. **Catheter-associated urinary tract infections (CAUTIs)**
   a. Most HAI CAUTI infections are the result of instrumentation of the urinary tract (CDC, 2018). CAUTI infections are those that occur within 48 hours of the placement of a urethral urinary catheter.
   b. Symptoms of CAUTI in the neonate include:
      1) Prolonged jaundice, fever (>38.0° C), hypothermia, apnea, bradycardia, lethargy, poor feeding, failure to thrive, emesis, and irritability (CDC, 2018; Fisher, 2017). Many of these symptoms are nonspecific for CAUTI in the neonate and require further investigation.
      2) Diagnosis with a CBC, blood culture, urinary analysis (UA), and urine culture.
      3) Treatment is indicated if the UA is gram-stained positive for bacteria, WBC greater than 5 per high powered field, nitrates, or leukocyte esterase (an enzyme that is released by WBC and is clinically significant); 10,000 colonies/mm^3 defines bacteremia (Fisher, 2017).
      4) Antibiotic use is based on sensitivities: ampicillin, gentamycin, cefotaxime, and ceftriaxone (not to be used in infants <6 weeks of age) for 7 to 10 days (Fisher, 2017). After 7 days of treatment, follow-up should be done to rule out recurrent infections (Fisher, 2017).

6. **Surgical site infections.**
   a. Recent study of 7379 neonates found a 2.6% surgical site infection (SSI) rate with perioperative variables being the most important factor (Gilje et al., 2017).
   b. SSIs result in prolonged hospitalizations independent of all other factors (Gilje et al., 2017).
   c. Neonatal SSIs are comparable to pediatric surgical infection rates and vary from institution to institution.
   d. Higher rates in neonates requiring gastroschisis repair and lower rates in neonates who have patent ductus arteriosus repairs (Segal et al., 2014).
   e. Antibiotic prophylaxis for surgery is indicated only for published clinical guidelines and timed for tissue and serum bactericidal effect once the incision is made (Berrios-Torres et al., 2017).
   f. Administration of antibiotic within 1 hour of the surgical incision unless it is vancomycin, which is within 2 hours of the surgical incision.
   g. In clean and clean contaminated procedures, no further antibiotic prophylaxis is recommended even with drains (Berrios-Torres et al., 2017).

7. Optimal staffing-to-patient ratios have not been established for NICUs, but low nurse–to–high patient ratios have been correlated with increased rates of nosocomial infections. Understaffing has also been correlated with periods of decreased hand hygiene compliance, leading to further infection rates (Ramasethu, 2017).

B. **Vaccination remains a critical component to preventing and controlling the spread of infection nationally and globally.**
   1. The four major strategies for protecting neonates are:
      a. Maternal immunization during pregnancy.
      b. Passive immunization with antibodies or immune globulins.
      c. Active immunization of neonates.
      d. Immunization of contacts to prevent transmission (herd immunity).
   2. Recommendations and schedules for vaccination use are constantly changing. Health care providers must review current guidelines from regulatory and advisory bodies for current practice standards.
      a. Guidelines and recommendations are available from the Advisory Committee on Immunization Practices (ACIP) of the CDC and can be found at https://www.cdc.gov/vaccines/acip/index.html.
      b. The Recommended Immunization Schedules for Persons Aged 0 Through 18 Years are updated annually and approved by the ACIP, the AAP, the American Academy of Family Physicians, and the American College of Obstetricians and Gynecologists. The 2018 schedule is available at https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf.

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CHAPTER 33

Renal and Genitourinary Disorders

Denise Maguire

OBJECTIVES

1. Relate congenital renal/genitourinary disorders to embryologic development.
2. Apply knowledge of normal renal anatomy and physiology to renal pathophysiology that presents in the neonatal period.
3. Explain the etiology of selected neonatal renal/genitourinary disorders.
4. Describe clinical manifestations and complications that may be associated with selected neonatal renal/genitourinary disorders.
5. Determine the appropriate management of each disorder discussed.
6. Formulate an appropriate plan of care for each disorder discussed.

Overview

Homeostasis of the newborn is dependent on a functional renal system. In utero, the placenta is the organ responsible for fluid and electrolyte homeostasis. After birth, the kidney must assume its role as the regulator. An understanding of basic principles in renal developmental physiology is essential for successful clinical management of sick preterm and term neonates. This chapter presents information on the anatomy and physiology of the kidney as a base from which to discuss selected renal/genitourinary disorders. Fetal renal function is closely linked to both the developmental stage of the kidney and the intrauterine or extrauterine environment of the fetus. Maternal exposure to a variety of teratogens may not only alter function of the fetal kidney but may also cause permanent impairment of renal development and function. The Barker hypothesis, as well as the theory of the developmental origins of disease, contend that adverse events in utero induce compensatory responses in the fetus, such as altered kidney development. These changes in organ structure may persist permanently and have long-term consequences for renal functions, such as the future development of hypertension. These considerations underscore the lifetime importance of optimal prenatal and neonatal care.

Fetal Development of the Kidney

A. **General concepts.**
   1. The fetal kidney develops from three successive structures: the pronephros, the mesonephros, and the metanephros.
   2. Nephrogenesis is the formation of new nephron units.
   3. Embryologic development of the urinary system begins within the first weeks after conception and progresses through three stages.
   4. Both the urinary and the genital systems develop from the same germ layer of the embryo.

B. **Pronephros.**
   1. Pronephros is a primitive and nonfunctional kidney that appears early in the fourth week of gestation, then disappears by the fifth week (Moore et al., 2016).
   2. Pronephroi degenerate but the ducts and tubes persist, which are then used by the mesonephroi (Moore et al., 2016).

C. **Mesonephros.**
   1. This intermediate kidney appears from 5 to 12 weeks' gestation and consists of glomeruli and tubules (Moore et al., 2016).
   2. The pronephric tube extends into the cell lining of the mesonephros to form the Wolffian duct. An outbranch of the Wolffian duct, called the *ureteric bud,* aids in the development of the metanephros (Merguerian and Rowe, 2018).
   3. The mesonephroi function as the intermediate kidney, then undergo involution through apoptosis (programmed cell death) in preparation for the next stage of development (Merguerian and Rowe, 2018).

D. **Metanephros.**
   1. Differentiation of the metanephros (a primitive form of the permanent kidney) starts around 5 weeks' gestation, and the first nephrons are formed by week 8 (Moore et al., 2016).

2. This primitive kidney is functional at around the ninth week of gestation and begins to form urine (Moore et al., 2016).
3. Interactions between the ureteric bud and the metanephric mesenchyme result in the formation of both the collecting duct system and the nephrons of the permanent kidney. The stalk of the ureteric bud becomes the ureter, and the cranial part of the bud branches to form the collecting tubules. This branching morphogenesis leads to the formation of the renal collecting system, with the first generations of the collecting tubules enlarging to form the major calices, while subsequent generations form the minor calices (Merguerian and Rowe, 2018; Moore et al., 2016).
4. Nephrogenesis is complete at 34 weeks of gestation, when each kidney contains its definitive complement of approximately 800,000 to 1.2 million nephrons (Abrahamson, 1991; Matsell and Hiatt, 2017).

E. **Positional changes of the fetal kidney** (Moore et al., 2016).
1. Initially the fetal kidneys are closely approximated and located down in the pelvis in the area of the sacrum. As the abdomen and the pelvis grow, the kidneys move upward and apart from each other. The kidneys attain their adult location in the ninth week of gestation.
2. Early in development, the hilum of the kidney (area where the veins, arteries, and ureters enter the kidney) faces ventrally (toward the abdomen). As the kidneys ascend upward, they also rotate medially, and by the ninth week of gestation the hilum is directed anteromedially. Eventually the kidneys are located on the posterior abdominal wall.
3. The kidneys become fixed once they come into contact with the suprarenal (adrenal) glands in the ninth week of gestation.

F. **Changes in blood supply of the fetal kidney** (Moore et al., 2016).
1. As the fetal kidneys change location, they obtain their blood supply from local blood vessels. Initially the renal arteries are branches of the common iliac arteries. Future blood is supplied from the distal aorta; then, as the kidneys rise upward, new branches to the aorta develop. Normally the old vessels involute and disappear.
2. The permanent renal arteries develop from branches of the abdominal aorta. The right renal artery is longer and often more superior.

Development of the Bladder and Urethra (Vogt and Springel, 2020)

A. **Formation**.
1. The bladder and urethra are formed during the second and third months of gestation.
2. During the fourth to seventh week of development, the cloaca begins to divide and develop. As the cloaca develops, portions of the mesonephric ducts are absorbed into the bladder wall.
3. Caudal portions of the ureters, which originate from the mesonephric ducts, enter the bladder.
4. During these processes, the ureteral orifices move cranially and the mesonephric ducts move closer together to enter the prostatic urethra, forming the trigone of the bladder.

Renal Function

A. **Intrauterine life.** The kidneys play only a minor role in regulating fetal salt and water balance because this function is maintained primarily by the placenta. The most important functions of the prenatal kidneys are the formation and excretion of urine to maintain an adequate amount of amniotic fluid (Matsell and Hiatt, 2017; Vogt and Springel, 2020), which also contributes to fetal pulmonary development and provides mechanical protection to the enlarging fetus (Wang et al., 2017).

B. **Renal blood flow.** Renal blood flow is low during fetal life, accounting for only 2% to 4% of the total cardiac output. This proportion increases after birth, from a value of 5% in the first 12 hours of life to 10% at the end of the first week (Matsell and Hiatt, 2017; Vogt and Springel, 2020).

Renal Anatomy

A. **Gross anatomy.**
1. Cortex: outermost portion of the kidney, which contains the glomeruli, proximal and distal convoluted tubules, and collecting ducts of the nephron.
2. Medulla: middle section of the kidney, which contains the renal pyramids, straight portions of tubules, loops of Henle, vasa recta, and terminal collecting ducts.
3. Renal sinus and pelvis: innermost portion of the kidney. The renal sinus contains the uppermost part of the renal pelvis and calyces, surrounded by some fat in which branches of the renal vessels and nerves are embedded.
4. Ureter: excretory duct of the kidney, which transports urine from the kidney to the bladder (Fig. 33.1).

B. **Microscopic renal anatomy: the nephron** (Hall, 2016).
1. The nephron is the functional unit of the kidney and produces urine. Each kidney contains about 800,000 to 1 million nephrons.
2. Each nephron contains a tuft of glomerular capillaries called the *glomerulus*, through which large amounts of fluid are filtered from the blood, and a

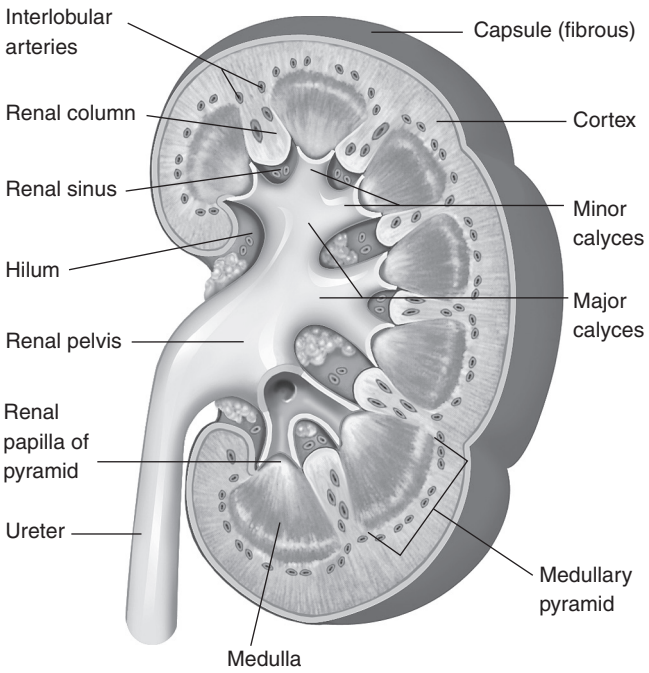

Fig. 33.1 Renal anatomy. *(From Patton K. T., & Thibodeau, G. A. [2016]*. Anatomy and physiology *[9th ed.]. St. Louis, MO: Elsevier.)*

long tubule in which the filtered fluid is converted into urine on its way to the pelvis of the kidney.

3. The glomerulus contains a network of glomerular capillaries that is encased in Bowman's capsule. Fluid filtered from the glomerular capillaries flows into Bowman's capsule and then into the proximal tubule, which lies in the cortex of the kidney.
4. From the proximal tubule, fluid flows into the loop of Henle, which dips into the renal medulla. Each loop consists of a descending and an ascending limb.
5. Collecting ducts empty into the renal pelvis of the kidney. Urine flows from the collecting ducts into the renal calyces and then into the ureters. Peristaltic contractions force urine down the ureters into the bladder.

Regulation of Postnatal Renal Hemodynamics (Solhaug and Jose, 2017)

A. **Postnatal regulation:** Postnatal regulation consists of a combination of related cardiac output, perfusion pressure, and renal vascular resistance. The low renal blood flow is the result of several factors, such as decreased number of glomeruli, lower systemic pressure, and higher renal vascular resistance.

B. **Cardiac output:** The proportion of cardiac output distributed to the kidneys is 4% to 6% in the first 12 hours of life and increases to 8% to 10% in the first week of life. In comparison, 25% of cardiac output is distributed to the kidneys in the normal adult.

C. **Systemic vascular resistance:** Systemic vascular resistance increases markedly after birth, which may cause a redistribution of blood flow to organs other than the kidneys and immediately contribute to the low neonatal renal blood flow.

D. **Contribution of structural changes:** New vascular channels from nephrogenesis, as well as the continued formation of new glomeruli and vascular remodeling, may influence renal hemodynamics postnatally.

E. **Vasoactive factors that regulate renal blood flow:** Several vasoactive agents participate in the regulation of renal blood flow in the postnatal maturing kidney.

1. **Renin–angiotensin system** is a powerful system to control blood pressure. Renin is a protein enzyme released by the kidneys when the arterial pressure is low. It acts on another plasma protein, angiotensinogen, to release an amino peptide, angiotensin I.
2. **Angiotensin I** rapidly converts to angiotensin II predominantly in the lungs, although other tissues, such as the kidneys and blood vessels, contain converting enzyme and can form angiotensin II.
3. **Angiotensin II** is an extremely powerful vasoconstrictor but is rapidly inactivated in the blood after 1 to 2 minutes. A second effect is to decrease excretion of sodium and water, which slowly increases the extracellular fluid volume (Hall, 2016).
4. **Natriuretic peptides:** atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and C-type natriuretic peptide (CNP). ANP and BNP are produced in the atria and ventricles, whereas CNP is found mainly in the brain, pituitary gland, vascular endothelium, and kidneys. The primary effects of ANP are (1) vasodilation and decrease in mean blood pressure; (2) increase in renal blood flow, glomerular filtration rate (GFR), and filtration fraction; (3) inhibition of sodium and water reabsorption in both proximal and distal tubules; and (4) decreased concentrating ability.
5. **Nitric oxide** is synthesized endogenously and is an important regulator of renal hemodynamics in the immature kidney. Nitric oxide can function as a vasodilator to counterbalance vasoconstrictors such as angiotensin II (Solhaug and Jose, 2017).
6. **Prostaglandins,** which are endogenously produced, can cause vasodilation. Renal prostaglandin production is increased during the perinatal period, and the urinary excretion of prostaglandin E is 5 times that noted at term (Solhaug and Jose, 2017).

F. **Glomerular filtration** (Vogt and Springel, 2020).

1. As blood passes through the capillaries, plasma is filtered through the glomerular capillary walls. Filtrate is collected in Bowman's capsule and enters the tubules, where composition is modified until it is excreted as urine.

2. Newborns have a limited ability to concentrate urine. Increasing glomerular perfusion pressures in the first few weeks of life result in increases in the GFR, which further improves as renal blood flow improves and superficial cortical nephrons mature during the first 2 years of life (Vogt and Springel, 2020).
   a. Factors that may contribute to decreased GFR at birth include:
      1) Small glomerular capillary area available for filtration.
      2) Structural immaturity of the glomerular capillary, which is associated with decreased water permeability.
      3) Decreased blood pressure.
      4) Increased hematocrit.
      5) Renal vasoconstriction, which results in decreased glomerular plasma flow.
   b. Neonates born at less than 34 weeks' gestation have a low GFR (0.5 mL/min) until nephrogenesis is completed.
3. Three primary factors determine GFR.
   a. Glomerular capillary hydrostatic pressure (the major controller of GFR).
   b. Hydrostatic pressure in Bowman's capsule.
   c. Capillary colloid osmotic pressure.
4. Additional factors that affect GFR.
   a. Capillary surface area.
   b. Permeability of capillary basement membrane.
   c. Rate of renal plasma flow.
   d. Changes in renal blood flow.
   e. Changes in blood pressure.
   f. Vasoactive changes in afferent or efferent arterioles.
   g. Ureteral obstruction.
   h. Edema of kidney.
   i. Changes in the concentration of plasma proteins.
      1) Dehydration.
      2) Hypoproteinemia.
   j. Increased permeability of the glomerular filter.
   k. Decrease in total area of the glomerular capillary bed.

G. **Tubular function** (Vogt and Springel, 2020).
1. Components of the tubular system include the proximal tubule, loop of Henle, distal tubule, and collecting ducts.
2. Tubules modify the glomerular ultrafiltrate, leading to production of urine, which is accomplished by the process of tubular reabsorption and secretion.
   a. Tubular reabsorption is the movement of substances into the peritubular capillary plasma from the tubular epithelium, which occurs by diffusion and active transport. The proximal tubule is the major site of reabsorption.
   b. Tubular secretion is the movement of substances into the tubular epithelium from the peritubular capillary plasma. Tubular secretion is necessary for regulation of fluid and electrolyte balance, along with other renal processes.
3. Regulation of fluids and electrolytes is an important tubular function.
4. Tubular function is altered in the neonate as a result of decreased renal blood flow and GFR.
5. Tubular portions of the neonatal nephron are smaller and less functionally mature, resulting in an altered ability to transport sodium, urea, chloride, and glucose, with decreased renal thresholds for many substances.
6. Rapid maturation of the proximal tubular cells occurs between 32 and 35 weeks of gestation.

H. Concentration and dilution mechanism (Vogt and Springel, 2020).
1. Maintenance of osmolality: The preterm and term neonate's ability to dilute urine is well developed, but concentrating ability is limited. A major function of the kidney is to maintain osmolality of extracellular fluid within the narrow range compatible with optimal cellular function.
2. Sites of urinary concentration and dilution.
   a. Loop of Henle.
   b. Collecting duct.
3. Factors responsible for the limited ability of the neonatal kidney to concentrate urine.
   a. Anatomic immaturity of the renal medulla.
   b. Decreased medullary concentration of sodium chloride and urea.
   c. Diminished responsiveness of the collecting ducts to arginine vasopressin.
4. Normal range of neonatal specific gravity is 1.002 to 1.010.
5. Maximum concentrating ability.
   a. Term neonate: 700 mOsm of water/kg.
   b. Preterm neonate: 600 to 700 mOsm of water/kg.
6. Capacity for urine dilution.
   a. Thirty to 50 mOsm of water/kg.
   b. Ability of neonate to excrete a hypotonic load is limited, presumably because of the low GFR.

I. Renal regulation of acid–base balance (Hall, 2016).
1. The kidneys regulate a powerful acid–base regulatory system.
   a. Molecules containing hydrogen atoms that can release hydrogen ions (H^+) in solutions are referred to as *acids*. The body produces acids mainly from the metabolism of proteins. These acids are called *nonvolatile* because they cannot be excreted by the lungs—they must be excreted by the kidneys.
   b. The term *alkalosis* refers to excess removal of H^+ from the body fluids, in contrast to the excess addition of H^+, which is referred to as *acidosis*.
   c. Excreting acidic urine reduces the amount of acid in extracellular fluid, whereas excreting alkaline urine removes base from the extracellular fluid.

2. The kidneys regulate extracellular H^+ concentration through three processes.
   a. Secretion of H^+.
   b. Reabsorption of filtered bicarbonate.
   c. Production of new bicarbonate.
3. Glucocorticoids can accelerate the renal processes of acidification (Wang et al., 2017).

J. **Renal regulation of potassium** (Wolf et al., 2017).
1. About 98% of potassium in the body is intracellular. Potassium is required for cell growth and division, DNA and protein synthesis, conservation of cell volume and pH, and optimal enzyme function.
2. The kidney is the major excretory organ for potassium.
3. Acidosis is associated with intracellular potassium release resulting in an increase in plasma potassium. Alkalosis results in a shift of potassium into cells and a consequent decrease in plasma potassium.
4. Acute metabolic acidosis causes the urine pH and potassium excretion to decrease. Acute respiratory alkalosis and metabolic alkalosis result in increases in urine pH and potassium excretion.
5. Potassium uptake into cells is stimulated by insulin, β-adrenergic agonists (e.g., albuterol and terbutaline), and alkalosis.

Clinical Evaluation of Renal and Urinary Tract Disease

With regard to incidence, defects of the kidneys and ureters occur in 3% to 4% of newborns; defects in shape and position are most common (Moore et al., 2016). About 20% of all congenital abnormalities are renal. The kidneys may be visualized after 16th to 17th week of gestation (Vogt and Springel, 2020).

A. **Antenatal history:** Particular attention should be given to medications, toxins, and unusual environmental exposures during the pregnancy (Vogt and Springel, 2020).

B. **Review the family medical history, including any prior fetal or neonatal deaths.** Although there is no established genetic basis for many congenital renal anomalies, certain disorders, such as renal hypoplasia/dysplasia, multicystic dysplastic kidney (MCDK), and vesicoureteral reflux, may be familial. Certain diseases, such as polycystic kidney disease and congenital nephrotic syndrome, have a clear genetic link.

PRENATAL DIAGNOSIS OF RENAL DISORDERS (BATES AND SCHWADERER, 2018; GIMPEL ET AL., 2018)

A. Prenatal findings that are associated with renal or urinary tract disease include hydronephrosis, renal cysts, hyperechoic kidneys, renal mass, oligohydramnios, and polyhydramnios. Hydronephrosis (dilation of the renal pelvis) is the most commonly identified renal anomaly.

B. Hydronephrosis may indicate upper urinary tract obstruction (ureteropelvic junction obstruction) and lower urinary tract obstruction (posterior urethral valves and prune-belly syndrome).

C. Prenatal renal cysts are associated with autosomal dominant polycystic kidney disease, MCDK, and cystic renal dysplasia.

D. Hyperechoic kidneys can result from tubular dilations (autosomal recessive polycystic kidney disease), dysplasia, or multiple microscopic cysts (Meckel–Gruber syndrome and nephrotic syndrome).

E. Oligohydramnios is not limited to renal disorders. However, it is associated with renal agenesis, renal dysplasia, and lower urinary tract obstruction.

F. Polyhydramnios is generally caused by gastrointestinal anomalies but may have a renal etiology in a small percentage of cases. Renal dysplasia, nephrotic syndrome, or inherited renal tubular defects may present with polyhydramnios.

G. Congenital renal tumors are rare. The most common tumor is a mesoblastic nephroma, which appears as a unilateral, single, solid mass on prenatal ultrasound.

POSTNATAL EVALUATION OF RENAL AND URINARY TRACT DISEASE (BATES AND SCHWADERER, 2018)

In the physical examination, findings that arouse suspicion of underlying renal defects include abnormal external ears, aniridia, microcephaly, meningomyelocele, pectus excavatum, hemihypertrophy, persistent urachus, bladder or cloacal exstrophy, abnormal external genitalia, cryptorchidism, imperforate anus, and limb deformities. Additional worrisome findings include hypertension or hypotension, ascites, and abdominal mass(es) (Vogt and Springel, 2020).

A genetics consultation may facilitate identification of a syndrome when two or more abnormal examination findings are identified.

A. A family history of renal agenesis in parents or siblings or polycystic kidney disease increases the risks of congenital kidney disease.

B. Hypertension in the newborn period is suggestive of renal disease and should be evaluated. Hypotension usually results from hypovolemia, hemorrhage, or sepsis, which may lead to acute kidney injury (AKI).

C. Delayed voiding longer than 12 hours may occur after stressful deliveries, but nearly all neonates will produce urine within 24 hours of birth. Prolonged anuria must be evaluated.

D. Palpable abdominal masses, in particular flank masses, most often originate from the urinary tract and must be evaluated.

E. Edema occurs when there is an imbalance between capillary hydrostatic and interstitial oncotic forces. The major renal causes include fluid overload secondary to a decrease in GFR from acute or chronic renal injury. Low intravascular oncotic pressure from urinary protein losses (congenital nephrotic syndrome) may also cause edema.

F. Ascites can arise as an imbalance between hydrostatic and oncotic pressures, but it can also occur secondary to decreased lymphatic drainage. The most common renal cause is urinary ascites from perforation of the ureter, renal pelvis, or bladder from obstruction (e.g., posterior urethral valves). Congenital nephrotic syndrome and renal vein thrombosis may also cause ascites.

G. Oligohydramnios (Potter) sequence may occur in infants with bilateral renal agenesis. The absence of fetal renal function results in anhydramnios, which causes fetal deformation from compression by the uterine wall. Features generally include wide-set eyes; depressed nasal bridge; beaked nose; receding chin; and posteriorly rotated, low-set ears. Other anomalies include a small, compressed chest wall and arthrogryposis. The condition is uniformly fatal. "Potter-like" features may be seen in infants with significant renal impairment and oligohydramnios. Such patients often have pulmonary hypoplasia and require careful respiratory management (Vogt and Springel, 2020).

H. Although a single umbilical artery is a relatively common anomaly seen in 0.5% to 1% of pregnancies, it has been associated with an increased risk of congenital malformations, especially genitourinary and chromosomal abnormalities (Ledbetter et al., 2018).

Laboratory Evaluation of Renal Function (Table 33.1)

A. Serum creatinine level is the simplest and most commonly used indicator of neonatal kidney function. The serum creatinine concentration immediately after birth reflects the maternal creatinine concentration, neonatal muscle mass, and GFR at the time of delivery.

1. In term infants, the serum creatinine level gradually decreases from 1.1 mg/dL to a mean value of 0.4 mg/dL within the first 2 weeks of life.

Table 33.1

Urine Evaluation of Renal Function

Evaluation	Discussion
Urine output	Anuria is absence of urine output. Oliguria is less than 0.5 mL/kg/hr. Ideally, urine output should be ≥2 mL/kg/hr.
Urine source	A clean-catch sample may be used for a urinalysis. If a culture is desired, a sterile sample must be obtained by a sterile catheterization.
Urine color and visual inspection	Cloudiness may represent a urinary tract infection or the presence of crystals. Yellow-brown to deep olive green color may represent large amounts of conjugated bilirubin. Porphyrins, certain drugs such as phenytoin, bacteria, and urate crystals may stain the diaper pink and be confused with bleeding. Brown urine suggests bleeding from the upper urinary tract, hemoglobinuria, or myoglobinuria. Hemoglobinuria occurs secondary to intravascular hemolysis, of which the most common etiology is ABO blood group incompatibility. In infants with myoglobinuria and hemoglobinuria, the urine may look red or brown and test dipstick-positive for blood, *but red blood cells are not present on microscopic examination of the urine.*
Specific gravity	Normal: 1.002 to 1.010. May be falsely elevated by high-molecular-weight solutes such as contrast agents, glucose or other reducing substances, or large amounts of protein. Urinary osmolality may be a more reliable measurement of the concentrating and diluting capacity of the kidney.
Hematuria	Defined as five or more red blood cells per high-powered field on microscopic evaluation. Causes include renal vein thrombosis, polycystic kidney disease, obstructive nephropathy, tumor, congenital malformations, urinary tract infection, and acute kidney injury. Extraurinary sources (vaginal, rectal, perineal, preputial) may also be the cause of apparent hematuria.
Proteinuria	Any form of renal injury, glomerular or tubular, will increase urinary protein excretion.
Glycosuria	Occurs when the serum glucose concentration exceeds the renal threshold. Isolated glycosuria with a normal serum glucose concentration is defined as renal glycosuria, a benign condition caused by an abnormality in the transport of proximal tubular glucose.
Microscopic analysis	May detect the presence of red blood cells, casts, white blood cells, bacteria, or crystals.

Adapted from Vogt, B. A., & Springel, B. A. (2020). The kidney and urinary tract of the neonate. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh (Eds.), *Fanaroff and Martin's neonatal-perinatal medicine* (10th ed., pp. 1676–1699). St. Louis, MO: Elsevier Mosby.

2. However, in preterm infants, the plasma creatinine level does not fall steadily from birth, but instead rises in the first 48 hours before beginning to fall to equilibrium levels (Vogt and Springel, 2020).

B. Failure of the serum creatinine level to fall or a persistent increase in serum creatinine suggests impairment of renal function. In general, each doubling of the serum creatinine level represents an approximately 50% reduction in GFR. For example, a rise in serum creatinine from 0.4 to 0.8 mg/dL represents a 50% reduction in GFR (Vogt and Springel, 2020).

C. Blood urea nitrogen (BUN) is used as an indirect measure of kidney function. The BUN may be elevated as a result of increased production of urea nitrogen in catabolic states, sequestered blood, tissue breakdown, or increased protein intake. Renal insufficiency is suspected if the BUN is less than 20 mg/dL due to intrinsic AKI, or greater than 30 mg/dL when due to prerenal azotemia (Vogt and Springel, 2020).

Radiographic Evaluation (Gimpel et al., 2018; Vogt and Springel, 2020)

A. Ultrasonography is the first-line diagnostic procedure for detecting, classifying, and following suspected renal disease. It offers a noninvasive evaluation without exposure to contrast agents or radiation. A Doppler-flow study of the renal arteries and aorta may be helpful in the evaluation of thrombosis, suspected renovascular hypertension, or AKI.

B. A voiding cystourethrogram (VCUG) is utilized to identify lower urinary tract obstruction and vesicoureteral reflux. Films of the urethra during voiding and of the bladder and ureters toward the end of voiding are essential.

C. Radioisotopic renal scanning may be used to locate anomalous kidneys, determine kidney size, and identify obstruction or renal scarring. Radioisotopic scans may also provide information about the relative blood flow to each kidney and the contribution of each kidney to overall renal function.

D. Abdominal computed tomography (CT) is useful in the diagnosis of renal tumors, renal abscesses, and nephrolithiasis. There has been recent concern related to the amount of radiation received with a CT scan (Pokora et al., 2016).

E. Fetal magnetic resonance imaging (MRI) provides detailed anatomy. The typical indication for fetal urinary tract MRI evaluation is a second- or third-trimester pregnancy with oligohydramnios, unusual location, or appearance of cysts or malformations of other organs. Regional availability and expertise in fetal MRI are still variable (Gimpel et al., 2018).

F. Genetic testing may be indicated.

Acute Kidney Injury (Table 33.2)

A. Previously referred to as *acute renal failure*, AKI is characterized by a deterioration in kidney function leading to an inability to excrete waste products and maintain fluid and electrolyte homeostasis. This condition is determined by a serum creatinine of more than 1.5 mg/dL (Vogt and Springel, 2020).

B. Oliguric AKI is characterized by a urine flow rate of less than 1 mL/kg/hr. Nonoliguric AKI is characterized by a urine flow rate greater than 1 mL/kg/hr.

C. The risk factors for developing AKI include very low birth weight (<1500 g); low 5-minute Apgar score; and neonatal conditions that decrease renal blood flow, such as septic shock, capillary leak, decreased cardiac output, and dehydration. AKI can also occur as a result of renal vascular thrombosis, renal congenital anomalies, nephrotoxins, intrarenal obstructions, intrinsic/extrinsic compression, and neurogenic bladder. The causes of AKI are multiple and fall into three categories: prerenal azotemia, intrinsic AKI, and obstructive renal failure.

D. Signs of AKI may include elevated serum creatinine and BUN, hyperkalemia, metabolic acidosis, and evidence of fluid overload or dehydration.

E. The half-life for medications excreted by the kidney (e.g., aminoglycosides, vancomycin) may also be prolonged.

EVALUATION OF ACUTE KIDNEY INJURY (VOGT AND SPRINGEL, 2020)

A. A careful review of the history should focus on prenatal ultrasound abnormalities, perinatal asphyxia, the prenatal or postnatal administration of potentially nephrotoxic drugs, and a family history of renal disease.

B. The physical examination should focus on signs of dehydration or volume overload, the abdomen, genitalia, and a search for congenital anomalies.

C. Electrolytes, BUN, creatinine, calcium, and phosphorus should be monitored frequently.

D. Urine should be sent for urinalysis, urine culture, and urine sodium and creatinine determination.

E. The fractional excretion of sodium and other diagnostic indices may be useful in differentiating prerenal from intrinsic AKI (Table 33.3).

F. Renal ultrasound is helpful in the identification of congenital renal disease and urinary tract obstruction.

MEDICAL MANAGEMENT OF ACUTE KIDNEY INJURY (VOGT AND SPRINGEL, 2020)

A. The prevention of AKI requires maintenance of an adequate circulatory volume, careful fluid and electrolyte management, prompt diagnosis and treatment of hemodynamic or respiratory abnormalities, and close monitoring of potentially nephrotoxic medications.

Table 33.2

Categories and Etiologies of Acute Kidney Injury

Category of Acute Kidney Injury	Cause
Prerenal Azotemia	
1. Respiratory distress syndrome 2. Hemorrhage 3. Septic shock 4. Increased abdominal pressures 5. Capillary leak 6. Congestive heart failure 7. Dehydration 8. Decreased cardiac output 9. Drugs that reduce renal blood flow: angiotensin-converting enzyme inhibitors, indomethacin, ibuprofen, amphotericin, tolazoline	Most common type, accounting for up to 85% of all cases. Often called prerenal azotemia, it is characterized by inadequate renal perfusion. Prompt treatment is followed by improvements in renal function and urine output.
Intrinsic Acute Kidney Injury	
1. Acute tubular necrosis (ATN) 2. Congenital anomalies a. Renal dysplasia/agenesis b. Polycystic kidney disease 3. Renal vascular causes a. Renal artery/vein thrombosis b. Disseminated intravascular coagulation 4. Infection/inflammatory disease a. Acute pyelonephritis b. Congenital syphilis and toxoplasmosis 5. Nephrotoxins 6. Intrarenal obstruction	ATN is the most common cause and appears to involve renal tubular cellular injury. The causes of ATN include perinatal asphyxia, sepsis, cardiac surgery, a prolonged prerenal state, and nephrotoxic drug administration.
Obstructive Renal Failure	
1. Congenital malformations a. Posterior urethral valves b. Bilateral ureteropelvic junction obstruction 2. Extrinsic compression (teratoma, hematocolpos) 3. Intrinsic compression (renal calculi, fungus balls) 4. Neurogenic bladder	Caused by urinary tract obstruction or compression and can usually be reversed by relief of the obstruction or compression.

Data from Askenazi, D., Selewski, D., Willig, L., & Warady, B. A. (2018). Acute kidney injury and chronic kidney disease. In C. A. Gleason & S. U. Devaskar (Eds.), *Avery's diseases of the newborn* (13th ed., pp. 1280–1287). Philadelphia, PA: Elsevier Saunders; and Vogt, B.A. and Springel, T. (2020). The kidney and urinary tract. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh (Eds.), *Fanaroff and Martin's neonatal-perinatal medicine* (10th ed., pp. 1676–1699). St. Louis, MO: Elsevier Mosby.

Table 33.3

Diagnostic Indices Related to Acute Kidney Injury (AKI)

Test	Prerenal (Azotemia) AKI	Renal (Intrinsic) AKI
BUN/Cr ratio (mg/mg)	>30	<20
FE_{Na} (%)*	≤2.5	≥3.0
Urinary Na (mEq/L)	≤20	≥50
Urinary Osm (mOsm/kg)	≥350	≤300
Urinary specific gravity	>1.012	<1.014
Ultrasonography	Normal	May be abnormal
Response to volume challenge	UO >2 mL/kg/hr	No increase in UO

BUN, Blood urea nitrogen; *Cr*, creatinine; FE_{Na}, fractional excretion of sodium; *Na*, sodium; *Osm*, osmolality; *UO*, urinary output.
* Fractional excretion of sodium (FE_{Na}) = $(U_{Na} \times P_{Cr})/(P_{Na} \times U_{Cr}) \times 100$, where U_{Na} = urine sodium; P_{Cr} = serum creatinine; P_{Na} = serum sodium; U_{Cr} = urine creatinine.
Data from Vogt, B.A. and Springel, T. (2020). The kidney and urinary tract. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh (Eds.), *Fanaroff and Martin's neonatal-perinatal medicine* (10th ed., p. 1685). St. Louis, MO: Elsevier Mosby.

B. The goal of medical management is to provide supportive care until there is spontaneous improvement in renal function.
C. With persistent oliguria, a urinary catheter should be placed to exclude lower urinary tract obstruction. If there is no improvement in urine output after bladder drainage is established, a fluid challenge of 10 to 20 mL/kg should be administered over 1 to 2 hours to exclude prerenal azotemia. A lack of improvement in urine output and increased serum creatinine suggest intrinsic AKI.
D. Fluids are generally restricted. Restriction guidelines are 30 mL/kg/day plus urine output and other measured losses (gastric/other drains).
E. Daily weights and careful intake and output measurements are necessary to follow volume status.
F. Nephrotoxic medications should be discontinued; troughs should be monitored closely to assess the risk of additional renal injury.
G. Potassium and phosphorus should be restricted in those neonates with hyperkalemia or hyperphosphatemia.
H. Metabolic acidosis, hyperkalemia, and hypertension may require treatment.

Renal Tubular Acidosis

A. Renal tubular acidosis (RTA) is defined as metabolic acidosis resulting from the inability of the kidney to excrete H^+ or to reabsorb bicarbonate. It may be a primary disorder or secondary to acquired renal injury. Poor growth may result from RTA (Vogt and Springel, 2020).
B. Generally, RTA is secondary to tubular damage from medications or obstructive uropathy (Vogt, B.A. and Springel, T. (2020)).
C. There are three main forms of RTA: type I (distal), type II (proximal), and type IV (hyperkalemic) (Table 33.4).

Developmental Renal Abnormalities

Many of the disorders of the kidney and urinary tract that present in infancy are the result of congenital malformations or inherited disorders.

A. **Unilateral renal agenesis** (Moore et al., 2016).
   1. Unilateral renal agenesis, or the congenital absence of the kidney, occurs in 1 in 1000 live births.

Part 3

Table 33.4

Three Types of Renal Tubular Acidosis

Type of RTA	Etiology	Presentation	Diagnosis	Treatment
Type I (distal)	Defect in the secretion of H^+ in the distal tubule Primary: sporadic; may be autosomal dominant or recessive Secondary: associated with other renal disorders; associated with acquired or hereditary diseases; due to tubular injury associated with drugs or toxins	Lethargy, polyuria, vomiting, dehydration, and failure to thrive	Urinary pH >6.5 in presence of a non–anion gap metabolic acidosis	Normalize blood and serum bicarbonate levels; Bicitra 2 to 3 mEq/kg/day suggested
Type II (proximal)	Defect in the proximal tubule, reduced reabsorption results in bicarbonate wastage Primary: familial or sporadic Commonly a component of Fanconi's syndrome	Symptoms associated with Fanconi's syndrome	Tubular wasting of sodium, potassium, glucose, phosphorus, and amino acids	Alkali supplementation of up to 10 mEq/kg/day
Type IV (hyperkalemic)	Impaired electrolyte transport in the distal tubule Hyperkalemia, resulting from abnormalities in aldosterone production or altered tubular sensitivity to aldosterone, leads to impaired ammoniagenesis May be induced with angiotensin-converting enzyme inhibitors or potassium-sparing diuretics	Dehydration and symptoms of hyperkalemia	Non–ion gap metabolic acidosis, hyperkalemia, elevated urine sodium, and diminished urine potassium	Mineralocorticoid supplementation may be needed, as well as treatment of hyperkalemia Alkali supplementation is generally required

From Vogt, B.A. and Springel, T. (2020). Fluid, electrolytes and acid-base homeostasis. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh (Eds.), *Fanaroff and Martin's neonatal-perinatal medicine* (10th ed. , pp. 613–631). St. Louis, MO: Elsevier Mosby.

2. Males are affected more often than females, and the left kidney is usually the one that is absent.
3. Unilateral renal agenesis often causes no symptoms and is usually not discovered during infancy because the other kidney usually undergoes compensatory hypertrophy and performs the function of the missing kidney.
4. Unilateral renal agenesis is associated with developmental defects, but they are not clinically evident until adolescence, when the patient presents with amenorrhea or dysmenorrhea (Vogt, B.A. and Springel, T. (2020)).

B. **Bilateral renal agenesis** (Moore et al., 2016).
1. Bilateral renal agenesis occurs in 1 in 3000 live births and is incompatible with postnatal life.
   a. Limited reports exist of serial amnioinfusions to support lung development, followed by dialysis and renal transplant after birth (Kara et al., 2018). George et al. (2017) reported that an infant born with normal lung function was treated with dialysis while awaiting transplant. Sugarman et al. (2018) warn about the complex ethical concerns raised by these interventions.
2. Renal agenesis results when the ureteric buds do not develop or the primordia (stalks of buds) of the ureters degenerate.
3. Bilateral renal agenesis is associated with oligohydramnios because little or no urine is excreted into the amniotic cavity.
4. Renal agenesis may be seen in infants with VACTERL association, caudal regression syndrome, branchio-oto-renal syndrome, and multiple chromosomal defects (Vogt, B.A. and Springel, T. (2020)). It may also occur in otherwise healthy infants.

C. **Horseshoe kidney** (Moore et al., 2016).
1. The poles of the kidneys are fused. The large U-shaped kidney usually lies in the pubic region, anterior to the inferior lumbar vertebrae.
2. Normal ascent of the fused kidneys is prevented because they are held down by the root of the inferior mesenteric artery.
3. A horseshoe kidney usually produces no symptoms because its collecting system develops normally and the ureters enter the bladder.
4. Approximately 7% of persons with Turner's syndrome have horseshoe kidney.

D. **Autosomal recessive polycystic kidney disease** (Moore et al., 2016).
1. Both kidneys contain many small cysts, which results in renal insufficiency.
2. Death of the infant usually occurs shortly after birth; however, an increasing number of these infants are surviving because of postnatal dialysis and kidney transplantation.

E. **MCDK** (Moore et al., 2016).
1. MCDK is a nonfunctional kidney, composed of multiple large cysts that resemble a cluster of grapes.
2. A possible etiology is failure of the ureteric bud to integrate and branch appropriately into the metanephros.
3. The majority of MCDKs undergo partial or complete spontaneous involution over time. The contralateral kidney, if normal, generally grows larger because of compensatory hypertrophy, allowing the child to maintain normal renal function.
4. MCDK does pose a risk of hypertension and malignancy. Surgical removal is reserved for children in whom the MCDK fails to involute or grows larger over time (Vogt and Springel, 2020).

F. **Ureteropelvic junction obstruction** (Vogt and Springel, 2020).
1. The most common cause of moderate to severe congenital hydronephrosis.
2. Ureteropelvic junction obstruction is more common in males and may be associated with other congenital anomalies, syndromes, or genitourinary malformations.
3. Many clinicians advocate antibiotic prophylaxis to prevent urinary tract infection, although this practice remains somewhat controversial.
4. Surgical repair is the treatment.

G. **Posterior urethral valves** (Vogt and Springel, 2020).
1. The most common cause of lower urinary tract obstruction, with an incidence of 1 in 5000 to 8000 live male births.
2. A posterior urethral valve is composed of a congenital membrane that obstructs or partially obstructs the posterior urethra.
3. At birth, the infant may present with a palpable, distended bladder and a poor urinary stream.
4. The VCUG is diagnostic for posterior urethral valves.
5. The initial treatment is placement of a urinary catheter and later primary ablation of the valves.

H. **Eagle–Barrett syndrome ("prune-belly" syndrome)** (Vogt and Springel, 2020).
1. Infants generally present with a distinct, flabby abdomen that is indicative of absent or deficient abdominal musculature.
2. Characterized by a triad of findings.
   a. Dilated, unobstructed urinary tract.
   b. Deficiency of abdominal wall musculature.
   c. Bilateral cryptorchidism.
3. The estimated incidence is 1 in 35,000 to 50,000 live births, with more than 95% of the cases occurring in males.
4. The two theories of pathogenesis are in-utero urinary tract obstruction and a specific mesodermal injury between the 4th and 10th weeks of gestation.
5. Cardiac, pulmonary, gastrointestinal, and orthopedic anomalies may also be present, often secondary to oligohydramnios.
   a. Treatment in the neonatal period involves the optimization of urinary tract drainage, the

management of renal insufficiency, and antibiotic prophylaxis.

I. **Exstrophy of the bladder** (Moore et al., 2016).
   a. A rare birth defect occurring once in every 10,000 to 40,000 live births, more often in males.
   b. The defect involves both the abdominal wall and the anterior wall of the urinary bladder. As a result, parts of the rectus muscles are absent, and the external and internal oblique transversus abdominal muscles are deficient.

Disorders of the Genitalia

A. **Undescended testes—cryptorchidism** (Merguerian and Rowe, 2018).
   1. The incidence ranges from 1% to 4.6% in full-term males and 1.1% to 45.3% in preterm males. During the first 3 to 6 months, the testicle may spontaneously descend.
   2. The number of spermatogonia per tubule is adversely affected if the testicle is not descended by 1 year, so it is recommended that orchiopexy be performed around 6 months to minimize germ cell loss.
   3. Bilateral impalpable undescended testes in a newborn male warrants a genetic and endocrine evaluation for a disorder of sexual differentiation.
      a. Failure to appreciate the significance of bilateral and impalpable undescended testes in the neonatal intensive care unit (NICU) could result in missed diagnosis of congenital adrenal hyperplasia in a virilized female neonate.
      b. The neonate with a unilateral undescended testis and a normal phallus may be referred for a urologic follow-up evaluation at 3 to 6 months of age. If at 6 months of age the testis remains out of position, surgical intervention should be undertaken to reposition the testis within the scrotum.
      c. Long-term issues associated with cryptorchidism include an increased risk of infertility and testicular malignancy.

B. **Testicular torsion** (Merguerian and Rowe, 2018).
   1. The newborn who presents in the delivery room with a painful, blue, and edematous hemiscrotum will likely have had an antenatal torsion.
   2. If the infant was born with a normal scrotal examination but subsequently develops scrotal swelling and erythema, the infant should undergo a Doppler ultrasound and surgical exploration if blood flow cannot be confirmed.

C. **Hypospadias** (Merguerian and Rowe, 2018).
   1. One of the most common abnormalities of the penis, occurring in 1 of every 250 to 300 male births. The diagnosis of hypospadias is established when the urethral meatus is not present in the normal glandular position; the meatus may be present anywhere along the ventral penile surface from the glans to the perineum.
   2. In addition, there is an asymmetrical or dorsally hooded foreskin, and the penis may be tethered, creating a significant bend (chordee).
   3. There are four main types (Moore et al., 2016).
      a. Glandular hypospadias, the most common type.
      b. Penile hypospadias.
      c. Penoscrotal hypospadias.
      d. Perineal hypospadias.
   4. Although the etiology remains unclear, hypospadias is thought to result from inadequate production of androgens by the fetal testes and/or inadequate receptor sites for the hormones (Moore et al., 2016). A family history is reported in 5% to 10% of cases.
   5. The infant must not undergo circumcision; the foreskin is crucial for use in the urethral reconstruction and correction of the chordee. However, up to 10% of patients with a hypospadias may have an intact foreskin, and the diagnosis is determined only after circumcision.
      a. Congenital adrenal hyperplasia in a female neonate may be misdiagnosed as hypospadias with undescended testis.
      b. It is recommended that infants with hypospadias and bilaterally descended testes have an outpatient urologic evaluation arranged within 2 to 6 months of age.

D. **Hydrocele** (Moore et al., 2016).
   1. Hydrocele, excess fluid in the scrotum, occurs when perinatal fluid passes into the patent processus vaginalis. It is a very common condition in newborns and usually resolves spontaneously within the first year of life.

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CHAPTER 34
Neurologic Disorders

Georgia Ditzenberger

OBJECTIVES

1. Identify the six primary stages of neurodevelopment and the congenital anomalies that result from defective development at each stage.
2. Define autoregulation.
3. Review a complete neurologic examination.
4. Examine birth injuries and patient care management.
5. Differentiate between the different types of intracranial hemorrhages and their origins, clinical presentation, and outcomes.
6. Recognize neonatal seizures, their distinguishing characteristics, and issues in patient care management.
7. Describe hypoxic–ischemic encephalopathy.
8. Describe the clinical implications of periventricular leukomalacia.
9. Distinguish the pathophysiologic factors, clinical presentation, and patient care management of early- and late-onset meningitis.

The human brain is an intricate, fragile organ requiring precise development from the moment of conception. Several crucial developmental landmarks pinpoint major events in the development of the human brain. If the process is interrupted, difficulties ranging from simple, easily treatable conditions to major neurologic malformations may occur. Neurologic problems account for a significant number of admissions into the neonatal intensive care unit each year. This chapter provides a comprehensive review of neurodevelopment, neurophysiology, and neuromalformations.

Anatomy of the Neurologic System (Blackburn, 2018; Moore et al., 2012; Volpe, 2018)

A. Embryologic development (Table 34.1).
   1. Primary neurulation (dorsal induction).
      a. Occurs within the first month of life, ending between 24 and 28 days of gestation.
      b. Induction events of dorsal aspect of embryo.
      c. Neural tube is formed by the invagination and curling of the distal neural plate.
      d. Closure of the neural tube gives rise to the central nervous system (CNS), including the cranial nerves.
      e. This evolution results in the formation of the skull and vertebrae.
      f. Inaccuracies of primary neurulation result in craniorachischisis totalis, anencephaly, myeloschisis, encephalocele, and myelomeningocele with Arnold–Chiari type II malformation.
   2. Prosencephalic development.
      a. Peak development is in the second and third months of gestation.
      b. Inductive interactive events that occur primarily at the rostral end on the ventral aspect of the embryo.
      c. This influences the formation of the face, forebrain, corpus callosum and septum pellucidum, optic nerves/chiasm, the hypothalamic structures (thalamus and hypothalamus [diencephalon]), and the cerebral hemispheres (telencephalon).
      d. Absence of olfactory bulbs and tracts is not uncommon.
      e. Disturbance in prosencephalic development causes facial and forebrain alterations.
         1) Holoprosencephaly (abnormal formation of telencephalon and diencephalon).
         2) Midline and midfacial defects.
            a) Hypotelorism (less common: hypertelorism).
            b) Cyclopia.
            c) Cleft lip with or without cleft palate.
         3) Agenesis of corpus callosum, corpus pellucidum.
      f. Most common karyotype is normal (chromosomal disorder is possible).
   3. Neuronal proliferation.
      a. Occurs initially at 2 months, with peak between 3 and 4 months of gestation.

Table 34.1

Major Events in Human Brain Development and Peak Times of Occurrence

Major Developmental Event	Peak Time of Occurrence
Primary neurulation	3 to 4 weeks of gestation
Prosencephalic development	2 to 3 months of gestation
Neuronal proliferation	3 to 4 months of gestation
Neuronal migration	3 to 5 months of gestation
Organization	5 months of gestation to years postnatal
Myelination	Birth to years postnatal

From Volpe, J. J. (2018). *Neurology of the newborn* (6th ed.). Philadelphia, PA: Elsevier Saunders.

b. Toxins and inherited diseases can significantly alter the number of neurons.
c. *Microcephaly* means "small head"; measurable by occipitofrontal head circumference.
d. *Microencephaly* means "small brain"; results from insufficient neurons; clinically referred to as *microcephaly.*
e. *Macrencephaly* means "large brain"; results from hypertrophy of the brain; seen in Tay–Sachs disease (degenerative disease of gray matter in infancy).
f. Insufficient neurons in the absence of apoptotic events are primary microencephaly; excess neurons can produce macroencephaly.
g. Chemical and environmental substances can reduce the number of neurons, causing microencephaly vera; clinically referred to as *microcephaly.*
h. Disorders of proliferation of small veins cause Sturge–Weber syndrome (6% unilateral, 24% bilateral facial lesions).

4. Neuronal migration.
a. Can occur as early as 2 months; peaks between 3 and 5 months.
b. By 6 months of gestation, the neurons have migrated to their final, permanent place in the cortex.
c. Neurons follow glial paths outward.
d. Cells migrate and differentiate into six cortical layers.
e. Migration is critical for development of the cerebral cortex and the deeper nuclear structures.
1) Basal ganglia.
2) Hypothalamus.
3) Thalamus.
4) Brainstem.
5) Cerebellum.
6) Spinal cord.
f. Dysfunction at this stage results in cortical malformation with abnormalities of neurologic function.
g. Seizures may be the first clinical manifestation in the early postnatal period.
h. Defects associated with abnormal migration range in severity and may be associated with other neurologic development.
i. Abnormal development of gyrus denotes a neuronal migration disorder.
j. Disorders include lissencephaly ("smooth brain"), pachygyria, agenesis of the corpus callosum, and schizencephaly (clefts found in the cerebral wall).

5. Neuronal organization.
a. Peaks at 5 months of gestation to several years after birth.
b. Provides the basis for brain function and its complex circuitry.
c. Includes cell differentiation, cell death, synaptic development, neurotransmitters, and myelination.
d. Achieves stabilization of cell connections.
e. Disorders due to organizational deficits and detrimental retardation (as with Down syndrome, fragile X syndrome, and mild Duchenne's muscular dystrophy).

6. Myelination.
a. Begins in the second trimester and continues into adult life.
b. Involves myelin deposition around axons.
c. Myelin, a fatty covering, insulates the circuitry; prevents leakage of current and enables rapid, efficient transmission of nerve impulses.
d. Enhances intercellular communication.
e. Deficiencies occur in some acquired and inherited diseases.

B. Brain anatomy (Fig. 34.1) (Blackburn, 2018; Moore et al., 2012; Volpe, 2018).
1. Cerebellum.
a. Promotes integrative muscle function.
b. Maintains balance.
c. Enables smooth, purposeful movements.

2. Cerebrum: main components of cerebral hemisphere.
a. Contains four lobes: frontal, parietal, occipital, and temporal.
1) Frontal lobes make up command center; concerned with decision making and other "executive" tasks.
2) Parietal lobes are responsible for hearing, understanding speech, and forming an integrated sense of self.
3) Occipital lobes process vision.
4) Temporal lobes are centers for smell with associative areas for memory and learning.
b. Corpus callosum: fiber bundles connecting the cerebral hemispheres.

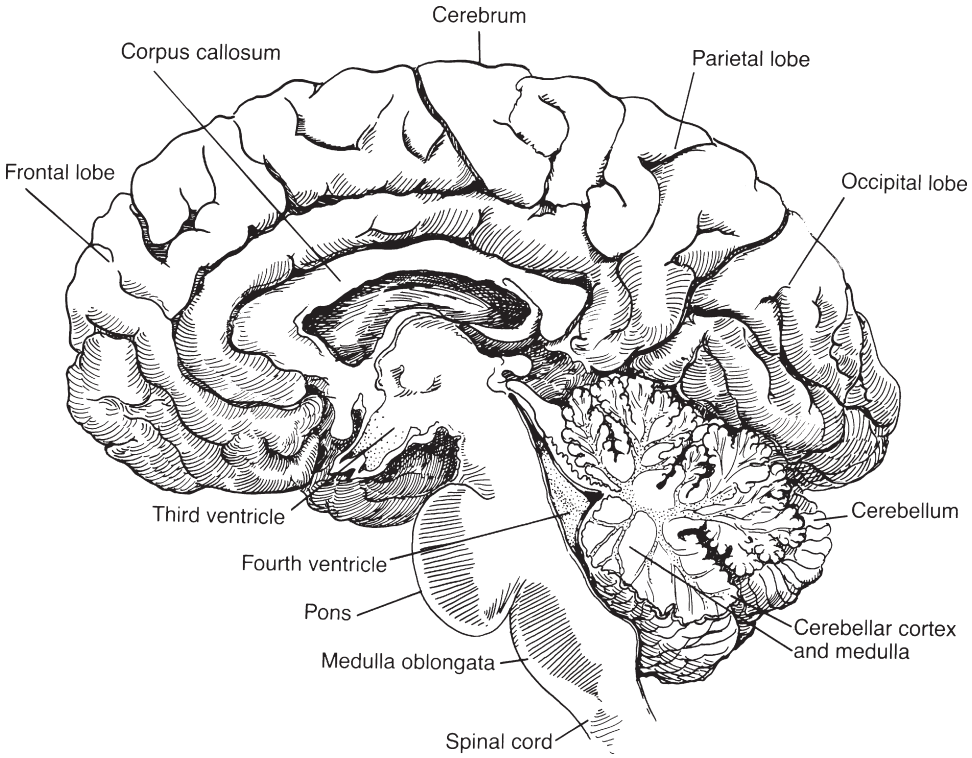


Fig. 34.1 Anatomy of the brain.

c. Cerebral cortex.
   1) Encompasses the mind and the intellect.
   2) Gray matter.
d. Lateral ventricles.
e. Third ventricle: fluid-filled space.
f. Thalamus: integrates sensory input.
g. Hypothalamus: regulates body temperature.

3. Brainstem.
   a. Relays input and output signals between higher brain centers and the spinal cord.
   b. Three main components.
      1) Medulla oblongata.
         a) Gives origin to cranial nerves VIII, IX, X, XI, and XII.
         b) Controls areas of the abdomen, thorax, throat, and mouth.
      2) Pons: carries information between the brainstem and the cerebellum.
      3) Midbrain: involved in eye movements.

Physiology of the Neurologic System (Blackburn, 2018; McLean et al., 2012; Volpe, 2018; Yager, 2012)

A. Glucose metabolism.
   1. Cerebral metabolism is influenced by the availability of glucose and oxygen.
   2. Glucose is transported from blood to brain by a glucose transporter found in capillaries.
   3. Serum glucose provides the brain with a glucose pool.
   4. The neonatal brain is glucose dependent. The CNS is quickly and significantly affected by hypoglycemia.
   5. Glycogen stores are minimal or nonexistent in the premature baby.
   6. The brain depends on adequate circulation to supply both oxygen and glucose to create enough energy for normal growth and metabolism.
   7. Anaerobic metabolism causes lactic acid buildup.
   8. Anaerobic metabolism produces significantly smaller amounts of energy.
   9. Newborn blood glucose levels less than 30 mg/dL are associated with significant increases in cerebral blood flow.
   10. Defining the lower limit of the neonatal blood glucose level is difficult because the infant's ability to present overt symptoms of hypoglycemia is not developed.

B. **Cerebral blood flow.**
   1. Cerebral blood flow is affected by pH (controlled by hydrogen ions and carbon dioxide levels), potassium, hypoxemia, osmolarity, and calcium ion concentrations.
      a. The brain increases cerebral blood flow to spare itself inadequacies.
      b. As pH decreases, cerebral blood flow increases.

c. As potassium levels increase, cerebral blood flow increases.
d. Hypoxemia causes an increase in cerebral blood flow to provide adequate oxygenated blood to the brain.
e. Increased osmolarity causes increased cerebral blood flow.
f. An increase in calcium ions causes a decrease in cerebral blood flow.
g. Cerebral blood flow increases when blood glucose levels fall to less than 30 mg/dL; the hypoglycemic brain recruits previously unperfused capillaries to maintain glucose levels. Degree and duration of hypoglycemia are significant.
h. Studies have shown that neonatal neurologic signs can be minimal or absent with subsequent abnormal cognitive development.

2. Autoregulation.
a. Maintains steady-state cerebral blood flow over a broad range of perfusion pressures.
b. Important vasoactive factors in the brain: hydrogen ions, potassium ions, adenosine, prostaglandins, osmolarity, calcium.
c. Cerebral blood flow increases with advancing gestational age and concomitant cerebral metabolic demands.
d. Normal arterial blood pressure in the preterm neonate is thought to be near or at the lower autoregulatory limit. This suggests an increased vulnerability to ischemic brain injury with modest hypotension, especially with decreasing gestational age.
e. Cerebral vasculature vasodilates maximally in response to hypoxemia, hypercapnia, and acidosis.
1) Hypotension leads to ischemia.
a) Ischemia damages blood vessels and surrounding elements supporting the blood vessels.
b) Blood flow to cerebral white matter is restored only after reperfusion of other brain regions.
c) Once adequate blood supply resumes, hemorrhage can occur into ischemic areas.
2) Hypertension leads to hemorrhage.

Neurologic Assessment (Blackburn, 2018; Rennie and Huertas-Ceballos, 2015; Volpe, 2018)

A. **History**.
B. **Observation**.
1. Determine behavioral state.
2. Note posture.
a. Gestational age determines posture.
1) Premature infants: open, extended position reflecting diminished tone.
2) Term infants: flexed position reflecting adequate tone.
b. Sequelae of intrauterine position may be evident.
c. Abnormal findings are as follows:
1) Hyperextension.
2) Asymmetry.
3) Flaccidity.
3. Note movements.
a. Symmetrical or asymmetrical body movements.
b. Note movement quality (jitteriness, seizures, tremors, and clonus).
c. Quantity (absent or pronounced).
4. Note respiratory activity.
a. Signs of distress.
b. Hypoventilation (apnea).
c. Quality of cry.
1) High pitched (consider meningitis, drug withdrawal, neurologic abnormalities).
2) Stridor (consider vocal cord damage or paralysis).
5. Observe skin.
a. Lesions (note number, size, shape, color, and texture).
1) Café-au-lait spots (six or more lesions of ≥1.5 cm; may indicate neurofibromatosis).
2) Port-wine facial hemangioma (consider Sturge–Weber syndrome).
3) Areas of depigmentation.
b. Abrasions, lacerations, bruises, and forceps marks (consider intracranial bleeding, injury).

C. **Physical examination** (Scher, 2013; Volpe, 2018).
1. Check the skull size, shape, symmetry, hair whorls, fontanelles, and sutures.
2. Measure frontal–occipital circumference (FOC).
a. Document less than 10th percentile (symmetrical vs. asymmetrical compared with total body growth; may indicate microcephaly).
b. Document greater than 90th percentile (symmetrical vs. asymmetrical compared with total body growth; may indicate macrocephaly).
3. Examine the face for abnormalities in structure.
a. Placement of ears.
b. Neck skinfolds.
4. Spine (intact, openings, masses).
5. Cranial nerve function.
a. Refer to Table 34.2.
b. May be difficult to assess in the preterm newborn.
c. Blink reflex requires intact cranial nerves III and VII.

Table 34.2

Cranial Nerves

Number	Name	Type of Nerve	Function	Bedside Testing Mechanism	Expected Results and Comments
I	Olfactory	Sensory	Smell	Soak cotton pledget in strong odor and place under nares	Startle
II	Optic	Sensory	Conveys visual information from retina to brain	Check PERL; funduscopic examination	PERL intact; presence of red reflex
III	Oculomotor	Motor	Motor fibers to eyelid (lid elevation), some eye muscles, pupil (constriction and accommodation), and light reflex	Check EOM, PERL	PERL intact; EOM full and conjugate
IV	Trochlear	Motor	Movement of superior oblique muscles of eye, uvula movement	Check EOM	EOM full and conjugate
V	Trigeminal	Mixed	Sensation of face, scalp, and cornea; motor of jaw (mastication)	Touch cheek	Turns cheek toward stimulus
VI	Abducens	Motor	Lateral gaze; abducts eyeball	Rotate infant	Movement of eyes in direction of travel
VII	Facial	Mixed	Facial muscle movement, lid closure, taste	Elicit cry and observe facial movement	Symmetrical facial movements
VIII	Auditory	Sensory	Hearing	Talk softly to baby or clap loudly near baby's ear	Quiets to voice; blinks to clap
IX	Glossopharyngeal	Mixed	Taste, swallow, gag	Elicit gag response	Strong gag response
X	Vagus	Mixed	Most extensive innervation of any cranial nerve; motor, sensory, and autonomic innervation of neck, thorax, abdomen; swallow and gag	Elicit cry	Strong, lusty cry
XI	Accessory	Motor	Movement of head and neck	Turn supine infant's head to side	Attempts to bring head to midline; full range of shoulder and neck
XII	Hypoglossal	Motor	Tongue movement and symmetry	Insert gloved finger into baby's mouth while sucking	Suck should be strong and steady without fasciculations, tongue symmetry

EOM, Extraocular movements; *PERL*, pupils equal and reactive to light.

Adapted from Scanlon, J. W., Nelson, T., Grylack, L. J., & Smith, Y. F. (1979). *A system of newborn physical examination*. Baltimore, MD: University Park Press; Hockenberry, M. J., & Wilson, D. (2011). *Wong's nursing care of infants and children* (9th ed.). St. Louis, MO: Elsevier Mosby; Fletcher, M. A. (1997). *Physical diagnosis in neonatology*. Philadelphia, PA: Lippincott, Williams & Wilkins; http://library.med.utah.edu/pedineurologicexam/html/newborn_n.html#02; and http://www.fpnotebook.com/Nicu/Exam/NwbrnNrlgcExm.htm.

d. Corneal reflex requires intact cranial nerves V and VII.
   1) Generally elicited only if one suspects brain damage.
   2) Consider testing integrity of reflex in the presence of eye damage.
e. Cranial nerves IX, X, and XII regulate the tongue, swallow, gag, and cry.
f. Rooting reflex starts at 28 weeks, with a complete response established by 32 weeks.
g. Sucking reflex present at 28 to 30 weeks but slow, weak, and unsustainable; mature and robust by 34 to 36 weeks of gestation.
h. Rooting and sucking reflexes test partial function of cranial nerves V, VII, and XII.
i. Swallowing tests cranial nerves IX and X.

6. Muscle tone.
   a. Evaluate head lag, ventral suspension, clonus, and recoil from extension.
   b. Check symmetry; briskness versus flaccidity.
7. Reflexes.
   a. Check primitive reflexes (automatisms).
      1) Blinking: an infant will close his or her eyes in response to bright lights.
      2) Palmar and plantar grasp (bilaterally): an infant's fingers or toes will curl around a finger placed in the area.

3) Babinski: as the infant's foot is stroked, the toes will extend upward and fan outward.
4) Moro: a quick change in the infant's position will cause the infant to throw back his or her head, extend his or her arms outward, and open the hands.
5) Startle: a loud noise will cause the infant to extend and flex the arms, while the hands remain in a fist.

b. Evaluate symmetry and strength of response of all primitive reflexes.
c. Consider clavicular or humeral fractures or brachial plexus injury in the presence of an abnormal Moro reflex.
d. Grasp varies with gestational age; if grasp is absent, consider nerve damage.

Neural Tube Defects (NTDs)

As the neural tube develops, developmental processes can be altered by intrinsic or extrinsic factors, resulting in defective closure or a reopening of the neural tube. Defects range from anencephaly to open or skin lesions of the spinal cord.

A. **Incidence and etiology** (Ditzenberger and Blackburn, 2014; Huang and Doherty, 2018).
1. NTDs are among the most commonly occurring congenital malformations of the CNS.
a. Incidence of NTDs in the United States is estimated as 0.5 to 5 per 1000 live births (Ditzenberger and Blackburn, 2014; Moore et al., 2012).
2. Risks for recurrence are significantly higher if a previous pregnancy has resulted in a child with an NTD. The risk may actually be nearly triple for subsequent pregnancies.
3. The etiology of NTDs is multifactorial. This complex interaction of genetic and environmental factors operates independently to determine individual and population risk. The majority of defects occur sporadically.
a. Environmental risk factors most commonly identified with development of an NTD include maternal febrile illness, maternal heat exposure in the first trimester, hyperglycemia secondary to maternal diabetes, lower socioeconomic status, dietary factors, and prenatal exposure to drugs.
4. The defects result from a failure in closure of the neural groove to form an intact neural tube. The type and severity of the defect are dependent on the location and extent of failure.

ANENCEPHALY (DITZENBERGER AND BLACKBURN, 2014; VOLPE, 2018)

A. **Incidence and etiology.**
1. Anencephaly is the most common and severe disorders of anterior neural tube closure, comprising over half of the NTDs (Huang and Doherty, 2018). It is a primary defect in anterior neural tube closure. Presentation of the anomaly is variable, may extend from the level of the lamina terminalis to the foramen magnum.
a. About 75% of infants are stillborn; of the infants who do survive into the neonatal period, it is uniformly lethal within the first months of life. The onset of the defect is estimated to occur no later than 24 days of gestation.
2. Incidence is 1.0 to 10.0 per 1000 live births (Huang and Doherty, 2018). Recurrence risk for parents who have had one affected child is 1.9% (Jones et al., 2013).
3. Genetic and environmental influences appear to be important in the development of the defect.

B. **Clinical presentation.**
1. General: no documented growth deficiency.
2. Craniofacial: commonly involves the forebrain and upper brainstem, resulting in absence of the calvaria; cerebral hemispheres are missing. The lower brainstem is present, with rudimentary function. Hypothalamus and cerebellum are frequently malformed. Varied facial features, cleft palate and/or lip, altered auricular development, and cervical abnormalities are also common (Huang and Doherty, 2018).
3. Musculoskeletal: malformation of the ribs, thoracic cage, abdominal wall, anterior spina bifida, and short neck.

C. **Associated findings.**
1. Polyhydramnios.
2. Diaphragmatic defects with or without herniation, hypoplastic lung.

D. **Diagnosis.**
1. Fetal ultrasound or radiographs in the second trimester to detect absence of vital structures.
2. Maternal serum screening at 16 to 18 weeks identifies infants at risk. Alpha-fetoprotein (AFP) is a major serum protein in the early embryo and is fetus specific. Leakage of fetal serum through an open NTD directly into the amniotic fluid results in elevation of AFP levels. These increases are detected by maternal serum and amniocentesis evaluation (Huang and Doherty, 2018).

E. **Treatment/prevention.**
1. U.S. Public Health Service recommends that women of childbearing age consume 0.4 mg of folic acid daily to decrease their risk for conceiving a child with an NTD. Periconceptional use of vitamins and folate have resulted in a 60% to 70% reduction in the recurrence of these malformations when given to women who had previously given birth to an infant with an NTD (Huang and Doherty, 2018). In the United States, cereals and bread products are enriched with folate.

2. As most anencephalic infants are stillborn or die within a few days of delivery, the parents must prepare for the death of their infant at a time when they would be anticipating the birth. Support for the family must consider their individual preferences and needs.
3. The opportunity for these infants to serve as organ donors is complex. Ethical and legal concerns over the diagnosis of brain death and persistent clinical signs of brainstem function have limited the donation of organs from anencephalic infants.

ENCEPHALOCELE

Defects are secondary to restricted failure of the anterior neuropore to close at approximately day 26 of gestation, resulting in extension of the brain tissue through a defect in the skull.

A. **Incidence and etiology** (Huang and Doherty, 2018).
   1. The defect occurs in 1 per 10,000 live births. In 70% to 80% of babies the lesion is found in the occipital region (Volpe, 2018).
   2. Precise mechanism for development is unclear.
   3. Genetic factors may be causative; autosomal recessive patterns of inheritance have been reported. Meckel's syndrome and Walker–Warburg syndrome are the most commonly associated syndromes.
   4. Environmental factors, including maternal teratogens, have been linked to development of encephalocele.
      a. Maternal febrile illness resulting in temperatures of 102.2° F (38.9° C) or greater within the first one third to one half of gestation have been found to be teratogenic (Jones et al., 2013).

B. **Clinical presentation.**
   1. Craniofacial: cranial defect through which brain protrudes. Defects are commonly occipital (80%), with frontal, temporal, and parietal composing the remainder. Lesions generally are covered by skin or membrane.

C. **Associated findings** (Huang and Doherty, 2018).
   1. Approximately 50% of infants presenting with an encephalocele have other major anomalies. Microcephaly, arrhinencephaly, cleft lip/palate, craniosynostosis, and hydrocephalus occur in approximately one half of the affected children. Agenesis of the corpus callosum occurs in two thirds of affected infants (Evans et al., 2018; Volpe, 2018).
   2. Though normal intelligence is reported in approximately 50% of cases, intellectual deficiencies occur.
   3. Hypotonia and associated motor defects.

D. **Diagnosis**.
   1. Evaluation of these defects is supported through the use of radiographs of the skull, transillumination of the defect, cranial ultrasound, and computed tomography (CT) or magnetic resonance imaging (MRI).
   2. Chromosomal studies should be undertaken if suspicion of a genetic syndrome is present.
   3. Careful history of maternal exposure to teratogens or adverse environmental events may provide clues to etiology.

E. **Treatment**.
   1. Based on the individual position and extent of the lesion.
      a. Neurosurgical relief is indicated for most lesions, especially if cerebrospinal fluid (CSF) is leaking from the lesion. Mortality and morbidity are dependent on the individual lesion. Of those children surviving initial repair, a significant number will have neurologic defects, paralysis, seizures, and deficits in muscular coordination.
   2. For those families who experience a child with an encephalocele, genetic counseling is essential, as recurrence risk is estimated at 3% to 5%, depending on the etiology of the defect.

SPINA BIFIDA

These spinal cord malformations include myelomeningocele and meningoceles and result from restricted failure of the posterior neuropore to close at approximately 26 days of gestation.

A. **Incidence and etiology** (Volpe, 2018).
   1. Overall incidence is 2 in 10,000 live births (Huang and Doherty, 2018).
   2. Etiology includes multifactorial inheritance, single mutant genes, chromosomal anomalies, and specific teratogens.
      a. Females are more commonly affected than males.
      b. The level of the myelomeningocele in the first affected infant has a direct effect on risk for subsequent infants. Recurrence risk for infants whose sibling had a lesion at T11 is 7.8%. If the index lesion was below T11, the subsequent risk was 0.7%.

B. **Clinical presentation** (Volpe, 2018).
   1. Defects are divided into two categories.
      a. Spina bifida occulta: Mildest form of the defect presenting with skin covering the opening in the spinal column. This developmental anomaly involves a separation of overlying ectoderm from the neural tube. Impairment of the mesoderm to develop between ectoderm and neural tube results in disturbance of vertebrae and mesodermal tissue.
         1) These lesions occur most commonly in the caudal region. Overt lesions include ectodermal abnormalities, dermal tracts, and sinuses. Vertebral defects are present in 85% to 95% of lesions.
         2) Approximately 80% of affected infants will exhibit a dermal lesion in the lumbosacral

region. These defects include cutaneous dimples, cutaneous abnormalities or masses, and abnormal collections of hair.

3) Neurologic deficits are unusual in the newborn; sensory abnormalities in legs, feet, or sphincter abnormalities may occasionally be present.

b. Spina bifida manifesta: Spinal dysraphic conditions result from defects in caudal neural tube formation.

1) Meningocele: restricted herniation of meninges at the site of defect. Defect is uniformly localized to the lumbar region, is closed defect with intact dermal covering (Huang and Doherty, 2018).

2) Myelomeningocele: characterized by herniation of meninges and spinal cord at the site of the defect. Lesions may or may not have vertebral or dermal covering. These defects are 4 times more common than meningoceles (Huang and Doherty, 2018).

a) Rarely occurs as an isolated malformation, commonly associated with CNS abnormalities (Huang and Doherty, 2018).

C. **Associated findings.**

1. Hydrocephalus is a common associated development either at birth or shortly after.
   a. Development correlates with the site of the lesion: 60% in patients with occipital, cervical, or thoracic lesions; 90% in infants with thoracolumbar, lumbar, or lumbosacral lesions (Huang and Doherty, 2018).
2. Infants with myelomeningocele experience serious urinary tract complications. These urinary issues are a major cause of death after the first year of life (Volpe, 2018).
3. Kyphosis at birth; scoliosis later in childhood.
4. Clubfeet secondary to neurologic and orthopedic abnormalities.
5. Dislocation of hips, delay in walking, asymmetry of legs.
6. Arnold–Chiari malformation occurs in 95% of patients with a lumbar lesion (Huang and Doherty, 2018). Downward displacement of the medulla and the fourth ventricle through the foramen magnum into the upper cervical canal sets in motion a chain of events that are potentially lethal secondary to brainstem dysfunction and hydrocephalus. Development of a hoarse, weak cry may indicate vocal cord paralysis and is a sign of herniation.
7. Tethered cord.
8. Seizure activity secondary to cortical dysgenesis occurs in 20% to 25% of infants with myelomeningocele (Volpe, 2018).

D. **Diagnosis**.

1. AFP elevation in maternal serum at 16 to 18 weeks.
2. Amniotic fluid acetylcholinesterase and amniotic AFP at 14 to 16 weeks.
3. Fetal ultrasound.
4. Radiographs, CT, cranial ultrasonography, and MRI are done to provide visual record of anomalies.

E. **Treatment**.

1. Scheduled delivery by cesarean section before onset of labor should be considered for the fetus with known meningomyelocele.
2. Clinical management is individualized to the type and position of the lesion.
   a. Early surgical repair is advocated for most infants to preserve cognitive function, improve prognosis for ambulation, and decrease mortality.
   b. Assessment of function at the level of the lesion allows for estimates of potential capabilities; motor, sensory, and sphincter function.
   c. Examine lesion and measure size.
   d. Culture specimen from lesion if sac is open. Wrap lesion with sterile gauze moistened with warm sterile saline solution; place a sterile feeding tube within the gauze mesh for intermittent infusion of warm saline solution. Maintain the infant in a prone kneeling position, and protect the knees from skin breakdown. Place a drape over the buttocks below the lesion; utilize the drape's adhesive backing to secure the drape to the body.
   e. Obtain immediate consultation.
      1) Neurosurgery.
      2) Urology: evaluation must be undertaken to demonstrate deformity and determine the type and frequency of follow-up management needed.
3. Secondary to the extensive associated finding for these defects, parents must be made aware of the need for continuing care and support. Often a team approach is needed to ensure that complications are minimized.

Neurologic Disorders

A. **Microcephaly** (Huang and Doherty, 2018; Volpe, 2018).

1. Definition.
   a. FOC ≥2 standard deviations below the mean for age and gender.
   b. Small brain implies neurologic impairment.
2. Risk factors.
   a. Maternal.
      1) Viral infections under the TORCH spectrum (*t*oxoplasmosis, *o*ther [syphilis], *r*ubella, *c*ytomegalovirus, or *h*erpes) (Schleiss and Marsh, 2018).

2) Exposure to radiation.
3) Metabolic conditions such as diabetes or phenylketonuria.
4) Use of prescription and/or street drugs, especially in the first trimester.
5) Genetic foundation may be autosomal recessive, autosomal dominant, or X-linked.
6) Malnutrition is the most common etiology worldwide.

b. Fetal.
1) Prenatal/perinatal insult: inflammation; hypoxia; birth trauma.

c. Neonatal.
1) Very low birth weight infant.
2) Hypoxic–ischemic encephalopathy (HIE).
3) Nutrition: most common worldwide cause.

3. Pathophysiology.
a. Neuronal proliferation defect.
b. Occurs between 3 and 4 months of gestational age.
c. Destructive microcephaly occurs when the normal brain suffers prenatal/perinatal insult.

4. Clinical presentation.
a. Small head, backward sloping of the forehead, small cranial volume.
b. Neurologic deficits rarely evident at birth.

5. Diagnostic evaluation.
a. Perform a complete physical examination, including neurologic assessment.
b. Elicit a thorough maternal history.
c. Use tests to confirm or rule out etiologic factors aligned with maternal history.
d. CT or MRI is performed.

6. Patient care management.
a. Record accurate measurement of FOC, length, and weight weekly.
b. Note percentiles and alert physician to abnormalities.
c. Document clearly any deviations from normal.
d. Obtain tests as ordered; note dates to follow up results.
e. Ensure that the family is informed.
f. Obtain consultations as needed: genetics, infectious diseases.

7. Outcome.
a. Dependent on severity.
b. May be associated with developmental delays.

B. **Hydrocephalus** (Porsors et al., 2016; Volpe, 2018).

1. Definition: excess CSF in the ventricles of the brain due to a decrease in reabsorption or overproduction.
a. CSF is in balance between formation and absorption.
b. CSF is produced at a rate of 0.35 mL/min from brain parenchyma, cerebral ventricles, areas along the spinal cord, and the choroid plexus (70% is from the choroid plexus).

2. Pathophysiology.
a. Excessive CSF production (rare).
b. Inadequate CSF absorption secondary to abnormal circulation.
c. Excess ventricular CSF secondary to aqueductal outflow obstruction causes obstructive, noncommunicating hydrocephalus (refer to Fig. 34.1 for a simplified diagram of the brain).
1) The condition is most common in newborn infants.
2) Obstructive hydrocephalus may progress rapidly.
d. Excess ventricular CSF with flow between the lateral ventricles and the subarachnoid space results in communicating, nonobstructive hydrocephalus (Fig 34.2).

3. Congenital hydrocephalus.
a. Risk factors.
1) Aqueductal stenosis.
2) Dandy–Walker cyst (cystic transformation of fourth ventricle).
3) Myelomeningocele with Arnold–Chiari malformation (herniation of the hindbrain, usually causing obstructive hydrocephalus).
4) Congenital masses and tumors.
5) Congenital infection (toxoplasmosis, cytomegalovirus infection).
b. Associated etiologies and/or congenital defects.
1) Spina bifida.
2) Encephalocele.
3) Holoprosencephaly.
c. Clinical presentation.
1) Large head.
2) Widened sutures.

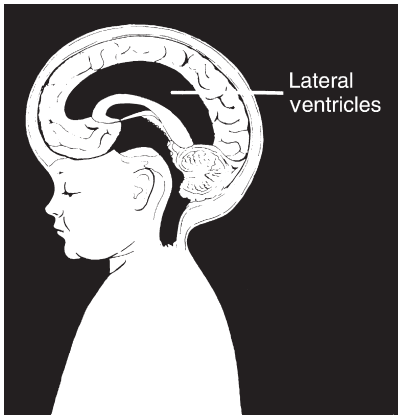


Fig. 34.2 Hydrocephalus. (*From Ross Laboratories. [1988]*. New perspectives on intraventricular hemorrhage. *Columbus, OH: Ross Laboratories.*)

3) Full (bulging) and tense fontanelles.
4) Increasing FOC.
5) "Setting-sun" eyes (may signify brain tissue damage).
6) Vomiting, lethargy, irritability.
7) Visible scalp veins.

d. Diagnostic evaluation.
1) Serial intracranial ultrasonography.
2) Neuroimaging techniques: CT, MRI, and cranial ultrasonography.

e. Patient care management.
1) Intrauterine diagnosis affords the family more options and allows time for preparation and anticipation.
2) Perform a thorough physical examination, assessing for further anomalies.
3) Obtain neurosurgery and genetics consultations.
4) Confirm diagnosis and cause.
5) Consider the possible need for reservoir placement versus ventriculoperitoneal (VP) shunt placement.
6) Support the infant by decreasing noxious stimuli (dim lights, minimal handling).
7) Position the head carefully.
8) Provide normal infant care as much as possible.
9) Involve parents in infant's care as soon as family is ready.
10) Allow parents to view an infant with a VP shunt or review pictured handouts.
11) Review VP shunt with parents preoperatively and postoperatively.
12) Prevent skin breakdown by not allowing the infant to put his or her head on the shunt side postoperatively.
13) Relieve the infant's probable stiff neck by holding the child's neck on the shunt side during feedings.
14) Review signs of infection or blocked shunt with the family.
a) Irritability.
b) Vomiting.
c) Increasing head size.
d) Lethargy.
e) Changes in feeding patterns.
f) Bulging fontanelle.
15) If incision site reddens, position infant on opposite side to relieve pressure from this area.

4. Posthemorrhagic hydrocephalus (Neil and Inder, 2018; Volpe, 2018).
a. Etiology.
1) Progressive dilatation of the ventricles after intraventricular hemorrhage (IVH) caused by injury to the periventricular white matter.
2) Two types: acute and chronic.
a) Acute.
(1) Rapidly appears—within days of the initial hemorrhage.
(2) Probably occurs secondary to malabsorption of CSF secondary to a blood clot.
b) Subacute, chronic.
(1) Inhibition of CSF flow.
(2) Blood from IVH.

b. Incidence.
1) Approximately 45% of infants with IVH have no evidence of hydrocephalus (Volpe, 2018).
2) Acute ventricular dilatation develops in approximately 50% of surviving infants with hemorrhage; in the majority, it resolves spontaneously or remains static (Blackburn, 2018; Neil and Inder, 2018; Volpe, 2018).

c. Clinical presentation.
1) Insidious following mild ventricular dilatation.
2) May be profound following severe ventricular dilatation.
a) Rapid increase in head size (begins days to weeks after ventricular dilatation present).
b) Episodic apnea and bradycardia.
c) Lethargy.
d) Increased intracranial pressure.
e) Tense, bulging anterior fontanelle.
f) Cranial sutures separating.
g) Ocular movement abnormalities.

d. Diagnostic evaluation.
1) Graph of weekly FOC measurements.
2) CT scan.
3) Cranial ultrasonography.
4) MRI.

e. Patient care management (Porsors et al., 2016; Verklan, 2012; Volpe, 2018).
1) Obtain daily FOC measurements.
2) Serial cranial ultrasonography.
3) Neurosurgical consultation.
4) Interventions to maintain lumbar or ventricular pressure at approximately 5 cm H_2O while evaluating for shunt placement.
a) Serial lumbar punctures or direct ventricular access may be helpful.
b) Administer medications that diminish CSF production rates.
(1) Furosemide (Lasix): 1 mg/kg/day.
(2) Acetazolamide (Diamox): up to 100 mg/kg/day.
5) Consideration given to placing a reservoir or VP shunt.
6) Observe the infant for signs of increasing intracranial hemorrhage and hydrocephalus.

7) Support the family: neonate is very susceptible to shunt infections and shunt malfunction.

f. Outcome (Blackburn, 2018; Verklan, 2012; Volpe, 2018).
1) Poor outcomes are likely when cerebral decompression does not occur after VP shunt placement.
2) Initial IVH severity is the major determining factor in posthemorrhagic hydrocephalus development.
3) In slightly more than 50% of the cases, severe hemorrhage results in progressive ventricular dilatation.
4) Without therapy, a considerable number of infants exhibit halted progression, with or without resolution.
5) Deficits are motor and/or cognitive.

C. **Craniosynostosis** (Evans et al., 2018).
1. Definition.
a. Premature closure of cranial sutures.
b. Occurs along one or more suture lines (see Fig. 34.3 for names and placement of cranial sutures).
2. Risk factors. Usually sporadic and without associated anomalies.
3. Pathophysiology.
a. Cause unclear. May be a defect in the mesenchymal layer of the ossification center within the skull.
b. Etiology includes developmental, mechanical, metabolic, and genetic factors that influence skull growth.
4. Incidence.
a. Reported as 1 in 2000 to 2500 births.
b. Sagittal craniosynostosis most common.
5. Clinical presentation.
a. Asymptomatic.
b. Cranial suture line reveals bony prominence; even and smooth bilaterally.
c. Inability to move the suture.
d. Abnormal cranial shape.
e. Later signs.
1) Increased intracranial pressure.

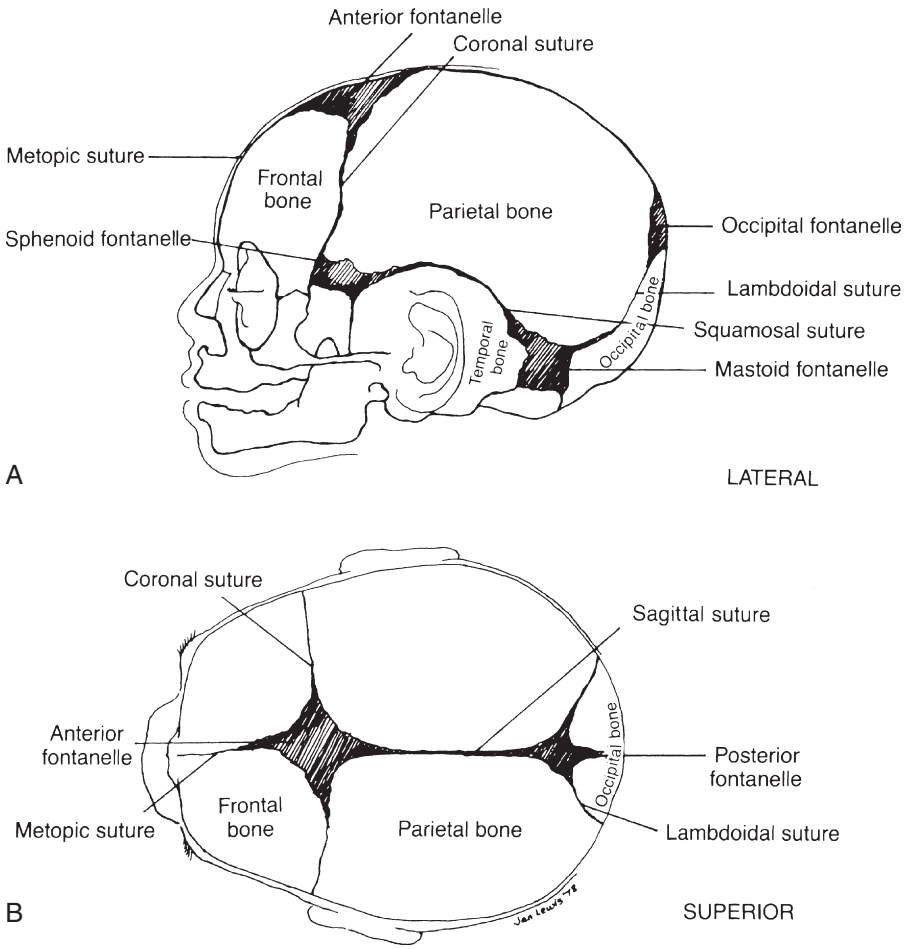


Fig. 34.3 **A** and **B**, Two views of the neonatal skull showing clinically important fontanelles and sutures. (*From Scanlon, J. W., Nelson, T., Grylack, L., & Smith, Y. F. [1979].* A system of newborn physical examinations *(p. 47). Baltimore, MD: University Park Press.*)

2) Increased irritability.
3) Possible separation of other sutures.

6. Diagnostic evaluation.
   a. Skull x-ray examination.
   b. High-resolution three-dimensional CT reconstruction scanning to determine the extent of premature bone fusion.
   c. Weekly graph of FOCs.
7. Patient care management.
   a. Thorough physical examination.
   b. Obtain neurosurgery consultation.
   c. Educate and support the family.
   d. Observe for signs of increased intracranial pressure.
      1) Irritability.
      2) Lethargy.
      3) Vomiting.
      4) Bulging fontanelle.
   e. Early surgical treatment is recommended.
8. Outcome.
   a. Surgically correctable.
   b. Good outcome; possible absence of sequelae.
   c. Cosmetically pleasing outcome.
   d. Multiple craniosynostoses associated with numerous syndromes.

D. **Cleft lip and cleft palate** (Evans et al., 2018).
1. Development of orofacial structures occurs before the seventh week of gestation. Cleft lip and palate result in medial and lateral nasal processes failing to fuse with maxillary process, producing cleft lip with or without cleft palate.

E. **Etiology and incidence.**
1. Orofacial clefts of the primary and secondary palate represent one of the most common structural defects; overall frequency is approximately 1 in 500 to 550.
2. Cleft lip and palate are the most common defect, followed by isolated cleft lip, and then cleft palate only.
3. Racial predilection exists, with Native American, white, and Hispanic populations experiencing increased incidence.
4. Sixty percent to 80% of infants affected with cleft lip are male. Cleft palate is more common in females than males (Moore et al., 2012).
5. The causes of most orofacial clefts are unknown and are nonsyndromic. The etiology of these defects is multifactorial, likely secondary to the interaction between environmental and genetic factors. Most cases represent sporadic events, but recurrence within families has been documented.
6. Seventy percent to 75% of cleft lip with cleft palate defects are nonsyndromic.
7. Recurrence risk is dependent on specific syndrome and genetic diagnosis. For families with one child affected with cleft lip and palate, risk is 2% to 5%, increasing to 10% to 15% if other family members have clefts. Risk for cleft lip only is less as cleft lip with or without cleft palate is genetically distinct from cleft palate.

F. **Clinical presentation.**
1. Presentation of the defect is variable, affecting the primary palate and/or the posterior palate.
   a. Unilateral cleft lip most commonly occurs on the left side.
   b. Bilateral cleft lip is usually accompanied by a cleft palate.
2. Defect may occur as a part of a syndrome of anomalies. Over 400 syndromes have been associated with orofacial clefting.
3. True median cleft is the rarest type of cleft and is commonly associated with serious risk for underlying CNS abnormalities, growth hormone deficiencies, adrenal hypoplasia, thyroid deficiency, and diabetes insipidus.

G. **Associated findings.**
1. Hypodontia in the area of the cleft, natal teeth.
2. Disruption of facial growth resulting in reduced facial height, flat facial profile, increased nasopharyngeal width, and a shortened mandible.
3. Feeding difficulties, failure to thrive.
4. Speech deficits and language delay.
5. Eustachian tube dysfunction, recurrent otitis media, and acquired conductive hearing loss.
6. Airway obstruction issues, especially if Pierre Robin sequence is associated.

H. **Diagnosis**.
1. Ultrasound evaluation with close attention to the oral and facial areas may provide a clue to the presence of the defect prenatally.
2. Careful physical examination after delivery as 25% of infants with cleft lip and/or palate have associated syndromes.

I. **Treatment**.
1. Secondary potential effects of these defects on respiratory, auditory, language, growth, and feeding; multidisciplinary team is important in long-term management.
2. Degree of defect may markedly alter the ability for the infant to breast- or bottle-feed effectively. A variety of feeding systems and nipples are available, and trial of many types may be needed to find the appropriate system.
3. Breastfeeding may be difficult, as an open palate will not assist in generating negative pressure needed for sucking. Expressed breast milk should be offered.
4. Growth velocity must be followed closely, as these infants are at higher nutritional risk.
   a. Dental appliances can be helpful to provide a palatal surface.
   b. Dentition patterns should be monitored closely, timing interventions with surgical intervention.

5. Auditory evaluations utilizing otoacoustic emissions or brainstem auditory evoked response are necessary if initial hearing screens are abnormal. As hearing loss may be responsible for speech distortion, development of speech must be closely monitored, and therapy provided as an ongoing portion of care.
6. Though site-specific, surgical correction of the lip and nasal deformities occurs first—usually within the first 3 to 6 months of life. Palatal repair occurs later at 9 to 12 months of age.
7. Airway management is a primary concern. Those infants with associated micrognathia and glossoptosis may require protective positioning and possible tracheostomy.
8. Genetic counseling is needed to assign potential risk and to exclude chromosomal disorder and single-gene defects.

J. **Birth injuries.**
1. Definition.
   a. Any injury that occurs during the entire phase of the birth process, comprising labor and delivery.
   b. Classification of the injury is anatomic or etiologic.
2. Risk factors.
   a. Abnormal labor time (long or short).
   b. Large size for gestational age.
   c. Cephalopelvic disproportion.
   d. Prematurity.
   e. Birth dystocia.
   f. Abnormal presentation (transverse, breech, face, and brow).
   g. Instrument-assisted extraction (vacuum or forceps).
3. Pathophysiology (see specific injury).
4. Specific injuries.
   a. Cephalohematoma (Hoppe and Benedetti, 2018).
      1) Pathophysiology.
         a) Subperiosteal hemorrhage.
         b) Does not extend across the cranial suture lines.
         c) Usually unilateral.
      2) Incidence approximates 1.5% to 2.5% of deliveries and is seen twice as often in males.
      3) Clinical presentation.
         a) Enlarges during the first few days after birth.
         b) Feels firm.
         c) Does not transilluminate.
         d) Presents bilaterally in 15% of patients.
         e) Linear fractures found in 5% of unilateral lesions and 18% of bilateral lesions.
      4) Diagnostic evaluation for presence of cranial fractures.
      5) Patient care management (Porsors et al., 2016).
         a) Provide supportive care to the family and their baby.
         b) Observe for hyperbilirubinemia.
         c) If sudden enlargement occurs, question infection.
         d) Educate the family.
         e) Assess neurologic status.
      6) Outcome.
         a) Bony calcified ring may develop; usually disappears within 6 months.
         b) Usually takes 2 weeks to 3 months for resolution.
         c) Essentially all cases resolve.
   b. Caput succedaneum.
      1) Pathophysiology.
         a) Hemorrhagic edema crossing cranial suture lines.
         b) Commonly seen after vaginal delivery.
      2) Clinical presentation.
         a) Evident at birth.
         b) Hemorrhagic scalp edema, causing discoloration at the site.
         c) Does not grow in size after birth.
      3) Diagnostic evaluation as per physical examination.
      4) Patient care management.
         a) No treatment is given.
         b) Educate and counsel the family.
      5) Outcome: resolution occurs during first few days of life.
   c. Subgaleal hemorrhage (Hoppe and Benedetti, 2018; Katheria and Finer, 2018; Neil and Inder, 2018).
      1) Pathophysiology.
         a) Hemorrhage beneath the scalp into the loose connective tissue below the aponeurotic membrane.
         b) Possible entry of blood into the subcutaneous tissue of the neck.
         c) Hematoma may cross suture lines in sufficient quantities to lead to exsanguination of the infant.
      2) Incidence.
         a) Approximately 1.54 per 10,000 births.
         b) Occurs much less often than caput succedaneum.
         c) Associated with vacuum extraction.
      3) Clinical presentation.
         a) Often a fluctuant mass of the scalp.
         b) May increase in size postnatally.
         c) Hypotonia, pallor, lethargy, seizures.
         d) Falling hematocrit levels.
      4) Diagnostic evaluation.
         a) Palpate: hemorrhage crosses suture lines, is firm but fluctuant to palpation.

b) Vital signs: monitor for symptoms of shock.
c) Serial hematocrit levels.
d) Monitor bilirubin levels during recovery.

5) Patient care management.
a) Rapid diagnosis and blood replacement are key to management. Observe for signs/symptoms of shock/hypovolemia.
(1) Monitor blood pressure, heart rate, and serial complete blood cell counts.
(2) Management for supporting organs, such as kidney, if shock occurs.
b) Infant may need blood transfusion on an emergent basis.
c) Ensure that infant receives vitamin K promptly.
d) Observe for hyperbilirubinemia.

6) Outcome: once the infant has survived the acute phase, recovery occurs in 2 to 3 weeks (Hoppe and Benedetti, 2018; Volpe, 2018).

d. Skull fractures.
1) Pathophysiology.
a) Linear fracture can occur.
b) Depressed fractures occur secondary to excessive force used with forceps and extreme molding.

2) Incidence.
a) Unknown.
b) Linear fracture fairly common finding.
c) Depressed fracture much less common than linear.

3) Clinical presentation.
a) Linear fracture: asymptomatic.
b) Depressed fracture.
(1) Presents with depressed surface of skull; indented, without craniotabes.
(2) Does not cross the suture lines.
(3) Possible marked separation of adjacent sutures.
(4) Most often occurs in right parietal bone.

4) Diagnostic evaluation.
a) X-ray examination.
b) CT scan.

5) Patient care management.
a) Obtain neurosurgery consultation.
b) Assess closely for neurologic deficits.
c) If lesion is less than 2 cm and patient is without neurologic deficits, follow clinically; spontaneous resolution expected within a few weeks.

6) Outcome.
a) Linear fractures usually heal completely within 3 months.
b) Depressed fracture outcome is dependent on degree of cerebral injury and success of therapy.

e. Brachial nerve plexus injuries (Hoppe and Benedetti, 2018; Porsors et al., 2016).
1) Pathophysiology.
a) Excessive stretching of brachial plexus during delivery.
b) Erb's palsy, involving cervical nerves V and VI. Denervation of the deltoid, supraspinatus, biceps, and brachioradialis leads to upper arm paralysis.
c) Klumpke's paralysis, involving cervical nerve VI to thoracic nerve I. Denervation of the intrinsics of the hand, flexors of the wrist, fingers, and sympathetics (Horner's syndrome) leads to lower arm paralysis.
d) Combination of Erb–Duchenne paralysis and Klumpke's paralysis, involving the entire arm from cervical nerve V to thoracic nerve I (entire arm paralyzed). Paralysis of the diaphragm will occur if injury involves cervical nerve IV.

2) Incidence: 0.5 to 2 per 1000 live births.

3) Risk factors.
a) Multiparous mother.
b) Prolonged labor.
c) Large size for gestational age.
d) Shoulder dystocia.

4) Clinical presentation.
a) Erb's palsy.
(1) Affected arm is abducted and internally rotated.
(2) The elbow is extended, with arm pronation and wrist flexion ("waiter's tip" position).
(3) Asymmetrical Moro reflex (absent in the affected arm), with a normal grasp.
b) Klumpke's paralysis.
(1) Swelling in shoulder and supraclavicular fossa; clavicle may be fractured.
(2) Involves intrinsic muscles of the hand, with a clawhand deformity.
(3) No grasp in the affected hand.
c) Erb–Duchenne–Klumpke paralysis.
(1) A combination of the earlier signs and symptoms.
(2) Occurs more often than isolated Klumpke's paralysis.
(3) Entire affected arm is flaccid.
(4) Moro and grasp reflexes are absent.

5) Diagnostic evaluation.
a) Obtain x-ray examination of affected arm and shoulder.
b) Obtain serial electromyographic studies.
c) Rule out fracture of the clavicle or humerus.
d) Rule out shoulder dislocation.
e) Rule out cerebral injury.

6) Patient care management.
   a) Obtain neurology consultation.
   b) Obtain serial electromyographic examinations to note improvements.
   c) Primary goal: avoid contractures of involved joints.
      (1) Begin passive range-of-motion exercise, beginning after the swelling and inflammation subside.
      (2) Exercise the arm with every diaper change.
      (3) Request a physical therapy consultation (infant may be able to benefit from splints at some point).
      (4) Educate the family about the importance of maintaining normal joint function.
         (a) Reinnervated musculature needs supple joints.
         (b) Will have wider choice of reconstructive procedures in the absence of contractures in the event there is no recovery.
7) Outcome.
   a) Generally spontaneous recovery occurs.
   b) About 88% fully recover by 4 months and 92% fully recover by 12 months (Hoppe and Benedetti, 2018; Volpe, 2018).
   c) If no appreciable recovery is noted by 3 months, surgical exploration may be warranted (Volpe, 2018).

f. Phrenic nerve paralysis (Hoppe and Benedetti, 2018; Volpe, 2018).
1) Pathophysiology.
   a) Diaphragmatic paralysis involving overstretching of cervical nerves III, IV, and V.
   b) Results from torn nerve sheaths with edema and hemorrhage.
   c) Eighty percent to 90% occur in association with brachial plexus injury, but it may also occur in isolation.
2) Clinical presentation.
   a) History of traumatic delivery, especially difficult breech delivery.
   b) First hours after birth.
      (1) Respiratory distress with cyanosis, tachypnea, hypoxemia, hypercapnia, and acidosis.
      (2) Diagnosis may be missed, as the elevated hemidiaphragm may not be present early in the course, especially with use of positive pressure ventilation.
   c) Next several days.
      (1) Improvement with oxygen and ventilatory support.
3) Diagnostic evaluation.
   a) Chest x-ray examination may not be useful, especially if positive pressure ventilation is in use.
   b) Ultrasonographic or fluoroscopic examination will show elevated hemidiaphragm and the paradoxical movement of the affected side with breathing.
   c) Serial ultrasonography to evaluate diaphragmatic function.
4) Patient care management.
   a) Administer oxygen and ventilatory support as needed.
   b) Place the infant affected side down (splint the affected side).
   c) Follow physical examination closely to note improvements.
   d) Family education and support because prolonged ventilatory support may be required.
5) Outcome.
   a) Mortality rate 10% to 15%.
   b) Majority recover within the first 6 to 12 months.
   c) Prolonged ventilatory support associated with 50% mortality rate.

g. Traumatic facial nerve palsy (Hoppe and Benedetti, 2018; Porsors et al., 2016; Volpe, 2018).
1) Pathophysiology.
   a) Trauma causes hemorrhage and edema into the nerve sheath, rather than a true disruption of the nerve fiber.
   b) Site of the lesion typically at or near the exit of the nerve from the stylomastoid foramen.
   c) Weakness of the facial muscles results.
2) Incidence: approximately 0.75% of term infants.
3) Clinical presentation.
   a) Varies with the degree of nerve involvement.
   b) Usually presents the first 2 days after birth.
   c) Persistently open eye on the affected side.
   d) Suck with drooling.
   e) Mouth drawn to normal side during crying.
   f) Corner of mouth does not pull down on affected side.
   g) Eyeball may roll up behind open eyelid.
   h) Usually does not increase in severity.
4) Patient care management.
   a) Artificial tears for the open eye.
   b) Possible need to tape or patch affected eye to protect cornea.

c) Support of parents.
d) Necessary to watch for signs of improvement.

5) Outcome.
a) High rate of spontaneous recovery by 7 to 10 days, especially between 1 and 3 weeks of age.
b) Detectable deficits rarely evident after several months.
c) For persistence beyond a few weeks, pediatric neurology should be consulted.

Intracranial Hemorrhages

A. **Subdural hemorrhage.**
1. Definition (Ditzenberger & Blackburn, 2014; Hoppe and Benedetti, 2018).
a. Due to laceration of the major veins and sinuses, usually associated with a tear of the dura overlying the cerebral hemispheres or cerebellum.
b. Occurrence with or without laceration of the dura.
2. Risk factors (Hoppe and Benedetti, 2018; Volpe, 2018).
a. Macrosomia.
b. Cephalopelvic disproportion.
c. Forceps delivery.
d. Vaginal breech delivery.
e. Premature delivery.
f. Malpresentation (breech, face, brow, foot).
g. Skull is unusually compliant and/or pelvic structures unusually rigid.
h. Labor is either very short (not enough time for dilation) or too long (head subjected to prolonged compression/molding).
i. Forceps, vacuum extraction, or rotational maneuvers required to effect delivery.
3. Pathophysiology (Hoppe and Benedetti, 2018; Volpe, 2018).
a. Excessive vertical molding and frontal–occipital elongation, or oblique expansion of the head; results in stretching of the falx and tentorium.
b. Venous sinuses are stretched, with possible rupture of the vein of Galen or cerebellar bridging veins.
c. Tear of the dura, including the falx or tentorium, may also occur.
4. Incidence.
a. Uncommon occurrence, accounts for less than 10% of intracranial hemorrhages.
5. Clinical presentation.
a. Decreased level of consciousness.
b. Seizure activity.
c. Asymmetry of motor function.
d. Determined by the extent of associated HIE injury.
e. Often minimal to no clinical symptoms for first 24 hours because of slowly enlarging hematoma.
f. On day 2 or 3: signs of increasing intracranial pressure due to block in CSF flow in posterior fossa.
1) Full fontanelle, irritability, lethargy.
g. Signs of brainstem disturbance.
1) Dilated, poorly reactive pupil on same side as the hemorrhage.
2) Respiratory abnormalities, facial paralysis.
3) Doll's eye reflex: normal to abnormal.
h. Chronic subdural effusion: present within the first 6 months of life with enlarging FOC.
6. Diagnostic evaluation.
a. CT scan.
b. MRI scan more effective if hemorrhage is in the posterior fossa.
c. Skull radiographs demonstrate skull fractures.
7. Outcome.
a. Major laceration of tentorium and falx with massive hemorrhage has poor prognosis.
b. Mortality rate approximately 45%.
c. Survivors develop hydrocephalus and other sequelae.
d. Concomitant hypoxic–ischemic injury critical factor in determining outcome.

B. **Primary subarachnoid hemorrhage** (Piña-Garza and James, 2013; Volpe, 2018).
1. Definition: an intracranial hemorrhage into the CSF-filled space between the arachnoid and pial membranes on the surface of the brain.
2. Pathophysiology.
a. Bleeding of venous origin in the subarachnoid space as a result of rupture of small vessels in the leptomeningeal plexus or bridging veins in the subarachnoid space.
b. Bleeding is not secondary to an extension of subdural hemorrhage, intraventricular hemorrhage, or cerebellar hemorrhage.
c. Self-limited.
d. May be precipitated by trauma (term infant) or hypoxia (preterm infant).
3. Incidence: common type of neonatal intracranial hemorrhage.
4. Clinical presentation.
a. Most commonly no symptoms develop.
b. Seizure activity may begin on day 2 of life, especially in the term infant.
c. Infant looks healthy between seizures: "well baby with seizures" (Piña-Garza and James, 2013; Volpe, 2018).
d. Recurrent apnea (more common in preterm infants).
5. Diagnostic evaluation.
a. Diagnosis of exclusion. Other forms of intracranial bleeding are eliminated by CT scan.

b. Lumbar puncture demonstrates uniformly blood-stained CSF.

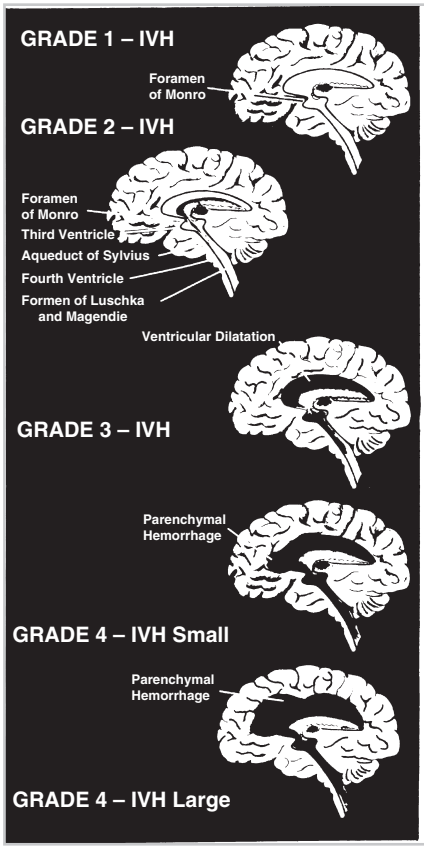
6. Outcome.
   a. Sequelae very uncommon.
   b. Ninety percent of term infants who exhibited seizures have normal follow-up.

C. **Intracerebellar hemorrhage.**

1. Definition: hemorrhage(s) within the cerebellum resulting from primary bleeding or extension of intraventricular or subarachnoid hemorrhage into the cerebellum.
2. Risk factors: association exists with respiratory distress, hypoxic events, prematurity, and traumatic delivery.
3. Pathophysiology.
   a. Intravascular, vascular, and extravascular factors (Hoppe and Benedetti, 2018; Volpe, 2018).
      1) Breech presentation and difficult forceps delivery secondary to a compliant skull, with external pressure causing occipital pressure.
      2) Vitamin K deficiency, thrombocytopenia.
      3) Vulnerable cerebral capillaries exposed to rapid colloid infusion, causing hypertensive spikes.
      4) Richly vascularized subpial and subependymal locations.
      5) Poor vascular support for subependymal and subpial germinal matrices.
      6) Extension of blood into the cerebellum associated with:
         a) Large volume of blood present with IVH.
         b) Increased intracranial pressure.
         c) Incomplete myelination of the cerebellum.
4. Incidence (Volpe, 2018).
   a. About 5% to 10% of neonatal deaths studied by autopsy.
   b. Higher in preterm infants than in term.
   c. Occurrence of 15% to 25% in premature infants born at less than 32 weeks of gestation or weighing less than 1.5 kg at birth.
5. Clinical presentation (Hill, 2005).
   a. May have a history of hypoxic–ischemic insult.
   b. Catastrophic deterioration with apnea, bradycardia, decreasing hematocrit values, and bloody CSF may occur.
   c. Signs appear within the first 3 weeks, most commonly within the first 2 days of life.
   d. Term infants may have a history of difficult breech delivery.
6. Diagnostic evaluation.
   a. Cranial ultrasonography (lack of symmetrical echogenicity may be important).
   b. CT scan necessary to define the hemorrhage.
   c. MRI provides definitive diagnostic information.
7. Outcome.
   a. More favorable in term infant than in premature infant.
   b. Poor outcome in premature infant.
   c. Probable neurologic deficits.

D. **Periventricular–intraventricular hemorrhage** (Blackburn, 2018; Hoppe and Benedetti, 2018; Porsors et al., 2016; Volpe, 2018).

1. Definition.
   a. Occurs once subependymal germinal matrix hemorrhage extends into lateral ventricles.
   b. Most extensive periventricular–intraventricular hemorrhage is a parenchymal intracerebral hemorrhage.
      1) Involves bleeding into the periventricular (i.e., intracerebellar) white matter and may also precipitate cerebral infarction.
      2) With time, on follow-up scans, may see formation of porencephalic cyst at the original hemorrhage site.
   c. See Fig. 34.4 for description and grading system (Papile, 2006).
      1) Small hemorrhage: grade 1 or 2.
      2) Moderate hemorrhage: grade 3.
      3) Severe hemorrhage: grade 4.
2. Risk factors.
   a. Prematurity: birth at less than 34 weeks of gestation; respiratory failure requiring mechanical ventilation.
   b. Associated with increasing arterial blood pressure and perinatal asphyxia.
   c. Associated clinical factors.
      1) Low 5-minute Apgar score.
      2) Asphyxia or birth trauma.
      3) Very low birth weight.
      4) Acidosis.
      5) Hypotension or hypertension.
      6) Low hematocrit.
      7) Respiratory distress requiring mechanical ventilation.
      8) Rapid administration of sodium bicarbonate.
      9) Rapid volume expansion.
      10) Infusion of hyperosmolar solution.
      11) Coagulopathy.
      12) Pneumothorax.
      13) Ligation of patent ductus arteriosus.
      14) Transport.
3. Pathophysiology.
   a. Occurs once subependymal germinal matrix hemorrhage extends into lateral ventricles.
   b. Most extensive periventricular–intraventricular hemorrhage is a parenchymal intracerebral hemorrhage.
      1) Involves bleeding into the periventricular (i.e., intracerebellar white matter) and may also precipitate cerebral infarction.



Grade 1 IVH: Subependymal hemorrhage in the periventricular germinal matrix. Often localized at the foramen of Monro.

Grade 2 IVH: Partial filling of lateral ventricles without ventricular dilatation.

Grade 3 IVH: Intraventricular hemorrhage with ventricular dilatation.

Grade 4 IVH (small and large): Parenchymal involvement or extension of blood into the cerebral tissue itself. Can be present to a lesser degree.

Correlation between the severity or extent of involvement and subsequent impairment is not absolute. Because outcomes are so varied, assessment of early symptoms and the practice of purposeful interventions are extremely important.

Fig. 34.4 Quantification of extent of intraventricular hemorrhage (IVH). Four grades of hemorrhagic involvement categorized IVH, as differentiated by Papile and Burstein. (*From Ross Laboratories. [1988].* New perspectives on intraventricular hemorrhage. *Columbus, OH: Ross Laboratories.*)

2) Only 10% to 15% of infants with hemorrhages.
3) With time, on follow-up scans, may see formation of porencephalic cysts at the original hemorrhage site.

4. Incidence.
   a. Incidence: 40% to 60% of very low birth weight neonates.
   b. Infants born at less than 28 weeks of gestation have a 3 times higher risk than infants born at 28 to 31 weeks of gestation.
      1) Primary site of bleeding is the germinal matrix in the subependymal area next to the caudate nucleus.
   c. Approximately 3.5% to 4.6% of term infants have a periventricular–intraventricular hemorrhage.
      1) More than half of these hemorrhages originated at the choroid plexus of the lateral ventricles.
      2) Timing of onset.
         a) About 50% occur by 24 hours of age.
         b) About 80% occur by 48 hours of age.
         c) About 90% occur by 72 hours of age.
         d) By 7 days of age, 99.5% have occurred.
         e) Twenty percent to 40% exhibit progression of the hemorrhage over 3 to 5 days.

5. Clinical presentation.
   a. Presentation ranges from unnoticeable to dramatic.
      1) Sudden deterioration.
      2) Oxygen desaturation.
      3) Bradycardia.
      4) Metabolic acidosis.
      5) Significant decrease in hematocrit.
      6) Hypotonia.
      7) Shock.
      8) Hyperglycemia.
      9) Tense anterior fontanelle.
   b. Symptoms of worsening hemorrhage.
      1) Full, tense fontanelles.
      2) Increased ventilatory support.
      3) Seizure activity.
      4) Apnea.
      5) Decrease in level of consciousness and/or activity.

6. Diagnostic evaluation.
   a. Optimal time to screen: 7 days of age because greater than 90% of all hemorrhages have occurred.
      1) If test result is normal, there is no need to recheck.

2) If test result is positive for periventricular–intraventricular hemorrhage, repeat test in 2 weeks.

b. Serial cranial ultrasonography has replaced CT as the principal diagnostic technique.
c. Lumbar puncture (CSF studies show elevated red blood cells, increased protein concentration, xanthochromia, and decreased glucose concentration).
d. Rule out septic shock or meningitis.

7. Patient care management.
   a. Prevent preterm birth, perinatal asphyxia, and birth trauma.
   b. Promote in-utero transport.
   c. Promote nonstressful intrapartum course.
   d. Provide efficient, expedient intubation.
   e. Appropriate handling; minimal stimulation with clustering of care activities as tolerated.
   f. Minimize noxious stimuli (dim the lights, quiet the environment).
   g. Avoid noxious procedures when possible.
   h. Avoid events associated with wide swings in arterial and venous pressures.
      1) Seizures.
      2) Excess motor activity.
      3) Apnea.
      4) Crying.
      5) Pneumothorax.
   i. Avoid administration of hyperosmolar solutions.
   j. Prevent blood pressure swings: give volume replacement slowly.
   k. Avoid overventilation leading to pneumothorax.
   l. Use two people for endotracheal suctioning.
   m. Use noninvasive monitoring of oxygen and carbon dioxide levels (maintain within normal limits).
   n. Monitor and maintain normal pH.
8. Correct abnormal clotting.
   a. Be alert to signs of a hemorrhage.
   b. Educate and support the parents.
9. Outcome.
   a. Grade 1 and grade 2 hemorrhages typically have resolution.
   b. Grade 3 hemorrhage evolves over 1 to 3 weeks. There may be destruction of the subarachnoid space leading to ventricular dilatation and hydrocephalus.
   c. Mortality rate is 50% with severe hemorrhage, 10% with moderate hemorrhage, and 5% with small hemorrhage.
   d. These hemorrhages are an important cause of morbidity and death in low birth weight infants.
   e. Hemorrhage alone does not account for all neurologic deficits.
   f. Approximately 50% of premature infants are free of neurologic symptoms.
   g. Approximately 25% to 30% of very low birth weight infants discharged from a level III neonatal intensive care unit have a periventricular–intraventricular hemorrhage without major neurodevelopmental sequelae.
   h. Outcome depends on degree of severity of hemorrhage.
      1) Small hemorrhage.
         a) Neurodevelopmental disability similar to that in premature infants without hemorrhage.
         b) Major neurodevelopmental disability in 10%.
      2) Moderate hemorrhage.
         a) Major neurodevelopmental disability in 40% during infancy.
         b) Mortality rate 10%, with progressive hydrocephalus in less than 20%.
      3) Severe hemorrhage.
         a) Major neurodevelopmental disability in 80%.
         b) Mortality rate 50% with hydrocephalus common in survivors.

Seizures (Piña-Garza and James, 2013; Porsors et al., 2016; Scher, 2012, 2013)

A. **Definition:** symptom of neurologic dysfunction (not a disease).
B. **Risk factors.**
   1. Metabolic encephalopathies.
      a. Decreased production of adenosine triphosphate.
   2. Ischemia.
   3. Hypoxemia.
   4. Hypoglycemia.
      a. Hyponatremia or hypernatremia.
      b. Hypocalcemia, hypomagnesemia.
      c. Inborn errors of metabolism.
      d. Pyridoxine dependency.
      e. Hyperammonemia.
   5. Structural.
      a. IVH.
      b. Intrapartum trauma.
      c. Cerebral cortical dysgenesis: result of abnormal neuronal migration.
      d. HIE, the most common diagnosis of neonatal seizures.
   6. Intracerebral meningitis.
      a. Bacterial infection.
         1) Group B β-hemolytic streptococci and *Escherichia coli* may account for up to 65% of cases.

2) Many other bacterial organisms may be implicated and include but are not limited to other streptococcus and staphylococcus species, such as group D streptococci, *Staphylococcus epidermidis*, *S. aureus*, *Listeria monocytogenes*, *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae*.

b. Nonbacterial infection: TORCH.

7. Withdrawal from maternal drugs.
   a. Uncommon cause of seizures (may cause jitteriness).
   b. Onset during first 3 days of life.
   c. Drugs.
      1) Narcotic analgesics.
      2) Sedative–hypnotics.
      3) Alcohol.
8. Familial (genetic).
   a. Onset in second and third days of life.
   b. Infant appears well between seizures.
   c. Self-limiting: within 1 to 6 months, seizures stop.
   d. Autosomal dominant inheritance.

C. **Pathophysiology:** seizures result from excessive simultaneous electrical discharge or depolarization of neurons.

D. **Incidence.**
1. 57.5 per 1000 infants less than 1500 g.
2. 2.8 per 1000 infants weighing 2500 to 3999 g.

E. **Clinical presentation.**
1. Subtle.
   a. Most frequent of neonatal seizures.
   b. Present in most term and premature newborn infants having seizures.
   c. Often unrecognized.
   d. Presentation varies.
      1) Horizontal deviation of the eyes.
      2) Pedaling movements.
      3) Rowing, stepping movements.
      4) Eye blinking or fluttering.
      5) Nonnutritive sucking.
      6) Smacking of lips.
      7) Drooling.
      8) Apnea (convulsive apnea usually does not occur by itself).
2. Tonic.
   a. Characteristic in premature infants weighing ≤500 g.
   b. Often seen with severe IVH.
   c. Generalized tonic extension of all extremities or flexion of upper limbs with extension of lower extremities.
   d. Often mimics decorticate posturing.
3. Multifocal clonic.
   a. Characteristic in term infants with HIE.
   b. Clonic movements migrating from one limb to another without a specific pattern.
4. Focal clonic.
   a. Uncommon.
   b. Presents as localized clonic jerking.
5. Myoclonic.
   a. Very rare in neonatal period.
   b. Multiple jerks of upper or lower limb flexion.

F. **Diagnostic evaluation.**
1. Perform physical examination.
   a. Rule out jitteriness.
      1) Characterized by trembling of hands and feet.
      2) No involvement of eye movements.
      3) Stopped by gentle, passive flexion of affected extremity.
   b. Note infant's history, which may provide a predisposed underlying etiology.
2. Laboratory work.
   a. Serum glucose level.
   b. Electrolyte levels (sodium, potassium, chloride, calcium, magnesium).
   c. Arterial blood gas analysis.
   d. Urea, ammonia.
3. Diagnostic study for sepsis.
   a. Lumbar puncture.
   b. Culture of blood, urine, and CSF specimens; bacterial and viral.
   c. Complete blood cell count and platelet count.
4. Electroencephalography (EEG), CT scan, cranial ultrasonography, MRI.
5. Skull films if etiology is trauma.
6. Twelve-lead electrocardiography.
7. Consideration of following laboratory tests:
   a. Blood pyruvate.
   b. Lactate.
   c. TORCH.
   d. Urinary drug screen.
8. Neurology consultation.

G. **Patient care management.**
1. Determine underlying etiology.
2. Resuscitate as necessary.
3. Obtain diagnostic studies as ordered.
4. Provide pharmaceutical therapy.
   a. Phenobarbital.
      1) Loading dosage: 20 mg/kg slow intravenous (IV) push for 10 to 15 minutes. Additional 5 mg/kg may be given 1 hour later for refractory seizures, to a maximum of 40 mg/kg.
      2) Closely monitor respiratory status.
      3) Maintenance dosage: 3 to 4 mg/kg/day, beginning 12 to 24 hours after the loading dose.
      4) Therapeutic range: 15 to 40 mcg/mL.
      5) Excretion.
         a) Metabolized by liver: 50% to 70%.
         b) Unchanged in urine: 20% to 30%.
      6) Consider as the drug of choice.

b. Fosphenytoin (Cerebyx).
   1) Loading dosage: 15 to 20 mg PE/kg IV over 10 minutes. Normal saline should be flushed before and after the dosing. (Fosphenytoin dose expressed in phenytoin equivalents [PEs]. Fosphenytoin 1 mg PE = 1 mg phenytoin.)
   2) May be given intramuscularly (IM).
   3) Maintenance dosage: 4 to 8 mg PE/kg/day slow IV push or IM 24 hours after loading dose.
      a) Term neonates older than 7 days of age may require up to 8 mg PE/kg/dose every 8 to 12 hours.
   4) Therapeutic range: 10 to 20 mcg/mL. Serum trough level of phenytoin measured (not fosphenytoin) 48 hours after the IV loading dose.
      a) Peak plasma concentrations: about the time that the IV infusion is complete; half-life is 4 to 10 minutes.
      b) Rapidly converted by the body to generate therapeutic levels of phenytoin.
   5) Excretion.
      a) Protein bound (approximately 90%).
      b) Displaced by bilirubin, increasing free drug levels. Caution with hyperbilirubinemia.

c. Phenytoin.
   1) Loading dosage: 15 to 20 mg/kg IV over at least 30 minutes. Flush with normal saline before and after dosing. Never given IM, and never give in central lines.
      a) Is very irritating to veins; extravasation may result in tissue necrosis.
   2) Maintenance.
      a) Dosage: 4 to 8 mg/kg/day slow IV push or per os (PO). *Caution:* Absorption is erratic with PO route.
      b) Therapeutic range: trough level of 6 to 15 mcg/mL 48 hours after loading dose and 10 to 20 mcg/mL after 2 weeks.

d. Lorazepam.
   1) Administer: 0.05 to 0.1 mg/kg slow IV push (for status epilepticus).
   2) Repeat dose based on clinical response.
   3) Note routes of excretion.
      a) By kidneys.
      b) Lipid soluble.
   4) Lorazepam produces anticonvulsant effect in minutes after administration.
   5) Monitor oxygenation and vital signs.
   6) Document precisely.

H. **Outcome**.
   1. Related to underlying etiology.

Hypoxic–Ischemic Encephalopathy (Laptook, 2012; McAdams and Traudt, 2018; Porsors et al., 2016; Scher 2013)

A. **Definition of HIE.**
   1. Hypoxemia and anoxia (diminished oxygen in blood supply; partial or complete). Moderate to severe hypoxia leads to metabolic acidosis.
   2. Ischemia (diminished blood supply perfusing the brain).
      a. Systemic hypotension.
      b. Occlusive vascular disease.
   3. Hypoxia and ischemia, which lead to neurologic dysfunction.
   4. Asphyxia.
      a. Impairment of gas exchange of respiratory gases—oxygen and carbon dioxide.
      b. Mixed respiratory and metabolic acidosis.
      c. Failure of systemic multiorgan systems, including heart, lungs, liver, and kidneys.

B. **Diagnosis**.
   1. History and risk factors.
      a. Antepartum risk factors: socioeconomic status, maternal thyroid disease, severe pregnancy-induced hypertension, fetal growth restriction, postdatism.
      b. Intrapartum risk factors: maternal pyrexia; persistent occiput posterior fetal position; acute intrapartum events, such as cord accident, uterine rupture, abruption; evidence of intrapartum hypoxia defined by composite of abnormal fetal heart rate, fresh meconium, and low Apgar scores.
   2. EEG.

C. **Incidence of HIE.**
   1. Approximately 1.5 per 1000 live births. About 0.3 per 1000 live births will have significant neurologic sequelae.
   2. About 2% to 4% of term infants.
   3. Approximately 60% of very low birth weight infants.
   4. Timing of insult occurrence (Volpe, 2018).
      a. Antepartum occurrence: 20%.
      b. Intrapartum occurrence: 30%.
      c. Antepartum–intrapartum occurrence: 35%.
      d. Postpartum occurrence: 10%.

D. **Clinical presentation and staging using Sarnat criteria. Refer to Table 34.3 for clinical presentation and staging of hypoxic–ischemic encephalopathy.**
   1. Stage I (mild encephalopathy): characteristic features.
      a. Hyperalert state.
      b. Normal muscle tone, active suck, strong Moro reflex, normal/strong grasp, and normal doll's eye reflex.

Table 34.3

Clinical Presentation and Staging of Hypoxic–Ischemic Encephalopathy

	Stage 1: Mild	Stage 2: Moderate	Stage 3: Severe
General			
1. Consciousness	Hyperalert	Lethargic; obtunded	Stupor; coma
2. Activity	Normal	Decreased	Absent
Neuromuscular Control			
1. Muscle tone	Normal	Mild hypotonia	Flaccid; absent
2. Posture	Mild distal flexion	Strong distal flexion	Intermittent decerebration
3. Stretch reflexes	Overactive	Overactive	Decreased; absent
Primitive Reflexes			
1. Suck	Weak	Weak or absent	Absent
2. Moro	Strong	Weak, incomplete	Absent
3. Tonic neck	Slight	Strong (stiff)	Absent
Autonomic Function			
1. Pupils	Dilated	Constricted	Variable; unequal
2. Heart rate	Tachycardia	Bradycardia	Variable
Seizures	None	Common	Uncommon

Adapted from McAdams, B. M., & Traudt, C. M. (2018). Brain injury in the term infant. In C. A. Gleason, S. U. Devaskar, & S. Juul (Eds.), *Avery's diseases of the newborn* (10th ed.). Philadelphia, PA: Elsevier Saunders.

c. Increased tendon reflexes.
d. Myoclonus present.
e. Hyperresponsiveness to stimulation.
f. Tachycardia possible.
g. Dilation of pupils, reactive.
h. Sparse secretions.
i. No convulsions (unless due to hypoglycemia or preexisting conditions that predisposed the infant to perinatal distress).
j. Electroencephalographic findings: within normal limits.

2. Stage II (moderate encephalopathy).
   a. Characteristic features.
      1) Lethargy.
      2) Hypotonia.
      3) Increased tendon reflexes.
      4) Myoclonus.
      5) Seizure activity frequent.
      6) Weak suck.
      7) Incomplete Moro reflex.
      8) Strong grasp.
      9) Overactive doll's eye reflex.
      10) Pupils constrictive and reactive.
      11) Respirations variable in rate and depth; respirations may be periodic.
   b. Critical period: infant's condition either improves or deteriorates.
   c. Indications of deterioration.
      1) No signs of improvement.
      2) Development of any of the following:
         a) Seizures.
         b) Cerebral edema.
         c) Lethargy.
         d) Abnormalities on EEG.
   d. Recovery.
      1) No further seizure activity.
      2) Electroencephalographic findings return to normal.
      3) Transient jitteriness.
      4) Improvement in level of consciousness.
3. Stage III (severe encephalopathy).
   a. Clinical course.
      1) Level of consciousness deteriorates from obtunded to stuporous to comatose.
      2) Mechanical ventilation is required to sustain life.
   b. Clinical features.
      1) Apnea/bradycardia.
      2) Seizures appearing within the first 12 postnatal hours; 50% to 60% of patients who do ultimately seize do so within the first 6 to 12 hours. Premature infants present with generalized seizures. Term infants demonstrate multifocal clonic seizures. All these infants display subtle seizures (Volpe, 2018).
      3) Severe hypotonia and flaccidity; suck, Moro, and grasp reflexes absent.
      4) Stuporous to comatose.
      5) Absent or depressed reflexes.
      6) Doll's eye reflex weak or absent.
      7) Pupils often unequal; variable reactivity and poor light reflex.
   c. Deterioration.
      1) Deterioration occurs within 24 to 72 hours.

2) Severely affected infants often worsen, sinking into deep stupor or coma.
3) Death may ensue.

d. Survivors.
1) Infants who survive to this point often improve in the next several days to months.
2) Feeding difficulties often develop secondary to abnormalities of suck and swallow. This is due to the poor muscle tone connected to involvement of cranial nerves for these functions.
3) Generalized hypotonia is common; hypertonia is uncommon.
4) Severe neurologic disabilities may ensue.

E. **Diagnostic studies.**
1. Valuable in assessing the nature of the brain insult and the extent of the brain injury.
2. Used to track the evolution of HIE.
a. Precise history.
b. Complete neurologic examination.
c. EEG.
1) Confirm or deny clinical diagnosis of seizures.
2) Provide prognostic information regarding severity of permanent brain damage.
3) Two common types of EEG: conventional EEG (cEEG) or amplitude EEG (aEEG).
a) cEEG: used to measure impact of neurologic insult and detect presence of seizure activity.
(1) Twelve to 16 sensors applied by specialist technician. Sensors are usually invasive.
(2) Usually recorded for 40 to 60 minutes.
(3) Provides information about entire cerebral cortex.
(4) Logistically challenging to schedule technician to interpret and neurologist to interpret study.
b) aEEG: measures, filters, and time-compresses raw EEG signal to create simplified pattern easy to interpret by nonneurologist.
(1) May be single (two sensors) channel to monitor single parietal channel or dual (four sensors) channels in parietal and central positions.
(2) Usually recorded continuously.
(3) Provides hemispheric information of the cerebral cortex.
(4) No technician needed for sensor application, and nonneurologist can interpret study.
(5) Abnormal aEEG is more specific (89% vs. 78%), has a greater positive predictive value (73% vs. 58%), and has a similar sensitivity (79% vs. 78%), as well as negative predictive value (90% vs. 91%) compared with abnormal neurologic examination by Sarnat criteria alone.
d. Evoked potentials.
e. Creatinine kinase and other biochemical/enzyme markers.
f. Lumbar puncture, CSF analysis.
g. CT scan.
h. Cranial ultrasonography.
i. Technetium scan.
j. MRI.
k. Intracranial pressure monitoring.

F. **Patient care management.**
1. Prevent perinatal hypoxia, ischemia, and asphyxia (anticipation of risk factors, appropriate intervention).
2. Perform prompt, efficient resuscitation by trained staff.
3. Maintain physiologic oxygenation and acid–base balance.
4. Correct fluid, electrolyte, and caloric abnormalities.
5. Monitor blood volume; avoid blood pressure swings and hypotension.
6. Maintain optimal perfusion.
7. Treat seizures.
8. Consider cerebral hypothermia.
a. Total body cooling.
b. Selective head cooling.
c. Goal of hypothermia: maintain brain energy phosphorylated metabolites, improve coupling between blood flow and oxidative metabolism, decrease release of excitatory transmitters that lead to seizures, reduce nitric oxide production, and decrease apoptosis.
d. See Table 34.4 for comparison between total body and selective cooling.
9. Perform a thorough neurologic examination.
10. Monitor and manage disturbances of other body organs.
a. Pulmonary.
b. Cardiac.
c. Hepatic.
d. Renal.
11. Educate and support the family.
12. Obtain neurology consultation.

G. **Outcome**.
1. Based on severity of brain insult; selective neuronal necrosis.
2. Death within newborn period in 20% to 50% of asphyxiated infants who exhibit HIE.
3. Overall neurologic sequelae with HIE at 3½ years of age: approximately 17%. With more follow-up data, the rate may change as cooling strategies have become widely used.
4. Factors associated with poor outcome.
a. Apgar score.
1) If score is 0 to 3 for 20 minutes or more, approximately 60% die.

Table 34.4

Comparison of Brain Cooling Trials

Parameter	CoolCap	Body Cooling
Mode of cooling	Head and systemic	Systemic only
Equipment	Cooling cap and radiant warmer	Cincinnati Sub-Zero Hyper-Hypothermia System; newborn-sized (22″ × 33″) cooling blanket
Target core: temperature	34° to 35° C	33.5° C
Target core: site	Rectum	Esophagus
Temperature control method at core site	Servo-control of abdominal skin temperature 36.8° to 37.2° C; manual control of CoolCap to achieve target core temperature at rectum	Servo-control of esophagus
Age at therapy initiation	<6 hours	<6 hours
Time to achieve target core temperature	2 hours	Approximately 1.5 hours
Duration of cooling therapy	72 hours	72 hours
Rate of rewarming after therapy cessation	0.5° C/hour	0.5° C/hour

From Laptook, A. R. (2008). Brain cooling for neonatal encephalopathy: Potential indications for use. In J. M. Perlman (Ed.), *Neurology: Neonatal questions and controversies* (pp. 66–78). Philadelphia, PA: Elsevier Saunders.

2) If score is less than 3 at 1 minute and less than 5 at 5 minutes, with abnormal neurologic signs (feeding difficulties, apnea, hypotonia, seizures):
   a) About 20% die.
   b) About 40% are normal.
   c) About 40% have neurologic sequelae.

b. Encephalopathy.
   1) Mild: no subsequent deficits.
   2) Severe: 75% die, 25% have sequelae.
   3) Term infants: 60% normal, 30% abnormal, and 10% die.
   4) Premature infants: 50% normal, 20% abnormal, and 30% die.
   5) Duration of abnormal neurologic signs: good indicator of severity of HIE injury.
   6) Disappearance of abnormal neurologic signs by 1 to 2 weeks: good chance of being normal (possibility of learning disabilities not ruled out).

5. Seizures early (first 12 hours of life) and/or difficult to control: associated with poorer prognosis.
6. Hyperactivity and attention difficulties: in infants with less severe encephalopathy.
7. Rapid initial improvement indicative of better outcomes.
8. Long-term sequelae based on:
   a. Site.
   b. Extent of cerebral injury.
   c. Duration of abnormal clinical presentation.

Periventricular Leukomalacia (Back and Miller, 2018; Neil and Inder, 2018; Scher, 2013)

A. **Definition of periventricular leukomalacia (PVL).**
   1. Ischemic, necrotic periventricular white matter.
   2. Principally ischemic lesion of arterial origin.
   3. Multicystic encephalomalacia with or without secondary hemorrhage into ischemic area.

B. **Pathophysiology**.
   1. Predisposition.
      a. Systemic hypotension severe enough to impair cerebral blood flow.
      b. Occurrence of focal cerebral infarction and cerebral ischemia.
      c. Major systemic hypotension.
      d. Episodes of apnea and bradycardia.
   2. Occurrence secondary to inadequate cerebral perfusion.
   3. Manifestation of HIE in premature infants.

C. **Incidence** (Volpe, 2018).
   1. Unknown.
   2. Approximately 3% to 10% of those with bilateral cystic leukomalacia.
   3. Increases to approximately 26% if noncystic PVL is included.

D. **Clinical presentation** (Back and Miller, 2018; Volpe, 2018).
   1. Acute phase: hypotension and lethargy.
   2. Six to 10 weeks later, characteristic picture.
      a. Irritable, hypertonic, increased flexion of arms and extension of legs.

b. Frequent tremors and startles.
c. Moro reflex may be abnormal.

E. **Diagnostic evaluation** (Neil and Inder, 2018; Scher, 2013).
1. Cranial ultrasonography.
2. CT scan.
3. MRI.

F. **Outcome** (Scher, 2013; Volpe, 2018).
1. Spastic diplegia (major motor deficit common in premature infants with PVL).
2. Motor deficits in premature infants; possible spontaneous resolution in first several years of life.
3. Significant upper arm involvement associated with intellectual deficits.
4. Visual impairment.
5. Lower limb weakness.
6. Outcome based on:
   a. Location.
   b. Extent of injury.

Meningitis (see Chapter 32)

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CHAPTER 35
Congenital Anomalies

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OBJECTIVES

1. Describe assessment strategies for the diagnosis of infants experiencing a congenital defect.
2. Identify methods of initial management and care for individual congenital anomalies.
3. List possible causative factors that result in common congenital abnormalities.
4. Verbalize the importance of parental involvement in the development of infants affected with congenital anomalies.

In North America, congenital malformations account for more than 20% of infant deaths (Moore et al., 2016a). In the United States, nearly 1 in 120 live-born infants will experience a chromosomal abnormality (Moore et al., 2016a). Every 4½ minutes an infant is born with a birth defect (https://www.cdc.gov/ncbddd/birthdefects/facts.html). Anomalies arising during gestation and present at birth are the leading cause of prenatal and postnatal morbidity. These statistics represent a significant challenge to health care providers and have life-changing implications for the families of these infants.

A congenital anomaly is defined as a physical, metabolic, anatomic, or behavioral deviation from the normal pattern of development (Moore et al., 2016a) (Box 35.1). This chapter presents information concerning the incidence, etiology, clinical presentation, and treatment modalities for some common abnormalities. The reader is directed to Chapter 20 for a foundation on genetics.

A. **Incidence**.
   1. The frequency of medically significant malformations diagnosed in the newborn period is documented as 2% to 4% of all live births (Parikh and Mitchell, 2015). These defects present as single or multiple defects, all with varying clinical significance.
      a. By 1 year of age, the incidence of congenital anomalies requiring surgery or interfering with normal functioning ranges from 4% to 7% (Lashley, 2005).
      b. Minor single-anomaly rates are estimated to be as high as 14% (Moore et al., 2016a). Estimates suggest 20% to 30% of babies with birth defects have two or more defects (Agopian et al., 2018).
      c. The identification of neonates with a major malformation is vital, as these infants have a five-fold increase in morbidity (Parikh and Mitchell, 2015).
   2. Birth defects are a significant cause of miscarriage and fetal death. Approximately 16% of confirmed pregnancies result in miscarriages or still births (Rousseaux and Bolon, 2013).
      a. Of recognized conceptions, 10% to 20% will end in spontaneous abortion secondary to abnormal genetic development. A significant number of unsuspected conceptions fail too early to be noticed.
      b. Fifty percent to 60% of all fetuses spontaneously aborted will have a detectable chromosomal abnormality (Lashley, 2005). Of those, trisomic abnormalities account for 50% of pregnancy losses (Parikh and Mitchell, 2015).

B. **Etiology.** The etiology of 50% to 60% of congenital anomalies is unknown (Moore et al., 2016a). Congenital malformations may have more than one cause, are often associated with multiple anomalies of major or minor significance, and have variable recurrence risks. Congenital anomalies may result from chromosomal disorders, single-gene defects, infective agents, teratogens, combinations of genetic and environmental factors, maternal metabolic factors, and mechanical constraints on the uterus. Historically, many believed advancing maternal age increased the risk for major congenital anomalies. However, studies suggest advanced maternal age may actually decrease chances for major anomalies, as anatomically normal fetuses are more likely to survive and others would be miscarried (Goetzinger et al., 2016). The role of advanced paternal age is unclear (Bajaj and Gross, 2015).
   1. Disorders resulting from genetic factors.
      a. Genetic factors are numerically the most frequent cause of congenital anomalies and are responsible for approximately 0.5% to 0.7% of all anomalies (Matthews and Robin, 2016). Chromosomal

Box 35.1

Terminology

Consistent language, definitions, and accurate presentation of dysmorphology are vital to understanding congenital anomalies.

1. Malformation: a primary morphologic defect of an organ or body part that results from an intrinsic abnormal developmental process (e.g., neural tube defect).
2. Deformation: alteration of a previously normal body part by unusual forces on normal tissue. Timing of event usually occurs in the fetal period as a secondary alteration, often involving cartilage, joints, and bones (e.g., clubfoot).
3. Disruption: extrinsic breakdown or interruption of a normal developmental process resulting in a defect of an organ or larger body system (e.g., amniotic banding sequence).
4. Dysplasia: abnormal organization of cells in tissue.
5. Syndrome: a recognized pattern of multiple anomalies derived from a single anomaly or mechanical factor (e.g., Down syndrome).
6. Sequence: a pattern of multiple anomalies related to a single prior anomaly (e.g., Pierre Robin sequence).
7. Association: a combination of anomalies known to occur together but not yet identified as a specific syndrome (e.g., VATER and CHARGE associations).

disorders account for 10% of all of the major malformations (Parikh and Mitchell, 2015). Of anomalies with known causes, 85% are due to genetic factors (Moore et al., 2016a).

b. Chromosomal errors are produced in the germ line of either parent, secondary to errors in fertilization, meiosis or mitosis (commonly nondisjunction and anaphase lag), and chromosome breakage and reunion (Lashley, 2005).
c. Embryos resulting from these unions display missing or extra chromosomes (numeric abnormality) or rearranged segments (structural abnormalities). Chromosomal aberrations result in defective zygotes, blastocysts, and early embryos.
d. Both sex chromosomes and/or autosomes may be affected.
e. Categories of genetic factors,
    1) Numeric abnormalities commonly result from nondisjunction of genetic material. This error in cell division occurs during mitosis or meiosis when a chromosomal pair or two chromatids of a chromosome fail to disjoin (Moore et al., 2016a). The end result is the loss or gain of one or more chromosomes.
        a) Trisomy: fertilization of an aneuploid gamete by a normal gamete, resulting in a zygote with three copies of a chromosome instead of two.
        b) Monosomy: zygote develops missing a specific chromosome.
        c) Mosaicism: Results secondary to nondisjunction in early cleavage division of a single zygote. The result is an embryo having two or more cell lines with different cell numbers (Moore et al., 2016a). Symptoms are generally less severe than if all cells are affected.
f. Numeric chromosomal abnormalities are frequently associated with intrauterine growth retardation, dysmorphic features, intellectual disability, and physical malformations (Matthews and Robin, 2016).
g. Structural abnormalities frequently result from chromosome breakage that results in a loss or rearrangement of the broken segment to a different location on the chromosome or to a different chromosome. The resulting change in structure is dependent on the final disposition of the broken pieces. Chromosome breakage may be caused by radiation, drugs, chemicals, and viruses (Moore et al., 2016a).
    1) Deletions are chromosome breaks that result in the loss of part of the chromosome. Breakage can occur at either end, resulting in a ring chromosome, or in the body of the chromosome. Microdeletions are submicroscopic chromosomal abnormalities that involve specific minute portions of chromosomes. Loss of chromosomal material is associated with serious malformation.
    2) Duplication anomalies result as a duplication of genetic material within, attached to, or as a separate fragment of the chromosome (Moore et al., 2016a). Though there is no loss of genetic material, individuals commonly experience intellectual disability or other birth defects.
    3) Inversion defects result when a chromosome segment is reversed. Risk for abnormality is dependent on the portion of the chromosome involved.
h. Single-gene or mendelian disorders are responsible for 0.4% of neonates who have major malformations (Parikh and Mitchell, 2015). The mode of mendelian inheritance for many major malformations is autosomal dominant (Parikh and Mitchell, 2015). Autosomal recessive or, less frequently,

X-linked, inheritance accounts for a minority of major malformations. The mechanism for development of abnormality is related to dysfunction of the gene or disturbance of the developmental pathway.

i. Multifactorial disorders result secondary to interaction of genes and additive environmental influences. In order for an abnormality to be expressed, a threshold of traits must be exceeded.
j. Disorders are familial but lack the inheritance traits of single-gene defects.
k. Most isolated single malformations, such as congenital heart defects, neural tube defects, and cleft lip and palate, develop secondary to multifactorial inheritance patterns (Parikh and Mitchell, 2015).
l. Recurrence rates are higher for first-degree relatives, are greater if a larger number of family members are affected, and are increased if the malformation is severe (Matthews and Robin, 2016).

2. Disorders resulting from exposure to teratogens that affect the developing fetus.
   a. A teratogen is defined as any external organism, substance, deficiency state, or physical agent capable of inducing abnormal structure or function in prenatal or postnatal life (Parikh and Mitchell, 2015).
   b. Environmental factors are causative for 7% to 10% of congenital anomalies (Moore et al., 2016a). The exact mechanism resulting in a disruption of embryonic development and induction of anomalies remains unclear, but environmental factors do not appear to exert effect until cellular differentiation begins.
   c. The majority of teratogenic agents exert their effect by interfering with cellular metabolic activity. The end result is failure of cellular replication, cell migration, cellular fusion, and death. Moore et al. (2016a) define the most critical periods of development as the time when cell division, cell differentiation, and morphogenesis are at their peak.
   d. The ability of a particular agent to exert a teratogenic effect is determined by the timing of the exposure (critical time once cellular differentiation has begun), dosage of the teratogen (the higher the dose, the greater the effect), the individual properties of the teratogen, and the genetic susceptibility of the mother and fetus (Matthews and Robin, 2016).
   e. The range of teratogenic agents is large and continues to increase. Teratogens can be infectious agents, drugs, chemical agents, radiation, and maternal factors.
   f. Exposure of the fetus to alcohol carries a significant risk throughout pregnancy and is considered to be the most common teratogen (Parikh and Mitchell, 2015). Accurate estimation of incidence rates of fetal alcohol spectrum disorder (FAS) is difficult due to frequently missed clinical diagnosis in the neonatal period (Wallen and Gleason, 2018). FAS is diagnosed from history and physical findings. No laboratory tests currently exist to quantify the amount of alcohol exposure to the developing fetus.
   g. Zika virus is an emerging infectious disease with serious nervous system anomalies. It also includes developmental anomalies of the eye, craniofacial, musculoskeletal, and pulmonary systems. The virus is spread via infected mosquitoes, sexual transmission, and maternal-to-fetus transmission. The result can be a series of congenital malformations, including microcephaly and other developmental abnormalities (Russo and Beltrao-Braga, 2017) (Fig. 35.1).

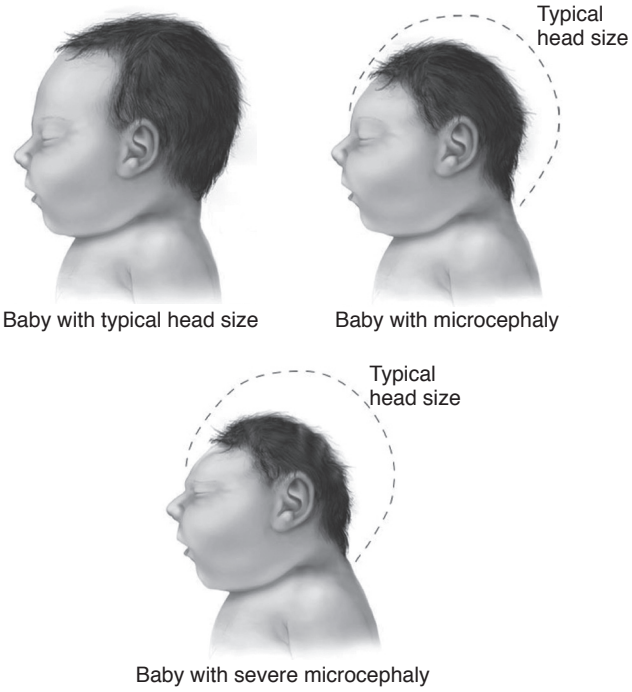

Fig. 35.1 Infant affected by Zika virus. Note microcephaly and arthrogryposis. *(Centers for Disease Control and Prevention, National Center on Birth Defects and Developmental Disabilities)*

C. **Evaluation.** When a newborn is identified as having one or more malformations, a detailed history and physical examination is needed to aid in accurate diagnosis. Infants with three or more minor anomalies have a much higher percentage of a major underlying malformation. However, many minor anomalies are of no medical concern. Combinations of some anomalies may be a sign of an underlying genetic syndrome (Askin, 2009).
   1. Family history should include the past three generations, with health information about all relatives—parents, siblings, grandparents, uncles, and aunts, as well as cousins.

2. A pedigree analysis should be developed. A genetic counselor or geneticist may be helpful in assisting to develop the pedigree.
   a. Reproductive losses and infertility.
   b. Relatives with intellectual disability or known malformations.
   c. Infants within the family with malformations or birth defects.
   d. Neonatal deaths, childhood deaths, stillbirths.
   e. Familial disorders or physical features common to the family.
   f. Consanguinity in parents.
   g. Ethnic background.
3. Prenatal and perinatal history should detail information about maternal and fetal well-being.
   a. Maternal age, parity, and health—including maternal illness and medications.
   b. Pregnancy mode (natural or assisted), complications.
   c. Teratogenic exposures, including alcohol, drugs, herbal preparations, medications, bacterial infections, viral infections, and parasitic infections.
   d. Duration of pregnancy, intrapartum course, prenatal testing, and duration.
   e. Fetal growth and behavior in utero—patterns of movement throughout pregnancy.
   f. Delivery mode, complications, condition of infant at delivery.
   g. Birth weight, length, and head circumference and whether measurements are appropriate for gestation.
4. Detailed physical examination is undertaken with attention to physical variations and malformations. It is essential to determine if an anomaly is isolated or part of a pattern of malformation. Variations are findings found in 4% or more of the population, and when found in isolation have no significance (Askin, 2009). Clinical photographs should be obtained. Photographs of any pertinent family members may also be helpful (Haldeman-Englert et al., 2018a). Photographing unusual features provides a permanent record, which may prove helpful at a later date. Most anomalies occur in early embryonic development, so attention must be directed to other organ systems that develop during the similar embryologic time. An example is ear malformations and renal syndromes.
   a. Growth parameters: weight, length, head circumference—assessment of proportionality and symmetry. Specific measurements of features for abnormality in shape, size, or symmetry should be undertaken. Measurements should be compared against gestational norms. Variation may reflect degree of prenatal insult.
   b. Estimation of gestational age.
   c. General appearance: posture, tone, and position.
   d. Systematic examination of all body surfaces.
      1) Head: size measured as occipital–frontal circumference, shape (assess for dolichocephaly, craniosynostosis, frontal bossing), size and number of fontanels (Haldeman-Englert et al., 2018b).
      2) Scalp: hair growth patterns, including placement of whorls, texture, pigmented areas, eyebrow length and pattern, eyelash length, or alterations in pigmentation. Scalp defects such as cutis aplasia may be a benign familial trait or a feature of a syndrome such as trisomy 13.
      3) Face: configuration, elfin, coarse, flat, triangular, round, birdlike, expressionless.
      4) Eyes: spacing of eyes, interpupillary distances, epicanthal folds, palpebral fissures (length and degree of slanting), iris and sclera color, colobomas, ptosis. Eye examination should include red reflex and presence of cataracts.
      5) Nose: appearance—beaked, pinched, upturned, flattened bridge, position on face, number and patency of nares, length of the columella.
      6) Mouth and chin: shape of palate and uvula, presence of cleft lip or palate, size of tongue or deformities, natal teeth, deformities of frenulum, shape of mouth, philtrum, and vermilion border, size and shape of chin.
      7) Ears: location, position, rotation, unilateral/bilateral defect, protruding/prominent shape, patency of auditory meatus, preauricular and postauricular pits and tags.
      8) Neck: length, webbed/redundant skin folds, posterior hairline, torticollis, bony abnormalities of the neck.
      9) Chest: shape, size, symmetry; location, spacing presence of supernumerary nipples, internipple distance.
      10) Cardiovascular: murmurs, bruits, pulses, blood pressure.
      11) Lungs: equality, character of breath sounds.
      12) Abdomen: integrity of abdominal wall, location and appearance of umbilicus, presence of masses, organomegaly, hypoplasia of musculature, omphalocele, gastroschisis. Umbilicus should be examined for number of vessels, hernias (Haldeman-Englert et al., 2018b).
      13) Genitalia: presence of ambiguity, size, appearance, underdevelopment or overdevelopment, descent of testicles in males.
      14) Anus: location and patency.
      15) Spine: neural tube defects, unusually pigmented lesions, hair tufts, dimples, sinuses, curvature of spine.

16) Extremities: proportions, symmetry, appearance, range of motion, number and placement of hands, feet, digits. Epidural ridges, creases, absence deformities, polydactyly, syndactyly, contracture deformities, clinodactyly, camptodactyly (Parikh and Mitchell, 2015). Single palmar crease, cortical thumb position, clubbing of feet, rocker bottom feet.
17) Skin: pigmentation, lesions, texture.

5. Diagnostic evaluation of a congenital abnormality.
   a. Radiographs, computed tomography (CT), ultrasound, and magnetic resonance imaging (MRI) are used to rule out structural abnormalities. These tests are also performed to investigate dysmorphic features that may be part of a syndrome or sequence.
   b. Cytogenic, molecular, and biochemical examination are useful in determining etiology of congenital anomalies.
   c. Chromosome analysis should be obtained for all infants with two or more major malformations, infants with growth restriction in association with anomalies, infants with multiple minor abnormalities, and infants with ambiguous genitalia.
      1) Karyotype analysis is performed on cells undergoing mitosis (Haldeman-Englert et al., 2018b). As chromosomes condense, they are stained and a representation of chromosome number results. Normal karyotype consists of 46 chromosomes—22 pairs of autosomes and one set of sex chromosomes.
   d. Microarray technology allows for detection and analysis of thousands of genes at the same time. Assay provides information about patterns of gene expression and interaction (Haldeman-Englert et al., 2018b). The focus of microarray-based techniques is centered on examination of chromosome number changes. Diagnostic confirmation of a microdeletion error is possible. Comparative genomic hybridization, single-nucleotide polymorphism or oligonucleotide arrays, and molecular analysis are being utilized in greater frequency to determine etiology of abnormalities (Haldeman-Englert et al., 2018b).
      1) Fluorescent in-situ hybridization (FISH) utilizes segments of fluorescently labeled DNA probes that attach to a specific segment of the chromosome and appear fluorescent under microscopic evaluation.
   e. Whole-genome sequencing involves the determination of all protein-coding gene sequence in the entire DNA. Rapid whole-genome sequencing is emerging in research. This technology allows highly precise and sensitive results as soon as 26 hours later (Bell, 2018).
   f. Biochemical studies are performed on ill neonates who have a condition that may be secondary to an inborn error of metabolism or for whom a specific diagnosis cannot be made. Laboratory studies should be obtained before treatment is begun. Presenting symptoms guide the specific tests to be ordered. Newborn screening using tandem mass spectrometry allows for a single drop of blood to effectively screen for 40 inborn errors of metabolism.
   g. Ophthalmologic examination may be useful, as abnormalities are often associated with neurologic or brain malformations.

D. **Genetic counseling.**
   1. The diagnosis of a congenital anomaly places the family in a crisis. Genetic counseling should be available to all parents of children with a major malformation or multiple anomalies.
      a. Genetic counseling is offered to prospective parents to help them evaluate risks for hereditary or genetic conditions based on the individual family pedigree (Parikh and Mitchell, 2015).
      b. Counseling allows for provision of information concerning diagnosis, needed care, impact of the illness, prediction for recurrence, and future support. Counseling is aimed toward assisting parents to make informed decisions.
      c. Counseling can be offered by any number of medical professionals (physician, geneticist, therapist, nursing). Counseling should be provided in a quiet location with all family members desired by the family present. A collaborative, multidisciplinary approach is optimal.
      d. Principles of genetic counseling.
         1) Supportive, nonjudgmental attitude.
         2) Respectful of family privacy, confidentiality.
         3) Sensitive to ethnic, cultural, and language differences.
         4) Supportive of family's movement through the grieving process.
         5) Content of counseling should consider medical issues, mechanisms causing the abnormality, a realistic prognosis, and a plan for treatment and support resources.
         6) Risk for recurrence and reproductive options.
         7) Assistance with family adjustment and social services as needed.

Specific Disorders

Congenital anomalies are divided into chromosomal and non-chromosomal.

ABNORMALITIES OF CHROMOSOMES

TRISOMY 21 (DOWN SYNDROME)

A. **Incidence and etiology.**

1. Most common autosomal chromosomal abnormality in live-born infants; occurring in 1 in 800 infants (Haldeman-Englert et al., 2018a).
2. Full trisomy 21 occurs in 94% of cases (all or large part of the chromosome). Affected individuals have 47 chromosomes (three of chromosome 21) (Fig. 35.2).
3. More than 90% of trisomy 21 cases result secondary to meiotic nondisjunction. Maternal age exerts a significant effect. Three percent to 5% of cases are de novo or caused by a balanced translocation that becomes unbalanced (Haldeman-Englert et al., 2018a).
4. Mosaic Down syndrome, presenting with variable phenotypic expression, is demonstrated in 3% of affected infants (Haldeman-Englert et al., 2018a). In this form some of the body's cells have the usual two copies of chromosome 21 and some have three.
5. More than 50% of trisomy 21 fetuses abort early in pregnancy.
6. Recurrence risk approximately 1% overall. For those parents who are known translocation carriers, the risk is substantially higher. Translocation carriers have recurrence risk of 100% (Bacino and Lee, 2016). Risk for carrier parent is dependent on the type of translocation and the sex of the parent (Jones et al., 2013).
7. The risk of having an infant with trisomy 21 is greatest in women who are more than 35 years of age. Younger women have a lower risk but represent half of mothers with Down syndrome babies, because the overall birth rate is higher at those ages (Bacino and Lee, 2016). Incidence of Down syndrome related to maternal age is as follows (Moore et al., 2016a):
   a. 20 to 24 years—1 in 1400.
   b. 25 to 29 years—1 in 1100.
   c. 30 to 34 years—1 in 700.
   d. 35 years—1 in 350.
   e. 37 years—1 in 225.
   f. 41 years—1 in 85.
   g. 43 years—1 in 50.
   h. Over 45 years—1 in 25.

B. **Clinical presentation.**

1. Craniofacial.
   a. Brachycephaly with flattened occiput, presence of third fontanel.
   b. Up-slanting palpebral fissures, iris speckled with Brushfield's spots, coloboma, cataracts, and glaucoma.
   c. Prominent epicanthal folds.
   d. Flattened facial profile, micrognathia, flattened nasal bridge.
   e. Small, posteriorly rotated, rounded ears; low-set and malformed ears (overfolding of superior helices), hearing loss.
   f. Prominent, protruding tongue; high-arched palate with tendency to keep mouth open (Bacino and Lee, 2016).
2. Musculoskeletal.
   a. Hypotonia: generalized—poor Moro reflex present in 80% of infants. Suck may be weak.
   b. Hyperflexibility of joints, dysplasia of pelvis: narrow acetabular angle.
   c. Clinodactyly of fifth digits, single or bilateral transverse palmar crease(s)—present in 50% of cases. Brachydactyly.
   d. Prenatal growth restriction, short stature, often 10% to 25% of affected children.
   e. Wide spacing between first and second toes (Bacino and Lee, 2016).
3. Skin.
   a. Short neck with excess nuchal skin.

C. **Associated findings.**

1. Prematurity.
2. Intellectual disability: present in all cases, variable degree, mild to moderate impairment (Moore et al., 2016a).
3. Hematologic: bone marrow dyscrasias, including neonatal thrombocytopenia and transient

Fig. 35.2 Neonate with trisomy 21 and hydrops fetalis. *(Courtesy Karen Wollman, parent of Renner.)*

self-resolving myeloproliferative disorders, have been described within the first year of life (Haldeman-Englert et al., 2018a). The World Health Organization classifies a rare subtype of leukemia as myeloid leukemia associated with Down syndrome (Moore et al., 2016a). This subtype has a favorable prognosis.

4. Gastrointestinal: duodenal atresia/stenosis—occurs in 2% to 5% of cases; esophageal atresia, imperforate anus, fistulas, webs.
5. Cardiac anomalies in approximately 50% of infants: endocardial cushion defect, ventral septal defect, patent ductus arteriosus, atrial septal defect, tetralogy of Fallot (Haldeman-Englert et al., 2018a).
6. Otitis media, hearing impairment.

D. **Diagnosis**.

1. Chorionic villus sampling at 9 to 12 weeks of gestation.
2. Amniocentesis at 16 weeks.
3. Maternal serum screening for low values of α-fetoprotein (AFP).
4. Ultrasound targeting growth, polyhydramnios, heart defects.
5. Standard chromosome banding techniques provide confirmation of trisomy 21 and differentiate those infants with nondisjunctional trisomy from a translocation. Generally, parental karyotype is not analyzed because it is normal in nearly all cases. (Haldeman-Englert et al., 2018a). However, in infants with verified translocation, each parent should have chromosome analysis to delineate carrier status because recurrence risk is much higher in these situations (Bacino and Lee, 2016).
6. FISH: FISH analysis using interphase peripheral blood cells and a chromosome 21–specific probe. Specifically, two genes (*DYRK1A* and *DSCR1*) appear to be the critical region of chromosome 21 (Bacino and Lee, 2016).

E. **Treatment**.

1. Initial treatment geared to expressed symptoms.
2. Parent education and support are essential for treatment of continuing health issues.
3. Ophthalmologic evaluation should be undertaken, as children with Down syndrome have greater incidence of cataracts, strabismus, myopia, and glaucoma (Haldeman-Englert et al., 2018a).
4. Monitor cervical spine for spinal cord compression.
5. Monitor growth, as velocity often decreases—weight and head circumference.
6. Screen for hypothyroidism.
7. Upper respiratory infections and ear infections are common.
8. Cardiac sequelae, including congestive heart failure.
9. Aimed at optimizing potential for intellectual and social growth.
10. Developmental delays—muscle tone increases with age; rate of developmental progress slows with age. Early developmental enrichment programs seem to be of the most value.
11. Social performance is usually above the expected level. Emotional problems are apparent in many affected individuals. Parents must be provided with resources for emotional and medical support.
12. After correction of associated congenital malformations, less than 50% of individuals with Down syndrome survive to age 60. Less than 15% survive to age 68 (Haldeman-Englert et al., 2018a).

TRISOMY 18 (EDWARDS SYNDROME)

A. **Incidence and etiology.**

1. Affected infants have 47 chromosomes (three of chromosome 18) (Fig. 35.3).
2. Occurs in 1 in 6000 births; females more often than males (3:1) (Moore et al., 2016a). Trisomy 18 is the second most common autosomal disorder. Associated with a high rate of intrauterine demise—5% of affected cases will survive to birth (Haldeman-Englert et al., 2018a). Recent advances in prenatal screening tests have resulted in an increase of prenatal diagnosis (Burke et al., 2013).
3. The majority of cases are caused by errors in meiotic nondisjunction; 95% of infants' have three copies of the entire chromosome 18, and 5% have either partial trisomy or mosaics of most of the long arm of 18 (Haldeman-Englert et al., 2018a).
4. Occurs more frequently as maternal age advances; mean maternal age is 32 (Jones et al., 2013).
5. Three patterns of presentation have been described,
   a. Severe: most body cells display abnormality. Handicaps are severe, with a short life expectancy.
   b. Mosaic form: some cells have the normal complement of genetic material, with the remaining cells having the typical pattern for trisomy 18. Infants are less severely affected and have a longer life expectancy.
   c. Partial: dependent on the portion of the chromosome affected. Infants with trisomy of the short arm of the chromosome have minimal handicaps, and few abnormalities are expressed. Infants with trisomy involving the entire long arm of the chromosome display the full spectrum of the syndrome. Infants with trisomy of the distal one third of the chromosome demonstrate a partial syndrome with less profound mental deficit and longer survival (Jones et al., 2013).
6. Estimate for risk of recurrence for future pregnancies is 1% over the maternal age–specific risk for any viable autosomal trisomy (Haldeman-Englert et al., 2018a). Infants whose defect is secondary to

Fig. 35.3 **A**, Female neonate with trisomy 18. Note growth retardation, clenched fists with characteristic positioning of fingers (second and fifth digits overlap third and fourth digits). **B**, Feet of another trisomy 18 infant showing characteristic rocker-bottom appearance as a result of vertical position of tali (ankle bones). Also observe prominent calcanei (heel bones). *(Courtesy Dr. A. E. Chudley, Department of Pediatrics and Child Health, University of Manitoba, Children's Hospital, Winnipeg, Manitoba, Canada.)*

a structural arrangement warrant parental karyotype analysis.

B. **Clinical presentation.**
   1. General: growth deficiency, hypoplasia of skeletal muscle, subcutaneous and adipose tissue (Haldeman-Englert et al., 2018a).
   2. Craniofacial: brachycephaly, up-slanted palpebral fissures, small/low nasal bridge, shortened hard palate, low-set malformed auricles, atresia of auditory canals, short palpebral fissures, microphthalmia, corneal opacities, colobomas, micrognathia, microstomia and high-arched palate, cleft palate (Jones et al., 2013).

3. Musculoskeletal: clenched hand, with index finger overlapping the third finger and the fifth finger overlapping the fourth, abnormal creases, low-arch dermal ridge pattern on six or more fingertips, hypoplasia of nails, short sternum, narrow pelvis with hip dislocation, rocker-bottom appearance to feet, hammer toes, clubfeet, and syndactyly between toes 2 and 3 (Jones et al., 2013).
4. Skin: redundant skin, mild hirsutism of back and forehead.

C. **Associated findings.**
1. Cardiac anomalies: varied. Occur in 50% or more of cases (Jones et al., 2013). Ventricular septal defects, patent ductus arteriosus, atrial septal defects, pulmonic stenosis, and coarctation of the aorta are most common (Haldeman-Englert et al., 2018a).
2. Renal anomalies: horseshoe kidneys, ectopic kidneys, double ureters, and cystic kidneys.
3. Genital abnormalities: cryptorchidism, hypospadias, bifid scrotum in males. Hypoplasia of labia, bifid uterus, ovarian hypoplasia, and prominent clitoris in females.
4. Abdominal: Umbilical hernias, omphalocele, Meckel diverticulum, incomplete rotation of colon.
5. Severe psychomotor deficits.

D. **Diagnosis**.
1. Chorionic villus sampling at 9 to 12 weeks of gestation.
2. Amniocentesis at 16 weeks.
3. Maternal serum triple screening revealing low levels of AFP, unconjugated estradiol, and total human chorionic gonadotropin. A large number of trisomy 18 cases can be detected with second-trimester screening utilizing the triple screen.
4. Ultrasound targeting growth retardation, oligohydramnios and polyhydramnios, heart defects, myelomeningocele, and limb abnormalities.
5. After delivery, standard chromosome banding assay or FISH.

E. **Treatment**.
1. Infants with full trisomy 18 are usually fragile, with a history of feeble fetal activity (Jones et al., 2013). Prognosis for infants with this disorder is poor. More than 90% of infants will succumb in the first 6 months of life; 5% will survive to 1 year (Haldeman-Englert et al., 2018a).
2. Children who survive the first year of life deal with feeding issues secondary to hypotonia, growth issues, and significant developmental disability. These children generally do not walk unsupported or develop expressive language, but they can be capable of limited verbal communication and some social interaction.
3. Once a diagnosis has been confirmed, decisions about extraordinary medical means for prolongation of life present nearly overwhelming challenges for families. Individual circumstances for each family must be considered (Jones et al., 2013). Most deaths result secondary to congestive heart disease, infection, and central apnea (Haldeman-Englert et al., 2018a).
4. For those infants surviving the immediate newborn period, care is supportive and individualized to the infant's needs.
5. Parents should be offered genetic counseling and provided with resources for support.

TRISOMY 13 (PATAU SYNDROME)

A. **Incidence and etiology.**
1. Affected infants are born with 47 chromosomes instead of the usual 46, with the extra genetic material located on chromosome 13. This abnormality is the rarest of the trisomies; severe external malformations are common, and only 5% survive to term (Jorde et al., 2016).
2. Defect occurs in 1 in 12,500 to 1 in 21,000 live births (Haldeman-Englert et al., 2018a), making it the fourth most common autosomal dominant disorder.
   a. Older mothers are more likely to have an infant with this aneuploidy defect.
   b. Slightly more boys than girls are affected (Jones et al., 2013).
3. The majority of cases result from chromosomal nondisjunction (Bacino and Lee, 2016).
4. The etiology for this disorder is trisomy of all or part of chromosome 13.
   a. Eighty percent of affected infants have three complete copies of chromosome 13.
   b. Mosaicism accounts for 5% of cases, with these infants demonstrating a wide range of expression from near normal to severe full pattern malformation.
      1) Survival for infants with mosaicism is usually longer.
      2) Survivors have significant neurodevelopmental delays (Bacino and Lee, 2016).
   c. Partial trisomy of the proximal segment is characterized by infants with severe intellectual disability and an overall pattern of full trisomy 13.
   d. Partial trisomy of the distal segment results in severe mental deficiency and characteristic phenotype (Jones et al., 2013).

B. **Clinical presentation.**
1. General: growth deficiency.
2. Craniofacial: cebocephaly, microcephaly, microphthalmia, coloboma, glaucoma, midline scalp defects, retinal dysplasia, cleft lip and/or palate (60% to 80%) (Jones et al., 2013), malformed ears, atresia of external auditory canals, deafness, prominent nasal bridge, short neck with excessive skin.
   a. Aplasia cutis congenita is a congenital localized absence of skin often involving the scalp along the midline. This is specific to the syndrome

occurring in 50% of cases (Haldeman-Englert et al., 2018a). Lesions are frequently noted on the scalp near the parietal hair whorl (Graham and Sanchez-Lara, 2016). Most defects are small and superficial; 20% involve absence of the skull, exposing the infant to hemorrhage and infection.

3. Musculoskeletal: polydactyly, single palmar crease, overlapping of fingers, flexion deformities of hands and wrists, prominent heel resulting in rocker-bottom feet, thin posterior ribs with or without missing rib, and hypoplasia of pelvis with shallow acetabular angle.
4. Genital abnormalities: males—cryptorchidism, abnormal scrotum; females—duplication or anomalous insertion of fallopian tubes, uterine cysts, hypoplastic ovaries.
5. Central nervous system (CNS): holoprosencephaly found in 50% of patients with incomplete development of the forebrain and olfactory and auditory nerves, seizure activity, apnea in early infancy, and severe mental deficiency (Haldeman-Englert et al., 2018a).
6. Skin: capillary hemangiomas, loose nuchal skin.

C. **Associated findings.**
1. Cardiac anomalies occur in approximately 80% of infants: ventral septal defects, dextrocardia, patent ductus arteriosus, atrial septal defects.
2. Renal abnormalities: polycystic kidneys, horseshoe kidneys, duplicated ureters.
3. Inguinal or umbilical hernias, single umbilical artery.

D. **Diagnosis**.
1. Chorionic villus sampling between 9 and 12 weeks of pregnancy.
2. Amniocentesis at 16 weeks.
3. Ultrasound targeting growth parameters, abnormalities of heart, kidneys, and brain.
4. After delivery, standard chromosome banding assay, FISH.

E. **Treatment**.
1. The presence of holoprosencephaly is the single most important finding predicting survival.
2. Prognosis is extremely poor—80% mortality in the newborn period has been documented (Haldeman-Englert et al., 2018a). Survivors frequently have seizures, severe intellectual disability, and failure to thrive.
3. Feeding issues are related to the smallness of the lower jaw, possible cleft lip and/or palate, and poor muscle tone.
4. The high rate of early mortality for this syndrome requires the parents to prepare for the infant's death as well as plan for supportive care. The desires of the parents must be considered, as care is designed for each patient.

22q11.2 DELETION SYNDROME. This syndrome has been referred to as *DiGeorge syndrome, Sprintzen syndrome,* or *velocardiofacial syndrome*. It is the most commonly occurring microdeletion syndrome in humans (Haldeman-Englert et al., 2018).

A. **Incidence and etiology.**
1. Occurs in 1 in 1000 fetuses (Haldeman-Englert et al., 2018a). This syndrome is extremely variable in expression and varies from patient to patient.
2. Inherited as an autosomal dominant pattern.
3. Individuals have an interstitial deletion of 22q11.2; 80% to 90% of patients have the same large deletion (Haldeman-Englert et al., 2018a).
4. Most 22q11 deletions occur as de novo lesions—less than 10% are inherited from an affected parent. Both parents must be tested to determine carrier status (Jones et al., 2013).

B. **Clinical presentation.**
1. Growth: postnatal onset of short stature (Jones et al., 2013).
2. Craniofacial: microcephaly, velopharyngeal insufficiency, palatal anomalies, small or absent adenoids, prominent nose with bulbous tip, narrow palpebral fissures, long face, retruded mandible with chin deficiency, small mouth—associated with swallowing abnormalities, hooded eyelids, hypertelorism, hearing deficits, and minor auricular abnormalities.
3. Musculoskeletal: limbs are slender, hypotonic; hands and fingers are hyperextensible (Jones et al., 2013).

C. **Associated findings.**
1. Cardiac defects are present and usually significant in 85% of patients. Most common defects include ventral septal defects, right aortic arch, tetralogy of Fallot, and aberrant left subclavian artery (Jones et al., 2013).
2. Atresia or hypoplasia of the thymus and parathyroid glands (Haldeman-Englert et al., 2018a).
3. Functional T-cell abnormalities: almost all have greater-than-average tendency to infections.
4. Hypocalcemia: usually due to hypoparathyroidism, occurs as a transient finding in neonates (60%) and is rarely lifelong (Habel et al., 2014). Seizures can occur—usually as a result of hypocalcemia.
5. Learning disabilities: 62% of patients will have normal or mild learning issues, with severe or moderate learning difficulties in 18% (Jones et al., 2013). Developmental delays in language and speech are common (Haldeman-Englert et al., 2018a).
6. IQ range is variable. Mean IQ low 70s. Attention and visual/spatial difficulties are often present (Habel et al., 2014).
7. Psychiatric disorders—schizophrenia and bipolar disorders. Schizophrenia develops in about 25% of adults (Kumar et al., 2015; Van et al., 2017).

22q11.2 is the strongest known genetic risk factor for schizophrenia.
8. Speech and language are often delayed. Speech pattern is frequently nasal secondary to poor pharyngeal musculature.

D. **Diagnosis**.
1. Defect is detected by FISH.

E. **Treatment**.
1. Death primarily secondary to cardiac defects—occurs in approximately 8% of infants (Jones et al., 2013).
2. Hypotonia is common, resulting in developmental delays. Early intervention, physical and speech therapy are helpful, especially with feeding issues.
3. Infants may require surgical intervention for palatal abnormalities to improve speech.
4. Gastroesophageal reflux and dysphagia can occur, requiring treatment (Habel et al., 2014).
5. Infants frequently demonstrate greater socialization skills than intellectual skills.
6. Onset of psychiatric symptoms is usually between 10 and 21 years of age—schizophrenia and depression are the most common conditions. Ongoing assessment and support are essential (Jones et al., 2013).

Sex Chromosome Abnormalities

TURNER'S SYNDROME

A. **Incidence and etiology.**
1. Affected individuals have monosomy—loss of all or part of one copy of the X chromosome in a female. Most 45,X conceptuses die early—0.1% survive to term, and the majority are spontaneously aborted (Haldeman-Englert et al., 2018a).
   a. Loss of the entire chromosome occurs in approximately 50% of cases (Haldeman-Englert et al., 2018). Occurs in approximately 1 in 2500 live-born phenotypic females (Haldeman-Englert et al., 2018a).
2. In 70% to 80%, the paternal X chromosome is missing (Jorde et al., 2016).
3. Mosaicism occurs in 30% to 40% and is associated with complex karyotypes, ring chromosomes, and deletions.
4. Disorder generally occurs as a sporadic event in a family (Jones et al., 2013).

B. **Clinical presentation.**
1. Growth: short stature.
2. Craniofacial: narrow palate, low-set ears with anomalous auricles, hearing loss, ptosis of eyelids, epicanthal folds, broad nasal bridge, low posterior hairline with appearance of a webbed neck.
3. Musculoskeletal: broad chest with wide-spaced nipples, pectus excavatum, short fourth metacarpal/metatarsal, marked lymphedema of extremities, bone dysplasia, dislocation of the hip, knee abnormalities (Granger et al., 2016).
4. Skin: excessively pigmented nevi, loose skin—especially posterior folds of neck.
5. Lymphatic: Impaired lymph drainage leads to distention of lymphatics and peripheral lymphedema, particularly of dorsa of hands and feet (Al Remeithi and Wherrett, 2015).

C. **Associated anomalies.**
1. Cardiac defects: bicuspid aortic valve, coarctation of aorta, valvular aortic stenosis, and mitral valve prolapse (Haldeman-Englert et al., 2018a).
2. Renal: horseshoe kidney, unilateral renal agenesis, duplications.
3. Gonads: ovarian dysgenesis with hypoplasia due to lack of germinal elements (Jones et al., 2013).
4. Performance issues: delayed motor skills, poor coordination, clumsiness, problems with nonverbal problem solving, depression, and poor self-esteem in young adults (Jones et al., 2013).

D. **Diagnosis**.
1. Ultrasound for short stature, cystic hygroma, lymphedema, monitoring of growth throughout gestation.
2. Standard chromosome banding assay or FISH.

E. **Treatment**.
1. Growth issues persist throughout childhood and adolescence. Growth is commonly normal within the first 3 years of life, decreasing during school-age years and more dramatically during teenage years when these girls do not get their usual growth spurt at puberty. Growth hormone therapy is generally begun at around 4 to 5 years of age. Significant improvement in final height has been achieved (Haldeman-Englert et al., 2018a).
2. Congenital lymphedema requires symptomatic treatment initially, presenting with edema of hands and feet secondary to faulty lymph drainage.
3. Ovarian function is affected, with primary ovarian failure occurring secondary to gonad dysplasia. The result can be delay in development of secondary sex characteristics and primary amenorrhea. Treatment options include cyclic estrogen replacement therapy for hypogonadotropic girls beginning at ages 13 to 14 (Haldeman-Englert et al., 2018a).
4. Ongoing evaluation of congenital heart defects is necessary secondary to the increased risk for dissection of the aorta. Coarctation of aorta must be surgically repaired.
5. With increasing age, greater incidences of osteoporosis, autoimmune thyroid disease, and chronic liver disease have been reported (Jones et al., 2013). Close monitoring for these conditions is needed.
6. For those infants for whom their physical appearance would be aided by plastic surgery, concerns

for the formation of keloid scars must be considered.

7. School performance may be affected primarily in word comprehension, perceptual thinking, and presentation (Haldeman-Englert et al., 2018a). Intelligence is usually normal.

KLINEFELTER'S SYNDROME

A. **Incidence and etiology.**
   1. Affects approximately 1 in 500 to 1 in 1000 males, making it the most common single cause of hypogonadism and infertility in males (Calogero et al., 2017).
   2. Chromosomal analysis reveals a 47,XXY karyotype. Mosaicism is present in 10% to 20% of Klinefelter syndrome patients (Bonomi et al., 2017).
      a. Parental sex chromosome nondisjunction due to the failure of chromosomes to separate at anaphase during meiosis I, meiosis II, or mitosis. This occurs equally during oogenesis and spermatogenesis (Bonomi et al., 2017). Rarely, nondisjunction can occur during early division of the fertilized egg.
      b. Advanced maternal age is related to an increased incidence for those whose defect is secondary to maternal factors. Up to a four-fold increase in Klinefelter syndrome cases was noted in women greater than 40 years of age (Bonomi et al., 2017).
      c. According to Jones et al. (2013), older fathers are at higher risk for producing a higher number of XY sperm, resulting in a higher risk of having an infant with Klinefelter's syndrome.
   3. Infants with XXY/XY mosaicism may have a greater potential for testicular function.
   4. Infants carrying the XXYY karyotype are more often developmentally delayed.

B. **Clinical presentation.**
   1. General: the phenotype of Klinefelter syndrome men encompasses a broad spectrum. Affected males frequently have long limbs, reduced upper-to-lower-segment ratio (Moore et al., 2016a). Tall and slim stature.
   2. Musculoskeletal: elbow dysplasia; fifth finger clinodactyly; tall, broad hips; narrow shoulders. Common radiographic findings include radioulnar synostosis or dislocation, elongated radius, scoliosis, kyphosis (Ali and Donohoue, 2016).
   3. Genital: hypogonadism, cryptorchidism, hypospadias, gynecomastia.

C. **Associated findings.**
   1. Cancers: teratoma, leukemia, breast most common.
   2. Scoliosis during adolescent years (Jones et al., 2013).
   3. School performance and behavioral issues: delayed speech and language development, difficulties with auditory processing and auditory memory. Aggressive behavior is observed (Moore et al., 2016a).

D. **Diagnosis**.
   1. Prepubescent males may have no significant dysmorphism. Condition may not be diagnosed until puberty, with incomplete development of secondary sex characteristics and infertility (Ali and Donohoue, 2016). Minor abnormalities are helpful in providing clues for diagnosis: penile size, skeletal defects. In retrospect, behavioral and psychological disorders may present themselves long before notable defects in sexual development.
   2. Karyotype testing, FISH to determine XXY, XXYY, or XXXY status.
   3. Some evidence exists showing earlier screening in the prenatal period results in more timely intervention and monitoring. This can be done via noninvasive prenatal testing (NIPT) (Close et al., 2017).

E. **Treatment**.
   1. As adolescence progresses, screening for scoliosis is needed.
   2. Deficient testosterone and elevated gonadotropin levels signal the need for hormone replacement. Boys must be monitored for prospective testosterone replacement as they near ages 10 to 12. Some males have incomplete or inadequate puberty. Replacement will assist in development of a more masculine physique, increased pubic and facial hair, and improved bone density and muscle mass (Jones et al., 2013). Delays in treatment can increase the risk for osteoporosis.
   3. The incidence of breast cancer for affected infants is 20 times higher than the general population, but only 1 in 5000 affected men. Routine mammography is not required (Jones et al., 2013). Incidence of mediastinal teratomas is 34 to 40 times that of nonaffected populations. Ongoing assessment of these individuals is needed.
   4. IQ range for affected individuals is variable, from well below to well above average. Assistance in school is commonly required, especially in the areas of reading and spelling. Monitoring for speech and learning issues should also be carried out (Ali and Donohoue, 2016). Emotional and behavioral problems persist and may increase throughout childhood. Formation of peer relationships may be difficult secondary to insecurity, shyness, and poor judgment activity. Support with psychological adjustment is needed.

Non-Chromosomal Abnormalities

MALFORMATION DISORDERS

Malformation sequences occur with a single, localized, poor formation of tissue that initiates a chain of subsequent defects (Jones et al., 2013). Expressed manifestations range

from nearly normal to severe and carry a variable recurrence risk.

OSTEOGENESIS IMPERFECTA. Clinically and genetically heterogeneous hereditary disease involving connective tissue disorders and skeletal dysplasia. The spectrum of osteogenesis imperfecta (OI) is broad, ranging from lethal to mild forms.

A. **Incidence and etiology.**
   1. The majority of OI cases are caused by structural or quantitative defects of type I collagen causing the full spectrum of OI types (I to IV). Overall incidence is 1 in 10,000 to 20,000 births (Palomo et al., 2017). Both dominant and recessive inheritance patterns exist (Marini, 2016).
   2. Twelve to fifteen clinical types are identified (Marini, 2016; Shaker et al., 2015). The six most common types are:
      a. Type I: autosomal dominant, resulting from mutations of the *COL1A1* gene on chromosome 17q21 (Jones et al., 2013). Characterized by bone fragility with onset of fractures after birth. Considered a mild form. The majority (85% to 90%) of OI cases are this type (Palomo et al., 2017).
      b. Type II (perinatal lethal): autosomal dominant inheritance pattern occurring secondary to a sporadic, dominant mutation in one of the two collagen genes (Jones et al., 2013). Characterized by multiple intrauterine fractures, pulmonary hypoplasia, CNS malformations, and hemorrhages.
      c. Type III (progressive deforming): primarily an autosomal dominant inheritance pattern, although rare autosomal recessive pattern has been identified (Jones et al., 2013). Most severe nonlethal form of OI (Marini, 2016). Characterized by significant physical disabilities.
      d. Type IV (moderately severe): autosomal dominant pattern resulting from mutations of the two collagen genes. Significant bone deformities are common.
      e. Type V (hyperplastic callus): autosomal dominant inheritance pattern that is not associated with collagen type I mutations (Jones et al., 2013). Moderate tendencies to fracture long bones.
      f. Type VI (hyperosteoidosis mineralization defect): pattern of inheritance is believed to be autosomal recessive (Forlino and Marini, 2016). Results from a mineralization defect; fractures occurring later between 4 and 18 months.

B. **Clinical presentation.**
   1. Type I.
      a. Growth: near-normal or normal growth pattern.
      b. Craniofacial: macrocephaly, triangular-appearing facies, hearing impairment, altered dentition with hypoplasia of dentin and pulp (Jones et al., 2013).
      c. Musculoskeletal: postnatal onset of mild limb problems; bowing of femur, tibia, scoliosis, hyperextensibility of joints, and osteopenia.
      d. Skin: translucent, easy bruising, blue sclerae secondary to partial visualization of the choroid.
   2. Type II.
      a. Growth: short-limbed growth deficiency with prenatal onset, low birth weight.
      b. Craniofacial: head is soft and boggy, with minimal calvarial bone palpable, large fontanelles, deep blue sclerae, shallow orbits; head assumes a triangular shape (Tiller and Bellus, 2018).
      c. Musculoskeletal: shortened and bowed limbs with extra skin, flexed and abducted hips, flattened vertebrae (Jones et al., 2013).
   3. Type III.
      a. Growth: prenatal onset of growth deficiency, extremely short stature.
      b. Craniofacial: macrocephaly, triangular facies, deep blue sclera, hearing loss, dentinogenesis imperfecta.
      c. Musculoskeletal: kyphoscoliosis, which may lead to respiratory distress (Jones et al., 2013), multiple fractures, and deformations of limbs at birth.
   4. Types IV to VI.
      a. Presentation less severe for these forms. Stature and growth may be mildly affected; fractures, if they occur, present later. Sclerae may be mildly affected or absent. Dentition is less commonly affected.

C. **Associated findings.**
   1. Conductive hearing loss secondary to deformity of the small bones of the ear.
   2. Platelet function is decreased due to defects in adhesion and clot retraction.
   3. Corneal clouding and keratoconus, megalocornea (Jones et al., 2013).
   4. Cardiac: floppy mitral valve.
   5. Scoliosis developing later, progressing during puberty, sometimes resulting in severe deformity in adulthood. Loss of height may occur secondary to progressive spinal osteoporosis in adults.

D. **Diagnosis.**
   1. Prenatal diagnosis is possible with ultrasonography and mutation analysis.
   2. Radiographs: entire skeleton, including skull, hands, feet, and lateral spine.
      a. Type I: femurs are short, broad, or crumpled. Fibulas may be thin.
      b. Type II: femurs are short and deformed but not crumpled. The long bones appear thin with bowing and deformations. Cranial bones are undermineralized, with wormian bones.
   3. Ultrasound of brain, heart, and kidneys.

4. Detailed family history, including measurements of family members.
5. Chromosomal study confirming genetic mutation on 17q21 and 17q22.1.

E. **Treatment**.
1. Depending on the type of OI, treatment will vary extensively. Type I patients may require little or no treatment, whereas type II patients may die before any treatment is begun. Types III and IV are the most complex, requiring intensive support. Treatment is focused on minimizing pain and prevention of future fractures.
   a. Initial treatment of fractures is aimed toward alignment of bones to avoid deformity, comfort measures, prevention of further deformity, optimizing function after healing, and prevention of further fractures.
   b. Laxity of ligaments and previous fracture abnormalities complicate the healing process.
   c. Lightweight splints or braces provide the first-line treatment; depending on previous bone damage, surgical procedures may be necessary to provide strengthening and support.
   d. Administration of bisphosphonates is currently the primary treatment (Forlino and Marini, 2016). The goal of treatment is decreased fractures, decreased bone pain, and improved vertebral shape. Bisphosphates adhere to mineralized surfaces, inhibit osteoclastic bone resorption, and have long half-lives.
   e. The use of growth hormone, which has anabolic effects on bone, and teriparatide, an anabolic agent that stimulates bone formation, may prove helpful adjuncts to treatment (Forlino and Marini, 2016).
   f. Future therapies include denosumab, sclerostin, cell-based therapies, and gene therapy (Forlino and Marini, 2016).
2. Early intervention for hearing loss is essential for development of language and later learning.
3. Dentition may be difficult or delayed; these children are more prone to cavities. Ongoing examination and treatment are vital.
4. Scoliosis may progress quickly for those nearing puberty—bracing is often ineffective. Early surgical fusion may provide the best option for treatment.
5. If a diagnosis has been made prenatally, operative delivery to avoid fractures and intracranial bleeding is recommended.

ACHONDROPLASIA

A. **Incidence and etiology.**
1. Achondroplasia occurs with a frequency of 1 in 25,000 live births (Tiller and Bellus, 2018).
   a. Most common skeletal dysplasia in humans (Jelin et al., 2017).
2. Defect has an autosomal dominant inheritance pattern. Eighty percent are sporadic occurrences of gain-of-function mutation in *FGFR3* (fibroblast growth factor receptor 3), representing a new mutation on chromosome 4p16.3 (Tiller and Bellus, 2018). This results in abnormal endochondral ossification.
   a. New mutations occur in the father's sperm and are associated with advanced paternal age (Tiller and Bellus, 2018).
   b. Transmitted as a fully penetrant autosomal dominant trait; each person who inherits the mutant gene will show the condition (Tiller and Bellus, 2018).

B. **Clinical presentation.**
1. General: small stature. Small at birth, with increasingly apparent growth deficiency secondary to failure of endochondral ossification.
2. Craniofacial: megalocephaly, small foramen magnum, low nasal bridge, flat midface, short flat nose with broad tip, anteverted nares, long philtrum, hypotelorism (Jones et al., 2013).
3. Musculoskeletal: short limbs, lumbar lordosis, mild thoracolumbar kyphosis, short tubular bones, vertebral anomalies, short trident hand, hyperextensible joints, shortened upper limbs, and flexion contractures at elbows.

C. **Associated findings.**
1. Mild hypotonia, especially in the trunk and extremities, with delayed milestones.
2. Bowing of the legs after ambulation has started.
3. Orthodontic problems related to maxillary hypoplasia.
4. Stenosis of the magnum and spine leading to compression of the upper cord and resultant symptoms of apnea, growth delays, hydrocephalus, quadriparesis, and sudden death.
5. Upper airway is often small, leading to obstructive apnea, snoring, and serous otitis media (Tiller and Bellus, 2018).

D. **Diagnosis**.
1. Chromosomal studies to confirm mutation on 4p16.3 chromosome. These may be performed prenatally. Usually ultrasound diagnosis isn't possible until late in second trimester.
2. Diagnosis is confirmed for achondroplasia through radiographic survey: calvarium is large with small foramen magnum and short base, lateral ventricles may be large, proximal long bones are shortened, fibulae longer than tibiae, metaphyseal flaring, short hand with trident shape of fingers, iliac bones are short and round, lumbar vertebrae have short pedicles and scalloping

E. **Treatment**.
1. Infants with known achondroplasia must be closely monitored for developmental delay, hypotonia, and abnormal growth patterns.

2. Unsupported sitting is associated with development of kyphosis. Infants should not be allowed to be carried in flexed positions before trunk muscle strength is adequate (Tiller and Bellus, 2018). Most infants lose kyphosis and develop lumbar lordosis when ambulation begins.
3. Hydrocephalus may develop within the first 2 years of life. Radiologic imaging of the skull as a baseline is recommended for monitoring; monthly head circumference should be obtained and plotted to determine abnormal growth.
4. Obstructive apnea may represent a serious threat. Treatment may consist of tonsillectomy or adenoidectomy. Evaluation for foramen magnum stenosis should be done.
5. Treatment for severe bowing of the legs is often deferred until full growth has occurred. Osteotomies provide needed corrections (Jones et al., 2013).
6. Close monitoring of auditory performance is needed, as shortened eustachian tubes may lead to middle ear infections and resultant hearing loss. Many infants require placement of tympanic membrane tubes.
7. Dental crowding is frequently encountered, requiring removal of one or more teeth.
8. Obesity develops toward late childhood and should be monitored closely.
9. Pharmacologic treatments are in clinical trials. These treatments are aimed at regulating *FGFR3* (Jelin et al., 2017).

SPECIFIC NEURAL TUBE DEFECTS

See Chapter 34.

DEVELOPMENTAL DYSPLASIA OF THE HIP (DDH). A wide spectrum of abnormalities that affect the femoral head and acetabulum.

A. **Incidence and etiology.**
   1. Defect occurs in 11.5 per 1000 live births, frank dislocations occurring in 1 to 2 per 1000 (White et al., 2018). Dislocations are described as syndromic or typical.
   2. Syndromic dislocations are associated with neuromuscular or dysmorphic conditions. These defects occur during weeks 12 to 18 of gestation, and are associated with arthrogryposis, myelodysplasia, or other specific syndromes (White et al., 2018).
   3. Typical dislocations present in healthy infants in prenatal or perinatal period.
   4. Risk factors include female gender, positive family history, incorrect swaddling of lower extremities, and breech presentation. Of these, breech presentation is likely the single most important risk factor, presenting in 2% to 27% of infants presenting in breech position (Shaw and Segal, 2016).
   5. In 60% of infants the left hip is affected, in 20% the right hip is affected, and in 20% both hips (White et al., 2018).
   6. Frank breech positioning with hips flexed and knees extended increases risk of dislocation.
   7. Etiology is multifactorial; interaction of genetic and environmental factors is considered to be causative.
   8. Ligamentous laxity secondary to circulating maternal hormone (relaxin) exerts an effect, resulting in hip dislocation. Familial ligamentous laxity has also been described.

B. **Clinical presentation.**
   1. The defect is considered a deformation anomaly. A full range of severity from a lax dislocatable hip to a nonreducible dislocation.
   2. Not all dislocated hips are present at birth.
   3. Not all dislocated hips present at birth are noted on examination in the newborn period.
   4. Anatomic changes are minimal in the neonate. As the hip becomes permanently dislocated, pathologic changes of the acetabulum, femoral head, hip capsule joints, and ligaments can occur. End result is degenerative changes in femoral head and acetabulum.
   5. Physical examination will demonstrate limitations in abduction, apparent shortening of the affected femur, and extra skin folds (Kelly, 2017 a, 2017b). These physical findings become more apparent after 6 months of age.

C. **Associated findings.**
   1. Associated with other postural adductus deformities such as torticollis, talipes equinovarus, and metatarsus deformities.
   2. Unilateral defects often have secondary problems with limb-length inequality, ipsilateral knee deformity, scoliosis, and disturbances in gait.

D. **Screening and diagnosis.**
   1. All newborns should be screened for DDH by physical examination at birth and at each well-child visit (Shaw and Segal, 2016).
   2. Physical tests are aimed at determining if the femoral head is fixed in the acetabulum. Tests should be repeated at intervals within the first year of life, as a dislocation may not be demonstrated for several months after delivery.
      a. Barlow's test: a reduced femoral head is adducted to determine if it becomes subluxated. This is a test of instability or laxity and has less clinical significance.
      b. Ortolani test: a subluxated or dislocated femoral head is reduced into the acetabulum with hip abduction. This is the most important clinical test for detecting newborn hip dysplasia.
      c. If the dislocation is a fixed type of lesion, Barlow's and Ortolani tests are not helpful, as the femoral head is locked outside of the

acetabulum. Diagnosis is made by palpation of the femoral head posteriorly.

d. Galeazzi sign: infant is placed supine, knees flexed to 90 degrees and hips in neutral abduction. The presence of asymmetrical knees and thigh and/or buttock folds is indicative of a positive sign. This indicates the femoral head is dislocated posteriorly. This is not evident in bilateral cases (White et al., 2018).

3. Radiographs are helpful but are difficult to interpret before 4 to 5 months of age secondary to the high percentage of cartilage in newborn infants.
4. Ultrasound screening of the cartilaginous femoral head and acetabulum has become common.
   a. Recommended after 3 to 4 weeks of age to confirm suspicious examination findings (Shaw and Segal, 2016).
   b. Used to detect in high-risk infant from 6 weeks to 6 months without clinical examination findings.

E. **Treatment**.

1. After delivery, unstable hips must be monitored closely. A percentage of unstable hips will stabilize, whereas others progress to subluxation or dislocation. The outcome of hip stability cannot be predicted; all newborns with clinical hip instability should be monitored closely and possibly treated.
2. Initial goal of treatment is reduction of the displaced femoral head and support of acetabular and femoral head growth. Reduction and stability of the femoral head are needed for normal growth and development of the hip joint.
3. For children 0 to 6 months of age, infants with reducible hip abnormalities are treated with the Pavlik harness (Fig. 35.4). The Pavlik harness is the most commonly used device to prevent adduction while allowing flexion and abduction. Length of treatment is dependent on the age of presentation. The harness encourages deepening and stability of the acetabulum. Progress is judged by serial physical examinations and ultrasonography. Treatment success is variable and dependent on stability of hips, dislocatability, and reducibility (White et al., 2018).
4. For those infants for whom harnessing is not effective or the lesion is fixed, surgical intervention with subsequent spica casting is required.
5. Ongoing developmental assessment of these infants is needed to monitor for secondary deformities.
6. Parents play a pivotal part in the success in management of harnessing therapy. It is vital for parents to have a clear understanding of the deformity and plan for care.

Fig. 35.4 Infant with dislocated hips in a Pavlik harness. *(Courtesy Jane Deacon, RNC, MS, NNP, The Children's Hospital, Denver, CO.)*

TALIPES EQUINOVARUS (CLUBFOOT)

One of the most common entities affecting the newborn foot.

A. **Incidence and etiology.**

1. Defect occurs in 1 per 1000 live births (Kelly, 2017a, 2017b).
2. Clubfoot is bilateral in 50% of cases, with males affected twice as often as females.
3. Classified as congenital, teratogenic, or positional (Son-Hing and Thompson, 2015).
4. The cause of congenital clubfoot is unknown.
   a. Causative factors are thought to be multifactorial, with strong influence from single autosomal dominant gene (Son-Hing and Thompson, 2015).
   b. Extrinsic causes: related to changes within the uterine environment, uterine abnormalities, oligohydramnios, and effects of uterine pressure during critical periods of development.
   c. Neural origin: neuromuscular pathologic conditions, resulting in muscle fibrosis, shortening of muscles, and development of contractures.
5. Within affected families, recurrence rates are 3% for subsequent siblings and 20% to 30% for offspring of affected parents (Son-Hing and Thompson, 2015).

B. **Clinical presentation.**

1. Classic deformity presents with numerous anatomic deformities. Clinically, the foot has a medial crease, with toes pointing toward midline; the sole of the foot is angulated medially; and the hindfoot is plantar flexed (White et al., 2018) (Fig. 35.5).
   a. The calf and foot of the clubfoot are smaller than the contralateral side.
   b. Infants may demonstrate dysplasia of bones, muscles, tendons, cartilage, skin, and neurovascular tissues distal to the knee of the affected extremity (White et al., 2018).
   c. Weight bearing is not possible secondary to position of the foot.

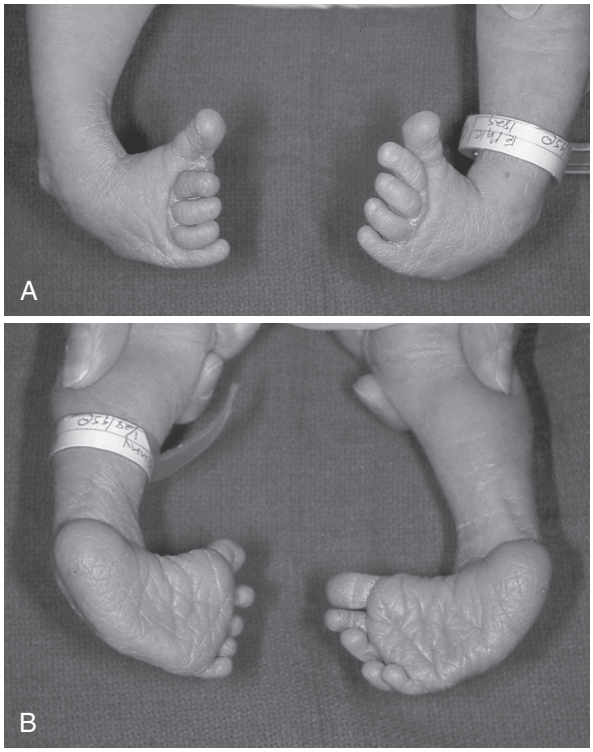

Fig. 35.5 Bilateral talipes equinovarus. Note structural deformity of hind part of foot. *(Courtesy Jane Deacon, RNC, MS, NNP, The Children's Hospital, Denver, CO.)*

d. Postural clubfoot presents without deep medial creasing and minimal to no calf atrophy.

C. **Associated anomalies.**
1. Deformity is associated with Smith–Lemli–Opitz, Larsen's, Freeman–Sheldon, and Poland's syndromes. These arthrogrypotic or neuromuscular defects result in rigid deformity with absence of skin creases, suggesting early in-utero involvement. These defects fail to improve without operative strategies.
2. Congenital hip dysplasia, neural tube defects, particularly myelomeningocele.

D. **Diagnosis**.
1. Physical examination and manipulation of the foot through range of motion.
2. Anteroposterior and lateral radiographs are helpful, assist with diagnosis of other bony abnormalities.

E. **Treatment**.
1. All clubfoot deformities should be evaluated by a pediatric orthopedist.
2. Depending on the lesion, operative and nonoperative methods are used to treat clubfoot deformities. Initial treatment for all congenital clubfoot is nonoperative; early treatment is more successful secondary to pliability of tissues and resilience to immobilization.
a. Manipulation, serial casting, and taping are first-line treatment, lasting for 3 to 6 months. Failure to achieve clinical and radiographic correction by 3 months of age may indicate the need for surgical correction (Son-Hing and Thompson, 2015).
b. Untreated clubfoot results in development of degenerative changes in foot joints. Long-term results of early surgical correction have yielded poor results with recurrence (White et al., 2018).
c. Nonoperative treatment consisting of casting, augmented with percutaneous tenotomy and occasionally tendon transfer, appears to provide some success. Recurrences of the deformity are common and require further casting or bracing (White et al., 2018).
3. Parents must be educated as to the importance of their role in ongoing treatment, as adherence to prescribed therapy is vital for a positive outcome.

POLYDACTYLY

A. **Incidence and etiology.**
1. Inherited as an autosomal dominant trait. Occurs in 2 per 1000 live births (Kelly, 2017a, 2017b). Approximately 30% of affected infants will have a positive family history.
2. Incidence is common: anomaly results from a duplication error in which a stimulus induces excessive limb bud formation.

B. **Clinical findings.**
1. Affected digits are often incomplete and lack muscular development. Defects are often bilateral (Fig. 35.6).
2. Abnormalities are divided into three classifications: soft tissue mass connected by a tissue pedicle, partial duplication involving the phalanges, and complete duplication of the digit with bony formation (Moore et al., 2016a).

C. **Associated findings.**
1. The anatomic placement of the digit varies and can be associated with genetic syndromes.
a. Preaxial or duplicate thumbs occur most commonly as an isolated lesion. Defect has been associated with Holt–Oram, Fanconi, and Ellis–Van Creveld syndromes.
b. Triphalangeal thumb; also referred to as a *thumbless, five-fingered hand*. Defect is associated with trisomies 13 and 15, as well as Blackfan–Diamond and Fanconi syndromes.

D. **Diagnosis**.
1. Physical examination.
2. Radiologic examination to identify bony defects.

E. **Treatment**.
1. Treatment is dependent on defect and may involve surgery.
2. Therapy is aimed toward preservation of function and motion, as well as provision of cosmetic remedy.
3. Education of parents as to the risks for recurrence and associated syndromes is essential.

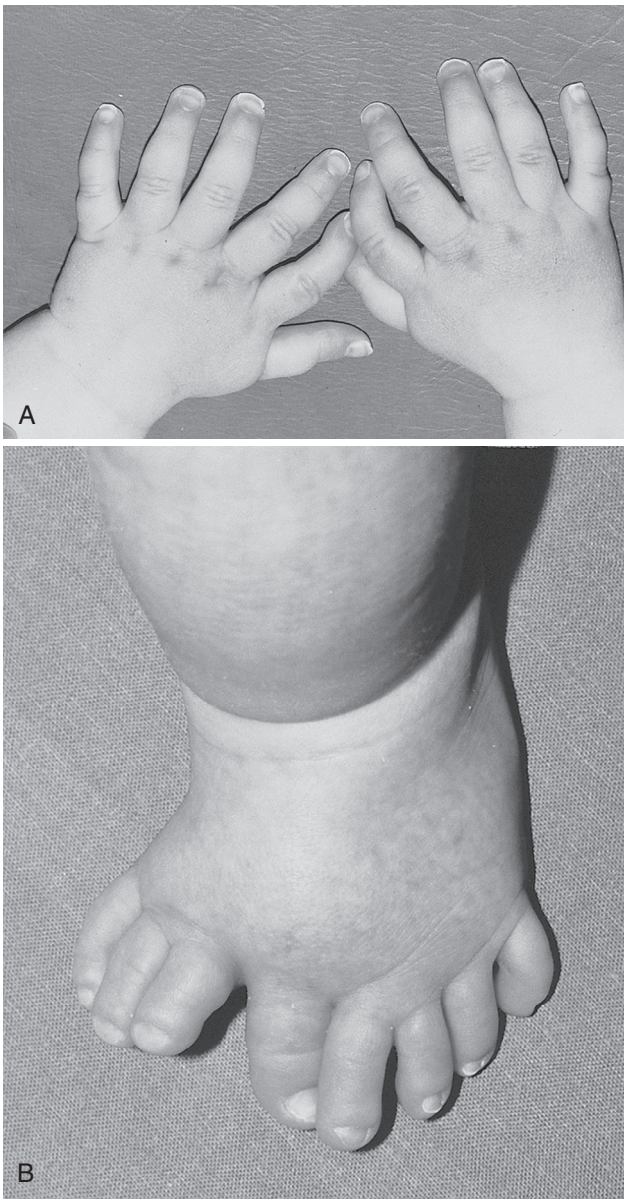

Fig. 35.6 Polydactyly of hands **(A)** and feet **(B)**. This condition results from formation of one or more extra digital rays during the embryonic period. *(Courtesy Dr. A. E. Chudley, Department of Pediatrics and Child Health, University of Manitoba, Children's Hospital, Winnipeg, Manitoba, Canada.)*

Deformation Abnormalities

AMNIOTIC BAND SYNDROME

A. **Incidence and etiology.**
   1. Amniotic band sequence occurs in 1 in 1200 live-born infants (Moore et al., 2016b).
   2. Etiology is primarily idiopathic, generally a sporadic event in an otherwise normal family, with little risk of recurrence. Defects are dependent on the degree of entanglement, timing of insult, and the body part affected. Two possible causes (Moore et al., 2016b):
      a. Exogenous-delamination of amnion due to rupture or tear.
      b. Endogenous-vascular disruption.
   3. Exceptions are presumed to occur secondary to trauma. Secondary to amnion rupture, strands of amnion encircle developing structures (Jones et al., 2013).

Fig. 35.7 A fetus with amniotic band syndrome showing amniotic bands constricting the left arm. *(Courtesy Professor V. Becker, Pathologisches Institut der Universität, Erlangen, Germany.)*

B. **Clinical findings.**
   1. Constriction bands commonly involve the distal portion of limbs, resulting in annular constrictions, pseudosyndactyly, intrauterine amputations, and umbilical cord constriction (Jones et al., 2013) (Fig. 35.7).
      a. Deformational defects result secondary to the primary insult.
         1) Loss of fetal movement can occur after tethering of a limb, resulting in foot or hand abnormalities.
         2) Constraint deformities result from a lack of amniotic fluid.
         3) Neurologic defects distal to the defect may occur.
         4) Defect may involve veins, arteries, and nerves, compromising circulation and growth of affected extremities.

C. **Associated findings.**
   1. Clubfeet occurs in 12% to 56% of affected infants. Treatment may be difficult due to the rigid position and paralysis secondary to nerve damage.
   2. Angular deformity, bone dysplasia, pseudarthrosis, and anterolateral bowing of the tibia may occur secondary to deep constriction bands in extremities.
   3. Syndactyly, brachydactyly.
   4. Cranial vault defects.
   5. If amniotic fluid has been leaking, features of oligohydramnios deformation may occur (Jones et al., 2013).

D. **Diagnosis**.
   1. No one feature consistently occurs, as this is a disruption sequence abnormality. No two infants will present with exactly the same defect.
      a. Physical examination, including vascular supply, joint function.
      b. Examination of the placenta for aberrant bands or strands of amnion, or rolled-up remnants of amnion at the placental base of the umbilical cord (Jones et al., 2013).
   2. Radiographs assist with definition and classification of defect.

E. **Treatment**.
   1. Dependent on anatomic position, associated abnormalities.
      a. If constriction is severe, early surgical relief is needed to preserve vascular, lymph, and nerve integrity.
      b. Deformities that pose no emergent threat are best repaired at ages 1 to 2 years. Repair may require a staged approach; repair is seldom completed in one surgery.
   2. Genetic counseling is necessary to educate parents as to the rare likelihood of recurrence. The appearance of some defects is significantly severe as to discourage further pregnancies, and accurate diagnosis of these defects is essential.
   3. Life expectancy is normal unless brain malformation or deep facial clefts are present.

TALIPES CALCANEOVALGUS

A. **Incidence and etiology.**
   1. Thought to be a postural defect secondary to intrauterine positioning, characterized by marked dorsiflexion of the entire foot at the ankle joint (White et al., 2018).
   2. Incidence of defect is estimated at 0.4 to 1 per 1000 births (White et al., 2018).
      a. More common after breech deliveries.
      b. Girls are affected more often than boys.

B. **Clinical findings.**
   1. Dorsum of the foot is, or is easily, positioned directly apposed to the anterior aspect of the leg (White et al., 2018).
      a. Soft tissues of the dorsal and lateral aspects of the foot are often contracted, limiting plantar flexion and inversion.

C. **Associated findings.**
   1. Increased association with hip dysplasia (White et al., 2018).
   2. May occur in conjunction with external rotation of the tibia and posteromedial bowing of the tibia.

D. **Diagnosis**.
   1. Physical examination provides the diagnosis for this condition.
      a. Reveals free mobility of the foot to passive manipulation.
      b. Forefoot is abducted and heel in an everted position. Plantar flexion of the foot is limited.
   2. Defect must be differentiated from congenital vertical talus, posteromedial bowing of the tibia, and neuromuscular abnormalities (White et al., 2018).

E. **Treatment**.
   1. Evaluation for hip dysplasia is essential; repeated examinations are needed.
   2. Generally, no treatment is required. This deformity usually resolves within first 6 months of life (Son-Hing and Thompson, 2015; White et al., 2018). Gentle stretching exercises can be done with diaper changes by caregivers.
   3. Infrequently, serial casting may be required; rarely ankle–foot orthoses are needed.
   4. Parents provide an active part in resolution of this condition and must be aware of the need for ongoing treatment and follow-up examinations.

Congenital Metabolic Problems

The process by which the body converts food into energy is complex. Disturbances in these processes result in a wide array of medical problems. The following section reviews some of the more common inborn biochemical disorders that affect the newborn.

INBORN ERRORS OF METABOLISM

A. **Incidence and etiology.**
   1. Inborn errors of metabolism are genetic biochemical disorders in which the function of a protein is compromised, resulting in alteration of the structure or amount of the protein synthesized.
   2. Genetic mutations produce deficiencies in enzymes, cofactors, transport proteins, and cellular processes. Interruptions of any of the steps in the formation of the coenzyme can lead to disease (Cederbaum, 2018).
   3. Inheritance can occur by multiple genetic mechanisms or via mutation (Cederbaum, 2018). Most mutations are inconsequential, but some mutations produce disease states that range from minor to severe.
      a. The majority of conditions are inherited as autosomal recessive traits resulting in a 25% recurrence risk in future offspring (Rezvani and Rezvani, 2016).

B. **Clinical presentation and findings.** Newborn metabolic diseases can be classified into three major groups based on clinical presentation (Harding, 2017):
   1. Disturbance of production or catabolism of complex molecules—includes lysosomal storage and peroxisomal disorders. Symptoms include somatic and neurologic abnormalities that develop

in utero, possibly clinically apparent at birth, and not affected by food intake.
   a. Clinical: may present with coarse or dysmorphic features, hepatosplenomegaly, hypotonia, hypertonia, large anterior fontanel, seizures, hydrops, and bone changes on x-ray.
   b. Laboratory: liver dysfunction, no acidosis, no hypoglycemia, normal ammonia, adrenal insufficiency.
2. Impaired energy production from food derivatives. This subgroup includes several inherited disorders. Typically differentiated as four different subgroups based on laboratory results, as clinical phenotype may be similar (Harding, 2017).
   a. Clinical (dependent on subgroup): global neurologic dysfunction, hypotonia, seizures, acidosis, vomiting, dehydration, dilated cardiomyopathy.
   b. Laboratory (dependent on subgroup): acidosis, ketosis, hypoglycemia, hyperammonemia, anemia, hypophosphatemia.
3. Accumulation of toxic metabolites with increasing food intake with a progressively deteriorating clinical course. These include errors of amino acids, urea cycle defects, organic acids, and sugar metabolism. These infants appear perfectly healthy at birth and a few days thereafter. This group is divided into four subgroups based on clinical and laboratory findings (Harding, 2017).
   a. Clinical (dependent on subgroup): initial presentation can occur very rapidly from vomiting and lethargy quickly progressing to coma or shock. Initial presentation often mimics sepsis. Other symptoms include liver dysfunction, jaundice, hepatomegaly, unusual odor and dehydration.
   b. Laboratory (dependent on subgroup): acidosis, hyperammonemia, hypoglycemia, ketonuria, neutropenia, alkalosis, direct hyperbilirubinemia, low blood urea nitrogen (BUN).

C. **Diagnosis**.
1. The newborn presenting with deterioration represents an emergency state. Septic evaluation should be undertaken to rule out infectious etiology. Metabolic workup is undertaken when the newborn's symptoms no longer fit the expected pattern for sepsis. The goals of treatment are rapid identification, treatment, and prevention of major sequelae. Multiple specialized laboratory tests exist for diagnosis.
   a. Mandatory screening of newborns: tandem mass spectrometry enables a single spot of blood to test for more than 40 inborn errors of metabolism. The only acutely presenting disorders not tested by expanded newborn screen include hyperammonemias and lactic acidoses (Cederbaum, 2018).
      1) All states require screening for phenylketonuria (PKU), hypothyroidism, and galactosemia.
      2) Expanded newborn screening is mandated by individual states.
      3) Collection of samples must be undertaken early (before 7 days of age) and repeated at prescribed intervals.
   b. Neuroimaging may provide early detection of cysts, calcifications, structural brain anomalies, and altered white mass echogenicity (Poretti et al., 2013).

Disorders of Metabolism

ERRORS OF AMINO ACID METABOLISM

PHENYLKETONURIA

A. **Incidence and etiology.**
1. PKU is the most common inborn error of amino acid metabolism that may result in intellectual disability (Merritt and Gallagher, 2018).
   a. Occurs more frequently in northern Europeans and East Asians, 1 per 10,000 live births (Harding, 2017).
   b. Gene location: chromosome 12q22-q24.1. Inherited as an autosomal recessive trait.
   c. Results from a deficiency of the liver enzyme phenylalanine hydroxylase to convert phenylalanine to tyrosine. It is the deficiency of this liver enzyme that is responsible for the development of brain disease.

B. **Clinical findings.**
1. After birth, the infant ingesting breast milk or formula will experience a gradual and persistent increase in plasma phenylalanine levels. Early symptoms include vomiting, poor feedings, hyperactivity, irritability, skin rashes, and urine odor. Untreated PKU will result in severe intellectual disability, hyperactivity, and seizures.
2. After 6 months of age, if untreated, developmental delays are evident, seizures, infantile spasms, and musty-smelling urine. Untreated infants demonstrate postnatal microcephaly.

C. **Diagnosis**.
1. Standard newborn screening is done with the infant receiving a regular diet.
2. DNA sequencing and mutational analysis are used to identify carriers in families and to assist with family genetic counseling.

D. **Treatment**.
1. Therapy consists of a low-protein diet and use of special amino acid–containing formula that does not have phenylalanine.
2. Parents must be counseled to understand the importance of continued dietary restrictions. A phenylalanine exchange system that allows for normal daily utilization of foods containing phenylalanine

while maintaining safe plasma phenylalanine levels is essential.

MAPLE SYRUP URINE DISEASE

A. **Incidence and etiology.**
   1. Maple syrup urine disease (MSUD) is a rare inborn error in 1 of 200,000 live births that is caused by a disturbance in the metabolism of leucine, isoleucine, and valine. The end result of this failure is an elevation of branched-chain amino acids (BCAAs) (Harding, 2017).
      a. Exception: older Mennonite colonies in Pennsylvania, Kentucky, New York, Indiana, Wisconsin, Michigan, Iowa, and Missouri demonstrate a frequency of 1 in 358 (Merritt and Gallagher, 2018).
   2. Inherited as an autosomal recessive trait. Males and females equally affected.

B. **Clinical findings.**
   1. Infants are usually well at the time of delivery, but after 2 to 3 days of feedings, infants demonstrate poor feeding and lethargy. Periods of hypertonicity and flaccidity mimicking a bicycling or boxing pattern may occur. The infant worsens, with high-pitched cry and hypotonia, eventually becoming obtunded and lapsing into a coma and death unless medical intervention is provided.
   2. Odor of maple syrup is evident on breath, in urine and feces, and in saliva.

C. **Diagnosis**.
   1. Laboratory findings include metabolic acidosis, ketonuria, hypoglycemia, elevation of the plasma BCAA leucine, isoleucine, and valine (Merritt and Gallagher, 2018).
   2. Standard newborn metabolic screening.
   3. Molecular diagnosis may be useful in target populations.
   4. Neuroimaging may demonstrate cerebral edema initially and then hypomyelination and cerebral atrophy (Kliegman et al., 2016).

D. **Treatment**.
   1. Initial therapy in the acute crisis includes hydration and parenteral nutrition modified to be BCAA-free and insulin therapy to manage catabolic stress. Peritoneal dialysis has also been utilized to decrease circulating plasma BCAAs.
      a. For those infants treated within 7 days of life, incidence of intellectual disability is diminished. Treatment delays beyond this time result in significant IQ deficiencies, and neurologic deficits are common (Kliegman et al., 2016).
   2. Long-term management requires a special formula devoid of BCAAs. The intake of formula must be carefully monitored. Supplemental isoleucine and valine may be needed.
   3. The long-term management of these infants requires that parents are vigilant in the provision of the diet and the need for follow-up.

ERRORS OF CARBOHYDRATE METABOLISM

GALACTOSEMIA. Defects in the enzyme involved with the metabolism of galactose may result in the development of galactosemia.

A. **Incidence and etiology.**
   1. The condition is caused by a nearly total deficiency of galactose 1-phosphate uridyltransferase (GALT).
   2. Enzymes involved in the galactose metabolic pathway are responsible for the conversion of galactose to glucose in the liver. The most common enzymatic deficiency is GALT (Merritt and Gallagher, 2018).
      a. Lactose is a disaccharide composed of galactose and glucose—deficiency of GALT enzyme blocks conversion, so infants are unable to metabolize lactose.
   3. Incidence is 1 in 60,000 live births (Merritt and Gallagher, 2018). There are milder forms with unclear clinical significance, which may be identified on newborn screening but currently do not require treatment.
   4. Inherited as an autosomal recessive condition.

B. **Clinical findings.**
   1. Infant appears normal at birth; once milk feeding begins, galactose and other metabolites accumulate in blood and urine. Some may be born with cataracts. Symptoms occur quickly—vomiting, poor feeding, diarrhea, jaundice, failure to thrive, hepatomegaly, hypoglycemia, lethargy.
   2. Jaundice; presenting in the first weeks of life, persisting.
   3. Later signs: multiorgan toxicity, with liver disease that progresses to cirrhosis, portal hypertension, splenomegaly, cataracts, ascites, sometimes progressing to renal Fanconi syndrome.
      a. *Escherichia coli* sepsis occurs as a complication in 10% of the affected infants (Merritt and Gallagher, 2018).

C. **Associated findings.**
   1. Speech defects—especially expressive speech, delayed speech, language and learning disabilities.
   2. Behavioral disorders, short attention span.
   3. Infertility: ovarian failure and amenorrhea and hypogonadism.
   4. Cataracts developing within 2 months of birth, reverse with treatment.

D. **Diagnosis**.
   1. Newborn screening demonstrating absence of the enzyme necessary for breakdown and metabolism of galactose.
   2. Laboratory: serum blood galactose levels, red blood cell galactose 1-phosphate levels, and elevated urine

galactitol. Albuminuria, hyperbilirubinemia, elevated alanine transaminase (ALT) and aspartate transaminase (AST) levels, elevated prothrombin time.
   a. Positive reducing substances in urine are present in severe hypergalactosemia.

E. **Treatment**.
   1. Initiation of a lactose-free diet is essential. This reflects a lifelong change; parents must receive appropriate counseling to ensure long-term success. Galactose 1-phosphate levels in red blood cells are monitored. This diet does carry a risk of vitamin D and calcium deficiencies, which require supplementation.
   2. With treatment, intellectual development may be normal or near normal. But even for infants who receive treatment, rates of intellectual disability remain higher.
   3. Communication problems continue throughout life despite speech therapy.

ERRORS OF FATTY ACID OXIDATION

MEDIUM-CHAIN ACYL-COENZYME A DEHYDROGENASE DEFICIENCY

A. **Incidence and etiology.**
   1. Defect involves an abnormality in the enzyme that encourages mitochondrial beta oxidation of fatty acids.
      a. Fatty acid oxidation provides energy as adenosine triphosphate during the Krebs cycle and as ketones during periods of caloric deprivation. When normal metabolism is disrupted, the quickly depleted glycogen stores lead to hypoglycemia.
   2. Medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency is the most commonly occurring fatty acid oxidation disorder, occurring in 1 in 20,000 infants (Sahai and Levy, 2018).
      a. MCAD deficiency is caused by *ACADM* gene, which codes the MCAD enzyme (Hamosh et al., 2016).
      b. A single mutation accounts for more than 70% of mutant alleles (Hamosh et al., 2016). Inherited as an autosomal recessive trait.

B. **Clinical findings.**
   1. Though severe enzyme deficiencies may manifest within the first days of life, presentation of symptoms is frequently in later infancy: after an infection, the infant experiences anorexia, vomiting, dehydration, lethargy, and hypoglycemia associated with seizures.
      a. High mortality rates, up to 25% to 50%, are common with initial episodes due to metabolic crisis (Hamosh et al., 2016). Thought to be causative in sudden infant death syndrome due to metabolic dyscrasias (Lane et al., 2018).
   2. Symptoms may mimic Reye's syndrome, death occurring from brain edema.

C. **Associated findings.**
   1. Carnitine deficiency develops as a result of excess excretion of acylcarnitine.
   2. Infants who die suddenly and have fat accumulation in the liver suggest a disorder of fatty acid oxidation.

D. **Diagnosis**.
   1. Chorionic villus sampling, amniocentesis, DNA analysis.
   2. Newborn screening.
   3. Laboratory studies: hypoglycemia, absence of moderate to large ketones in urine. Plasma ammonia values may be increased; AST and ALT may also be elevated.
   4. MCAD enzyme may be assayed in cultured skin fibroblasts (Lane et al., 2018).

E. **Treatment**.
   1. Symptomatic hypoglycemia is treated aggressively. Intravenous glucose and caloric support must be provided quickly.
   2. Prevention of hypoglycemia is the cornerstone of therapy; avoid free fatty acid mobilization during times of catabolic stress and relative insulin deficiency.
   3. Limit fasting to no more than 12 hours, particularly if infant is experiencing an associated illness.
   4. Diagnosis and treatment of associated carnitine deficiency.
   5. Infants with MCAD often have a sibling who has died of sudden infant death syndrome. Accurate diagnosis and genetic counseling are essential.

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CHAPTER 36
Neonatal Dermatology

Catherine Witt

OBJECTIVES

1. Name three functions of the skin.
2. Describe two ways in which the skin of a newborn or preterm infant differs from that of an adult.
3. Identify three factors that affect the appearance of the neonate's skin.
4. Identify two nursing interventions that provide protection for the preterm infant's skin.
5. Recognize three common skin lesions that are normal variations in the newborn infant. Describe their appearance and treatment, if any.
6. Describe three common vascular lesions in the neonate, their appearance, and appropriate treatment.
7. Identify two syndromes associated with vascular lesions.
8. Evaluate two pigmented lesions occurring in the newborn infant and list implications associated with each.
9. Name two types of infectious skin lesions and select the appropriate treatment.

Careful assessment of the skin is an important element of the neonatal physical examination. The appearance of the skin gives the nurse important clues regarding gestational age, nutritional status, function of organs such as the heart and liver, and the presence of cutaneous or systemic disease. It is important for the clinician to be familiar with normal variances in the skin of the newborn infant as well as those variances that signify disease.

Proper care of the neonate's skin can directly affect mortality and morbidity, especially in the preterm infant. The skin is the first line of defense against infection. Proper skin care can protect the integrity of the skin and prevent breakdown.

Anatomy and Physiology of the Skin

A. **Anatomy of the skin—three main layers** (Fig. 36.1).
   1. Epidermis: outermost layer, which functions as a barrier against outside penetration. The epidermis is subdivided into the following:
      a. Stratum corneum: outermost layer, consisting of closely packed dead cells that are consistently brushed off and replaced by lower levels of the epidermis. These cells are flatter and have thicker walls than other cells. The cells are held together by intracellular lipids, which aid in forming the protective barrier of the skin.
      b. Lower layers of epidermis: contain keratin-forming cells that create the outer layer of skin as well as melanocytes, which produce melanin, or pigment. Despite racial differences in pigmentation, the number of melanocytes in a given surface area of skin is the same (Hoath and Narendran, 2015; Moore et al., 2016).
   2. Dermis: directly under epidermis; 2 to 4 mm thick at birth. The dermis is composed of:
      a. Collagen and elastic fibers that connect the epidermis and dermis and provide the skin with the ability to stretch and then to return to normal shape.
      b. Blood vessels and nerves that carry sensations of heat, touch, pain, and pressure from the skin to the brain and provide protection against injury, infections, or other invasions.
      c. Sweat glands, sebaceous glands, and hair shafts.
   3. Subcutaneous layer: fatty tissue functions as insulation, protection of internal organs, and calorie storage.

B. **Functions of the skin.**
   1. Physical protection.
      a. Mechanical.
         1) Tightly packed, thick-walled cells, held together by intercellular lipids, provide a protective barrier against transepidermal water loss and external invasions.
         2) Process of constant sloughing and replacement of stratum corneum prevents colonization of the skin surface by bacteria and other organisms.

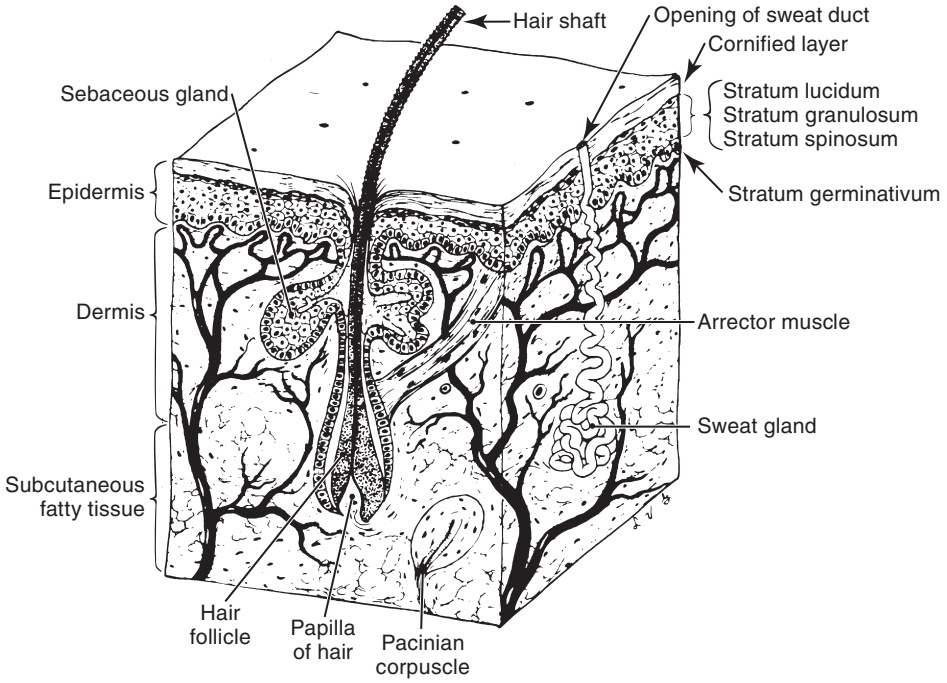

Fig. 36.1 Several layers and structures of human skin. *(From Francis, C. C., & Martin, A.H. [1975]. Introduction to human anatomy [7th ed.]. St. Louis, MO: Mosby.)*

b. Chemical/bacterial.
   1) Acidic surface of skin (pH 5 to 6) provides defense against bacteria and other microorganisms (Association of Women's Health Obstetric and Neonatal Nurses [AWHONN], 2013).
   2) Production of melanin protects against damage from ultraviolet-light radiation.

2. Heat regulation.
   a. Production and evaporation of sweat.
   b. Dilation and constriction of blood vessels.
   c. Insulation of body by subcutaneous fat.
3. Sense perception: heat, touch, pain, and pressure.

C. **Differences in newborn/preterm skin.**

1. Basic structure is same as that of the adult. However, the epidermis and stratum corneum do not reach full adult functioning until around 1 year of age (AWHONN, 2013). Less mature neonates have less mature skin epidermis and dermis and minimal subcutaneous fat.
2. Skin adaptation occurs rapidly during the first few weeks after birth. The full-term infant will achieve a stratum corneum that is structurally and functionally equivalent to the adult by approximately 2 weeks of age. The preterm infant will also experience accelerated skin maturity, although it may take as long as 4 to 8 weeks in the extremely preterm neonate (Hoath and Mauro, 2015; Mathes and Williams, 2015; Paller and Mancini, 2015). The acid mantle of the epidermis develops over 5 to 6 weeks, with the pH value decreasing from around 6.0 in the newborn to 5.1, which is comparable to adult levels (AWHONN, 2013).
3. The earlier the gestational age, the thinner and more gelatinous the skin, with fewer layers in the stratum corneum and a thinner dermis with fewer elastic fibers. Transepidermal water loss is inversely related to gestational age, with a 25-weeks-gestation neonate having nearly 4 to 5 times the transepidermal water loss as a term infant (Dell, 2015; Hoath and Mauro, 2015). Subcutaneous fat is accumulated predominantly during the third trimester.
   a. Preterm babies have little fat, resulting in an inability to maintain body temperature and blood glucose level.
   b. Brown fat, which is important for temperature regulation in the newborn infant, begins to differentiate between 26 and 30 weeks' gestation (Ward and Hisley, 2016).
4. Immature skin is thinner and therefore more permeable.
   a. An infant, especially a preterm infant, quickly absorbs topically applied medications and chemicals (Mathes and Williams, 2015; Paller and Mancini, 2015).
   b. Greater permeability allows for greater insensible water loss in the preterm infant.
   c. Higher surface area–body weight ratio also allows for greater absorption of chemicals and greater transepidermal water loss.
5. Fewer fibrils connect the dermis and epidermis, and they are more fragile in term and preterm skin than in the skin of an adult. The stratum corneum is thinner in the term and preterm infant. Risk of

injury from tape, monitors, and handling is increased, especially in the preterm infant; this type of injury includes removal of the outermost layer of the dermis with removal of tape or electrodes (August et al., 2017; AWHONN, 2013).

6. Sweat glands are present at birth, but full adult functioning is not present until the second or third year of life. Although present in the preterm infant, sweat glands are immature and function poorly before 36 weeks of gestation (Hoath and Narendran, 2015).
   a. The newborn infant has limited ability to tolerate excessive heat.
   b. Vasodilation to increase heat loss can result in hypotension and dehydration caused by increased insensible water loss.

Care of the Newborn Infant's Skin

A. **Term newborn infant.**
   1. Initial bath with water and a mild soap.
      a. Plain water or mild soaps with a neutral pH should be used for bathing neonates (Cooke et al., 2018).
      b. Safety of bacteriostatic soaps has not been determined. These products may be too harsh for the neonate's skin and may negatively affect normal skin colonization (AWHONN, 2013).
      c. As soon as the body temperature is stable (>97.7° F [36.5° C]), it is advisable to bathe the healthy term infant to decrease the caregiver's risk of exposure to blood-borne pathogens. Standard Precautions, including the use of gloves, should be adhered to when handling the infant who has not been bathed after delivery and during any invasive procedure in which the caregiver may be exposed to body fluids (AWHONN, 2013).
   2. Parents may prefer to give the first bath themselves.
   3. Vernix caseosa contains fats and proteins that protect the skin from the amniotic fluid and bacteria in utero and is thought to aid in skin maturation after birth. Vernix insulates the stratum corneum and should not be removed during the initial bath (AWHONN, 2013; Danby et al., 2015).
   4. When possible, avoid puncturing the skin of babies with suspected maternal infections.
   5. Routine use of emollients is not recommended in the term infant. Creams and emollients that contain perfumes are drying and may irritate the infant's skin. Products that change the pH of the skin decrease the bacteriostatic properties. If cracking or fissures develop in the skin, a nonperfumed emollient such as white petrolatum may be used (AWHONN, 2013; Danby et al., 2015).

B. **Preterm infant.**
   1. Keep skin clean with water. Mild, nonalkaline soap may be used on soiled areas as needed; otherwise, plain water is acceptable. Preterm infants should be bathed infrequently during the first 2 months of life to avoid excessive drying of the skin and to avoid overstimulation, stress, and fatigue (AWHONN, 2013).
   2. Handle infant gently and minimally to avoid trauma.
   3. Minimize use of tape and other adhesives as much as possible. Use care when removing tape to avoid stripping the epidermis (AWHONN, 2013; Hoath and Narendran, 2015).
      a. Use of adhesive solvents is not recommended. Cotton balls soaked with warm water can be used effectively for removing tape and other adhesives.
      b. Gelled adhesives and pectin-based barriers are good alternatives to tape, as removal causes less trauma to the skin (Hoath and Narendran, 2015).
      c. Pectin or hydrocolloid layers applied before adhesives may protect the skin from damage when endotracheal tubes or catheters are secured (AWHONN, 2013).
      d. Benzoin and other adhesive bonding agents form a strong bond between the adhesive and the epidermis, increasing the risk of stripping the epidermis when the adhesive is removed. Use of these agents with preterm infants should be avoided.
   4. Increased permeability of the skin allows absorption of some medications and products such as alcohol and povidone–iodine (Danby et al., 2015). When these substances are used for an invasive procedure, it is recommended that they be removed completely with water as soon as possible to prevent absorption or chemical burns.
   5. The skin should be disinfected before any invasive procedure. Although chlorhexidine gluconate has been shown to be more effective than other agents in reducing skin colonization, it has not been approved for use in infants less than 2 months of age. Chlorhexidine gluconate is available in single-use applicators that contain 70% alcohol, but may be drying to the neonate's skin or cause burning or other injury (AWHONN, 2013; Danby et al., 2015).
   6. Emollient creams that are free of preservatives and perfumes may be of benefit to the preterm infant as they decrease transepidermal water loss and skin breakdown when cracking, excessive dryness, or fissures are present (AWHONN, 2013; Mathes and Williams, 2015). Humidity at levels of 70% to 90% during the first week after birth reduces insensible water loss and evaporative heat loss in extremely low birth weight infants. Humidity should be gradually decreased to 50% after the first week. Transepidermal water loss in extremely low birth weight infants decreases after the first week after birth. Decreasing humidity to around 50% may improve skin barrier maturation (Agren, 2015).

7. Transparent adhesive dressings can be used over wounds and abrasions and to secure intravenous (IV) catheters and central lines (Houth and Narendran, 2015).

C. **Umbilical cord care.**
   1. Sterile cutting of the cord at delivery, rapid drying of the umbilical cord, and keeping the cord clean are effective in preventing umbilical infections. The use of antimicrobial creams or ointments has not been shown to be more effective in preventing infection than keeping the cord clean and dry (Stewart and Benitz, 2016).
   2. Some studies have suggested that chlorhexidine may be of benefit in cord care, particularly in circumstances in which infection risk is increased, although cord separation time may be lengthened (Stewart and Benitz, 2016).
   3. Bathing does not increase the rate of omphalitis or cause a delay in cord separation.
   4. It is normal for the cord to appear slightly mucky, with small amounts of cloudy, mucus-like material at the junction of the cord and abdominal skin.
   5. Omphalitis is characterized by serosanguineous drainage, inflammation of the surrounding tissues, and a foul odor. Poor feeding, lethargy, and fever may also be associated. Suspected omphalitis should be treated immediately with IV antibiotics.

Assessment of the Newborn Infant's Skin

A. **Factors affecting the appearance of the skin.**
   1. Gestational age.
   2. Postnatal age.
   3. Nutritional status and hydration.
   4. Racial origin.
   5. Type and amount of available light.
   6. Hemoglobin and bilirubin levels.
   7. Environmental temperatures.
   8. Oxygenation status.

B. **Definitions used to describe skin lesions** (Paller and Mancini, 2015). See Table 36.1.

Common Skin Lesions

A. **Normal variations in newborn skin.**
   1. Cutis marmorata.
      a. Bluish mottling or marbling effect of the skin.
      b. Physiologic response to chilling caused by dilation of capillaries and venules.
      c. Disappears when infant is rewarmed.
      d. May be a sign of stress or overstimulation in newborn infant.
      e. Common in infants with trisomies 18 and 21.
      f. If condition persists in infants 6 months of age or older, it may be a symptom of hypothyroidism or a vascular abnormality such as cutis marmorata telangiectasia (Paller and Mancini, 2015).
   2. Harlequin color change (Fig. 36.2).
      a. A difference in the amount of blood flow in the right and left sides of the body results in a sharply demarcated difference in color between one side and the other. This is most often seen in the dependent half of the body when the infant is lying on his or her side. When the infant's position is reversed, the color changes to the other side. This condition may also be seen when the infant is lying flat. It is most often visible in the trunk. It may last from a few seconds to a few minutes and changes with activity or changes in position.

Table 36.1

Definitions Used to Describe Skin Lesions

Terminology	Definition
Macule	A pigmented, flat spot that is visible but not palpable. Macules greater than 1 cm in diameter are referred to as a patch.
Papule	A solid, elevated, palpable lesion, with distinct borders less than 1 cm in diameter.
Plaque	A solid, elevated, palpable lesion, with distinct borders, greater than 1 cm in size.
Nodule	A solid lesion, elevated with depth, up to 2 cm in size.
Tumor	A solid lesion, elevated with depth, greater than 2 cm in size.
Vesicle	An elevated lesion or blister filled with serous fluid and less than 1 cm in diameter.
Bulla	A fluid-filled lesion larger than 1 cm.
Pustule	A vesicle filled with cloudy or purulent fluid.
Petechiae	Subepidermal hemorrhages, pinpoint in size. They do not blanch with pressure.
Ecchymosis	A large area of subepidermal hemorrhage.
Wheal	Area of edema in the upper dermis, creating a palpable, slightly raised lesion.
Ulcer	Erosion of skin with damage to the epidermis into the dermis. Will usually leave a scar after healing.

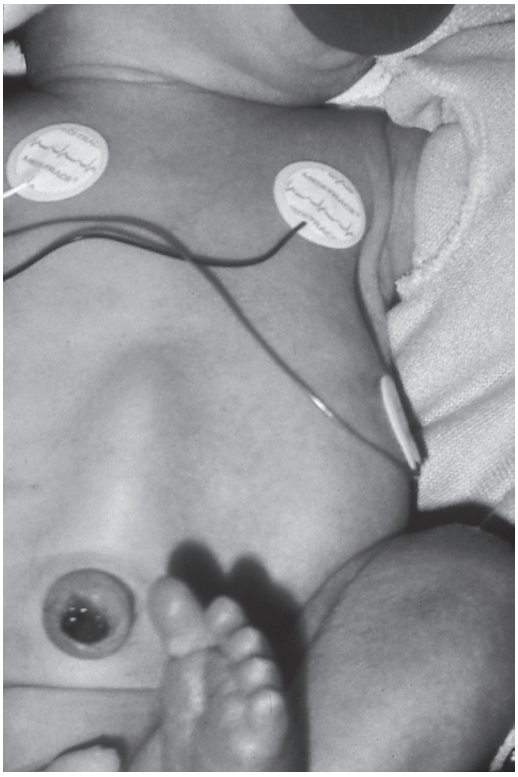

Fig. 36.2 Harlequin color change. *(Courtesy Jane Deacon, RNC, MS, NNP, The Children's Hospital, Denver, CO.)*

Fig. 36.3 Erythema toxicum. *(Courtesy Jacinto Hernandez, MD, The Children's Hospital, Denver, CO.)*

   b. Caused by immaturity or temporary disturbance of the autonomic regulation of the cutaneous vessels. It is more common in preterm neonates.
3. Erythema toxicum (newborn rash) (Fig. 36.3).
   a. Small white or yellow pustules surrounded by an erythematous base (erythematous base is caused by histamine release) (Reginatto et al., 2017).

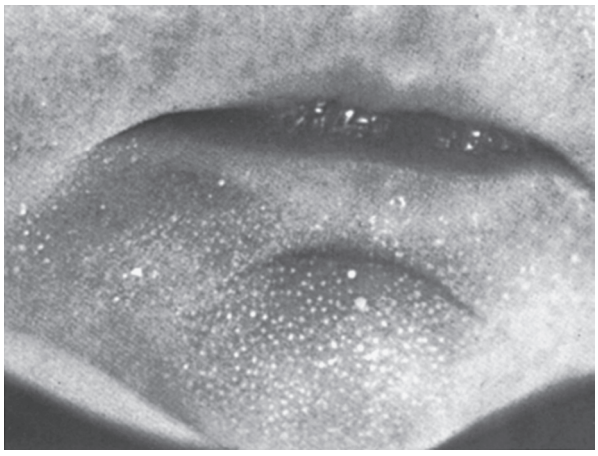

Fig. 36.4 Milia. *(Courtesy Jacinto Hernandez, MD, The Children's Hospital, Denver, CO.)*

   b. Benign, found in up to 35% of newborn infants (Reginatto et al., 2017).
   c. Seen in neonates and infants up to 3 months of age.
   d. Lesions come and go on various sites of face, trunk, and limbs, although they are never seen on the palms of the hands or soles of the feet (Lucky, 2015).
   e. Cause unknown, but condition may be exacerbated by handling or by chafing from linen.
   f. Differential diagnosis: may resemble a staphylococcal infection. Diagnosis can be confirmed by smear of aspirated pustule showing numerous eosinophils.
   g. No treatment is necessary. Lotions or creams may exacerbate condition.
4. Milia (Fig. 36.4).
   a. Multiple yellow or pearly white papules about 1 mm in size; epidermal inclusion cysts composed of laminated, keratinous material. They occur on the brow, cheeks, and nose.
   b. Milia are observed in about 40% of term infants (Lucky, 2015).
   c. No treatment is necessary. They resolve spontaneously during the first few weeks after birth.
5. Epstein's pearls (Fig. 36.5).
   a. Oral counterpart of facial milia. They can be seen on the midline of the palate or on the alveolar ridges.
   b. Epstein's pearls occur in approximately 60% to 90% of neonates (Lucky, 2015).
   c. When seen on the vestibular or lingual surfaces of the alveolar ridges they are referred to as *Bohn's nodules* (Lucky, 2015).
6. Sebaceous gland hyperplasia.
   a. Tiny (<0.5 mm) white or yellow papules found on the nose, cheeks, and upper lips of newborn infants.

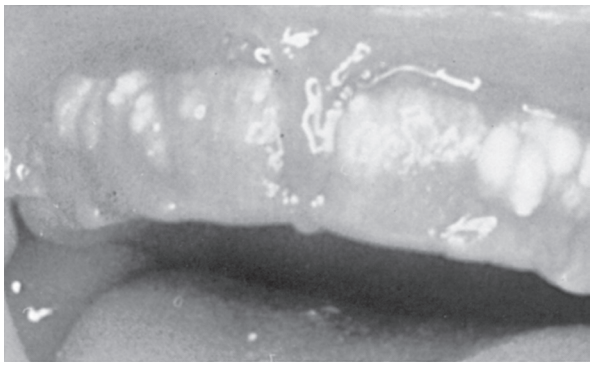

Fig. 36.5 Epstein's pearls. *(Courtesy Jacinto Hernandez, MD, The Children's Hospital, Denver, CO.)*

b. Common in term infants but rarely seen in preterm infants.
c. Represent overactivity of the sebaceous follicles and are a manifestation of maternal androgen stimulation.
d. They resolve without treatment within a few weeks.

7. Miliaria. Caused by occlusion of sweat ducts by keratin, resulting in retention of sweat. There are two main types of miliaria.
   a. Miliaria crystallina: clear, thin vesicles 1 to 2 mm in diameter that develop in the epidermal portion of the sweat glands. They are seen over the head, neck, and upper aspect of the trunk in newborn infants. Can be present at birth (Paller and Mancini, 2015).
   b. Miliaria rubra: commonly referred to as "prickly heat"; results from prolonged occlusion of pores, leading to release of sweat into the lower epidermis. Condition appears as pink or white papules and vesicles 2 to 4 mm in diameter, with an erythematous base. The lesions are generally found in the flexure areas, such as the neck, groin, and axillae, as well as on the face and the upper aspect of the chest. Correcting the cause of the overheating will resolve the lesions.
8. Diaper dermatitis.
   a. May be caused by chafing from diapers, by prolonged contact with urine or feces, or by sensitivity to chemicals in disposable diapers or in detergent used in laundering cloth diapers.
   b. The best treatment is prevention by frequent diaper changes and by protection of the skin with a barrier product containing zinc oxide and/or petrolatum. The skin should be cleansed with warm water after voiding or stooling. The barrier ointment should not be scrubbed off between applications. Stool can be gently wiped away with only the soiled layer of the barrier removed. (AWHONN, 2013; Blume-Peytavi and Kanti, 2018).
   c. Cornstarch and baby powder should not be used. They provide a medium for growth of bacteria and yeast, and inhaled particles are irritating to the respiratory tract (AWHONN, 2013).
   d. *Candida* diaper dermatitis: see 2. under E. Infectious lesions.

B. **Lesions resulting from trauma.**
1. Forceps marks.
   a. Forceps marks are red or bruised areas seen over the cheek, scalp, or face of infants after forceps delivery.
   b. The neonate should be examined for underlying tissue damage or other signs of birth trauma such as scalp abrasions, fractured clavicles, or facial palsy.
2. Subcutaneous fat necrosis.
   a. A hard, circumscribed, red or purple nodule under the dermis in the subcutaneous tissue. Nodules appear on the trunk, extremities, or face, usually during the first 2 weeks of life. They may grow larger initially and then resolve spontaneously within several weeks.
   b. Subcutaneous fat necrosis has been attributed to trauma, cold stress, shock, and asphyxia and is caused by crystallization of the subcutaneous fat cells. It has also been reported in neonates being treated with therapeutic hypothermia for hypoxic–ischemic encephalopathy (Thomas et al., 2016).
   c. Hypercalcemia may be associated with subcutaneous fat necrosis in infants with multiple nodules. Hypocalcemia has also been reported, possibly because of the underlying cause of the nodules. Serum calcium levels should be monitored (Thomas et al., 2016).
3. Scalp lacerations.
   a. Scalp lacerations may be caused by trauma during delivery, placement of scalp electrodes, or fetal blood pH sampling.
   b. Treatment consists of keeping the area clean and dry and assessing for infection.
4. IV extravasations.
   a. Vascular access sites in the infant should be assessed hourly to evaluate line patency and detect extravasation. The IV catheter should be removed immediately if patency is not certain or if signs of extravasation are apparent. If an infiltration of a vesicant medication has occurred, treatment should be determined before removing the catheter (AWHONN, 2013).
   b. If extravasation occurs, using a multiple-puncture technique has been reported to help avoid swelling at the site and further tissue damage (AWHONN, 2013). Using aseptic technique, make several puncture holes with a 25-gauge needle over the area of swelling and gently

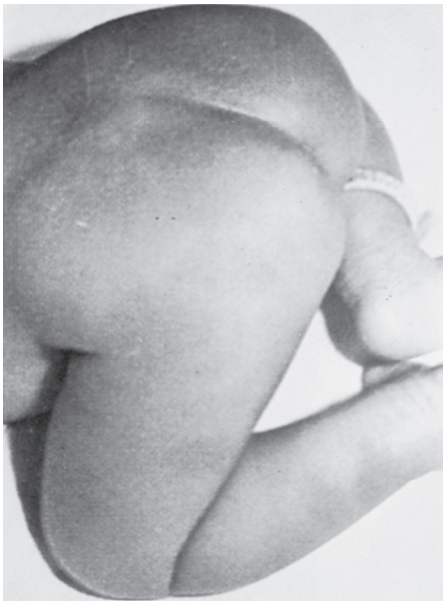

Fig. 36.6 Hyperpigmented macules (mongolian spots). *(Courtesy Jacinto Hernandez, MD, The Children's Hospital, Denver, CO.)*

Fig. 36.7 Giant pigmented nevus. *(Courtesy Catherine L. Witt, Aurora, CO.)*

squeeze fluid out of the tissue, or allow the fluid to leak out on its own. Hyaluronidase injected into the tissue surrounding the site may decrease tissue damage, and phentolamine can be used as an antidote for infiltration of vasoconstrictive agents such as dopamine or norepinephrine, although evidence from randomized controlled trials is minimal (AWHONN, 2013; Maly et al., 2018).

c. Application of an occlusive hydrocolloid dressing may aid in healing (AWHONN, 2013).

C. **Pigmented skin lesions.**

1. Hyperpigmented macules (Fig. 36.6).
   a. Large macules or patches, gray or blue-green, seen most commonly over the buttocks, flanks, or shoulders.
   b. Most common pigmented lesion seen at birth, occurring in 80% of African American, Asian, and Hispanic infants and only occasionally in lighter-skinned infants (Kane et al., 2017; Lucky, 2015).
   c. Hyperpigmented macules are caused by the increased presence of melanocytes dispersed in the dermis.
   d. The spots fade somewhat during the first few years after birth, particularly as surrounding skin darkens, but may persist into adulthood.
   e. It is important to document size and location to avoid the question of nonaccidental trauma.
2. Congenital melanocytic nevi (pigmented nevi) (Fig. 36.7).
   a. Dark brown or black macules or papules that may or may not be hairy. Nevi may occur anywhere on the body, with the "bathing trunk" area being the most common site.
   b. Caused by collection of melanocytes under the skin.
   c. Most are small, less than 2 cm, with smooth surfaces. Large nevi (>10 cm) are rare (Price and Marghoob, 2015).
   d. Pigmented nevi are generally benign. Malignant changes may occur but are rare before puberty in small nevi (Paller and Mancini, 2015; Price and Marghoob, 2015).
   e. Close observation for changes in size or shape is indicated, with possible surgical excision. Large, unusually shaped nevi may be difficult to assess for changes and should be followed closely (Price and Marghoob, 2015).
   f. Pigment-specific lasers such as the Q-switched or ruby laser have been used with increasing success (Simons et al., 2017).
   g. A hairy nevus present over the spine may be associated with spina bifida or meningocele (Price and Marghoob, 2015).
   h. Pigmented nevi may also be associated with neurofibromatosis or tuberous sclerosis. Magnetic resonance imaging (MRI) should be considered for individuals with large or multiple nevi (Price and Marghoob, 2015).
3. Transient neonatal pustular melanosis (Fig. 36.8).
   a. Superficial vesiculopustular lesions that rupture during the first 12 to 48 hours after birth, leaving small, brown, hyperpigmented macules. The macules may be surrounded by very fine white scales. They often rupture before delivery, presenting as macules.
   b. Benign; found in up to 5% of African American infants and in about 0.2% of white neonates (Paller and Mancini, 2015; Ramamurthy et al., 1976).
   c. No treatment is necessary. The macules generally fade during the first few weeks or months after birth.

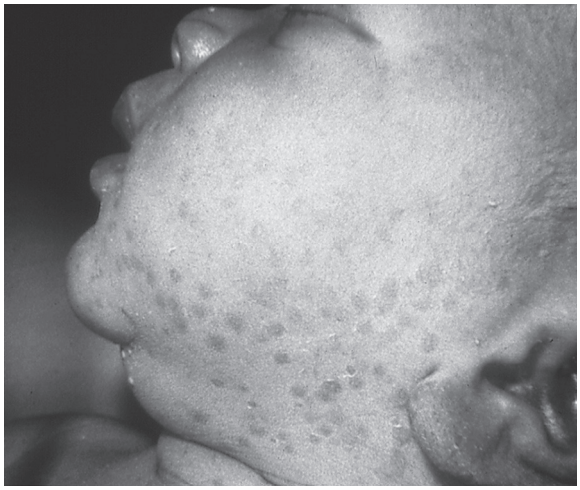

Fig. 36.8 Neonatal pustular melanosis. *(Courtesy Jane Deacon, RNC, MS, NNP, The Children's Hospital, Denver, CO.)*

Fig. 36.9 Café-au-lait spots. *(Courtesy Jacinto Hernandez, MD, The Children's Hospital, Denver, CO.)*

d. Aspirating the contents of the vesicles will reveal a variable number of neutrophils and few or no eosinophils.

4. Café-au-lait macules (Fig. 36.9).
   a. Tan or light brown macules or patches with well-defined borders.
   b. When less than 3 cm in length and fewer than six in number, they are of no pathologic significance.
   c. Six or more macules may be an indication of neurofibromatosis (Paller and Mancini, 2015; Price and Marghoob, 2015).
      1) Neurofibromatosis is a condition in which tumors form on cutaneous nerves and along the thoracic, brachial, and lumbar nerve trunks. Cranial nerves may also be affected.
      2) It is an autosomal dominant disorder.
      3) Café-au-lait macules may be the only finding of this disease in the neonatal period.
5. Ash leaf macules.
   a. White macules in the shape of an ash leaf or thumbprint; seen primarily over the trunk or buttocks.
   b. Found in 90% of infants with tuberous sclerosis, although up to 5% of white infants will have hypopigmented macules (Paller and Mancini, 2015; Siegel et al., 2015).
   c. May be difficult to see in fair-skinned infants. Use of a Wood's (ultraviolet) lamp will aid in examination.
   d. Infants with unexplained seizures should be examined for these macules.
   e. May also be a normal finding or may be associated with neurofibromatosis.

D. **Vascular lesions.**
1. Nevus simplex.
   a. Nevus simplex (stork bite) refers to macular pink areas of distended capillaries found on the nape of the neck, the upper eyelids, the nose, or the upper lip. They have diffuse borders, blanch with pressure, and become pinker with crying.
   b. These are the most common of vascular birthmarks, seen in 30% to 50% of newborn infants (Kane et al., 2017).
   c. The lesions tend to fade by the first or second year, with the exception of those on the nape of the neck, which may persist.
2. Port-wine stain.
   a. A flat vascular nevus is present at birth. It is usually pink in infancy but may be red or purple. The nevus may be small or may cover almost half of the body. It is flat, sharply delineated, and blanches minimally. Facial lesions are the most common.
   b. Port-wine stains consist of mature capillaries that are dilated and congested directly below the epidermis. The cause is unknown.
   c. The nevus does not grow in area or size. It will not resolve and should be considered permanent. The lesion may become darker and thicker with age.
   d. The pulsed-dye laser has been successful in significantly lightening most port-wine stains. The laser works by causing intravascular coagulation (Perruchoud et al., 2016). Light-colored facial lesions have the best results; red or purple lesions that are thick and nodular respond less well. Most infants require several treatments, and up to 10% of lesions recur several years after treatment (Rozas-Muñoz et al., 2016).
   e. Sturge–Weber syndrome (Fig. 36.10).
      1) Port-wine stains that are confined to a pattern similar to that of the branches of the trigeminal nerve.

Fig. 36.10 Sturge–Weber syndrome. *(Courtesy Jacinto Hernandez, MD, The Children's Hospital, Denver, CO.)*

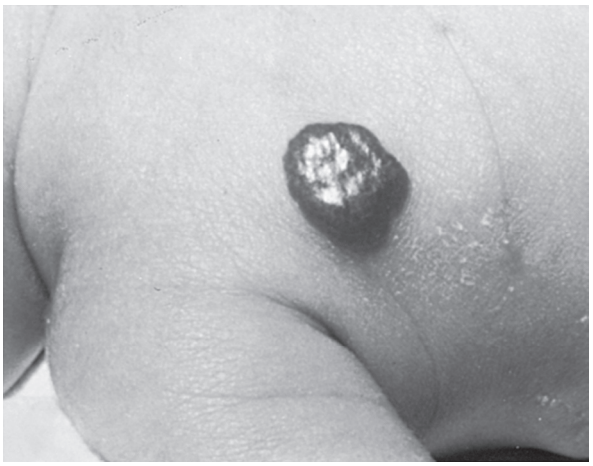

Fig. 36.11 Strawberry hemangioma. *(Courtesy Jacinto Hernandez, MD, The Children's Hospital, Denver, CO.)*

2) Their central feature is disordered proliferation of endothelial cells, particularly in the small capillaries and veins. It is associated with atrophic changes in the cerebral cortex and calcium deposits in the walls of small vessels and areas of affected cortex (Rozas-Muñoz et al., 2016).
3) Manifestations of the disease may include glaucoma, headaches, focal seizures, hemiparesis, and cognitive impairments (Rozas-Muñoz et al., 2016).

3. Infantile hemangioma (strawberry hemangioma) (Fig. 36.11).
   a. Raised, lobulated, soft, bright red tumor located on the head, neck, trunk, or extremities. These lesions may also occur in the throat, where they can cause airway obstruction, requiring a tracheostomy in extreme cases.
   b. Caused by proliferation of capillaries occupying the dermal and subdermal layers in association with endothelial proliferation.
   c. About 50% to 60% are present at birth, and 90% are evident by 2 months of age (Haggstrom and Chamlin, 2015; Paller and Mancini, 2015). The lesions occur in approximately 1% to 2% of newborn infants and are more common in preterm infants (10% to 15% will have lesions), with females predominating (Haggstrom and Chamlin, 2015; Paller and Mancini, 2015). They are also more common in white infants and in twins or higher-order multiples. The lesions may also be familial (Paller and Mancini, 2015).
   d. Infantile hemangiomas will generally increase in size during the first 6 months and then become stable in size before undergoing gradual spontaneous regression, with most leaving no trace. This may take several years. Infants will often have more than one lesion.
   e. Treatment of choice is to allow the lesion to regress spontaneously. If the lesion is interfering with vision, is bleeding or ulcerating, or is impinging on other vital functions, treatment should be considered (Fernando et al., 2016).
      1) Propranolol is the primary treatment for infantile hemangiomas. The mechanism of action is unclear (Fernando et al., 2016). In cases where propranolol is contraindicated or not well tolerated, systemic corticosteroids may be used (Darrow et al., 2015). Pulsed dye laser therapy may be useful in ulcerated hemangiomas.
   f. The infant should be monitored for signs of impingement on vital organs or functioning, such as stridor, poor feeding, and difficulty in swallowing, which would make treatment necessary.
   g. The cosmetic concerns of parents require a caring, supportive approach. Pictures illustrating spontaneous regression may be helpful.
4. Compound hemangioma.
   a. Infantile hemangiomas that lie above and deep below the skin surface.
   b. It involves the dermis and subcutaneous tissue and appears as a bluish-red discoloration under the overlying skin.

c. The compound hemangioma has poorly defined borders and may feel cystic, like a "bag of worms," when palpated. Like the infantile hemangioma, the compound hemangioma will increase in size during the first 6 to 12 months and then involute spontaneously (Darrow et al., 2015).
d. Treatment is not indicated unless the lesion is interfering with vital functions, including airway obstruction, in which case propranolol or systemic corticosteroid treatment may be helpful (Darrow et al., 2015).
e. Kasabach–Merritt phenomenon.
1) Vascular anomalies resembling a hemangioma associated with sequestration of platelets and thrombocytopenia (Haggstrom and Chamlin, 2015).
2) Treatment consists of propranolol or systemic corticosteroid therapy. Transfusions of platelets and blood are frequently necessary (Darrow et al., 2015; Haggstrom and Chamlin, 2015). The lesion may resolve spontaneously.
3) Significant bleeding or impingement of vital organs may occur (Haggstrom and Chamlin, 2015).
f. Klippel–Trenaunay–Weber syndrome.
1) Syndrome consists of cutaneous capillary malformations such as a port-wine stain, hypertrophy of a limb with associated vascular anomalies, and hypertrophy of underlying bone and soft tissue (Rahimi et al., 2017; Volz et al., 2016).
2) No specific treatment for the disease other than treating individual symptoms such as pain. Severe limb hypertrophy may require orthopedic consultation, with possible amputation of the affected limb. Pulsed dye lasers have been used with some success (Rahimi et al., 2017).

E. **Infectious lesions.**
1. Thrush.
a. A fungal infection of the mouth or throat caused by *Candida albicans*.
b. Very common in infants.
c. Manifested as patches of adherent white material scattered over the tongue and mucous membranes.
d. Treated with an oral antifungal preparation such as nystatin (Mycostatin).
2. *Candida* diaper dermatitis.
a. Fungal infection of skin in the diaper area; may include buttocks, groin, thighs, and abdomen.
b. Caused by *C. albicans*.
c. Manifested as a moist, erythematous eruption, often with white or yellow satellite pustules.
d. Treatment consists of an antifungal cream or ointment preparation, such as nystatin, applied to the rash several times per day. Oral antifungal treatment may be recommended in cases of persistent *Candida* dermatitis.
3. Systemic *Candida* infection.
a. Very low birth weight infants are at risk of having systemic, invasive fungal infections, with invasion of the fungus beyond the stratum corneum.
b. Improving the barrier function of the skin by minimizing trauma and maintaining a sterile environment may help prevent onset of this infection.
4. Herpes.
a. Neonatal herpes simplex infection is a significant viral infection in the neonate.
b. Rash appears as vesicular or pustular rash (Fig. 36.12).
c. Seventy percent of infants with herpes will have subsequent rash but not necessarily before other signs and symptoms of illness develop. Therefore, the absence of vesicles does not eliminate the possibility of disease (Baley and Gonzales, 2015).
d. Treatment with an antiviral agent, such as acyclovir, should begin immediately when vesicles are noted or disease is suspected. The earlier treatment is begun, the better the outcome (Baley and Gonzales, 2015).
5. Scalded skin syndrome (also known as bullous impetigo, toxic epidermal necrolysis, Ritter's disease, and nonstreptococcal scarlatina).
a. An inflammatory skin disorder generally caused by the phage strain of group II *Staphylococcus aureus*. May follow an upper respiratory tract infection or otitis media.
b. Manifested as a widespread, tender erythema, followed by blisters ranging from small vesicles to large bullae. Caused by the release of an endotoxin that acts on the stratum granulosum of the

Fig. 36.12 Herpes simplex vesicles in axilla. *(Courtesy Jane Deacon, RNC, MS, NNP, The Children's Hospital, Denver, CO.)*

epidermis. The blisters, which frequently begin in the diaper area and spread to the rest of the body, rupture, leaving large, raw, scaldlike areas.

c. Treatment includes isolation and aseptic handling to prevent further infection in the infant and the spread of bacteria to others. The infant is treated systemically with antibiotics. Many of the strains in the phage strain of group II *S. aureus* are resistant to penicillin, so methicillin or vancomycin may be required. A topical antibiotic ointment, such as bacitracin, may be applied locally (Hennigan and Riley, 2016).

6. Congenital viral infection.
   a. Petechiae and purpuric macules erupt on the head, trunk, and extremities of affected infants. The lesions are often described as "blueberry muffin" spots and are caused by dermal erythropoiesis (Fig. 36.13).
   b. The lesions generally disappear in 2 to 3 weeks. Treatment is based on the underlying disorder.
   c. Although the lesions are most often associated with rubella, they are also seen in association with other congenital infections, such as cytomegalovirus, toxoplasmosis, syphilis, and herpes.
   d. Affected infants may also have growth restriction, jaundice, hepatosplenomegaly, and thrombocytopenia (Baley and Gonzales, 2015).

F. **Hereditary and miscellaneous lesions.**

1. Epidermolysis bullosa (EB).
   a. Disease characterized by the formation of vesicles and bullae over various parts of the body. Skin is extremely fragile. The underlying genetic defect may be autosomal dominant or recessive, with four major subtypes having been identified: EB simplex (EBS), junctional EB (JEB), dystrophic EB (DEB), and Kindler syndrome (Bruckner and O'Regan, 2015; Hoath and Narendran, 2015). Subtype diagnosis is made by skin biopsy. All subtypes have a range of severity in the lesions that present.
   b. Vesicles may appear spontaneously or in response to minor trauma such as routine handling. In all subtypes, vesicles and bulla may appear from simple skin friction.
   c. Lesions may appear at birth or a few weeks later.
   d. Esophageal lesions may also occur. The life span of severely affected patients is generally short. Treatment is supportive care, minimizing trauma and infection (Bruckner and O'Regan, 2015).
2. Collodion baby.
   a. Term describes an appearance rather than a disease. These babies are born covered with a tight, shiny, transparent membrane that cracks and peels off after a few days. An abnormal epithelium then appears with varying severity (Hoath and Narendran, 2015). Up to 20% will have normal skin after exfoliation (Kane et al., 2017) (Fig. 36.14).
   b. Treatment consists of liberal application of sterile olive or mineral oil several times a day to hydrate and lubricate the skin, careful handling, a humidified environment, and prevention of infection.

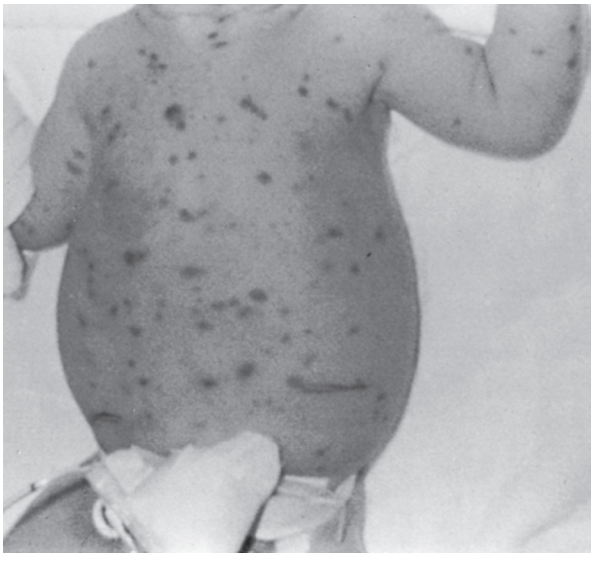

Fig. 36.13 "Blueberry muffin" rash. *(From Clark, D. [2000]. Atlas of neonatology [p. 56]. Philadelphia, PA: W. B. Saunders.)*

Fig. 36.14 Collodion infant. *(From Solomon, L. M., & Esterly, N. B. [2001]. Neonatal dermatology [p. 115]. Philadelphia, PA: W. B. Saunders.)*

3. Ichthyosis.
   a. Ichthyosis is a disease involving excessive scaling of the skin caused by excessive production of stratum corneum cells or faulty shedding of the stratum corneum (Foley et al., 2015). There are four types of ichthyosis.
      1) Ichthyosis vulgaris: an autosomal dominant disease, usually appearing after 3 months of age. This is the most common and most benign of the ichthyosis disorders, occurring in approximately 1 in 250 infants (Kane et al., 2017). It consists of fine white scales and excessively dry skin due to an abnormal granular layer of the epidermis (Kane et al., 2017). Moisturizing emollients and keeping the skin hydrated are the main treatments.
      2) X-linked ichthyosis: an X-linked recessive disorder caused by reduced or absent steroid sulfatase due to a deletion of the *STS* gene on chromosome Xp22.32 (Kane et al., 2017). It appears at birth or during the first year of life. It occasionally occurs in a collodion baby. The disorder consists of large, thick, dark brown scales over the entire body, with the exception of the palms and soles. Keeping the skin well hydrated and use of emollients are recommended.
      3) Lamellar ichthyosis: an autosomal recessive trait that is manifested at birth as bright red erythema and universal desquamation. Some infants resemble collodion babies. Scales are large, flat, and coarse and may be less prominent in infancy than later in childhood. Eversion of the lips and eyelids may occur, and the palms and soles may be thickened. Hyperkeratosis may be seen on skin biopsy, although this is not diagnostic of the disorder (Kane et al., 2017). Blockage of sweat glands by hyperkeratosis may impair sweating and increase the risk of overheating.
      4) Bullous ichthyosis: autosomal dominant disorder characterized by recurrent formation of bullous lesions, erythroderma, and excessive dryness and peeling. As the child grows, the involvement generally becomes limited to small, thick, hard scales, most often found in the flexure regions. Hyperkeratosis may be seen on the palms and soles. Infection in the neonatal period with *S. aureus* is of primary concern because of the widespread skin breakdown (Avril and Riley, 2016).
   b. Treatment of ichthyosis is limited to use of topical preparations to hydrate and lubricate the skin. Daily baths with a water-dispersible bath oil, with use of alpha-hydroxy acid ointments, may be helpful (Kane et al., 2017).
   c. Drying soaps and detergents should be avoided.
   d. Optimal nutrition is essential (Avril and Riley, 2016).
   e. Care must be taken to prevent infection of dry or cracked skin.
4. Harlequin fetus.
   a. The harlequin fetus previously was considered to have a severe form of ichthyosis but is, in fact, a rare autosomal recessive mutation in the *ABCA12* gene (Kane et al., 2017). The harlequin fetus has hard, thick, gray or yellow scales that cause severe deformities of skeletal and soft tissues.
   b. The condition is untreatable, and most infants die within a few hours or days of life.
5. Cutis aplasia.
   a. Term refers to congenital absence of skin, either as a midline defect, a posterior scalp defect, or several small or large defects involving the upper and lower extremities (Fig. 36.15).
   b. Lesions heal slowly over several months, leaving a hypertrophic or atrophic scar.
   c. May be associated with other defects, such as cleft lip and palate, heart disease, tracheoesophageal fistula, and other midline defects. It is seen in approximately 50% of infants with trisomy 13 (Jones et al., 2013).

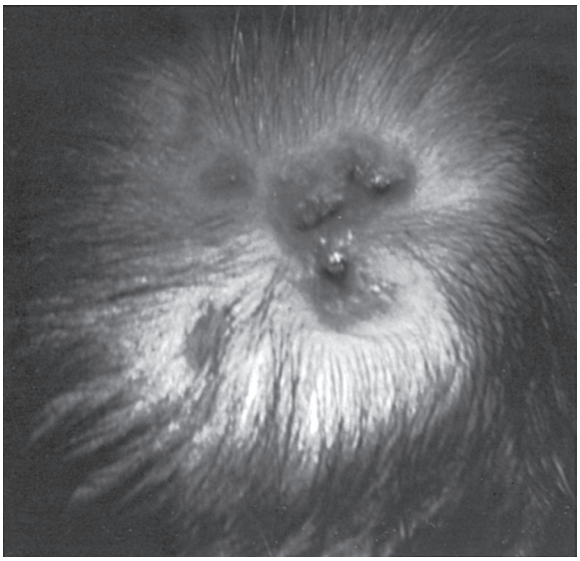

Fig. 36.15 Cutis aplasia. *(Courtesy Jacinto Hernandez, MD, The Children's Hospital, Denver, CO.)*

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CHAPTER 37

Ophthalmologic and Auditory Disorders

Debbie Fraser and William Diehl-Jones

OBJECTIVES

1. Describe the normal anatomy of the eye.
2. Identify the normal anatomy of the ear.
3. Identify the major function(s) of each structure.
4. Describe the components of a nursing assessment of the eyes and ears in the neonate.
5. Describe the nurse's role in assisting the physician with neonatal eye examinations.
6. Discuss the factors to consider in universal hearing screening of newborns.
7. Discuss each of the seven types of eye disorders in the neonatal period—traumatic injuries to the eye, conjunctivitis, nasolacrimal duct obstruction, cataracts, retinoblastoma, infections (TORCH diseases), and retinopathy of prematurity—there is (1) an overview of the pathogenesis and (2) a description of the commonly used treatment modalities, outlining the specific nursing care measures designed to meet the needs of neonates with these disorders.
8. Outline the most common causes of hearing loss in the newborn.
9. Outline teaching points for the family of a newborn at risk for hearing or vision problems.

An examination of the neonate's eyes and ears is an important, though often neglected, portion of a physical assessment. There is a great deal of clinically significant information that the astute nurse can glean from a thorough evaluation of these systems. Evidence of intrauterine infection, birth trauma, congenital malformations, disease, and a variety of genetic abnormalities can be detected during the nurse's assessment of the neonate's eyes and ears.

This chapter provides the neonatal nurse with a review of the following: normal anatomy of the eye and ear, together with the major function(s) of each structure; essential components of an assessment of the newborn's eyes and ears; an overview of the most common eye disorders in the neonate; and common treatment modalities and nursing measures used in the treatment of various ocular disorders in the newborn. The elements of a universal hearing screening program for newborns are addressed, as are the most common causes of hearing loss in neonates.

Anatomy of the Eye (Fig. 37.1)

PROTECTIVE STRUCTURES

A. **Eyelids:** shade the eyes during sleep, protect from excessive light or foreign objects, spread lubricating secretions over the eyeball.
B. **Conjunctiva:** mucous membrane lining the inner aspect of the eyelids (palpebral) and the eyeball to the periphery of the cornea (bulbar).
C. **Lacrimal system:** manufactures and drains away tears; cleans, lubricates, and moistens the eyeball.
D. **Bony orbit or socket:** surrounds and protects the eyeball. Most important opening within the orbit is the optic foramen, through which the optic nerve, ophthalmic artery, and ophthalmic vein from each eye pass en route to the brain.

THE EYEBALL

A. **Outer layer (fibrous tunic).**
   1. Cornea: transparent; reflects light rays.
   2. Sclera: the "white" of the eye; normal bluish appearance in newborns; connective tissue shell, which gives shape to the eyeball and protects the inner components.
B. Middle layer (vascular tunic): the uveal tract.
   1. Iris and pupil: a circular pigmented diaphragm with a central hole; controls the amount of light entering the eye.
   2. Ciliary body: the anterior portion of the choroid.
   3. Choroid: a vascular, pigmented membrane that lines most of the internal surface of the sclera, absorbs light rays, and nourishes the retina.
C. **Inner layer: the retina.**
   1. Extends from the ora serrata to the optic nerve.
   2. Functions in image formation. Multiple cell layers that receive, transduce, and process light:
      a. Photoreceptors (rods and cones).
      b. Bipolar cells.

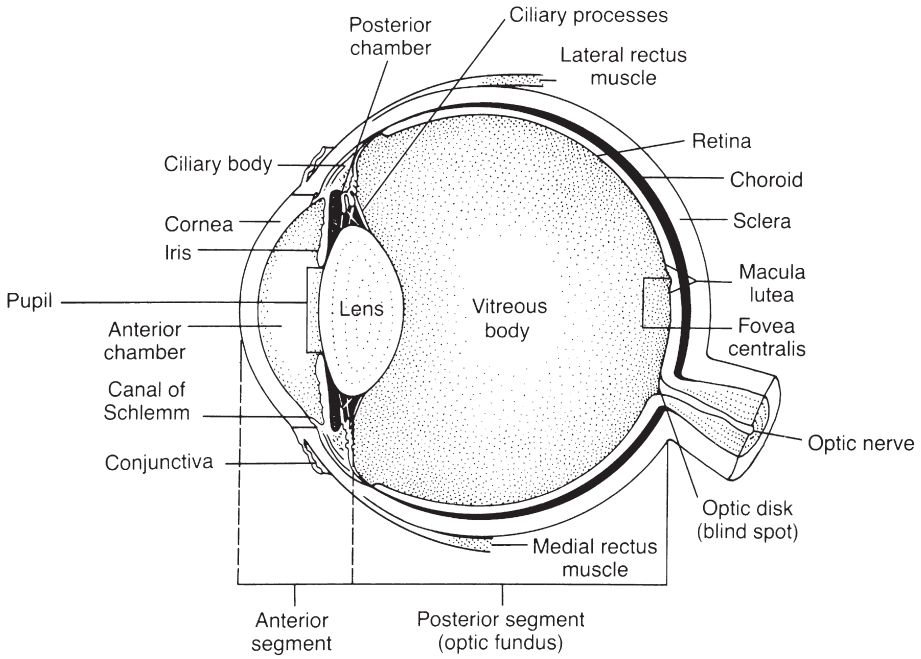

Fig. 37.1 Cross-section of eyeball. *(From Boyd-Monk, H. [1987]. The structure and function of the eye and its adnexa.* Journal of Ophthalmic Nursing and Technology, *6[5], 176–183.)*

c. Horizontal cells.
d. Amacrine cells.
e. Ganglion cells.

3. Optic disc: retinal blood vessels enter the eye, and the optic nerve exits the eye. Blind spot in field of vision because optic disc has no photoreceptors.
4. Optic nerve: second cranial nerve.
5. Macula: center of the retina; area of greatest density of photoreceptors and location of sharpest vision.

D. **Anterior cavity (filled with aqueous humor).**
1. Anterior chamber: behind the cornea, in front of the iris.
2. Posterior chamber: behind the iris, in front of the suspensory ligament and lens.
3. Ciliary body: behind lens; produces aqueous humor, which circulates to anterior chamber.
4. Canal of Schlemm: drainage duct for aqueous fluid.

E. **Lens:** a biconvex, transparent capsule that refracts light; the most important focusing mechanism of the eye.
1. Lens remains cloudy until 30 to 34 weeks of gestation.

F. **Posterior cavity (filled with vitreous humor):** lies between the lens and the retina. Contributes to intraocular pressure, gives shape to the eyeball, and holds the retina in place.

EXTRAOCULAR MUSCLES

A. **Musculature.** Six muscles move each globe. The muscles of each eye work in conjunction with each other.

B. **Innervation.** The extraocular muscles are innervated by the oculomotor (third cranial) nerve, the abducens (sixth cranial) nerve, and the trochlear (fourth cranial) nerve.
1. Pupillary reflex is functional by 36 weeks.

C. **Function** (Blackburn, 2013; Gardner et al., 2016).
1. At birth, newborns have a visual acuity of 20/400 (Standring, 2016).
2. A healthy term newborn is able to fix on an object and follow it up to 90 degrees in a horizontal arc.
3. Newborns prefer black-and-white patterns and the human face.
4. Color discrimination develops at around 3 months of age (de Alba Campomanes and Binenbaum, 2017).

Patient Assessment

HISTORY

A. **Pregnancy:** first-trimester infections (e.g., rubella), unknown rashes, fever, sexually transmitted disease, vaginal discharge, medications.

B. **Birth history:** gestational age, duration of labor, use of forceps.

C. **Family history:** incidence of ocular disorders, especially retinoblastoma; systemic diseases.

EXAMINATION (DE ALBA CAMPOMANES AND BINENBAUM, 2017; JOHNSON, 2016)

The examination is performed with the baby in a quiet, alert state. To facilitate the spontaneous eye-opening, use

an auditory stimulus, change the infant's position from supine to upright, or dim the lights (Johnson, 2016). Eye prophylaxis may make the examination more difficult.

A. **External assessment.**
   1. General facial configuration: should be symmetrical. Note distance between the eyes; hypertelorism: increased width between the eyes; hypotelorism: decreased width between the eyes.
   2. Spontaneous eye movements: note range of motion and conjugation (the ability of the eyes to move together). Infants can track and follow objects with both eyes. Erratic or purposeless movements may be observed during the first few weeks of life. Median focal distance for the term neonate is about 8 inches (20 cm).
B. **Reaction to light or visual stimuli:** strong blink reflex to bright light or stimulation of the lids, lashes, or cornea. A somewhat unsteady gaze can be observed shortly after birth, with ability to fixate on a stimulus for 4 to 10 seconds and refixate every 1 to 1.5 seconds. Ability to maintain fixation and to follow does not occur until 5 to 6 weeks of age.
C. **Pupils:** shape should be round, and reaction to light should be equal; constriction to both direct and contralateral stimulation should occur. The red reflex should be elicited bilaterally; normally appears as a homogeneous bright red-orange. Opacities or interruptions may indicate cataracts or retinoblastoma.
D. **Eyelids:** note symmetry, epicanthal folds, bruising or edema, lacerations, ptosis, and presence of lacrimal puncta.
E. **Conjunctivae:** should be pink and moist; redness or exudate is abnormal.
F. **Corneas:** may be somewhat less than transparent or slightly hazy in the first few days of life in both premature and term infants. Sclerae may be bluish in premature or small babies as a result of thinness.
G. **Irises:** should be similar in appearance; note pigmentation. A coloboma, or keyhole pupil, may be associated with congenital anomalies. Brushfield's spots are silvery gray spots scattered around the circumference of the iris—strongly associated with Down syndrome.
H. **Lenses:** should be clear and black with direct illumination. Examination of the anterior vascular capsule of the lens is a useful adjunct to determination of gestational age in preterm infants between 27 and 34 weeks.

Pathologic Conditions and Management

BIRTH TRAUMA

A. **Pathophysiology**.
   1. Direct result of duration and difficulty of delivery.
   2. Improperly applied forceps.
   3. Compression of cranial nerves.
B. **Clinical presentation.**
   1. Petechiae, ecchymoses, edema, and/or lacerations of pinna, lids, conjunctiva, or globe.
   2. Bright red patches on conjunctiva (subconjunctival hemorrhage): occurs in at least 13% of births (Pineles and Isenberg, 2016).
   3. Droopy eyelids.
C. **Complications:** These injuries are generally mild and transient, often resolving spontaneously.

CONJUNCTIVITIS

Conjunctivitis is an inflammatory reaction resulting from invasion of the conjunctivae by pathologic organisms.

ETIOLOGY

A wide variety of infectious agents are capable of producing conjunctivitis in the newborn infant. The most common causes in North America include:

A. ***Neisseria gonorrhoeae:*** peripartum transmission, onset 3 to 4 days.
B. ***Chlamydia trachomatis:*** peripartum transmission, onset 5 to 7 days.
C. ***Staphylococcus aureus:*** acquired during the neonatal period, onset 5 to 14 days.
D. **Herpes simplex:** peripartum transmission, onset 6 to 14 days.

Neisseria gonorrhoeae

A. **Incidence:** One third of neonates born vaginally to infected women develop ophthalmic gonococcal infection (Embree, 2016). May be higher in areas with poor perinatal care or irregular antibiotic eye prophylaxis after birth.
B. **Onset of symptoms of infection:** usually between days 3 and 4 of life.
C. **Clinical presentation.**
   1. Edema of the eyelids.
   2. Purulent discharge.
   3. Redness/hyperemia of the conjunctivae.
D. **Diagnostic findings.**
   1. History.
      a. Maternal history of sexually transmitted disease.
      b. Age at onset of infection.
   2. Physical examination.
      a. Clinical signs of inflammation.
      b. Purulent discharge.
   3. Laboratory.
      a. Gram stain shows gram-negative diplococci.
      b. Culture positive for gonococci from conjunctival surface or exudate.
E. **Nursing care.**
   1. Isolate infant in accordance with infection control guidelines.
   2. Irrigate eyes with sterile normal saline solution hourly until discharge is eliminated.

3. Promptly administer appropriate systemic therapy. Topical antimicrobial therapy is not required.
   a. Penicillin-sensitive *N. gonorrhoeae*: aqueous crystalline penicillin G, intravenous (IV) or intramuscular (IM), for 10 days (Pammi et al., 2016).
   b. Penicillin-resistant *N. gonorrhoeae*: ceftriaxone, 25 to 50 mg/kg (maximum 125 mg) IV or IM in a single daily dose (de Alba Campomanes and Binenbaum, 2017).
4. Parents of infected infant should be referred for evaluation and treatment.

F. **Complications**.
1. Infants with gonococcal conjunctivitis are at risk of having corneal ulceration, perforation, and subsequent visual impairment.
2. Systemic complications involving the blood, joints, or central nervous system may occur in a small number of infants.

Chlamydia trachomatis

A. **Incidence**.
1. The most common cause of conjunctivitis in the neonatal period, especially in areas with poor perinatal care or irregular administration of erythromycin eye prophylaxis after delivery. Chlamydial eye infections occur in up to 1% of births in developed countries (Pineles and Isenberg, 2016).
2. About 20% to 50% of babies born vaginally to mothers with a *C. trachomatis* infection of the cervix will develop conjunctivitis; 5% to 20% develop pneumonia (Darville, 2016).
3. Prevention of infection in the newborn infant is dependent on prenatal detection and treatment of the mother or on the use of an effective form of eye prophylaxis at birth (e.g., erythromycin ointment).

B. **Onset:** Symptoms are usually observed between 5 and 7 days of age.

C. **Clinical presentation:** Symptoms vary from mild conjunctivitis to intense edema of the lids with purulent discharge. A pseudomembrane may be present over the conjunctiva.

D. **Diagnostic findings.**
1. Identification of *Chlamydia* antigen.
2. Stains of conjunctival scrapings.
3. Culture of conjunctival scrapings.

E. **Patient management.**
1. Therapy of choice is oral erythromycin (estolate preparation) for 14 days (Darville, 2016).
2. Topical therapy alone is inadequate to eradicate the organism from the upper respiratory tract.
3. Parents of infected infants should be referred for evaluation and therapy.

F. **Complications:** Infection is spread via the nasolacrimal system to the nasopharynx, leading to *Chlamydia*-related pneumonia.

NASOLACRIMAL DUCT OBSTRUCTION

A. **Pathophysiology**.
1. Lacrimal apparatus consists of glandular tissues that produce tears (lacrimal glands) and structures responsible for drainage of tears (upper and lower puncta, canaliculi, lacrimal sac, and nasolacrimal duct). System functions to clean, lubricate, and moisten the eyeball.
2. Term and preterm newborn infants have the capacity to secrete tears (reflex tearing to irritants) but usually do not secrete emotional tears until 2 to 3 months of age.
3. Congenital obstruction is usually caused by an imperforate membrane at the distal end of the nasolacrimal duct.
4. Congenital nasolacrimal obstruction is the most common abnormality of the neonate's lacrimal apparatus. Incidence of this condition is about 5% of all newborns (de Alba Campomanes and Binenbaum, 2017).

B. **Clinical presentation.**
1. Usually within the first few weeks of life.
2. Persistent tearing (epiphora): need to rule out congenital glaucoma.
3. Crusting or matting of the eyelashes: "sticky eye."
4. Spilling of tears over the lower lid and cheek: a "wet look" in the involved eye(s).
5. Absence of conjunctival infection.
6. Mucopurulent material refluxing from either punctum when gentle pressure is applied over the involved nasolacrimal sac.

C. **Nursing care.**
1. Conservative management, with daily massage of the nasolacrimal sac in an attempt to rupture the membrane at the lower end of the duct.
2. Technique consists of placing the index finger over the common canaliculus to block the exit of material through the puncta and stroking downward firmly.
3. Digital pressure increases hydrostatic pressure in the nasolacrimal sac, which may cause a rupture of the membranous obstruction.
4. If a mucopurulent discharge is present, antibiotic eyedrops (sodium sulfacetamide) or ointment (erythromycin) may be required.
5. Cleansing of eyes: eyes should be cleaned with moist compresses, with secretions mechanically removed.
6. Duration of conservative management: conservative management is advocated for the first year of life.
7. Resolution: the majority of nasolacrimal obstructions resolve spontaneously or with massage by 1 year of age.

8. Surgical treatment: unresolved obstructions can be successfully treated surgically; tear duct probing is done, with the infant under general anesthesia, after the first year of life.

D. **Complications**.
1. Acute dacryocystitis: inflamed, swollen lacrimal sac.
2. Fistula formation.
3. Orbital or facial cellulitis.

CATARACTS

Congenital cataracts are the main treatable cause of visual impairment in infancy. To ensure optimal visual development, congenital cataracts should be surgically removed within 6 weeks of birth (de Alba Campomanes and Binenbaum, 2017).

A. **Pathophysiology**.
1. Lens: the lens is a biconvex, transparent capsule that refracts light. It is the most important focusing mechanism of the eye.
2. Cataract: a cataract is an opacity of any size or degree in the lens of the eye.
3. Path of light: normally the light from an object passes directly through the lens to a focal point on the retina, producing a sharp image. Cataracts result in a degraded image or no image at all.
4. Visual impairment: cataracts lead to varying degrees of visual impairment, from blurred vision to blindness, depending on the location and extent of the opacity. In neonates, cataracts may be transient, disappearing spontaneously within a few weeks.

B. **Etiology or precipitating factors.**
1. Idiopathic (30%): developmental variation, not associated with other abnormalities.
2. Genetically determined (30%): most common mode of inheritance—autosomal dominant.
3. Congenital rubella: cataracts are present in one third of newborns with congenital rubella syndrome (Reef and Plotkin, 2016).
4. Other congenital infections.
   a. Toxoplasmosis.
   b. Cytomegalovirus (CMV) infection.
   c. Herpes simplex.
   d. Varicella.
5. Metabolic disorders (e.g., galactosemia).
6. Chromosomal abnormalities (e.g., Down syndrome, trisomy 13, Turner's syndrome).
7. Clinical syndromes (e.g., Crouzon's disease, Pierre Robin syndrome).
8. Prematurity.

C. **Clinical presentation.**
1. White pupil (leukocoria).
2. Searching nystagmus (at 1 to 2 months of age). The presence of nystagmus is a marker for poor visual prognosis.

D. **Diagnostic findings.**
1. History.
   a. Family history of ocular disease or systemic disorders.
   b. Pregnancy, especially first-trimester intrauterine infections.
2. Physical examination.
   a. Normally, when light is directed at the pupils, they appear black to the naked eye of the examiner.
   b. Examine to detect a white pupil by shining a light into each eye, with the light source held to one side.
   c. If the opacity is small, it may be identified only when the pupils are dilated and with the use of an ophthalmoscope.
   d. Consider other diseases of the eye that may produce a white pupil (e.g., retinoblastoma).

E. **Nursing care.**
1. Eye examination: assist the physician in carrying out a thorough eye examination of the newborn. This includes administering drops to dilate the pupils before the examination and supporting the infant's head to facilitate examination.
2. Parental education: in collaboration with the physician, assist parents in understanding the nature, possible cause, and treatment of cataracts in the newborn infant, together with the prognosis for future vision. Surgery is indicated whenever the cataract is likely to interfere with vision.
3. Explore any feelings of guilt the parents may have in relation to the cause of the cataracts; provide appropriate support.
4. Encourage parent–infant attachment: neonate may not be able to see the parents but can learn to recognize their voices, smell, and touch.
5. Care for the patient postoperatively.
   a. Prevent increased intraocular pressure. Keep the neonate comfortable, well fed, and free of pain to decrease crying.
   b. Administer eyedrops or ointments as ordered postoperatively.
   c. Apply clean eye patches or protective shields to protect the eye from rubbing or bumping and to prevent irritation from light.
   d. Monitor for complications of cataract surgery. These are relatively infrequent but include infection within the eye, glaucoma, and retinal detachment. Note any increased redness or haziness of the eye, increased tearing, photophobia, or cloudiness of the cornea. Increased crying, irritability, disruption in sleeping patterns, or rubbing of the eye may indicate pain.
   e. Assist the parents in understanding the essential role of optical correction devices, such as glasses or contact lenses, in their infant's vision and development.

f. Promote appropriate visual stimulation and foster normal infant development by teaching parents about newborn visual preferences (e.g., black-and-white contrast or medium-intensity colors, the human face, geometric shapes, checkerboard designs).

F. **Complications**.
1. Varying degrees of visual impairment, leading to developmental delay.
2. Presence and/or severity of associated ocular defects, such as microphthalmos and glaucoma.

G. **Outcome.** Visual prognosis depends not only on the extent of cataracts, age at removal, surgical outcome, and rapid optical correction but also on the nature of other associated anomalies of the eye or syndromes.

RETINOBLASTOMA
(DE ALBA CAMPOMANES AND BINENBAUM, 2017)

Retinoblastoma is the most common ocular malignancy in children, with an incidence of 1 in 15,000 to 20,000 live births.

A. **Clinical presentation.**
1. Leukocoria (54%).
2. Strabismus (19%).
3. Loss of visual acuity (4%).
4. Red eye (5%).

B. **History**.
1. Family history of retinoblastoma.

C. **Physical examination.**
1. Examine for presence of red reflex and to detect a white pupil.
2. Consider congenital cataracts as an alternative cause of leukocoria.

D. **Treatment**.
1. Enucleation.
2. Chemotherapy.
3. Focal destruction of the lesion.

E. **Complications**.
1. Loss of vision in the affected eye.
2. Survival is greater than 90% with early recognition and treatment.
3. Long-term survival is 50% if spread outside the eye has occurred.

CONGENITAL INFECTIONS

The developing eyes are highly vulnerable to the damaging effects of prenatal infection (de Alba Campomanes and Binenbaum, 2017), and ocular abnormalities may in fact be the predominant manifestation of the disease. A number of the congenitally acquired infections are associated with abnormal ocular conditions, including cataracts, chorioretinitis, corneal opacities, and glaucoma. The most common of these infections are toxoplasmosis, rubella, CMV, and herpes (see also Chapter 32).

CONGENITAL RUBELLA SYNDROME

In the prevaccine era, rubella was a common childhood infection. Since the introduction of vaccinations, congenital rubella syndrome occurs infrequently. Between 2001 and 2006, only four cases of congenital rubella syndrome were reported in the United States (Baley and Gonzalez, 2015).

A. **Pathophysiology**.
1. Timing of infection: consequences of the transplacental infection are determined primarily by the timing of the viral insult.
2. Infection in the first trimester of pregnancy presents the greatest hazard to organogenesis, including that of the eyes.

B. **Incidence.** Ocular abnormalities are frequently seen in congenital rubella, with "salt-and-pepper" retinopathy being the most common ocular abnormality (Reef and Plotkin, 2016).

C. **Clinical presentation.**
1. Gestational age: Findings in the infant exposed to rubella in utero depend on the gestational age at which the infection occurred.
2. Ocular manifestations.
   a. Cataracts: in approximately 30% of patients.
   b. Pigmentary retinopathy.
   c. Microphthalmos.
   d. Glaucoma.
3. Other common manifestations include severe hearing loss, intrauterine growth restriction, hepatomegaly, thrombocytopenia, and cardiac anomalies (see also Chapter 32).

D. **Nursing care.**
1. Virus shedding may continue for months after birth. Infants with suspected congenital rubella should be isolated from other newborn infants and from pregnant women (both in the hospital and at home after discharge).
2. See E. Nursing care, under Cataracts.

E. **Outcome**.
1. Prognosis: depends on severity of symptoms and number of organ systems involved.
2. Mortality rate: in first year of life may approach 80% when multisystem involvement occurs.
3. Multiple disabilities: common in surviving infants.
4. Consequences of congenital rubella: may not be evident at birth but may become apparent in subsequent months.

CYTOMEGALOVIRUS

A. **Pathophysiology**.
1. CMV can cause a perinatal viral infection.
2. Congenital illness is most severe if infection occurs early in pregnancy, the period of greatest susceptibility of the developing fetus. Congenital infections can result from either a primary or recurrent maternal infection.

B. **Etiology**.
   1. Ubiquitous virus: CMV can cause infection in all age groups.
   2. Route of transmission: Infection may be acquired transplacentally, during birth (via the cervix), or through breast milk. In seropositive mothers, the risk of transmission through breast milk is 30% to 59%.
   3. Transfusion: An important possible cause of morbidity in premature infants is transfusion-acquired CMV. All premature infants should receive seronegative blood products.

C. **Incidence**.
   1. The most common congenital viral infection, affecting 0.15% to 2% of all newborns in the United States (Baley and Gonzalez, 2015).
   2. In the presence of primary acute maternal infection, 30% to 40% of fetuses are affected (Baley and Gonzalez, 2015).

D. **Clinical presentation.**
   1. A diagnosis of congenital CMV infection can rarely be made on the basis of clinical findings alone. Only 5% to 10% of neonates infected with CMV will have symptoms at birth. When symptomatic CMV is present, disseminated disease can occur involving all major organ systems.
   2. Laboratory diagnostic methods (e.g., isolation of the virus from the urine) must be used if this condition is suspected.
   3. Chorioretinitis is present in 10% to 20% of infants with symptomatic CMV (Britt, 2016).
   4. Other eye abnormalities include conjunctivitis, microphthalmos, strabismus, cataracts, and optic atrophy.
   5. Other manifestations include intrauterine growth restriction, microcephaly, hepatosplenomegaly, jaundice, and bleeding disorders (see also Chapter 32).

E. **Nursing care.**
   1. Limited research suggests some benefit from IV ganciclovir or oral valganciclovir.
   2. Use of gowns and good handwashing technique are essential to prevent the spread of infection.
   3. Seronegative pregnant women should not care for infants with known or suspected infection.
   4. These infants require long-term follow-up.

F. **Complications**.
   1. Cytomegalic inclusion disease.
   2. Sensorineural hearing loss, the most important late sequela, and the most common cause of congenital nonfamilial hearing loss (Britt, 2016).
   3. Chorioretinitis or optic atrophy.

G. **Outcomes**.
   1. Mortality rate: overall mortality rate for symptomatic congenital infection is up to 30% (Britt, 2016).
   2. In 10% to 15% of infants who are free of symptoms at birth, neurologic sequelae, such as microcephaly, neurodevelopmental delay, or sensorineural deafness, may develop in the first 2 years of life.

TOXOPLASMOSIS (PEYRON ET AL., 2016)

A. **Pathophysiology.** Fetal damage occurs as a direct result of inflammation caused by the presence of cysts in the tissues, including the eyes.

B. **Etiology.**
   1. Maternal infection by the protozoan *Toxoplasma gondii* in the first and second trimesters of pregnancy is often associated with transplacental infection of the fetus.
   2. Infection is acquired through contact with the excrement of infected cats and ingestion of improperly cooked meat.

C. **Incidence**.
   1. The incidence of maternal infection varies considerably according to geographic location. Estimates in the U.S. population suggest a seroconversion rate of between 2 and 10 in 1000 during pregnancy (Peyron et al., 2016).
   2. The risk of transmission for an infection acquired during pregnancy averages 30% and increases with gestational age (Peyron et al., 2016).

D. **Clinical presentation.**
   1. Congenital *T. gondii* may be present at birth, in the first few months of life, or with sequelae from a previously undiagnosed infection.
   2. Eighty percent to 90% of infected infants are symptomatic at birth (Peyron et al., 2016).
   3. Chorioretinitis is the most common manifestation (Peyron et al., 2016).
   4. Other manifestations include hydrocephalus, intracranial calcifications, hepatosplenomegaly, jaundice, and bleeding disorders (see also Chapter 32).

E. **Specific nursing care.**
   1. Nursing care includes pharmaceutical treatment of *Toxoplasma* infection by administering sulfadiazine and pyrimethamine. These agents will eradicate the cysts and improve outcome but may not reverse the damage already done.
   2. Give supportive care to the family, with sensitivity to feelings of guilt they might have.
   3. Teach parents to recognize the signs of sequelae, including visual impairment in infancy (e.g., failure to fix and focus on objects or faces).

F. **Outcome**.
   1. Prognosis for infants with congenital infection is markedly improved with prompt initiation of treatment.
   2. Eighty percent of treated infants with moderate to severe disease have normal psychomotor development.

3. Recurrent eye lesions develop in 10% of treated infants with mild disease and in up to 30% of treated infants with moderate or severe disease.

RETINOPATHY OF PREMATURITY

Retinopathy of prematurity (ROP) is a vasoproliferative retinopathy that occurs primarily in low birth weight infants (Fierson et al., 2013).

A. **Pathophysiology**.
   1. Human retina is avascular until 16 weeks of gestation. After this time, a capillary network begins to grow, starting at the optic nerve and branching outward toward the ora serrata (edge of the retina).
   2. Nasal periphery is vascularized by about 32 weeks of gestation, but the process is not complete in the more distant temporal periphery until 40 to 44 weeks. Most cases of ROP begin at 31 to 32 weeks of gestation.
   3. After premature birth, this process of normal vasculogenesis may be arrested as a result of injury from some noxious agent(s) or stressor(s).
   4. Vasoproliferation: The arrest of normal vasculogenesis is later followed by a phase of rapid, excessive, irregular vascular growth and shunt formation (vasoproliferation), stimulated by vascular endothelial growth factor (VEGF) and stromal cell–derived factor 1α (SDF-1α).
   5. Area of new growth generally forms an abrupt ridge between the vascular and avascular retina, particularly in the temporal periphery.
   6. ROP may resolve if the vasculature in the area recovers and resumes advancing normally, allowing the retina to become completely vascularized.
   7. If the new vasculature proceeds to develop abnormally, these capillaries may extend into the vitreous body and/or over the surface of the retina (where they do not belong). Leakage of fluid or hemorrhage from these weak, aberrant blood vessels may occur.
   8. Blood and fluid leakage into various parts of the eye can result in scar formation and traction on the retina.
   9. Traction may pull the macula out of its normal position, thus affecting visual acuity. If the macula is slightly out of position, vision will be mildly affected.
   10. Tractional exudative retinal detachment results in blindness.

B. **Etiology**.
   1. Complex multifactorial disorder.
   2. Possible risk factors (de Alba Campomanes and Binenbaum, 2017; Owen et al., 2017; Sun et al., 2015).
      a. Prematurity/low birth weight: most important clinical factor associated with ROP.
      b. Supplemental oxygen, hypoxia, and hyperoxia.
      c. Pulmonary insufficiency.
      d. Growth hormone deficiency.
      e. Ventilator support.
      f. Asphyxia/acidosis/shock.
      g. Blood transfusions.
      h. Steroid exposure.
      i. Sepsis.
      j. Patent ductus arteriosus.
      k. Intraventricular hemorrhage/seizures.
      l. Nutritional deficiencies, such as vitamin E and vitamin A.
      m. Hyperglycemia.
      n. Prenatal complications such as preeclampsia.
      o. Gender—ROP is more common in males.

C. **Incidence**.
   1. Incidence of ROP appears to increase significantly as birth weight and gestational age decrease. Over 80% of infants born at less than 26 weeks' gestation will develop some form of ROP compared with only 50% at 29 weeks (Sun et al., 2015).

D. **Stages of retinopathy.**
   1. Standardized approach for describing ROP, developed by the International Committee for the Classification of Retinopathy of Prematurity (2005) according to five stages.
      a. Stage 1: demarcation line within the plane of the retina separating the avascular and vascular retinal regions.
      b. Stage 2: ridge or elevation at the junction of the avascular and vascularized regions of the retina.
      c. Stage 3: ridge with extraretinal fibrovascular proliferation, either:
         1) Continuous with the posterior edge of the ridge.
         2) Posterior but disconnected from the ridge.
         3) Into the vitreous.
      d. Stage 4: subtotal retinal detachment.
         1) Extrafoveate.
         2) Involving the foveae.
      e. Stage 5: total retinal detachment.
   2. Aggressive posterior ROP: significant dilation and tortuosity of posterior pole vessels, present in zone I or II.
   3. "Plus" disease: an indicator of activity. Signs (in increasing order of severity) include:
      a. Engorgement and tortuosity of vessels of the posterior pole in two or more quadrants.
      b. Iris vessel engorgement.
      c. Pupil rigidity.
      d. Vitreous haze.
   4. Pre–plus disease: abnormal vessels, dilation and tortuosity in two or more quadrants not yet sufficient for a diagnosis of plus disease.
   5. Zones for classification of ROP (Fig. 37.2).
      a. Zone I: extends from the optic disc to twice the disc–foveal distance—a radius of 30 degrees.

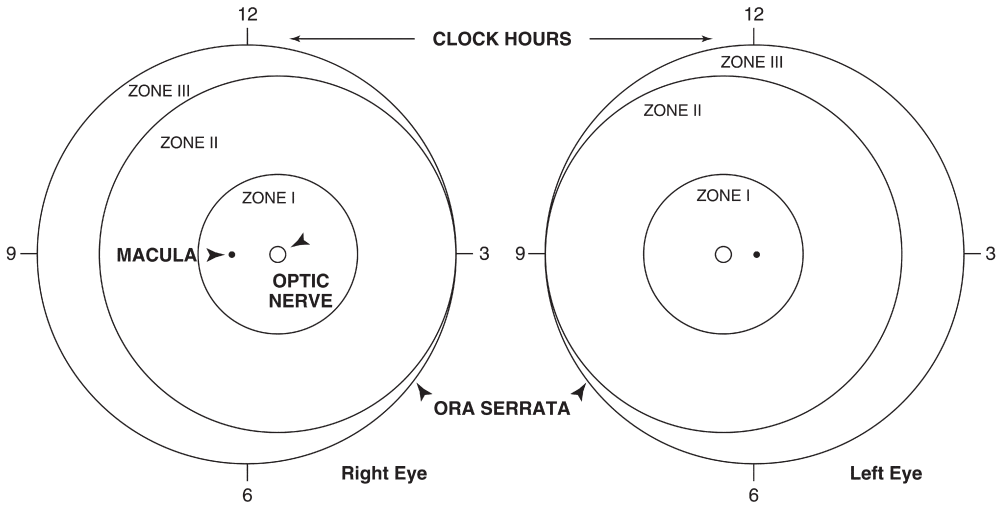

Fig. 37.2 Zones in retinopathy of prematurity. *(From George, D. S. [1988]. The latest on retinopathy of prematurity.* MCN: American Journal of Maternal Child Nursing, 13*[4], 254–258.)*

b. Zone II: extends from the periphery of the nasal retina (ora serrata) in a circle around the anatomic equator.
c. Zone III: anterior to zone II; present temporally, inferiorly, and superiorly but not in the nasal retina.

E. **Physical examination.**
1. All infants born at less than 30 weeks of gestation or with a birth weight of less than 1500 g and selected high-risk infants between 1500 and 2000 g or gestational age greater than 30 weeks with an unstable clinical course should have their eyes examined by a trained pediatric ophthalmologist when in stable clinical condition, 4 to 6 weeks after birth (approximately 31 to 33 weeks of postconceptional age) (Fierson et al., 2013). Infants born at less than 25 weeks of gestation may benefit from an ROP screen before 31 weeks to detect early aggressive ROP (Fierson et al., 2013).
2. Dilation of pupils: Infant's pupils should be dilated with a mydriatic agent before examination to facilitate optimal evaluation. Cycloplegic mydriatic agents (e.g., cyclopentolate, tropicamide) have rapid onset of action, with peak ophthalmic effects between 20 and 60 minutes. The excess eyedrops should be wiped away promptly to avoid systemic absorption. Absorption can also be minimized by applying gentle pressure over the nasolacrimal duct for 1 minute after instillation of the eyedrops. It is necessary to protect eyes from bright light after mydriasis. Assess for symptoms of systemic absorption (e.g., tachycardia, restlessness) and notify physician immediately if symptoms are present.
3. Documentation: Location and extent of any retinopathy should be precisely documented and classified according to the guidelines developed by the International Committee for the Classification of Retinopathy of Prematurity (2005).
4. Follow-up.
   a. Infants who are found to have areas of retinal immaturity on initial examination should have repeated examinations every other week and, subsequently, every 2 to 3 weeks until vascularization has reached the ora serrata.
   b. If ROP is present during the initial examination, the infant should be examined weekly or every other week, depending on the severity of clinical findings.

F. **Prevention**.
1. Precautions while using oxygen: Although the role of oxygen in the pathogenesis of ROP is unclear, cautious and judicious administration and monitoring of oxygen remains one possible preventive measure.
   a. Continuous assessment and monitoring of the infant receiving oxygen to control arterial oxygenation. Cautious administration of oxygen while carrying out nursing procedures such as suctioning.
   b. Ongoing assessment of the oxygen delivery system, including calibration of oxygen analyzers, monitoring fractional inspired oxygen, checking/recording ventilator settings, circuit, and oxygen saturation monitors.
   c. Use of oxygen blenders to deliver precise oxygen concentrations.
   d. Lowering oxygen saturation alarm limits may decrease the incidence of ROP, but may increase mortality (Fang et al., 2016).
2. Sensory stimulation: Provide a variety of forms of sensory stimulation to the infant, appropriate to level of development and behavioral cues.

3. Assessment: Assess newborn's ability to fix and focus.
4. Assistance: Assist the physician in carrying out a safe, minimally stressful eye examination of the newborn.
5. Protection against bright light: Protect the infant's eyes from bright light by shielding the incubator with a blanket and reducing the light in the nursery. The use of eye pads should be evaluated according to the principles of developmental care.
6. Parent education: Provide accurate parent education about the possibility of ROP (when parents are ready to receive information about potential non–life-threatening complications). Ensure that parents understand the importance of timely and appropriate follow-up (Fierson et al., 2013).
7. Follow-up: Unit-specific procedures for ensuring appropriate screening and follow-up should be in place and communicated to all members of the health care team, including those responsible for care after discharge.

G. **Treatment**.
1. Timing of treatment: Ablative treatment may be initiated for the following (Fierson et al., 2013):
   a. Zone I ROP: any stage with plus disease.
   b. Zone I ROP: stage 3 with no plus disease.
   c. Zone II: stage 2 or 3 with plus disease.
   d. The number of clock hours may not always be the determining factor for the strong consideration of ablative treatment.
   e. Treatment should be started within 72 hours of the finding of treatable disease to decrease the risk of retinal detachment.
2. Laser photocoagulation.
   a. Uses either an argon or diode laser to coagulate the avascular periphery of the retina.
   b. Laser surgery can be performed in the nursery with sedation and analgesia rather than general anesthesia.
   c. Is more difficult when the retina is not readily visualized (pupils cannot be dilated, presence of hemorrhage).
   d. Has fewer systemic and ocular side effects than cryotherapy and carries less risk of damage to adjacent structures (Bashour, 2013). Is less painful than cryotherapy.
   e. Complications: cataracts (Sabri et al., 2018); burns to the cornea, iris, or lens; retinal, periretinal, or vitreous hemorrhage; photocoagulation of the fovea; and late-onset retinal detachment.
3. Nursing care for the infant undergoing laser photocoagulation.
   a. Preoperatively, the infant should be given nothing by mouth for 4 to 6 hours; phenylephrine with cyclopentolate (Cyclomydril) and sedation and analgesia should be given as ordered.
   b. Intraoperatively, monitor the baby and give medications as indicated.
   c. After laser photocoagulation, the infant's respiratory status, oxygen saturation, and vital signs should be monitored.
   d. Assess the eyes for drainage and edema.
   e. Medications such as cyclopentolate and the combination dexamethasone, neomycin, and polymyxin B sulfate (Maxitrol) may be ordered to reduce postoperative complications.
4. Cryotherapy.
   a. Although the use of cryotherapy is decreasing, it continues to be used in some centers.
   b. Supercooled probe is used to freeze the avascular retina, preventing vessel proliferation.
   c. Invasive procedure requires anesthesia.
   d. Complications include scarring; edema; conjunctival hematoma or laceration; strabismus; retinal, periretinal, or vitreous hemorrhage; conjunctival tissue proliferation; macular hole or distortion; and late-onset retinal detachment (Wu and Kuo, 2017).
5. Anti-VEGF therapy.
   a. Still in the experimental stage, bevacizumab (Avastin) is a monoclonal antibody that inhibits angiogenesis.
   b. Avastin is administered as an intraocular injection to suppress the development of blood vessels in the retina.
   c. A randomized controlled trial comparing Avastin with laser therapy found a reduced length of hospital stay with no difference in neurodevelopmental outcomes with Avastin (Kennedy and Mintz-Hittner, for the BEAT-ROP Cooperative Group, 2018).
   d. Reported side effects of anti-VEGF agents include recurrent neovascularization, retinal hemorrhage, and retinal detachment (Pertl et al., 2015).
6. Vitreoretinal surgery results in reattachment of the retina in 40% to 90% of the cases depending on the stage; however, after macular detachment, visual prognosis is poor, even if the retina is successfully reattached (Karacorlu et al., 2017).
7. Provide emotional support and appropriate community referrals for parents whose infant will have significant visual impairment.

H. **Complications**.
1. Mydriatic eyedrops and eye examinations can produce hypertension, reflex bradycardia, and apnea as a result of drug effects and vagal stimulation.
2. Varying degrees of visual impairment (e.g., myopia) may require corrective lenses to improve visual acuity.
3. Additional complications include the following:
   a. Strabismus (20%).
   b. Glaucoma.

c. Cataracts
d. Amblyopia.
e. Astigmatism (40%).
f. Retinal detachment and blindness.

I. **Outcome**.
1. Ninety percent (or more) of cases of acute ROP resolve spontaneously, with little or no visual loss.
2. Timely treatment has been shown to decrease the risk of blinding complications of ROP by 50%. A significant number of visual impairments may result, especially in the presence of disease in zone I.

Anatomy of the Ear (Fig. 37.3)

EXTERNAL EAR

A. **Auricle**.
1. Thin plate of elastic cartilage covered by skin.
2. Collects air vibrations.

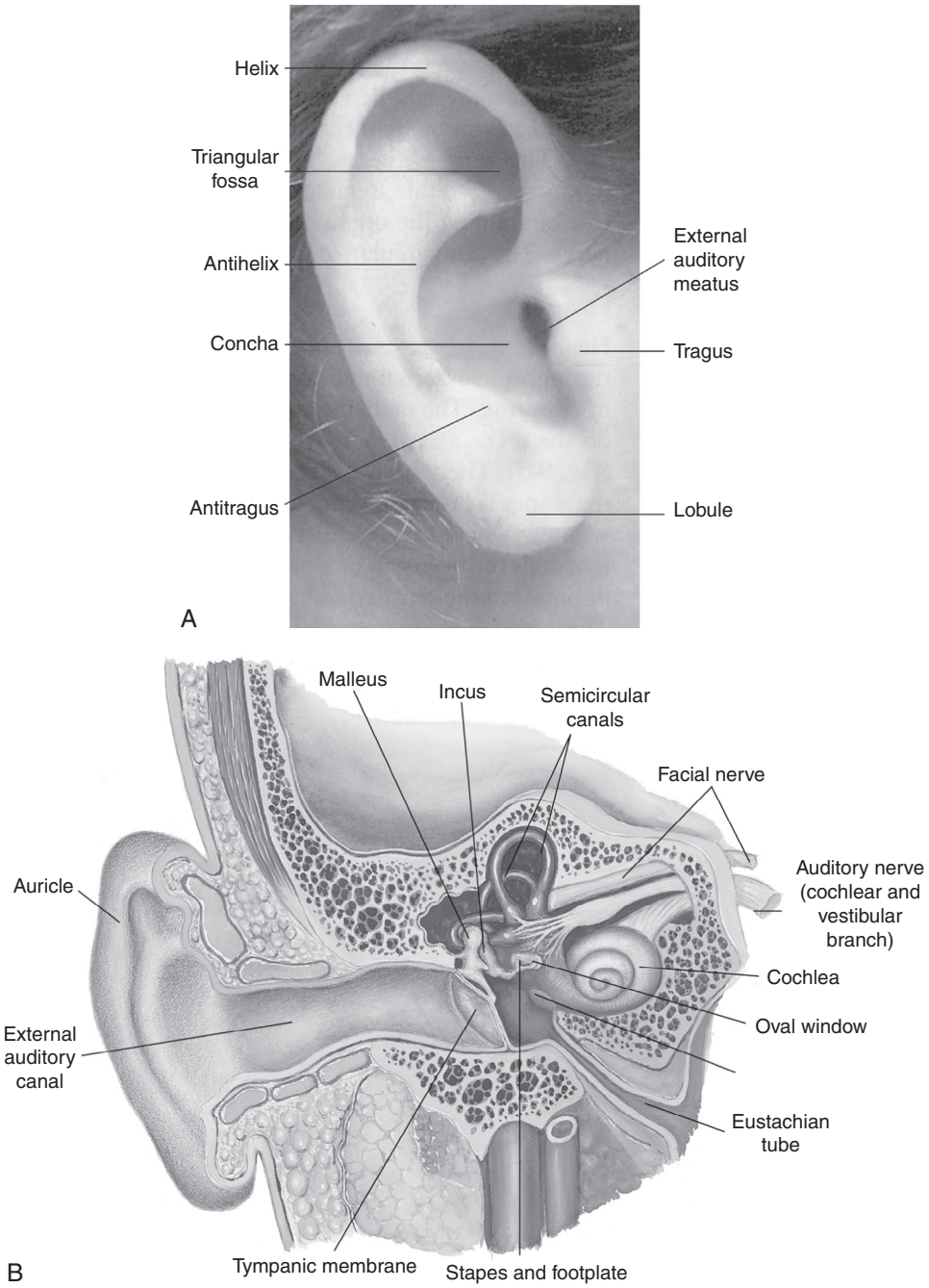

Fig. 37.3 **A,** Different parts of the auricle of the external ear. **B,** Anatomy of the ear. *(From Seidel, H. M., Ball, J. W., Dains, J. E., & Benedict, G. W. [2006].* Mosby's guide to physical examination *[6th ed.]. St. Louis, MO: Elsevier Mosby.)*

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3. Possesses extrinsic and intrinsic muscle.
4. Supplied by branches of facial nerve.
5. Consists of tragus, helix, concha, and lobule.

B. **External auditory meatus.**
1. Curved tube leading to tympanic membrane.
2. Framework composed of elastic cartilage (outer one third) and bone (inner two thirds).
3. Lined by skin; outer one third has hair, sebaceous, and ceruminous glands.
4. Auriculotemporal nerve and auricular branch of vagus nerve provide sensory output.
5. Lymph drainage is to parotid, mastoid, and cervical lymph nodes.
6. At birth, meatus is shorter and less curved than in the adult.

MIDDLE EAR

A. **Slit-like air-containing cavity within petrous (bony) portion of the temporal bone.**
B. **Has roof, floor, anterior, posterior, medial, and lateral walls.**
C. **Lateral wall is the tympanic membrane.**
1. Tympanic membrane is thin, fibrous membrane.
2. Sound waves move tympanic membrane medially.
3. Obliquely placed, concave laterally.
a. Depression in concavity is called the *umbo*.
b. Umbo is produced by the tip of the handle of the malleus ("hammer").

D. **Contains the auditory ossicles.**
1. Ossicles include malleus, incus ("anvil"), and stapes ("stirrup").
2. Malleus and incus can be recognized on otoscopic examination.
a. Tensor tympani muscle inserts on malleus; dampens vibrations.
3. Stapes inserts on the oval window of the semicircular canal.
a. Stapedius muscle inserts on stapes; dampens vibrations.
4. Movement of tympanic membrane moves ossicles.
5. Movement of ossicles induces compression waves in fluid (perilymph) in cochlea.

E. **Communicates to the nasopharynx via the eustachian (auditory) canal.**
1. Eustachian tube equalizes air pressure between the middle ear and the nasopharynx.

INNER EAR

A. **Cavity in petrous portion of temporal bone, medial to middle ear.**
B. **Consists of bony labyrinth and membranous labyrinth; the latter is lodged within the former.**
1. Membranous labyrinth filled with endolymph.
2. Bony labyrinth consists of vestibule, semicircular canals, and cochlea.
a. Vestibule forms base of semicircular canals.
b. Semicircular canals (superior, posterior, and lateral) arise from vestibule; filled with perilymph.
c. Movement of perilymph in semicircular canals induced by axial movement.
d. Transduced by vestibular branch of cochlear nerve.
e. Cochlea composed of two continuous chambers (scala tympani and scala vestibule) filled with perilymph and a medial chamber (cochlear duct) filled with endolymph.
f. Sensory ("hair") cells stimulated by compression waves that cause relative movement of membranes within cochlea.

Innervation

A. **Sensory afferents from cochlea and vestibule transmitted by branches of vestibulocochlear (eighth cranial) nerve.**
1. Vestibular branch forms vestibular ganglion, which receives nerves from different regions of the vestibule.
2. Cochlear nerve has motor and sensory branches.

B. **Motor efferents to tensor tympani and stapedius muscles.**
1. Tensor tympani supplied by mandibular branch of trigeminal nerve.
2. Stapedius supplied by the facial nerve.

C. **Vestibulocochlear and facial nerves enter the inner ear via the internal acoustic meatus.**

Patient Assessment

HISTORY

A. **Pregnancy:** first-trimester infections (e.g., CMV), unknown rashes, fevers, flu-like illnesses.
B. **Family history:** incidence of hearing loss, ocular disorders.
C. **History of risk factors:** see B. Etiology, under Hearing Loss.

EXAMINATION

During all interactions, care providers should observe the neonate's response to sound. A more focused assessment is performed with the baby in a quiet, alert state.

A. **General assessment.**
1. General facial configuration: The ears should be symmetrically positioned with the helix of the ear on or above an imaginary line drawn from the inner to the outer canthus of the eye toward the ear. Ears that fall below that line are termed *low-set* and are often associated with genetic syndromes and other congenital malformations.

2. The development of the pinna correlates with the infant's gestational age. The pinna of a term infant is firm, with prompt recoil.
3. Presence of preauricular pits or skin tags may be familial or associated with other anomalies, especially of the renal system. Pits may also communicate with the brain or inner ear and lead to infection.
4. Poorly developed or malformed ears are associated with hearing loss and other anomalies (Johnson, 2016).
5. Otoscopic examination of the newborn ear is not part of a routine examination. Visually inspect the auditory canal to ensure patency.
6. As part of a complete assessment, physical features of syndromes associated with sensorineural hearing loss should be identified.

HEARING LOSS

Hearing loss in the newborn population is estimated to occur at a rate of between 1 and 3 in 1000 live births (Williams et al., 2015). Low birth weight neonates demonstrate failure rates of 5% to 10% (Volpe et al., 2018). Hearing loss occurs across a continuum and can be classified as mild, moderate, or severe. Some types of hearing loss, such as those caused by congenital infections, are progressive or manifest well beyond the newborn period. Ongoing monitoring is needed for those infants with risk factors but who have normal hearing at birth (Vohr, 2015; Volpe et al., 2018).

A. **Pathophysiology**.
   1. Conductive: dysfunction of the outer or middle ear prevents sound transmission.
   2. Sensorineural: results from damage to the sensory nerve endings in the cochlea or impairment of the auditory nerve.
   3. Mixed: a combination of conductive and sensorineural hearing loss.

B. **Etiology**.
   1. Risk factors (Vohr, 2015; Volpe et al., 2018).
      a. Familial.
      b. Craniofacial anomalies: especially those involving the pinna and ear canal.
      c. Hyperbilirubinemia: at levels requiring exchange transfusion.
      d. Bacterial or herpes meningitis.
      e. Low Apgar scores (<5 at 1 minute, <6 at 5 minutes).
      f. Ototoxic drugs.
         1) Gentamicin.
         2) Vancomycin.
      g. Intrauterine infections.
         1) CMV.
         2) Rubella.
         3) Syphilis.
         4) Herpes.
         5) Toxoplasmosis.
      h. Syndromes associated with hearing loss.
   2. Idiopathic (up to 50% of cases).

HEARING SCREENING

A. **Examination of all newborns.** The Joint Committee on Infant Hearing (2007) recommends universal hearing screening for all newborns. Prompt detection of hearing loss facilitates interventions aimed at preventing speech, language, and cognitive development impairments.

B. **Methodology.**
   1. Evoked otoacoustic emissions.
      a. Measures sound waves generated in the inner ear in response to clicks or tone bursts generated by small microphones placed in the infant's auditory canals.
      b. Advantages: results are specific to each ear; not dependent on the infant's state; short test time.
      c. Disadvantages: inaccurate in the presence of debris in the ear canal; infant must be relatively inactive during the test; does not test neural transmission of sound.
   2. Auditory brainstem response.
      a. Using three scalp electrodes, measures brain waves generated in response to mechanically generated ticks.
      b. Advantages: ear-specific results; unaffected by ear canal debris.
      c. Disadvantages: infant must be in a quiet state.

C. **Follow-up:** Hearing screening identifies infants at risk for hearing loss but is not diagnostic. Infants who fail screening tests must be referred for further testing and intervention.

Part 3

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PART 4
Professional Practice

CHAPTER 38
Foundations of Neonatal Research

Alice S. Hill

OBJECTIVES

1. Identify nurses' research competencies according to educational preparation.
2. Describe the research process and key components of research studies.
3. Identify neonatal nurses as research consumers who implement research translational strategies through clinical evidence-based practice.
4. List questions to ask when critiquing research literature.
5. Be informed about the rights of research subjects and the ethical conduct of research.

Research and Generation of Nursing Knowledge

Research refers to systematic inquiry or investigation governed by scientific principles and conducted to expand knowledge and increase understanding. The research process describes a logical and orderly progression from development of a question through the conduct of a study, analysis of resultant findings, dissemination of conclusions, translation into practice, and implementation. The questions asked and the methodology that guide inquiry reflect underlying values and beliefs, worldview, or philosophy. Scientific method describes prescribed rules of logic and imposed controls, ensuring that the knowledge generated is truthful. Research generates empirical (i.e., experienced) knowledge. Although nursing, as a science-based profession, strongly subscribes to empirical research, the body of nursing knowledge is enriched by diversity in ways of knowing. Nonresearch bases for nursing knowledge—tradition, authority, trial and error, personal experience, intuition, and commonsense reasoning—have powerful influences and are part of nursing tradition; however, nonresearch knowledge does not permit scientific predictability, nor does it provide for scientific rationale and justification for nursing actions. Within the nursing profession, research promotes health and well-being of patient populations through a variety of applications. Research improves practice by providing answers to clinical questions, evaluating the effectiveness of nursing interventions and programs of care, and expanding the body of nursing knowledge. Increasing emphasis on evidence-based practice, research-based practice, best practices, practice guidelines, and outcomes-focused research mandates that research occupy a central role in nursing. All nurses have a role related to research (LoBiondo-Wood and Haber, 2018). Although not all nurses will do research, every nurse is a consumer of research. Research findings are an essential component of evidence-based practice. At the time of this writing, a search in PubMed using the terms "evidence-based practice nursing" yielded 17,838 hits. One of the earliest articles dates from 1974. The past three decades are marked by mounting emphasis on empirical proof as the base for nursing care, as well as on the evaluation and synthesis of knowledge supporting nursing actions. There is a significant need in nursing for well-constructed systematic and integrative reviews of the literature (McGrath, 2012). Pressure for evidence-based practice is also related to cost containment and demonstrating the value of nursing care, as well as cost-effectiveness of nursing interventions. Although nurses in general increasingly subscribe to the principles of evidence-based practice, nursing leadership and organizational support play an essential role in the implementation of evidence-based practice (Ahrens and Johnson, 2013). Therefore, neonatal clinical nurse specialists, nurse managers, and nursing administrators are critical in moving research into practice. Evidence-based practice shares elements with conducting research (Raines, 2012) and requires knowledge of the "doing" of research to evaluate existing evidence (Table 38.1).

Independently planning and conducting research require advanced knowledge. Assuming that any nurse can do research is like assuming any nurse can insert a peripheral intravenous central catheter line. Both require specific education and skill development. The conduct of research

Table 38.1

Processes of "Doing" and "Using" Research in Nursing

Research	Evidence-Based Practice
Formulate a question or hypothesis	Specify a clinical problem
Choose study design	Conduct literature review
Plan study methods and procedures	Gather evidence
Collect data	Critically appraise evidence
Analyze data and generate findings	Develop practice guideline
Disseminate results	Apply the practice change
Translate findings into practice	Evaluate patient/family outcomes and share results

Adapted from Raines, D. A. (2012). Quality improvement, evidence-based practice, and nursing research . . . Oh my! *Neonatal Network*, *31*(4), 262–264; and Melnyk, B. M., & Fineout-Overholt, E. (2011). Making the case for evidence-based practice and cultivating a spirit of inquiry. In B. M. Melnyk and E. Fineout-Overholt (Eds.), *Evidence-based practice in nursing and healthcare: A guide to best practice* (pp. 3–24). Philadelphia, PA: Wolters Kluwer.

requires expertise in research design and methods as well as statistical analysis. Research is differentially emphasized in the curriculum of nursing academic programs. Table 38.2 illustrates general research competencies based on educational preparation. The American Association of Colleges of Nursing (AACN) specifies research competencies as essentials in baccalaureate (2008), master's (2011), and doctoral nursing practice (2006). In addition, AACN emphasizes research and development of nursing science as the center of PhD education in nursing (American Association of Colleges of Nursing, 2010).

Bridging the gap between doing and using research is the role of translational science. Though various terms are used, translational science, knowledge translation, and implementation science, in general, all refer to moving science "from the bench to the bedside," including both practice and policy (Curran et al., 2011). Translation, the in-between step, is a science unto itself, with theory and methods guiding how and why knowledge is transmitted into practice. Translational science, the underpinning of

Table 38.2

Nursing Research Education

Program	Educational Preparation*,†,‡,§
ADN	Appreciate the importance of research in nursing and assist in problem identification and data collection.‡ Identify problems, collect data, apply research findings in care delivery.§
B.S.N.	AACN B.S.N. Essential III. Translation of current evidence into practice. Basic understanding of research process and translation to practice, appraise sources of information, participate in translation of evidence into practice, collaborate in collection and dissemination of evidence, understand nursing quality and safety measures.¶
Master's	AACN Master's Essential IV. Translation and integration of scholarship into practice. Integration and translation of multiple information sources to improve practice and subsequent outcomes for patient aggregates, ethical protections for research participants, articulate evidence base for practice, work collaboratively to improve outcomes and promote policy change through generation, dissemination, and implementation of knowledge, apply practice guidelines, rigorous examination of database evidence to guide nursing practice.¶¶
DNP	AACN DNP Essential III. Clinical scholarship and analytical methods. Determine best evidence for practice through critical appraisal, design and implement outcome evaluation of practice, design and conduct quality improvement processes, develop evidence-based practice guidelines, work collaboratively as a practice specialist to generate knowledge, dissemination to improve outcomes.**
Ph.D.	Develop the science of nursing. Research intensive, develop in-depth knowledge in substantive area, knowledge of the philosophy of science, integrative scientific perspective, generate knowledge, conduct original research, research ethics, leadership in the conduct of research, communication and dissemination of findings.†

**AACN*, American Association of Colleges of Nursing.

†American Association of Colleges of Nursing. (2010). *The research-focused doctoral program in nursing pathways to excellence*, Washington, DC: American Association of Colleges of Nursing. Retrieved from http://www.aacnnursing.org/Portals/42/Publications/PhDPosition.pdf

‡ Retrieved from http://www.aacn.nche.edu/publications/position/nursing-research

§ Adapted from Ayers, D. M., & Coeling, H. (2005). Incorporating research into associate degree nursing curricula. *Journal of Nursing Education*, *44*(11), 515–518.

¶ American Association of Colleges of Nursing. (2008). AACN Essentials – Baccalaureate. Retrieved from http://www.aacnnursing.org/Education-Resources/AACN-Essentials

¶¶ American Association of Colleges of Nursing. (2011). AACN Essentials – Master's. Retrieved from http://www.aacnnursing.org/Education-Resources/AACN-Essentials

** American Association of Colleges of Nursing. (2006). AACN Essentials – DNP. Retrieved from http://www.aacnnursing.org/Education-Resources/AACN-Essentials

evidence-based practice, examines the nature of evidence and its evaluation, synthesis of evidence, informatics, the study of knowledge-to-action gaps, factors promoting and hindering knowledge transfer, methods of knowledge transfer, and evaluation of effects (Curran et al., 2011).

Whether doing or using research, nurses assume several roles related to research ethics. Nurses independently conducting research comply with regulations governing human research subject participation. Nurses also may serve as staff on research projects conducted by others. Finally, nurses care for patients and their families who are involved in research. In all of these roles, nurses promote safety and protection of rights. General ethical issues to consider when enrolling critically ill participants into a research study include the participant's decision-making ability, that a fully informed consent is provided and understood, and that the benefits and risks ratio is weighed (Richmond and Ulrich, 2007). Neonatal intensive care unit (NICU) nurses face particular research ethics challenges given the vulnerable nature of infants and their parents (Strandås and Fredriksen, 2015).

Research Process and Components of a Research Study

The nursing process and research process represent an organized approach to critical thinking and share several similarities (Table 38.3). In essence, every patient is an "*n* of 1" research study. Regardless of the topic investigated, a research study contains several key elements (Houser and Bokovoy, 2006; LoBiondo-Wood and Haber, 2018).

A. **Question:** All research derives from a purpose and begins with a problem or general question, which is refined to form specific research aims, questions, or hypotheses.
   1. The research questions or hypotheses are the focal point of a research study, driving all other aspects of the investigation, including method choices.
   2. Each element of a research project fits the stated questions or hypotheses.
   3. Analysis and study results directly relate to stated aims, questions, or hypotheses.

B. **Background:** The framework is derived from a review of the literature that establishes what is currently known regarding the study topic and identifies the gaps in knowledge that the study will address.
   1. When a study is derived from an existing theory, the theoretical framework portrays the variables and their relationships as prescribed by the theory.
   2. A conceptual framework is a description of concepts, defined for the purposes of the research, and their relationships.

C. **Method:** In some readings, the term *method* is used to define what was done to collect the data (e.g., observation, questionnaire, interview, physiologic measure); however, here *method* is defined as the entire description of how the study is conducted.
   1. Design: the plan for data collection, much like a recipe or pattern. There are two general types of research design.
      a. Descriptive (sometimes divided into descriptive and exploratory).
         1) Designs involve depicting the study sample "as is."
         2) Provide information to help understand the variables of interest in the defined sample.
      b. Experimental.
         1) The investigator manipulates independent variables and measures the response in dependent variables.
         2) Intervention studies are by nature experimental.
      c. The design determines the number of subject groups, the timing of data collection, and control of extraneous variables that may produce bias.
      d. These design choices contribute to scientific validity of the study and are related to how subjects are selected, the control of extraneous variables, and how the independent variables are applied.
      e. Designs are described according to internal and external validity. Designs offer differing strengths and weaknesses relative to internal and external validity (Table 38.4).
         1) Internal validity refers to the lack of bias and random variation that support obtaining accurate results in the population studied.
         2) External validity refers to the generalizability of results to a wider population.
   2. Sample: represents who or what is studied.
      a. Made up of units of analysis, such as individuals, nursing units, or hospitals.
      b. Typically selected from a larger population.
      c. Specific strategies for sampling determine if results from a sample can reasonably be generalized to the larger population.

Table 38.3

Similarities of the Research Process and the Nursing Process

Nursing Process	Research Process
Client assessment	Identification of problem
Nursing diagnosis	Questions or hypotheses
Plan of care	Method
Evaluation	Findings
Revision of plan	Implications and dissemination

Adapted from Gillis, A., & Jackson, W. (2002). *Research for nurses: Methods and interpretation*. Philadelphia, PA: F. A. Davis.

Part 4

Table 38.4

Levels of Bias Control in Research Design

Level	Designs	Independent Variable Control*	Control Group	Outcomes Present at Enrollment
A	Randomized concurrent controlled trial Quasi-randomized concurrent trial Randomized pre–post design	Yes	Yes (concurrent)	No
B	Cohort concurrent study Pre–post study	No	Yes (may or may not be concurrent)	No
C	Ex post facto study Case–control study	No	Yes (may or may not be concurrent)	Yes
D	Descriptive	No	No	Yes or no

* Independent variable or intervention controlled by investigator.

Adapted from Jacob, R. F., & Carr, A. B. (2000). Hierarchy of research design used to categorize the "strength of evidence" in answering clinical dental questions. *Journal of Prosthetic Dentistry*, *83*(2), 137–152.

1) Probability sampling: Each individual in the population has an equal chance of being included in the sample. Probability sampling is not always feasible, particularly in nursing research dealing with small patient populations. In this situation, nonprobability sampling, meaning every individual will not have the same chance of being selected, is employed.

d. Sample size is a factor in the selection of analysis strategies.

3. Variables: the attributes or properties measured in a research study.
   a. Variables are defined both conceptually and operationally.
      1) Conceptual definition: variable is described in the abstract (e.g., hypertension).
      2) Operational definition: defines the variable in measurable terms. For example, hypertension will be defined as a systolic blood pressure greater than 100 mm Hg in the term neonate.
   b. *Instruments* and *tools* are terms used interchangeably to indicate operational measures.
   c. The quality of measurement is critical to research. Validity and reliability describe instrument measurement characteristics.
      1) Validity is the degree to which an instrument measures what it is purported to measure. The instrument truly measures the variable.
      2) Reliability refers to the ability of the instrument to obtain consistent results (i.e., reproducibility) over time or across administrators.
4. Setting: portrays where the study is conducted and the conditions surrounding it.
5. Procedure: describes in stepwise fashion how the study was carried out.
6. Analysis: uses statistical or analytic techniques on the data collected to answer the research questions or compare findings with stated hypotheses.
7. Results: include a description of the study sample as well as findings from the analysis based on stated aims, questions, or hypotheses.
8. Conclusion: includes discussion of study findings, implications, limitations, and recommendations for future research. Practice recommendations are supported by the study results.

Quantitative Research

A. **Numeric data are analyzed using a statistical approach specified as part of the planning for the research project.**

B. **Descriptive statistics include measures of frequency (percentages, count), central tendency (mean, median, mode), and dispersion (standard deviation, variance, range).**

C. **Inferential statistics are based on probability and allow judgments to be made about the population and hypotheses to be tested.** In general, inferential statistics test either how things differ or how things are related.

D. **Statistical significance means that the particular finding is not likely due to chance alone.**
   1. The investigator sets an alpha or probability level that will be acceptable in interpreting results (often alpha is set at $p < 0.05$).
   2. The p value is the probability associated with the test statistic calculated from the study data. If the p value is equal to or less than alpha, the test is statistically significant.
   3. Statistical significance is not always consistent with clinical significance, meaning that the magnitude of

the effect may be more relevant or important in clinical practice (Page, 2014).

Qualitative Research

A. **Maintains the same rigor as quantitative research.**
B. **Focus is on an in-depth understanding of a phenomenon, with particular emphasis on the subject's reports of personal experience, used to increase understanding of phenomena perceived by individuals, groups, and cultures** (Creswell and Poth, 2017).
C. **Participant observation, focus groups, and interviews are methods frequently employed in qualitative research.**
D. **The specific research approach stems from an underlying philosophical perspective.** Types of perspectives commonly used in nursing qualitative research include phenomenology, grounded theory, and ethnography (Creswell and Poth, 2017).
   1. Phenomenology: seeks to understand the lived experience of individuals.
   2. Grounded theory: symbolic interaction forms the basis for understanding social processes and behavior.
   3. Ethnography: describes a cultural group.
E. **The analysis is inductive and interpretive.**
F. **The process of conducting qualitative research and components of the research project are parallel with those of quantitative research.** Qualitative research entails defined specifying aims, defined approach, description of sampling and data collection procedures, analysis consistent with philosophical approach and aims, and actions to maintain rigor (validity) (Creswell and Poth, 2017).

Areas of Exploration in Neonatal Nursing

A. **Research supports generation of knowledge guiding evidence-based practice.**
B. **Contemporary topics in neonatal nursing research include the following:**
   1. Consequences of pain experiences in the neonate and pain management.
   2. Initiation of oral feeding in preterm infants and feeding schedules.
   3. Promotion of breastfeeding in preterm infants.
   4. Empowerment of families and family-centered care.
   5. Safe care delivery and patient safety.
   6. Cost containment.
   7. Promotion of optimal developmental outcomes.
   8. NICU nursing staff recruitment, training, and retention.
   9. NICU design and environment effects on infants and nursing staff.
   10. Ethical challenges in NICU care.
   11. Prevention of hospital-acquired infections.
   12. Care of drug-exposed neonates.
   13. Nutritional needs of high-risk infants.
   14. Innovations in care delivery structure and process.
   15. Neural protection measures such as head cooling or whole-body cooling.
   16. Skin-to-skin contact.
   17. Skin care practices.

Nurses as Consumers of Research

A. **Every nurse is a consumer of research whether or not direct participation in research activities occurs** (Box 38.1).
B. **Nursing activities involving consumption of research.**
   1. Individually reading current research articles and attending conference research presentations to expand knowledge and support practice.
   2. Conducting reviews of evidence.
   3. Types of evidence review (Doolen, 2017).
      a. Systematic review—combine studies on specific problem or questions, the basis for evidence-based practice.
      b. Meta-analysis—statistical combining of findings from primary research studies to form aggregate results.
      c. Integrative review—address the broadest base of existing knowledge.
   4. Research critique and appraisal is a systematic approach to reading and assessing research articles to assess applicability of knowledge in practice and use in further research. Key questions to ask when reviewing a research article are provided in Box 38.2.

Box 38.1

Research Applications in Practice

Clinical practice committee
Quality improvement committee
Process improvement protocol
Policies
Procedures
Standards
Critical pathways
Protocols
Guidelines
Journal club
Product review committee

Box 38.2

Research Critique and Appraisal

Is there a clear statement of the problem and purpose?
Are the research questions or hypotheses unambiguous and stated in measurable terms?
Does the background establish a theoretical or conceptual framework and show gaps in knowledge?
Does the background define key concepts and their measures and describe relationships among study concepts?
Is the literature review comprehensive and current?
Do the purpose, questions/hypotheses, design, method, and analysis fit together logically?
Is the design clearly described?
Are possible extraneous variables identified and controlled?
Are the sample characteristics described and sampling exclusion and inclusion criteria reported?
To whom can study results be generalized?
Is the sample size adequate to address the research questions or hypotheses?
Is loss of subjects explained?
Is the measurement of study variables described?
Are study measures valid and reliable?
Are study procedures described?
How were extraneous variables controlled?
Is the analysis described and are the statistics appropriate for addressing the questions/hypotheses?
Do the reported results address the research questions/hypotheses?
Are the findings interpreted and compared with current knowledge?
Are conclusions justifiable on the basis of the stated findings?
Are statistically significant findings also clinically significant?
Are limitations of the study presented?
Is application of findings discussed?
Are future research directions outlined?

C. **Research utilization.**
   1. Refers to specific application of research findings, irrespective of research method, in practice and includes critique of studies, synthesis of findings, assessing applicability to practice, development and implementation of research-based guidelines, and evaluation of practice change (Iowa Model Collaborative et al., 2017).
      a. The Iowa Model (Fig. 38.1) is an example of research-based practice that includes generation of practice-related questions and systematic assessment of research findings used to change caregiving.
      b. The Iowa Model emphasizes a variety of research sources of data and is not limited to randomized controlled trials.

D. **Evidence-based practice emphasizes a systematic appraisal of the best evidence combined with clinical expertise and patient/family values and preferences to develop best practices** (LoBiondo-Wood and Haber, 2018).
   1. Systematic review of data-based literature, grading studies according to level of evidence, with highest priority given to systematic review or meta-analysis of randomized controlled trials (Box 38.3).
   2. Evidence-based practice is exemplified by the Cochrane Collaboration, an organization that has established robust criteria for the systematic evaluation of research studies resulting in recommendations for practice.
   3. Evidence-based practice in general refers to established criteria for sources of knowledge and acceptable research methods (LoBiondo-Wood and Haber, 2018).

E. **The Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) and the National Association of Neonatal Nurses (NANN) have been instrumental in establishing research-based practice programs, addressing such issues as normal birth, mental health, patient safety, transition of the late preterm infant initiative, neonatal skin care, transition of the preterm infant to an open crib, management of neonatal hypotension, transport standards, neonatal pain assessment, and insertion of peripheral catheters** (http://www.awhonn.org/page/researchpriorities, 2018; http://nann.org/education/research, 2018).

Ethics in Research and Nurses as Advocates

A. **Whether nurses are investigators conducting research or caring for patients who are research participants, careful consideration of ethics in research is essential.**

B. **It is important that nurses maintain a clear distinction between research and practice and between the roles of researcher and care provider.** Practice is aimed at caregiving to aid the well-being of an

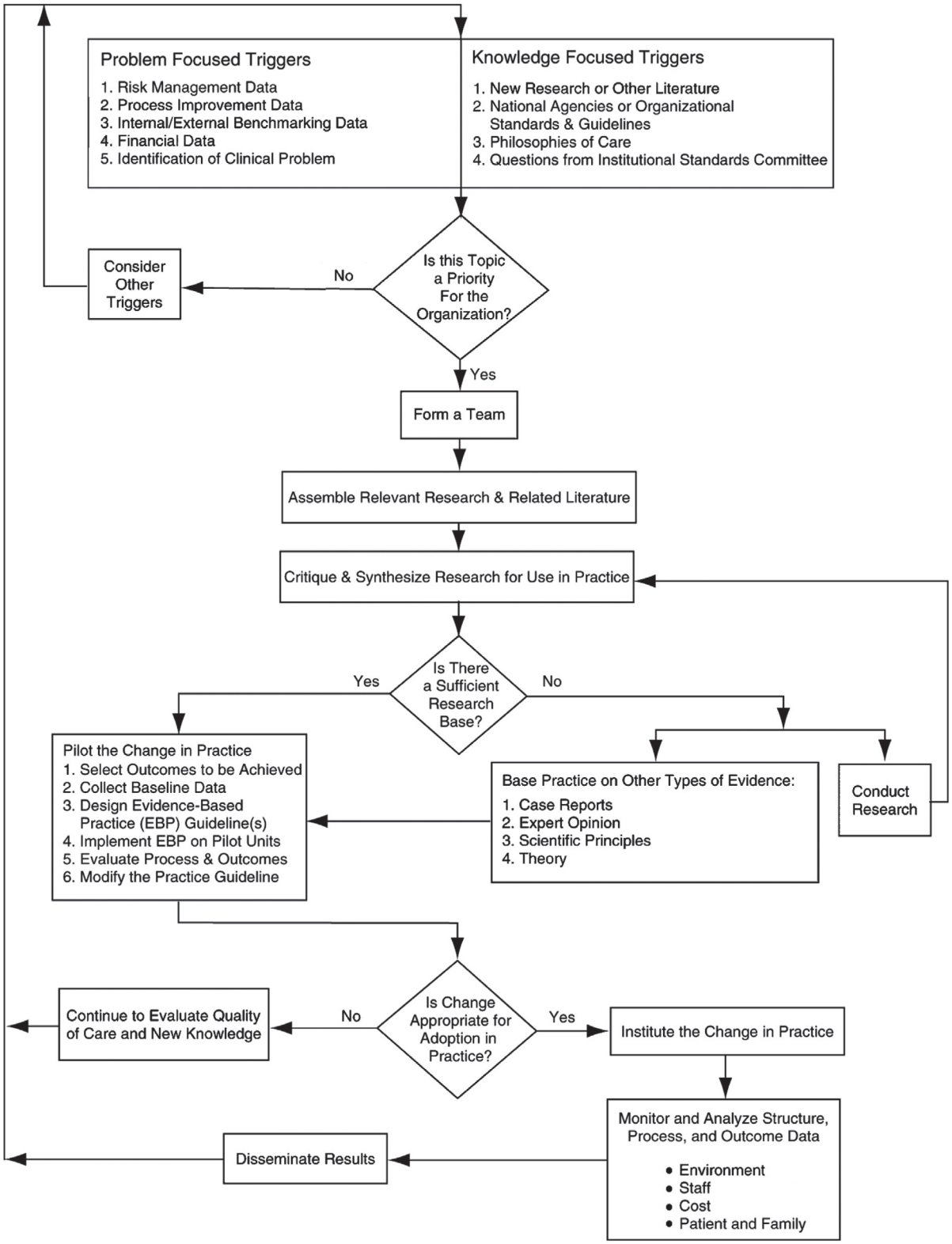

Fig. 38.1 Iowa Model of research-based practice to promote quality care. *(From Titler, M. G., Kleiber, C., Steelman, V. J., Rakel, B. A., Budreau, G., Everett, C. L. Q.,…Goode, C. J [2001]. The Iowa Model of evidence-based practice to promote quality of care.* Critical Care Nursing Clinics of North America, 13*[4], 497–509.)*

Box 38.3

Levels of Research Evidence

Meta-analysis of randomized controlled trials
Single randomized controlled trial
Single well-designed controlled study without randomization
Single well-designed quasi-experimental study
Systematic reviews of nonexperimental research
Well-designed single nonexperimental study
Expert opinions, committee reports, consensus panels

Adapted from Agency for Health Care Policy and Research. (1994). *Clinical Practice Guideline No. 9: Management of cancer pain* (AHCPR Publication No. 94-0592). Rockville, MD: Department of Health and Human Services; and Guyatt, G., Drummond, R., Meade, M. O., & Cook, D. J. (2015). *Users' guides to the medical literature: A manual for evidence-based clinical practice* (3rd ed.). New York, NY: McGraw-Hill.

Box 38.4

Elements of Informed Consent

- Complete explanation of study purpose and procedures
- Duration of involvement and time commitment clearly stated
- Full disclosure of study risks
- Description of potential adverse effects and how they will be treated
- Identification of any costs that are subject's responsibility
- Accurate description of potential benefit to self and/or society
- Description of deviations from standard care
- Indication of alternatives if an intervention is to be tested
- Permission for use of medical records
- Protection of confidentiality
- Specification of possible limits to confidentiality (e.g., mandatory reporting)
- Duration of identifiable data retention
- Permission to withdraw at any time
- Permission to refuse to answer any questions
- No coercion, including assurance that refusal will not change care or other entitlements
- Opportunity to ask questions
- Consent language and literacy at the level of signatory's understanding
- Receipt of copy of consent

individual, whereas research involves gathering of data to generate knowledge (Connor, 2014).

C. **The ethical principles guiding human research include autonomy, beneficence, and justice.**
   1. Autonomy: the ability to make an informed choice, free of coercion, regarding participation in research. The components of informed consent are provided in Box 38.4. Consent for research participation must be obtained by a member of the research team who is qualified to explain the study and answer questions. In neonatal research, parents provide consent for infant participation.
   2. Beneficence: the research benefits must outweigh the risks. Children are considered a vulnerable group, and federal mandates require that risks to a child must be minimal when there is no direct benefit to the child. When a research project involves more than minimal risk, the direct benefit to the child must outweigh the risk.
   3. Justice: relates to who is represented in the research sample. Groups that bear the burden for research participation should also be groups that will ultimately benefit from the results.

D. **Subject selection should be free of discrimination and represent a broad population.**

E. **Several documents provide guidelines for the protection of human subjects in the United States.**
   1. The Belmont Report (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) was developed within the Department of Health, Education, and Welfare (now the Department of Health and Human Services [DHHS]).
   2. All research sponsored by any federal agencies, including the National Institute for Nursing Research (an institute under the National Institutes of Health and part of the DHHS), must comply with standards for human participation in research listed under Title 45, Code of Federal Regulations, Part 46, "Protection of Human Subjects" (DHHS, 2009).
   3. The Office for Human Research Protections is specifically charged with ensuring the safety and welfare of people participating in DHHS research (additional information is available at http://www.hhs.gov/ohrp/index.html).
   4. To ensure the protection of human subjects, all research should be approved by a peer review group. All research supported by federal funds requires review by an institutional review board (IRB), a specific type of peer review group established according to federal regulations.
   5. Nurses conducting research should become familiar with regulations protecting human subjects. For nurses in practice, understanding of rights in research, particularly informed consent, provides a basis for advocacy and ensuring the protection of patients who are also research participants (Ballard et al., 2011). Concerns about research ethics should be raised with the local peer review group or IRB.

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CHAPTER 39
Ethical Issues

Tanya Sudia and Anita Catlin

OBJECTIVES

1. Explore how the principles of biomedical ethics can be applied in the neonatal intensive care unit (NICU).
2. Identify alternative theoretical and case analysis approaches to examining ethical issues in the NICU.
3. Identify the rare, but at times appropriate, use of conscientious objection for the neonatal nurse.
4. Examine the nurse's role when ethical issues arise in the NICU.
5. Recognize the contribution of medical and nursing organization position statements in providing guidance on ethical dilemmas.
6. Recognize the role of the hospital ethics committees in exploring and resolving ethical issues in the NICU.

Ethical issues are ever present in the neonatal intensive care unit (NICU). Each technological advance brings ethical questions to the forefront of care. How far can and should the limits of viability be extended? How can we minimize the social, emotional, and financial costs associated with NICU care? Are we providing adequate palliative care in the NICU? What circumstances may rise to the level of conscientious objection for the neonatal nurse? These are among the poignant questions that warrant ongoing ethical analysis.

Nurses, nurse practitioners, physicians, and other members of the NICU health care team have professional obligations to patients. In this chapter, the emphasis is placed on the obligations and role of the nurse in collaboration with other NICU team members. For nurses and physicians, these obligations are based on the professional codes of practice and means of ethical conduct. For example, the practice of medicine evolved from the founding obligation of *Primum non nocere*, a Latin phrase meaning "First, do no harm." This has become a guiding ethical obligation for health care professionals, regardless of their practice setting.

Nurses also focus on ethical guidance as established by professional nursing organizations. For the NICU nurse, primary professional guidance is provided through the American Nurses Association (ANA) *Code of Ethics for Nurses with Interpretive Statements* (ANA, 2015); the ANA *Position Statement on Ethics and Human Rights* (ANA, 2016); and the National Association of Neonatal Nurses (NANN) *Position Statement on NICU Nurse Involvement in Ethical Decisions* (NANN, 2016b). These key documents provide the foundation for ethical practice in the NICU.

Examining Ethical Issues in the NICU

In the NICU, ethical dilemmas arise when ethical principles and well-intended actions compete. For example, when a neonate with overwhelming sepsis and intraventricular hemorrhage begins to exhibit multisystem failure, conflict may arise regarding continuation of the most aggressive technical care measures versus deceleration of those measures to focus on more intensive palliative care. Thus, the ethical dilemma in this situation is avoiding causing harm yet doing good, ensuring that actions taken are in the best interest of this neonate now.

Among the questions that can arise are: What are best-interest actions for the neonate? Who decides what those actions should be? What happens when members of the health care team disagree about the aggressiveness of treatment? What if one or both parents disagree about the best interests of the neonate? Questions such as these and the related ethical issues encountered in the NICU often arise from very complex situations that are best addressed by a team approach.

Nurses, physicians, and other members of the NICU health care team need to have a framework for understanding and resolving the ethical issues that arise (Callister and Sudia-Robinson, 2011). Although there are many different philosophical perspectives one can use to examine ethical issues, health care professionals need to be able to directly translate those theories to bedside care. This chapter's discussion of ethical approaches focuses on models from the field of applied ethics. The following sections are designed to assist the nurse to recognize and examine ethical issues as they arise in the NICU.

Principles of Biomedical Ethics

The most well-known framework for examining biomedical ethical issues was originally developed by Beauchamp and Childress in 1979. Commonly referred to as the *Principle Approach* or the *Principles of Biomedical Ethics,* the model provides the health care team with four key principles to examine: beneficence, nonmaleficence, respect for autonomy, and justice. All four principles must be considered when examining ethical situations (Beauchamp and Childress, 2013).

BENEFICENCE

The principle of beneficence focuses on the act of doing good or performing actions with the intent of benefiting another person (Beauchamp and Childress, 2013). It is an action-based principle; thus, there is a requirement to act or perform actions that lead to direct benefit. In accordance with this principle, the health care team must examine their actions and overall plan of care to determine the intended direct benefit for the neonate. An important point to remember is that as the neonate's condition changes, an ongoing consideration of beneficence should occur. For example, revisiting all decisions made to use technology to extend an infant's life should have dates set when such therapies are initiated. Goals of care should be reassessed along the therapeutic trajectory (NANN Position 3063, 2016a). Workman (2007) suggests that when uncertainty exists in whether a patient will live, informed consent should be asked for a "trial of care." Thus, family members would understand that the outcome of the trial may not be positive.

To illustrate the principle of beneficence in the NICU, consider the case of a neonate who is born extremely premature and with an extremely low birth weight. The parents agree with a plan of aggressive treatment. However, at approximately 4 days of age, the neonate has a grade 4 intraventricular hemorrhage, severely distended abdomen, poor perfusion, and signs of failing organs. The plan of care that was benefiting this neonate several days ago no longer has the same effect. The care measures that have been in place are not having a direct beneficial effect and must be reexamined with the parents.

NONMALEFICENCE

The principle of nonmaleficence obligates health care providers to avoid directly causing harm to a patient. Specifically, the plan of care must avoid causing intentional harm. Using the previous example of a neonate in multisystem decline, the NICU team would need to evaluate the continuing use of aggressive therapies with a neonate who is physiologically progressing through the dying process. The plan of care should not involve measures solely and directly intended to cause the neonate's death, but rather to focus upon relief of suffering. Measures that are implemented should not cause harm without any direct benefit.

The key aspect of this principle resides in the intent of the health care provider's action. One principle used in neonatal ethics is known as the *principle of double effect* or the *rule of double effect (RDE)* (Beauchamp and Childress, 2013). According to Beauchamp and Childress (2013), for an act to be considered morally justifiable under the RDE, the following four conditions must be met: (1) the actual act must be good or morally neutral; (2) the intent must be limited to the good effect; (3) the bad effect cannot serve as the means to the good effect; and (4) the good effect must outweigh the bad effect.

The RDE is best illustrated by the administration of increasing amounts of morphine in a neonate at the end of life who is exhibiting air hunger. A nurse administers morphine with the intent of relieving suffering, and in the process the patient's respirations slow considerably to the point of cessation. The nurse's intent was not to cause the patient to stop breathing. Rather, the nurse's intent was to ease the patient's suffering. Thus, upon ethical examination of this situation, the conclusion would be that this nurse did not act in a maleficent manner toward the patient.

RESPECT FOR AUTONOMY

The principle of respect for autonomy emphasizes the right of an individual to make decisions for himself or herself. In health care, this principle is reflected in both the right to make decisions about a treatment plan and the right to refuse treatment. When an adult is the patient, the health care team seeks permission for treatment by means of informed consent. True informed consent is an actual process that involves more than obtaining a signature on a form or legal document. During the informed consent process, the patient should be provided with accurate, sufficient, and understandable information. The patient can then weigh the pros and cons of the proposed treatment options, including no treatment, and, after adequate consideration, the patient can express an informed decision regarding his or her preferences.

In the NICU, parents serve as the legal surrogate decision makers for their neonate. NICU staff can assist parents in their decision-making role by keeping them well informed of the neonate's condition and by objectively presenting treatment options. Parents' preferences for care must be reassessed as the neonate's condition warrants, because their preferences may change in either direction. For example, parents who expressed a desire for very aggressive treatment may later decide that deceleration of care may be in the infant's best interest. Other parents may decide to continue aggressive care as planned, even though a grim prognosis is present. Regardless, for parents to act in their infant's best interest, they need to be kept informed of all options, as well as the likely outcomes of the options.

Respect for the health care team and treating their moral distress is also essential. If parents (or other providers) are insisting upon care that a nurse or team member feel is causing harm or suffering to the infant, members of

the team have the right to conscientiously object to participating in this form of care. Catlin and colleagues (2008) have defined conscientious objection as follows: "For the nurse, conscientious objection may occur when the nurse interprets that the specific treatment that has been ordered for a patient is harmful or causing suffering. The nurse does not wish to provide this form of therapy and feels sincerely and has felt for some time that this situation warrants a conscientious objection. The nurse objects to the nature of the orders for treatment, willing to assist in other forms of treatment and not wishing to abandon the patient." Catlin has encouraged treating the infant with the "dual track method" when disagreement with parents occurs. The infant should receive the ongoing curative care that the parents are advocating for but also be shown the dignity and human caring that any dying person deserves. Actions that cause pain, such as blood gases or laboratory sticks, should be minimized. Activities that increase comfort should be maximized, such as dimming the lights or allowing the infant to feel the sun. Encouraging the parents, or nurses if parents are absent, to hold, dress, and comfort the infant, even if attached to life-sustaining equipment, respects the infant's personhood. Workman (2007) discusses continuing diligently to try to reach consensus with the parents but also always showing them respect and support.

JUSTICE

The principle of justice focuses on the fair distribution of the benefits, risks, and costs among members of society in relation to health care needs. In the NICU, questions of justice frequently arise. For example, two mothers are about to give birth to neonates who will require care in the NICU. The births will occur within an hour of each other. One neonate is extremely premature and will have a less than 20% chance of survival. The other neonate will have a 75% chance of survival. If the neonate with only a 20% chance of survival is born first, should he or she occupy the last available NICU bed, or should that bed be reserved for the more viable neonate?

Questions of justice are difficult to resolve at the bedside. Yet pursuing these questions is an important step in achieving balance in health care. Vawter and colleagues (2010) have written a policy for the state of Minnesota on the distribution of health resources during a flu pandemic. Moving toward examining justice from a societal perspective provides an opportunity to develop and frame a health policy that will assist in refining hospital policies and further translate back to the bedside.

UTILIZATION OF THE PRINCIPLE APPROACH IN THE NICU

When ethical issues arise in the NICU, the principle approach can assist the health care team to organize its assessment and analysis of the situation. Examining the proposed plan of care with full consideration of benefits and burdens to the neonate and benefit and burden to the family can provide insight into competing goals. Fully engaging the parents in the decision-making process as early as possible will assist them in exercising their rights as surrogate decision makers for their neonate. Introducing the parents to other parents who have been in a similar situation may be helpful. The National Perinatal Association Family Advocacy Network supplies consultation to neonatal units and support to parents and can be reached at the nationalperinatal.org website. Raising justice-related questions will help clarify how this neonate's case affects the institution and how related cases affect public policy. However, it is important to remember that all principles should be considered and that no one principle is inherently given precedence over the other three principles (Beauchamp and Childress, 2013).

Other Approaches to Ethical Issues

In addition to the principle approach to ethical issues, there are many ethical theories and case analysis models. It is beyond the scope of this chapter to adequately address all these perspectives; however, NICU nurses should be encouraged to further explore them in clinical ethics textbooks.

ETHICAL THEORIES

Three of the theories commonly referenced in bioethics are Kantianism, utilitarianism, and liberal individualism. Although these theories can assist nurses in examining ethical issues broadly, they do not provide direct guidance for resolving issues at the bedside.

KANTIANISM

Kantianism, or deontology, is an obligation-based theory from the 1700s. This theory requires that individuals act with a sense of obligation and that their actions should be as if a universal law. Ruiz (2001) gave an example of applying Kantian theory to developmental care for neonates. Written at a time when this mode of therapy was not universally accepted, Ruiz helped us to see that application of new evidence beneficial to newborns is an ethical imperative. The deontological directive to apply evidence once we know it has more recently been addressed by Camicia (2018) for the adult population.

UTILITARIANISM

The focus of utilitarianism is on utility, or the maximization of the goodness of an act (Beauchamp and Childress, 2013). According to this theory, the decision maker is challenged to identify the greatest good while balancing the interests of all affected individuals. For example, the health care team may desire to provide aggressive treatment to a neonate who will require a succession of very expensive surgical procedures. The family may be unable to

pay for any of the treatment. Under utilitarianism, it may be determined that providing care for this infant would not maximize utility of resource allocation for the community, and thus this infant might not receive the costly extensive care that was recommended by the health care team. Falk and Chong (2008) discuss the need for the nursing curriculum to include teaching on micro and macro allocation of health care therapies.

LIBERAL INDIVIDUALISM

Liberal individualism addresses the rights, both positive and negative, that individuals in our society possess. A positive right requires someone to do something for another individual, such as a health care provider's duty to treat those in need of immediate care. A negative right keeps individuals from being directly harmed by others. For example, an individual may request that no experimental treatments be performed on him. Without explicit consent, his right cannot be overridden.

Case Analysis Model

Apart from ethical theories and principles, a model for analyzing ethical cases was developed and refined for bedside use by Jonsen and colleagues (2002). Their model provides four components that health care providers should examine for each case: the medical indications, patient preferences, quality of life, and contextual features.

MEDICAL INDICATIONS

Health care providers can begin by summarizing the neonate's diagnosis and prognosis. The treatment plan, along with the benefits and burdens, would also be discussed.

PATIENT PREFERENCES

In the NICU, the health care providers would obtain the parents' preferences for their neonate's treatment plan. It would be important to ask the parents what their goals are for the infant. Considering the current and/or proposed treatment plan, the NICU team should also ask parents how they view the benefits and burdens for their infant. It is important to elicit parental preferences, as well as any other concerns the parents may have.

QUALITY OF LIFE

This component of the model provides an opportunity to examine quality of life from the perspective of the health care team and to relate that to the stated parental preferences. This may require additional conversation with the parents to ensure correct interpretation of their values by the NICU team.

CONTEXTUAL FEATURES

The contextual features incorporate a variety of factors, including religious beliefs and practices, financial concerns, family issues, potential conflicts of interest among the care providers or within the institution, and the legal implications of treatment options (Jonsen et al., 2002).

The case analysis model can be useful as an initial step in examining or identifying ethical issues in the NICU. It does not provide a directive for decision making, but it illuminates the issues so that further conversation and progressive steps can be taken toward resolution.

The Nurse's Role in Ethical Issues

The NICU nurse plays a critical role in both direct care of the neonate and support for the parents. The nurse can help prevent some ethical issues from arising by engaging the parents in both conversation and care from the time of admission throughout the neonate's hospitalization. Parents will need help understanding and coping with the complex dimensions and implications of their infant's NICU admission (Sudia-Robinson, 2011b). They will also need extensive nursing support to more actively engage in the care of their neonate (Franck and Axelin, 2013; Skene et al., 2012), regardless of prognosis (Currie et al., 2016).

Optimal NICU care includes comprehensive family support delivered by a dedicated interdisciplinary team of care providers (Hall et al., 2015; Hall et al., 2016). Hall and colleagues (2015), with input from NICU parent groups, are leading the development of the National Interdisciplinary Consensus Model, which focuses on outlining program standards for the psychosocial support of parents of infants admitted to a NICU. Coordinated care commences upon NICU admission and incorporates family support services throughout the trajectory of care. Family-centered developmental care, as well as palliative care and bereavement support, should be provided in the NICU and beyond the immediate grief time frame. This approach also highlights the need for comprehensive postdischarge support for parents, as well as for NICU staff education and support.

ADEQUATE COMMUNICATION WITH PARENTS

In the NICU, nurses, along with other members of the health care team, have an obligation to keep the parents thoroughly informed of the options for care and the associated risks and benefits (Janvier et al., 2014; Sudia-Robinson, 2011a; Sudia-Robinson and Freeman, 2000) and provide them with adequate support services throughout this process (Hall et al., 2016). To adequately involve parents in the decision-making process, health care providers need to move beyond merely imparting information. Parents must have the information but also know how to interpret the information they receive. This has been described in various health care situations as the transparency model (King, 1992). Truth telling is an important nursing virtue (Hodkinson, 2008), but one that must be done with compassion and caring.

Nurses can assist in this process by incorporating the transparency model into their daily interactions with parents. Telling parents what the neonate's ventilator settings are or stating the latest blood gas results represents a nurse simply giving information to parents. The problem with this approach is that parents may or may not know how to interpret the information given to them. Information without a comprehensive explanation or without the proper context is merely data and does not help parents move toward understanding. However, when a nurse explains what the ventilator settings mean for their particular neonate in relation to the course of the neonate's disease process, the nurse is actively helping parents to begin to better understand and think about the information they are given by the health care team. Nurses need to remember that sharing knowledge is different from helping with comprehension or understanding. Therefore, when nurses assist parents to understand their neonate's overall condition, nurses are preparing parents to make more informed decisions for their neonate.

Not all parents will want to be fully engaged in the decision-making process for their neonate. Sometimes parental preferences for involvement will change during the neonate's hospitalization. For example, some parents may be so intimidated by the NICU initially that they may not ask many questions and may agree with whatever is presented to them. As time passes, however, they may begin to ask more questions and move toward desiring to become more involved in daily care. It is important to recognize differences in parental preferences while continually reassessing parental desire for involvement in daily care and decision making as the neonate's condition changes.

SUPPORTING THE NICU TEAM

At times the NICU nurse may feel torn between support for the parents and support for the health care team. This can occur when the health care team advocates one plan of care and the parents disagree with the team's recommendation. For example, the NICU team may recognize that the neonate is in multiorgan system failure and that death is imminent, yet the parents continue to request that aggressive medical intervention continue. The section on autonomy earlier discusses conscientious objection and the "dual track" methodology, which can assist the nurse.

Assessing Ethical Advisories From Maternal Child Organizations

When a dilemma arises, neonatal nurses can often find guidance from organizations such as the American Nurses Association Center for Ethics and Human Rights, the American Medical Association (AMA) Virtual Mentor, American Society of Reproductive Medicine, National Association of Neonatal Nurses, American College of Obstetricians and Gynecologists, American Academy of Pediatrics, and the National Perinatal Association. All of these organizations have studied ethical issues and published advisory position statements.

Consulting the Hospital Ethics Committee

Nurses also have the option of reaching out for an ethics consultation. The Joint Commission requires all health care facilities to have access to ethics experts. When significant differences in the desired plan of care arise between stakeholders, it can be beneficial to initiate an ethics consultation. In most institutions, a nurse, physician, social worker, other staff, or parent can request an ethics consultation. The focus of the consultation should be the actual process rather than the outcome. Ethics committee members can sometimes aid in clarifying the issues and various perspectives presented. The process must be respectful of all perspectives and give full consideration of all possible options. The product of an ethics consultation will be a set of recommendations, not a mandate for a trajectory of care.

The ethics committee can be of assistance to the NICU in situations other than actual case consultation. Hospital ethics committees can serve as important resources about both ethically and legally permissible courses of action that can guide policy development in the NICU. Some ethics committees also prepare educational materials for families to make them aware of the process and how to access committee members (Mitchell and Truog, 2000). The ethics committee members can also help nurses resolve moral distress over unsolved dilemmas. The neonatal nurse may wish to become a member of the ethics committee (Catlin, 2014).

Summary

Nurses are in a unique position to recognize ethical issues as they arise in the NICU. Understanding key ethical concepts and ethical principles can assist in further understanding and resolution of ethical issues. Supporting parents throughout the process by providing information in an understandable context and providing adequate psychosocial support is imperative for collaborative, ethical decision making and optimal care in the NICU.

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CHAPTER 40
Legal Issues

M. Terese Verklan

OBJECTIVES

1. Identify how an attorney may use the nursing process for litigation.
2. Define standards of care and guidelines for establishing the standard of care.
3. Define malpractice and the conditions that constitute malpractice.
4. Define concepts of liability and negligence.
5. Discuss the importance of documentation in the patient's record and guidelines for charting.
6. Discuss the nurse's role in informed consent.
7. Identify scope-of-practice issues in providing patient care functions.
8. Identify the risks and benefits of possessing professional liability insurance.

In the past, the specialty of obstetrics was considered the "high-risk" area for malpractice suits and loss of licensure. Today litigation is not uncommon in our own area of specialization. Neonates are seen as a "special" population that is afforded extra protection (Verklan, 2012). Thus, neonatal nurses must be cognizant of the minimum standards of professional conduct that they, as health care providers, must adhere to. The purpose of this chapter is to familiarize the nurse with the concepts and ramifications of legal concerns as they pertain to the realm of neonatal intensive care nursing. Topics that will be discussed include standards of care, liability, documentation, informed consent, scope of practice, and professional liability insurance.

Nursing Process

A. **The nursing process forms the foundation for nursing education, practice, and documentation, regardless of whether the nurse graduated from a diploma, associate degree, or baccalaureate program.** Although the phrase *nursing process* is often omitted from practice standards and teaching strategies, nursing documentation should continue to be reflective of the nursing process. Failure to follow the following five steps of the nursing process is the number-one cause of all patient injuries:
   1. Assessment: gathers data related to the neonate's physiologic and psychosocial status.
      a. Vital sign records, flow sheets, and nursing progress records.
      b. Body and organ-system findings (e.g., cardiopulmonary findings).
      c. Laboratory and diagnostic reports.
      d. Medical progress notes.
      e. Intake and output.
      f. Progress notes from other disciplines (e.g., respiratory, social work, pharmacy).
      g. Information from the family.
   2. Diagnosis: correctly identifies the neonate's condition using the data obtained from the assessment step, from documents on the nursing care plan, and in the progress notes.
   3. Planning: develops a plan of care that incorporates all aspects of the neonate's condition.
      a. Uses a multidisciplinary approach.
      b. Documents interventions and anticipated outcomes for the targeted diagnosis on the nursing care plan.
      c. Incorporates evidence-based findings into practice.
   4. Implementation: carries out the plan of care.
      a. Follows neonatologist and/or advanced practice nurse (APN) orders, provides direct care, supervises the care given by another, teaches and/or counsels the family, provides referrals for care by other disciplines.
      b. Documents all pertinent information on the neonate's medical record.
   5. Evaluation: evaluates the neonate's response to the plan of care as outlined by the multidisciplinary team, noting any revisions or changes to the plan.
      a. Implementation process is not complete without evaluating the effectiveness of the intervention.

b. Communicates patient response to treatment to family and members of the multidisciplinary team.
c. Documents pertinent findings in the patient's medical record.
d. Revises plan of care based on the patient's response and anticipated outcomes.

B. **The attorney, as well as all interested parties involved in the legal process, will use the steps of the nursing process to:**
1. Interpret the medical record.
2. Identify possible deviations from the standard of care.
3. Speak the same language as the nurse.
4. Generate questions that will be used to depose a nurse defendant.
5. Use the reports of expert witnesses, who will outline how the nurse did or did not follow the nursing process.

Standard of Care

The standard of care outlines the minimum criteria by which proficiency is defined in the clinical area. When the standard is not specifically referred to in the state nurse practice act, it becomes a guideline for practice rather than law. In the legal system, the standard of care is established by defining what a reasonable and prudent nurse would have done in the same or similar circumstances. The issue of excellence in practice or quality of care given does not pertain to the argument—what is being sought is reasonableness and prudence. A reasonable and prudent nurse is a nurse with like education, background, and experience who would behave in a corresponding manner, given a parallel set of events. The plaintiff attorney has the burden to prove that the standard(s) do exist and that the defendant nurse failed to meet the standard(s).

In addition, it is expected that the standard of care given to neonates everywhere is the same. "A neonatal nurse is a professional nurse who provides skilled nursing care for low-risk, high-risk and critically ill neonates, high-risk neonates, and their families. The neonatal nurse has specialized knowledge and develops and maintains clinical competence through standardized practice and continuing education" (Association of Women's Health, Obstetric and Neonatal Nurses [AWHONN] and National Association of Neonatal Nurses [NANN], 1997, p. 8). "Although neonatal nurses may provide basic neonatal care, they may also focus on an area of expertise, as for example, intensive or critical neonatal care, transport, lactation, grief, extracorporeal membrane oxygenation or developmental care" (AWHONN, 2012; AWHONN and NANN, 1997; NANN, 2013).

Ewing v. Aubert (1988) set out that a maternal–child nurse is held to the standard of care of a nurse practicing in the maternal–child specialty. Neonatal nurses, a subspecialty within maternal–child nursing, must be cognizant of what the professional practice standards are for that subspecialty: A nurse who practices her profession in a particular specialty owes to her patients the duty of possessing the degree of knowledge or skill ordinarily possessed by members of her profession actively practicing in such a specialty under similar circumstances. It is the nurse's duty to exercise the degree of skill ordinarily employed, under similar circumstances, by members of the nursing profession in good standing who practice their profession in the same specialty and to use reasonable care and diligence, along with his or her best judgment, in the application of his or her skill to the case (*King v. Department of Health & Hospitals*, 1999).

The quality of the nursing care provided is judged according to national standards, making obsolete the "locality rule." The locality rule permitted nurses to be judged according to the standard of care evidenced by nurses working in the same geographic area, reflecting the community's accepted practices. Recognition of national standards by professional neonatal nursing organizations and accreditation agencies is reflected in clinical policy and procedure manuals. In addition, accredited schools of nursing across the nation have similar curricula and textbooks, and nurses attend similar continuing education conferences. Thus, it is expected that the professional nurse will be and remain competent and continually updated on the standards of care and practice (American Nurses Association [ANA], 2018; AWHONN, 2012; NANN, 2013).

Five basic types of evidence are used to establish the legal standard of care: (1) state and federal regulations; (2) institutional policies, procedures, and protocols; (3) testimony from expert witnesses; (4) standards of professional organizations; and (5) current professional literature.

STATE AND FEDERAL REGULATIONS

These agencies establish the standards of care and scope of practice. The national standards tend to be written in broad language to permit flexibility without compromising standards to accommodate differences within each state. The standard of practice is also defined by the state nurse practice act as mandated by each state's legislature. Here the scope of practice is delineated for each level of nursing (e.g., licensed vocational nurse, registered nurse, APN). For example, a registered nurse may not delegate the act of assessment and the formulation of a nursing diagnosis to any assistive personnel who are unqualified to perform this task (ANA, 2012). In addition, standards of nursing practice are regulated by the state board of nursing, the department of health, The Joint Commission (TJC), and the Health Care Financing Administration, in addition to other regulatory agencies (Urubek, 2016).

INSTITUTIONAL POLICIES, PROCEDURES, AND PROTOCOLS

The hospital's policies, procedures, and protocols also outline the standard of care. The policy establishes the purposes for performing a procedure, whereas the procedure is the guideline for how that procedure should be carried out. These guidelines must reflect the national and state standards of care, should be reviewed at least annually, and should be revised to reflect current acceptable nursing practice (Urubek, 2016). In addition, these guidelines must be (1) prepared by a qualified committee of professionals who practice in the specialty, (2) consistent with current research and practice literature, (3) archived for the length of liability, and (4) accessible to staff (Urubek, 2016). The policy and procedures manual should be approved by both the unit and the hospital's nursing and medical administrations.

Being unaware of the policy and procedures for the standard clinical practice at your institution is not an acceptable excuse for not being held accountable for your practice. The policy and procedures manual is often one of the first documents requested by both the plaintiff and defense attorneys because it is the best source for specific standards by which to evaluate a specific nurse's care. Because the statutes of limitations endure for 18 to 21 years and standard care practices change dramatically across the years, keeping the policy and procedures manual will also help to determine what the standard of care was at the time the neonate was hospitalized.

TESTIMONY FROM EXPERT WITNESSES

A nurse expert is typically required to articulate what the standard of care is or was in the situation in which the nurse has deviated from the usual and customary standard of care. A nursing expert opinion requires that the person expressing that opinion possess special skill, knowledge, and experience in the neonatal area and knowledge of the standards applicable at the time of the occurrence (Starr, 2016). The judge and jury have little knowledge related to neonatal physiology, pathophysiology, and the relevant neonatal nursing care. They therefore need assistance in understanding just what a reasonable and prudent nurse would have done in the given circumstances (e.g., did the nurse meet the accepted standard of care?).

Both liability and damages have to be proved in nursing malpractice cases. Thus, two types of experts are usually necessary: a nurse to address the nursing standard of care and a physician to determine causation, that is, to link the breach of standard to the injuries suffered by the neonate. Professional nursing philosophies dictate that nurses be the only witnesses permitted to testify as experts outlining what the nursing standard of care is in a nursing malpractice suit. However, it is the quality of the expert's experience and education that determines the competency and credibility of the testimony (Starr, 2016).

STANDARDS OF PROFESSIONAL ORGANIZATIONS

Professional associations represent the interests of nurses. The ANA has developed standards with measurable criteria that define professional nursing practice (ANA, 2018), as well as standards for neonatal nursing (ANA, 2013). Specialty organizations such as the NANN, AWHONN, American Association of Critical-Care Nurses (AACN), and National Association of Pediatric Nurse Associates and Practitioners (NAPNAP) have adapted these standards to define the standards of care and professional practice guidelines applicable to the care of neonates. For example, AWHONN publishes the *Neonatal Nursing Clinical Competence and Education Guide* (2012).

CURRENT PROFESSIONAL LITERATURE

Current texts and journal articles, although technically hearsay, aid in establishing the legal standard of care. A number of journals specific to the care of neonates focus on clinical, management, and research articles. Clinical articles are useful in helping to determine the applicable standard of care at the time of the malpractice suit, whereas nursing textbooks provide information related to the standard of care associated with nursing techniques and care (Iyer, 2011a). Research articles are beginning to assume more importance in the legal arena because of the desire to document evidence-based practice. Evidence-based practice is defined as the incorporation of the current best evidence in clinical decision making. Increased use of websites such as Medline and CINAHL for research/clinical information has led to an increase in the critique of published literature by nurses. Hospitals holding Magnet status must demonstrate that nurses participate in research utilization or they will lose their designation. Despite this, the integration of research findings into clinical practice is slow, taking as long as 10 to 15 years. However, keeping theory and clinical practice on par with the literature and remaining current with regard to continuing education will assist the nurse in ensuring that his or her professional standards are synonymous with those of his or her peers.

FURTHER ISSUES: PRACTICE GUIDELINES AND ETHICAL STANDARDS

Standards of care are often confused with practice guidelines. Standards of care are the basis for proving that the nurse had a duty to the patient and that there was a breach of that duty. Clinical practice guidelines, with reference to the standards of care, are meant to assist the health care provider in the delivery of care in specific clinical circumstances. For example, *Guidelines for Perinatal Care* outlines recommendations regarding nurse providers, nursing ratios, staffing guidelines, and outreach education for inpatient perinatal care facilities providing basic, specialty, and subspecialty care (American Academy of Pediatrics and

the American College of Obstetricians and Gynecologists, 2017). Critical pathways are another example of a practice guideline that is modified to reflect the neonate's clinical progress. Therefore, the difference between a standard of care and a practice guideline is that the standard always must be adhered to, whereas the guideline suggests a voluntary approach to achieve a desirable patient outcome (Iyer, 2011a; NANN, 2010).

The ethical standards of nursing practice may also be the issue in a malpractice suit: The Mississippi Board of Nursing charged Terry Lynn Hanson, a registered nurse, with abuse of neonatal patients. It was noted that her clinical practices included holding a baby around its neck with only one hand, carrying babies by holding them under their axillae, carrying naked babies around the neonatal intensive care unit (NICU) and washing them in the unit's sinks and that she endangered the babies by rapidly flipping the levers on the incubators when attempting to stimulate them. The board, finding her guilty on all charges, revoked her license. Nurse Hanson appealed to the Supreme Court of Mississippi, who held that her behavior constituted a reckless disregard of the health and safety of the neonates. The court also ruled that she was negligent by holding babies under the axillae, permitting their bodies to dangle; and that removing them naked from incubators to bathe and weigh them in different areas of the NICU compromised thermoregulation and exposed them to risks of infection; and that overstimulation increased the risk of intraventricular hemorrhage (Tammelleo, 1998, p. 1).

Malpractice

The term *malpractice* means negligence on the part of the nurse, in that she or he has violated the standards of ordinary nursing practiced by nurses of similar background in the same specialty of nursing. Malpractice is professional misconduct that may be intentional or unintentional. If the individual is acting in a personal capacity, then the individual would be subject to negligence, as malpractice is limited to the omission, lack, or misuse of a professional skill. By undertaking professional services to the patient, a nurse represents that she or he possesses, as a duty, the degree of learning and skill ordinarily possessed by nurses of good standing practicing in the same community under similar circumstances. It is the nurse's further duty to use the care ordinarily exercised in like cases by reputable members of the profession practicing in the same or a similar locality and under similar circumstances. The nurse is to use reasonable diligence and best judgment in the exercise of her or his skills and learning in an effort to accomplish the purpose of employment. A defendant nurse must violate one of these duties before being found to have committed malpractice (Fulginiti et al., 2007, p. 1375).

It must be emphasized that the nurse need possess only the knowledge and skill possessed by the average reasonable, prudent nurse and must exercise reasonable care, skill, and judgment in carrying out her or his professional work. The nurse need not be perfect or able to predict every single difficulty or uncertainty regarding the patient. However, the nurse must act in a careful or prudent fashion in the delivery of professional care while exercising reasonable care, skill, and judgment. Occasionally an unexpected situation arises so quickly that one's actions in hindsight may not be considered to have been the perfect course of action.

A mistake in judgment is not considered malpractice: A mistake in judgment on the part of the nurse is not evidence of negligence. If a nurse possesses reasonable and ordinary skill and uses care ordinarily used in like or similar situations by nurses of reasonable and average skill practicing in the community at the time in question, she or he is not guilty of negligence even though her or his judgment may be subsequently proven incorrect (Fulginiti et al., 2007, p. 1375).

Liability

Today nurses are recognized as professionals who are responsible and accountable for the care they give to their patients. If the nurse is liable to the patient because of negligent conduct, that nurse can be held legally responsible for the harm caused to that patient (Cady, 2016). Harm must result from the act, because without damage, no legal wrong has been committed. Baby R was born after a difficult labor, including the presence of meconium and episodes of hypoxia. Routine orders for the admission were given despite the presence of risk factors for hypoglycemia. Over the next 3 hours of life, the baby's glucose values decreased from 104 mg/dL to 28 mg/dL. The nurse fed the baby but did not notify the physician. The neonate continued to experience hypoglycemia throughout the night. The glucose level increased to normal parameters after a feeding in the morning. The physician examined the baby shortly after the feeding, noting that she was at risk for hypoglycemia. No further orders were given, such as the need to begin intravenous glucose. A neonatologist was not consulted. Later that day profound hypoglycemia was evidenced by seizure activity. Nursing did not notify the physician of the seizure activity until later in the evening when the seizures became worse. The physician returned to the nursery and examined Baby R. Once the seizures were observed, the baby was transferred to another hospital. The hospital settled for $1.75 million before trial (Laska, 2005).

The plaintiff, the party bringing the suit, must prove the following four elements in a malpractice case:

1. The nurse had a duty to her or his patient.
2. There was a breach of that duty.
3. Harm or damages did occur to the patient.
4. Breach of that duty resulted in harm (proximal cause).

An infant, born in a depressed state, had Apgar scores of 3 and 8 at 1 and 5 minutes, respectively. Although his condition

was improving, he continued to have raspy breathing that required suctioning. It was alleged that the defendants failed to provide adequate special care and observation, causing the baby to suffocate on its own secretions. The neonate was discovered in a cyanotic state 2 hours after birth. Resuscitative techniques restored the heartbeat in 18 minutes. He was transferred to another hospital, declared to be brain-dead, and was removed from life support 4 days later. The plaintiff claimed that resuscitation was both delayed and improperly performed. The defendants argued that the baby appeared normal, that the cause of the respiratory arrest was unknown, and that inborn errors of metabolism caused the death. They also countered that failure to respond to resuscitation does not imply negligence (Du Page County [IL] Circuit Court, Case No. 94 L-318 [Laska, 1997]).

In this case the plaintiff proved that the defendant owed a duty to the neonate, in that the baby and his parents should expect the care received to be at least equal to the standard of care. However, the plaintiff was not able to prove that the defendant breached the duty (failure to respond to resuscitation does not imply negligence) or that there was proximal cause (inborn errors of metabolism may have contributed to or caused the injury). Thus, despite the neonate's death (damages), a malpractice suit cannot be won if all four elements are not present.

A. **The costs of liability when a neonate is involved are high for three reasons:**
   1. The costs of health care for a damaged infant with a normal life expectancy are high.
   2. The longer statute of limitations for minors may permit charges to be made years later, applicable to other medical malpractice actions.
   3. There is sympathy toward the family, who may not be able to afford the needed care for the child, as opposed to the deep pockets of a corporation, who may be seen as uncaring and will not miss the money anyway.

B. **Although an individual nurse is accountable only for his or her own practice, three additional theories of liability may be pursued against a facility or its management** (Lewis and Krulewicz, 2011; Rottkamp, 2011):
   1. *Respondeat superior*, which in essence says that the employer is given the responsibility and accountability for the actions or intentions of the employee. This doctrine:
      a. Holds an employer liable for the negligent acts of employees that arise in the course of the employment (i.e., employers are held responsible for the acts of those whom they have a right to supervise or control).
      b. Holds the institution responsible for ensuring that the policies and procedures meet the standard of care and that employees follow these policies.
      c. Will not impose liability in most circumstances on a nursing supervisor for negligent acts of the nursing personnel he or she is supervising. This responsibility rests with the person who makes changes in the policies and procedures.
      d. Obligates the nursing supervisor to ensure that the licensed and unlicensed nursing personnel under his or her supervision are able to provide patient care safely. If the supervisor does not document the personnel's deficiencies and use the chain of command, she or he can be held liable for any damages that befall a patient.
      e. Holds that negligent employees are always liable for their own conduct.
   2. *Corporate negligence* holds the institution's management and board of trustees liable for any breach of their duties:
      a. The institution must provide a safe physical setting and monitor the quality of care provided, along with the equipment necessary for patient care.
      b. An equipment standard must be implemented.
         1) The institution must have a management plan documenting competency validation for the proper use of medical equipment by the institution's employees (TJC, 2019).
         2) The institution may also name the equipment manufacturer as a third-party defendant in an attempt to shift the blame (Verklan, 2012). Shortly after birth, Baby Wright's blood pressure decreased, necessitating a transfer to the special care unit. Dr. Bloom ordered a bolus of normal saline (unconcentrated) to be given over 30 minutes. Nurse Diltz offered to prepare the bolus. The hospital stocked both the unconcentrated and the concentrated normal saline solutions in the same place. Nurse Diltz obtained a vial of the concentrated sodium chloride that had "CONCENTRATE" and "CAUTION: MUST BE DILUTED FOR I.V. USE" in large red letters. There was also a written warning in red letters that the fluid was a 14.6% solution. Nurse Diltz did not read the physician's order, nor did she note the label on the sodium chloride vial. The fluid bolus was subsequently administered to Baby Wright. After the second bolus, Baby Wright suffered severe brain damage. The Wrights sued Abbott Laboratories, the suppliers of the concentrated sodium chloride solution. Abbot never sent a warning letter to the hospital despite the Food and Drug Administration's warning to change the labeling and package inserts for the concentrated and unconcentrated normal saline products. The plaintiffs argued that Abbott had a duty to warn the hospital about the dangers of inadvertent

administration of the wrong solution and that the failure to warn the hospital was the proximate cause of Baby Wright's brain injury. The court granted summary judgment for Abbott (not guilty). It also found the hospital and its staff should have been aware of the dangers of stocking the look-alike products together, and therefore, Abbott Laboratories did not have a duty to warn the hospital of the risk. The court also found that had Nurse Diltz simply read the physician's orders and the label on the vial, the concentrated solution would not have been given (*Wright v. Abbott Lab.*, 2001).

c. The facility may be found liable for advertising a service for which it lacks the proper equipment or personnel or for failure to keep these services at the acceptable standard of care.
d. The institution must verify the credentials of those who apply for clinical privileges (e.g., APNs) and must also query the National Practitioner Data Bank at the time clinical privileges are requested, and subsequently every 2 years, regarding those who hold practice privileges. The data bank maintains records of disciplinary action taken on licenses, hospital privileges, and payment in conjunction with malpractice suits. In addition to health care organizations, professional societies and attorneys have access to the data bank. Each APN should be familiar with the data bank and should periodically verify that the information it contains regarding her or him is accurate.
e. Clinical competencies must also be evaluated and documented every 3 years (TJC, 2019).

3. *Apparent/ostensible authority* holds an institution liable for the acts and omissions of an independent contractor (Lewis and Krulewicz, 2011; Rottkamp, 2011).
   a. The hospital should maintain a file for each agency nurse that contains her or his nursing license, required certifications, and a current competency skills checklist.
   b. APNs working within the hospital must be aware that patients view them as hospital employees even if they are in private practice, and as such the hospital may be held liable for their acts.

C. **An area of considerable controversy in the liability arena relates to risk management and quality assurance activities** (Keohane et al., 2018; Liang and Mackey, 2011).
1. Quality assurance, more commonly called *quality management* today, focuses on evaluation of the quality of patient care, continuous quality improvement, and total quality management. The department and its activities may or may not be integrated with risk management.
2. Risk management is an internal systematic process aimed at preventing injuries and accidents and reducing financial liability for the institution. Occurrence, variance, or incident reports are reviewed to evaluate and anticipate risk associated with the provision of services.
   a. By documenting occurrences and maintaining related records, such as the organization's claims history, quality assurance and utilization review activities, and risk management and analysis, this area may have information valuable for a plaintiff's malpractice case.
   b. Many jurisdictions have provided a protective shield for quality assurance and risk management activities, which renders the materials generated and the thought processes engaged in during those activities "privileged" or otherwise nondiscoverable (defendant cannot be asked to produce the materials).
3. Risk management works closely with quality assurance, as information from risk management activities may be helpful in improving the quality of patient care. TJC links these areas in that such information must be accessible to all components of the quality assessment departments (TJC, 2019).

D. **Scope of practice.** Each state has its own nurse practice act, composed of statutes passed by its legislature and defining the boundaries of nursing practice. These laws vary from state to state in their demarcation of nursing practice. In contrast to state medical practice acts, the nurse practice statutes delineate nursing responsibilities in broad, universal nomenclature that generally must be examined with reference to the pertinent local law. The crucial issue regarding the scope of practice is whether the procedure performed by the nurse is legally within or beyond the scope of a nursing license to practice (Jacoby and Scruth, 2017).

Numerous areas of medical and nursing practice overlap one another, especially in the NICU. Depending on the unit and its written protocols, the same procedure may be considered within the realm of medicine when performed by a physician and within the realm of nursing when performed by a nurse. These gray areas have evolved partly in response to the nurse's increased level of educational preparation and advanced practice role and partly in response to the high-tech environment found in the NICU. Neonatal nursing is considered a specialty area of practice, and the high-risk neonatal nursing in the NICU is considered a subspecialty area of practice. Certification for both the low-risk and the high-risk neonatal nurse is available through several specialty organizations (ANA, AACN Certification Corporation, National Certification Corporation [NCC], NAPNAP).

Increasing the scope of practice, autonomy, and authority is likely to result in greater exposure to liability situations. Critical legal liability and scope-of-practice problems arise whenever the nurse assumes patient care functions of an independent nature that:

1. Have long been held to be solely within the province of physicians.
2. Are not the subject of standing orders.
3. Lack definition in the nurse practice act.
4. Are not generally recognized as legitimate nursing functions by accredited professional organizations.

The standard of care and liability for negligence may be determined by (Starr, 2016):

1. Nurse's level of training and experience.
2. Manuals and textbooks written for the specialty.
3. Actions and inactions of the nurse.
4. Protocols and instructions referred to by the nurse.
5. The accepted professional nursing practice.

The following case highlights many of these principles. Dr. Seal remained with Baby T, born at 0130 after a difficult labor and traumatic forceps delivery, for approximately 1 hour before the baby was taken to the nursery. He left the hospital at approximately 0300, with instructions to the nurse that the medical student was in charge but that he was to be called if needed. Nurse Bowles was concerned about Baby T from the outset, taking vital signs every 15 minutes. She called the medical student at 0345 and 0400, both times at which she was reassured that the baby looked "fine." Nurse Bowles did not call Dr. Seal. The nurse's aide assigned to Baby T did not take vital signs as ordered and fell asleep twice during the shift. Baby T's condition required transport to another hospital, where he was diagnosed with hypovolemic shock related to a subgaleal hematoma, likely the result of the forceps delivery. The plaintiffs brought a negligence suit against the hospital after the baby's death, alleging that the hospital personnel failed to take proper action when Baby T displayed signs of distress. The jury returned a verdict against the hospital for $800,000, which was reduced to $650,000 because Dr. Seal agreed to a pretrial settlement of $150,000 (Tammelleo, 1995).

The reasonable, prudent nurse, besides being responsible to the patient, is also accountable to herself or himself and to the profession (Jacoby and Scruth, 2017). Both the nurse and the employer have the responsibility to determine the level of competence of the nurse who is asked to provide care outside her or his specialty area. The right of a nurse's refusal to "float" has been upheld by the Wisconsin Supreme Court (*Winkelman v. Beloit Memorial Hospital*): A nursery nurse, Nurse Winkelman, was asked to float to a unit that provided postoperative and geriatric care. She discussed the situation with the supervisor, indicating that she had never floated, that she was exclusively a nursery nurse, and that she was not qualified to provide the type of care being requested. It was her opinion that the floating would put the patients and her license at risk, and thus, the hospital in jeopardy. The supervisor gave her three options, (a) float, (b) find another nurse to float, or (c) take an unexcused absence day. Nurse Winkelman left the hospital and later received a letter informing her that the hospital took her actions to be a voluntary resignation. Although she denied that she had ever resigned, the hospital refused to reinstate her. Nurse Winkelman filed a complaint of wrongful discharge against the hospital. The case was decided in her favor, and the hospital appealed. The Supreme Court affirmed that she had identified the fundamental policy that provides for only qualified nurses to render care and that nurses who provide care for which they are not qualified are subject to sanctions under the law (Tammelleo, 1992).

Advanced Practice

Coincident with evolving health care delivery systems, neonatal APNs can be found in hospitals, ambulatory care centers, and private practice. The APN is often the only health care provider in many rural areas. According to the ANA, APNs are those who have further knowledge and practice experiences that have prepared them for specialization, expansion, and advancement in the practice role (ANA, 2018).

1. Specialization: focusing on one aspect of the field of nursing.
2. Expansion: acquisition of new practice skills.
3. Advancement: encompassing both specialization and expansion and involving:
   a. New integration of theories and skills.
   b. Graduate education.

The licensing statute in each state controls advanced practice and thereby protects the use of the title of APN. All states have defined the scope of the APN by the board of nursing, with several states having the state board of nursing and the state medical board jointly oversee licensing and scope of practice for APNs. An APN is a nurse with a graduate degree in nursing who is practicing in an advanced clinical role. APNs are able to conduct comprehensive health assessments and demonstrate expert skill in the diagnosis and treatment of complex clinical issues evidenced by individuals, their families, and communities. The APN functions with a high degree of autonomy in the formulation of clinical decisions to manage acute and chronic illness and promote wellness. Education, research, management, leadership, and consultation are integrated into their clinical role. They collaborate with nurses, physicians, pharmacists, and others who influence the health care arena (ANA, 2018).

In the neonatal area, the two recognized APNs are the neonatal nurse practitioner and the clinical nurse specialist. As APN roles continue to expand, there will be further debate on what constitutes nursing functions.

A. **Neonatal nurse practitioner** (ANA, 2018; AWHONN, 2012; NANN, 2013).

1. One of the most common APNs found in the tertiary care setting.
2. Is responsible for managing a caseload of neonatal patients with general supervision, collaboration, and consultation from a physician.
3. Exercises independent judgment in the assessment, diagnosis, and initiation of delegated medical processes and procedures by using extensive knowledge of pathophysiology, pharmacology, and physiology.
4. Is involved in education, consultation, and research.
5. Has successfully graduated from a master's program (after the year 2000) with certification through the NCC.

B. **Clinical nurse specialist.**
1. Focuses on patient care, staff education, research, and consultation.
2. Responsibilities are (ANA, 2018; AWHONN, 2012; NANN, 2013):
   a. Acting as a resource for neonatal nurses, neonatal nurse practitioners, and other care providers.
   b. Establishing and evaluating patient care standards.
   c. Assessing and identifying educational needs of the family, nursery, and community.
   d. Designing and implementing appropriate educational programs based on identified needs.
   e. Providing consultation to health care providers.
   f. Initiating research projects, participating in data collection, and instituting changes based on research findings (evidence-based practice).

By virtue of the necessary education and training required to become an APN, they are held to a higher standard than a registered nurse. Thus, the standard of care expected of the APN is the degree of care expected of any reasonable and prudent APN who practices in the same specialty.

A major legal issue relates to the permissible scope of practice and how independent of physician oversight the APN may be. The nurse practice act, in reference to the APN, has been broadened to include diagnosis and treatment, areas that were exclusive to those holding medical credentials. All states have passed legislation that defines the scope of practice.

The most common areas in which APNs have incurred liability are as follows (Guido, 2013; Iyer, 2011b):

1. Conduct exceeding their scope of expertise resulting in damages.
2. Conduct exceeding physician-delegated authority resulting in damages.
3. Practicing independently in a state that stipulates that APNs must have a sponsoring physician.
4. Failure to refer the patient to a physician when the APN's skills are exceeded.
   a. Is the most common cause of action.
   b. APNs must also refer the patient in a timely manner when they recognize the patient's condition requires increased medical attention.
5. Negligence in their delivery of health care.
6. Failure to adequately diagnose the patient's condition.

Documentation (Yankowsky, 2017)

A. **It is a professional responsibility of the nurse to document on the medical record. This will:**
1. Facilitate care.
2. Enhance continuity and coordination of care.
3. Assist in the evaluation of the patient's response to treatment.
4. Provide a legal and official record of the care provided.

B. **Thus, the medical record is used by the attorney as a tool to provide evidence in legal proceedings because it also verifies that the nurse:**
1. Provided the standard of care.
2. Did so within the scope of his or her nurse practice act.
3. Provided "routine care." Negligence could be proved if this information is absent or inappropriate. Flow sheets that list these routines, along with times, dates, patient and caregiver identification, and nursing care outcomes, are valuable in providing a means of documenting repetitious nursing activities.

C. **Although nursing notes need to be as complete as possible, the comment "If it's not documented, then it wasn't done" doesn't always hold true.** Patient care is always the number-one priority. Once the emergency is past, the nurse should strive to document the events, using as much detail as possible. However, if the needs of other patients were placed on hold during a crisis, those needs must be met immediately once the crisis is past. When the medical record is incomplete, the nurse may testify as to what constitutes her or his usual practice.

D. **The most common charting systems in the NICU are** (Iyer and Koob, 2011):
1. Flow sheets.
   a. Decrease the need to document repetitive, routine nursing functions in the narrative notes.
   b. Have column-and-row format organized according to time and/or shift.
   c. Use abbreviations, symbols, and check marks to enter information.
2. Narrative charting.
   a. Patient care is documented by using chronologic format.
   b. Entries describe the neonate's status, interventions, evaluation of care, medical treatments and

equipment (e.g., ventilator, bed, phototherapy lights) used and the neonate's response to care.

3. Problem-oriented charting.
   a. Problem list outlines the patient's priority problems.
   b. Updates should be entered on a regular basis as problems resolve and new ones emerge.
   c. Documentation may be directly on the care plan or in the narrative notes.
   d. Specific format is followed.
      1) S = subjective information that the patient tells the nurse.
      2) O = objective information the nurse observes (including laboratory results).
      3) A = assessment of the earlier-mentioned data, leading to a nursing diagnosis.
      4) P = plan that the nurse will implement to address the care issue.
4. Problem, intervention, and evaluation of problems (PIE) charting: uses flow sheets, progress notes, and nursing diagnoses.
5. Charting by exception.
   a. Narrative notes are completed only when the neonate's progress and/or condition deviates from the expected or when an untoward occurrence arises.
   b. Charting system contains nursing care plans, nursing database, flow sheets, and progress notes.
   c. Standards of practice, determined by the institution, are incorporated into the charting system to record routine, repetitive nursing interventions (e.g., observation of intravenous site, checking ventilator settings).
6. Electronic medical record.
   a. Uses a single, easily accessible site to store a detailed account of the neonate's delivery, transition, and hospital course.
   b. Accuracy in patient information is enhanced as the nurse relies less on human recall.
   c. Patient monitoring is automatically uploaded into the appropriate space (e.g., vital signs from cardiopulmonary monitoring: blood pressure, heart rate, oxygen saturation, etc.).
   d. The nurse requires training on the documentation system/computer used to input and retrieve patient-related data.
   e. To access the medical record, an electronic signature and password/code must be entered. This is unique for each health care provider and must never be shared.
   f. Only health care providers/staff that are caring for the patient have a legal right to access the medical record.

E. **Table 40.1 outlines the advantages and disadvantages of each charting strategy.**

F. **Guidelines for documentation** (Iyer and Koob, 2011; Verklan, 2012).
1. Sign at the end of every entry by using full name and credentials or only initials (full name and credentials noted in the appropriate space). Ensure that no vacant lines are left. An empty space may later prompt someone to fill in a "missing" piece of information.
2. Cosigning means that you have observed and/or approved the care given and that you are accepting joint responsibility (and liability) for that care. Nurses who are required by hospital policy routinely to countersign documents or information in the patient's chart should protect themselves in one of two ways:
   a. By personally verifying the information being recorded.
   b. By noting in the record that the signature is included in accordance with hospital policy and is not based on personal knowledge of the information in question.
3. Illegible, sloppy handwriting with spelling and grammatical errors will convey a negative impression of the nurse.
4. Late charting is always suspect because it is typically key information that is added. Chart the information as soon as possible, beginning with the words "late entry for [date and time]."
5. To correct a mistaken entry:
   a. Draw one line through the entry.
   b. Write "mistaken entry" above the line. (The term *error* is no longer advised because juries tend to associate it with a clinical error.)
   c. Initial or sign document and add date next to "mistaken entry."
   d. What if a nurse is instructed not to chart an error by the attending physician? Nurses who accede to the demands of a physician to cover up the true facts of an unusual clinical episode by deliberately not mentioning it in the patient's chart not only may be subject to possible loss of licensure but also, in flagrant circumstances, even subject themselves to criminal action, leading to a fine or jail sentence.
6. Avoid inappropriate comments concerning:
   a. The patient's or family's personality traits or idiosyncrasies (unless such remarks are relevant to the infant's treatment).
   b. Subjective views to the effect that the patient or family is a potential litigant.
   c. Admissions of legal liability with respect to untoward medical or nursing events. Examples are:
      1) "The IV infiltrated because the night staff forgot to check it" (Solberg, 1986, p. 13).
      2) "Patient going into shock. Could not get Dr. Jones to come. We never can!!!" (Fox and Imbiorski, 1979).

Table 40.1

Advantages and Disadvantages of Charting Systems

Charting Systems	Advantages	Disadvantages
Flow sheets	Easy to use. Decrease time spent.	No note on narrative sheet. Duplication of documentation on narrative sheet.
Narrative charting	Easy to document events as they occur in time.	Information may be disorganized and may not contain all elements of nursing process. Key patient issues may vary from shift to shift and from nurse to nurse; thus, it may be difficult, years later, for hospital, nurse, and/or attorney to tease out relevant information related to specific patient complaint.
Problem-oriented charting	Documentation is organized. All disciplines use same progress notes, permitting increased collaboration and continuity of care.	Continuing same format on all patient problems becomes redundant, with same information appearing over and over. Time consuming because of repetitious nature of note.
PIE charting	Documentation is organized. Evaluation of each problem requires only the information that is specific to that particular problem, intervention, and evaluation.	Novice nurses may have difficulty where there is no traditional care plan but instead an ongoing plan of care that is documented daily.
Charting by exception	Complete, detailed patient information is easily accessible to the health care provider. Standard of practice for documentation outlines expected normal findings.	Exceptions to the standards of practice may not be documented because nurses become accustomed to "checking off" the flow sheets.
Computerized medical record	Improves legibility of the record, decreasing misinterpretation and error. Correct spelling is already in the system.	The selection of phrases or words doesn't always reflect the neonate's condition, as computerized records are "built" for the entire hospital. The nurse may have to input additional notes.
	Patient information can more easily/quickly be located, retrieved, and filed.	Accidently "choosing" the wrong descriptive phrase from the dropbox may result in a misleading or inaccurate assessment.
	Uses a standardized and structured format for inputting data, as well as mandatory areas that require population (care plans, flow sheets, nursing assessments).	Because the nurse is charting on the same computer, he or she may inadvertently chart the assessment on a different neonate.
	All entries are time-stamped. Also, the time the individual accesses the medical record is time-stamped.	Privacy, security and confidentiality may be endangered. Hospital policy as well as the HIPAA provide for stern penalties, including punitive actions.
	Use of bar codes allows the information to be scanned immediately into the medical record.	Misinformation may be difficult to correct, as the error may not be detected and the medical record can be viewed by the entire appropriate health care community.
	Policies and procedures may also be on the same computer for quick, easy access when needed.	

HIPAA, Health Insurance Portability and Accountability Act; *PIE*, problem, intervention, and evaluation.

Data from Iyer, P. W., & Koob, S. L. (2011). Nursing documentation. In P. W. Iyer, B. J. Levin, K. C. Ashton, & V. Powell (Eds.), *Nursing malpractice. Volume II: Roots of nursing* malpractice. Tucson, AZ: Lawyers & Judges Publishing, Kindle edition.

7. Document occurrences accurately and concisely. For example, the neonate's parents (plaintiffs) may have a different view of what actually took place. In a malpractice action, the burden of proof rests with the plaintiff. In the case of *Coleman v. Touro Infirmary of New Orleans* (1993), the plaintiff alleged that the defendants had been negligent by failing to treat an abruptio placentae before the premature delivery of the infant and that the defendants' actions or inaction had caused the child's death. There were several discrepancies between the patient's recollection of events and the medical

record. The court consulted the chart and the physician, determined that the nurses' notes stated another set of events, and concluded that the plaintiff failed to prove any act or omission by the obstetrician or hospital that resulted in the wrongful death of the Coleman infant.

8. Document objectively.
   a. Avoid using "appears to be" and "seems to be." These phrases are not consistent with the judgments/diagnosis made by the critical thinking nurse.
   b. Quantify in measurable aliquots when possible. For example, "approximately 30-cc emesis" gives more information than "large emesis."
   c. The patient record is not an appropriate place to refer to an incident report having been made. What should be documented is a factual account of what transpired and what was done. Incident reports enable the hospital or agency to make necessary investigations of the situation while the patient is still hospitalized, to identify situations of increased risk, and to trend these events to determine whether they are preventable (Iyer and Koob, 2011).
9. Document promptly:
   a. Any significant changes in the patient's status.
   b. Nursing actions undertaken to intercede in the situation, including notifying the physician of the concern. Note the time of the phone call notifying the physician, the information relayed, any orders received, and what you did next.

The case of *Mark and Debbie Easter, etc. v. Baylor University Medical Center* (Laska, 1993) illustrates the way in which nurses can place themselves in a liability situation by ignoring the previously noted standard of conduct. The defendant was a 29-week gestational age neonate delivered by cesarean section at the defendant hospital. His serum potassium was not measured during the first 6 days of his life, and the blood glucose level was measured once on the day of his birth. As a result, hyperkalemia and hypoglycemia were undetected until he had a severe episode of bradycardia and/or cardiac arrest, stopped breathing, and required cardiopulmonary resuscitation. He suffered permanent brain damage. A subsequent laboratory report revealed severe hyperkalemia and hypoglycemia; however, the report was not forwarded to the neonatologists for approximately 7 hours. The plaintiff brought a complaint of gross negligence for failure to properly diagnose and timely treat the hyperkalemia and hypoglycemia. The jury returned a $4,500,000 verdict.

Medical records are crucial in a court case because they provide the sequence of events, the time frame in which they occurred, and the participants in the care of the patient. Dylan Keene was born at 0107 May 15, 1986. He was discharged from the NICU to the regular nursery at 0630 with a one-page discharge note that noted "watch for sepsis, hold antibiotics pending complete blood count [CBC] results and cultures." The medical records for the next 24 hours went missing. Dylan was diagnosed with septic shock and seizures at 0230 May 16, 1986. Testing determined he had sepsis and meningitis that resulted in profound brain damage. He was discharged from the hospital June 18, 1986. His parents brought a malpractice suit against the hospital on May 12, 1995, alleging that there was a failure to properly diagnose and treat for sepsis and meningitis. The plaintiffs requested names of health care providers involved in the treatment and care of Dylan on May 14, 15, and 16, 1986, including those involved in the decision to not give antibiotics on those dates. The hospital records for these dates could not be located. The judge applied a default sanction against the hospital, as the loss of the records for which the hospital was responsible had deprived the plaintiffs of their day in court. The plaintiffs were awarded $4,108,311.66 (*Keene v. Brigham and Women's Hospital*, 755 N.E.2d 725-MA 2002 [Tammelleo, 2002]). If a nurse is named in a suit or is called to testify with regard to what took place, sometimes many years later, the chart serves as a memory aid. Statements contained in the medical record are not, in themselves, admitted into evidence; rather, the testimony of the witness concerning the particular event, as reinforced by the medical record, becomes the direct evidence given under oath. Most cases in which the hospital records cannot be located appear to be those in which the amount of damages in question is significant and the hospital appears to be liable; seldom do "missing" records ever favor the defendant hospital (Tammelleo, 2002).

Informed Consent

Legally, for a person to be able to give informed consent, that person must have the capability of "capacity." This usually entails that the person (1) has reached the age of majority and (2) can understand the information that is being given by the health care provider. Neonates therefore do not meet the criteria to give informed consent legally. Thus, the parents typically are the surrogate decision makers for the neonate, as long as they appear to be acting in the best interests of their infant. If the parents are married to each other, either may consent on behalf of the neonate. However, in situations involving divorce, custody battles, and teenaged and foster parenting, issues related to informed consent and patient privacy can become convoluted (Guido, 2013). A guardian *ad litem* may be appointed by the court to act in the neonate's best interests instead of or in addition to the parent(s). To meet the legal standard of informed consent, the surrogate decision maker must receive sufficient information regarding the proposed plan of treatment, including the risks and benefits of treatment, alternative treatment strategies, and the repercussions of not consenting (Guido, 2013). The only exception to treating

before obtaining informed consent is when delay of treatment could place the neonate at risk of further harm, such as in an emergency situation.

It is outside the boundaries of the practice of the staff nurse to provide the patient and/or family with information regarding medical–surgical risks and benefits of treatment or to suggest alternative medical–surgical therapies. It is appropriate for the nurse to inform the physician that the family members need further clarification to enable them to come to a decision comfortably. Obtaining the informed consent is the responsibility of the physician and/or the APN if appropriate, providing the treatment. Ideally, the treating physician should also be responsible for obtaining the signatures on the appropriate form once the parent(s) have consented, because she or he is truly the only one who can ensure that the parent(s) have no further questions and fully comprehend all treatment issues.

A. **If nurses are required to obtain patient and/or family signatures on consent forms, they should limit their clarification of patient and/or family understanding to two questions:**
   1. Has your physician discussed your baby's surgery (i.e., treatment approach) with you?
   2. Are you ready to sign this consent form? This means that you consent to the procedure.

B. **It is recommended that the name of the person able to give informed consent on behalf of the neonate be recorded in the medical record or nursing care plan once identified** (Guido, 2013).

C. **What if the parents or guardian will not give consent?**
   1. If physicians heed the parents' wishes and do not treat the infant, they may be guilty of child abuse or neglect, because laws stipulate that parents must provide needed medical care. Denial of this care can constitute a form of child neglect or abuse.
   2. If physicians proceed to treat the infant, ignoring parental objections, they could be liable for battery because their touching of the infant was intentional and there was a lack of consent.
   3. Physicians may petition the court for an authorization to provide the infant with the necessary treatment (i.e., obtain a court order). The most common example of physicians' seeking court orders to intervene in treatment is that of refused consent for blood transfusions based on religious beliefs. This request is almost always granted—certainly in emergency situations.

D. **When parents refuse treatment for other reasons, the court will base its decision on several factors** (Guido, 2013).
   1. The infant's overall health and development.
   2. The immediacy of danger to the infant if treatment is withheld.
   3. The risks and benefits of the proposed treatment.

Professional Liability Insurance

There is a growing trend to hold nurses personally liable for their acts of negligence, especially when they have assumed additional responsibility as APNs. Some believe that nurses should not carry insurance because this only provides them with "deep pockets," making them more attractive to the plaintiff. Others insist that being well insured will serve as good protection. How much insurance is enough? Is the insurance coverage provided by the employer enough, or should nurses also invest in a personal policy for additional protection? These questions need to be answered by the individual nurse after examination of her or his practice.

A. **Principal benefits afforded by an individual malpractice policy** (Guido, 2013).
   1. Insurer's agreement to defend all malpractice claims filed against the nurse. Also generally included are claims alleging assault, battery, invasion of privacy, and defamation of character and claims that the nurse/APN practiced outside the scope of his or her license.
   2. Insurer's agreement to pay the amount that the nurse is legally liable to pay the plaintiff, up to the limits of the policy.
   3. Coverage of all costs associated with an appeal of an adverse verdict.
   4. Coverage for instructional and supervisory activities, as well as off-duty and non–hospital-related nursing activities, such as volunteer work.

B. **Reasons to obtain malpractice insurance** (Guido, 2013).
   1. The hospital may have liability insurance policies that limit coverage and cover employees only when they work as hospital employees. No institutional policy covers a nurse for any acts or omissions that occur outside the normal work environment.
   2. Hospital's policy is designed to meet its needs and may not be able to protect the nurse's best interests.
   3. If the hospital decides that what you did was not covered under its policy, it will not defend you. In fact, the hospital may actually assume an adversarial position to demonstrate that you are the legally responsible party. The institution may bring an indemnity claim against the nurse for monetary contributions if the nurse's actions or failure to act resulted in the patient's original injury. You will now have to defend yourself on your own.
   4. Hospital policies do not have supplementary payments for the nurse's additional expenses related to investigating the claim or loss of work while defending the claim. The nurse will have to pay for his or her own out-of-pocket expenses.
   5. You will be protected if the hospital is not insured. The case of *Wake County Hospital System v. National Casualty Co.* (1992) alleged nursing malpractice of a neonatal nurse. The hospital had a

self-insured retention, or a deductible, of up to $750,000 per person/event before its commercial insurance coverage became effective. The defendant nurse's policy was deemed to be excess coverage over other valid and collectible insurance. The U.S. District Court ruled that self-insurance by a hospital is not really insurance in the legal sense. It also ruled that the nurse's insurer had to pay the full amount awarded in the case. This case is a good illustration of a nurse's needing her or his own malpractice coverage.

6. When an insurance carrier makes payment to a plaintiff on the basis of malpractice, the insurer is legally entitled to sue the nurse to obtain reimbursement for the amount paid.
7. Cost of a policy for staff nurses is low; however, the insurance for the APN may cost several hundred dollars a year.

C. **Most health care providers do carry their own professional liability insurance. There are two types of insurance policies** (Guido, 2013).
   1. Claims-made policy: covers damages only when the damages occurred during the policy period (when the policy was in effect) and only if the claim is reported to the insurance company during the policy period or the extending reporting endorsement (tail). This is typical of policies held by institutions.
   2. Occurrence-basis policy: covers damages occurring during the period covered by the policy, even if the claim is made after the policy period has ended. This is typical of policies held by individuals.
      a. Preferable for neonatal nurses because the lawsuit may not be filed until an extended period after the infant is discharged from the hospital.

D. **There are differences in coverage between an institutional and an individual liability policy** (Guido, 2013).
   1. Institutional liability policy.
      a. Employer purchased and provided as typical "claims-made" coverage.
      b. Institution is the primary insured party, holding fullest rights and responsibilities.
      c. Policy covers specific professional activities in the work environment.
      d. Institution may be able to sue the nurse for all or part of the money paid in settlement, judgment, and legal fees.
      e. Insurance company employs the attorney; the individual nurse may not have a right to select counsel.
      f. Individual nurse has no right to refuse or authorize settlement.
   2. Individual liability policy.
      a. Commercially purchased insurance that typically has an "occurrence" coverage.
      b. Individual nurse is the primary insured party.
      c. Policy covers specific professional activities of the insured at any time and place.

E. **All nurses can practice preventive legal maintenance by avoiding 18 legal pitfalls** (Guido, 2013; Monarch, 2002).
   1. Neglecting to make safety a high priority.
   2. Failing to spot and report possible violence. For example, the number of kidnapping occurrences has increased in recent years. Nurses play a role in the security plan by wearing photographic identification badges, enforcing visiting policies, and, along with risk management, developing a preventive program to anticipate neonatal kidnapping.
   3. Not following institutional policies and standards of care.
   4. Responding unwisely in a short-staffing or floating situation. Courts have generally upheld the validity of the hospital's floating policy; thus, a nurse's refusal to accept the assignment may place the nurse in jeopardy. It is suggested that the prudent course is to accept the assignment after clearly informing the nurse manager or charge nurse concerning your limitations and concerns.
   5. Neglecting to use due care in physical procedures, such as the dispensing of medications.
   6. Not checking equipment.
   7. Assuming that others are responsible for your duties.
   8. Assuming responsibility for informed consent.
   9. Wrongfully disclosing confidential information.
   10. Making reckless accusations.
   11. Failing to act like a professional.
   12. Confusing licensure issues with malpractice.
   13. Failing to communicate.
   14. Failing to monitor and assess.
   15. Failing to listen to information provided by family and friends and to the patient's or parent's requests for assistance.
   16. Neglecting to follow principles of risk management.
   17. Not following documentation principles.
   18. Confusing legal and ethical questions.

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APPENDIX A

Newborn Metric Conversion Tables

Table A.1

Temperature Conversion: Fahrenheit (F) to Centigrade (C)

°F	°C	°F	°C	°F	°C	°F	°C
95.0	35.0	98.0	36.7	101.0	38.3	104.0	40.0
95.2	35.1	98.2	36.8	101.2	38.4	104.2	40.1
95.4	35.2	98.4	36.9	101.4	38.6	104.4	40.2
95.6	35.3	98.6	37.0	101.6	38.7	104.6	40.3
95.8	35.4	98.8	37.1	101.8	38.8	104.8	40.4
96.0	35.6	99.0	37.2	102.0	38.9	105.0	40.6
96.2	35.7	99.2	37.3	102.2	39.0	105.2	40.7
96.4	35.8	99.4	37.4	102.4	39.1	105.4	40.8
96.6	35.9	99.6	37.6	102.6	39.2	105.6	40.9
96.8	36.0	99.8	37.7	102.8	39.3	105.8	41.0
97.0	36.1	100.0	37.8	103.0	39.4	106.0	41.1
97.2	36.2	100.2	37.9	103.2	39.6	106.2	41.2
97.4	36.3	100.4	38.0	103.4	39.7	106.4	41.3
97.6	36.4	100.6	38.1	103.6	39.8	106.6	41.4
97.8	36.6	100.8	38.2	103.8	39.9	106.8	41.6

Note: °C = (°F − 32) ∞⅝. Centigrade temperature equivalents are rounded to one decimal place by adding 0.1 when second decimal place is 5 or greater. The metric system replaces the term "centigrade" with "Celsius" (the inventor of the scale).

Table A.2

Length Conversion: Inches to Centimeters

1-inch increments. Example: to obtain centimeters equivalent to 22 inches, read "20" on top scale, "2" on side scale; equivalent is 55.9 cm.

Inches	0	10	20	30	40
0	0	25.4	50.8	76.2	101.6
1	2.5	27.9	53.3	78.7	104.1
2	5.1	30.5	55.9	81.3	106.7
3	7.6	33.0	58.4	83.8	109.2
4	10.2	35.6	61.0	86.4	111.8
5	12.7	38.1	63.5	88.9	114.3
6	15.2	40.6	66.0	91.4	116.8
7	17.8	43.2	68.6	94.0	119.4
8	20.3	45.7	71.1	96.5	121.9
9	22.9	48.3	73.7	99.1	124.5

One-quarter (¼) inch increments. Example: to obtain centimeters equivalent to 14 ¾ inches, read "14" on top scale and "¾" on side scale; equivalent is 37.5 cm.

10 to 15 Inches

	10	11	12	13	14	15
0	25.4	27.9	30.5	33.0	35.6	38.1
¼	26.0	28.6	31.1	33.7	36.2	38.7
½	26.7	29.2	31.8	34.3	36.8	39.4
¾	27.3	29.8	32.4	34.9	37.5	40.0

16 to 21 Inches

	16	17	18	19	20	21
0	40.6	43.2	45.7	48.3	50.8	53.3
¼	41.3	43.8	46.4	48.9	51.4	54.0
½	41.9	44.5	47.0	49.5	52.1	54.6
¾	42.5	45.1	47.6	50.2	52.7	55.2

Note: 1 inch = 2.540 cm. Centimeter equivalents are rounded one decimal place by adding 0.1 when the second decimal place is 5 or greater; for example, 33.48 becomes 33.5.

Table A.3

Weight (Mass) Conversion: Pounds and Ounces to Grams

Example: To obtain grams equivalent to 6 pounds, 8 ounces, read "6" on top scale, "8" on side scale; equivalent is 2948 g.

	POUNDS														
Ounces	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
0	0	454	907	1361	1814	2268	2722	3175	3629	4082	4536	4990	5443	5897	6350
1	28	482	936	1389	1843	2296	2750	3203	3657	4111	4564	5018	5471	5925	6379
2	57	510	964	1417	1871	2325	2778	3232	3685	4139	4593	5046	5500	5953	6407
3	85	539	992	1446	1899	2353	2807	3260	3714	4167	4621	5075	5528	5982	6435
4	113	567	1021	1474	1928	2381	2835	3289	3742	4196	4649	5103	5557	6010	6464
5	142	595	1049	1503	1956	2410	2863	3317	3770	4224	4678	5131	5585	6038	6492
6	170	624	1077	1531	1984	2438	2892	3345	3799	4252	4706	5160	5613	6067	6520
7	198	652	1106	1559	2013	2466	2920	3374	3827	4281	4734	5188	5642	6095	6549
8	227	680	1134	1588	2041	2495	2948	3402	3856	4309	4763	5216	5670	6123	6577
9	255	709	1162	1616	2070	2523	2977	3430	3884	4337	4791	5245	5698	6152	6605
10	283	737	1191	1644	2098	2551	3005	3459	3912	4366	4819	5273	5727	6180	6634
11	312	765	1219	1673	2126	2580	3033	3487	3941	4394	4848	5301	5755	6209	6662
12	340	794	1247	1701	2155	2608	3062	3515	3969	4423	4876	5330	5783	6237	6690
13	369	822	1276	1729	2183	2637	3090	3544	3997	4451	4904	5358	5812	6265	6719
14	397	850	1304	1758	2211	2665	3118	3572	4026	4479	4933	5386	5840	6294	6747
15	425	879	1332	1786	2240	2693	3147	3600	4054	4508	4961	5415	5868	6322	6776

Note: 1 pound = 453.59237 g; 1 ounce = 28.349523 g; 1000 g = 1 kg. Gram equivalents have been rounded to whole numbers by adding 1 when the first decimal place is 5 or greater.

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