12

THE SKIN

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LEARNING OBJECTIVES

After completing this chapter, the reader should be able to:

- Understand normal skin development.
- Analyze the physiologic function of the fetal and neonatal skin.
- Discuss common inherited disorders and their effect on fetal and neonatal skin development and function.
- Identify maternal health issues that have a potential impact on fetal and postnatal skin development and function.
- Evaluate common disorders that affect the skin and their implications across the life span.

INTRODUCTION

The skin, or integumentary system, is the largest organ in the body. It modulates multiple functions, including protection, sensation, metabolic functions, and thermoregulation. It does so by forming a physical barrier to the environment, harmful microorganisms, ultraviolet radiation, toxic agents, and mechanical injuries. The skin functions as a conduit for sensation and a metabolic organ that allows or limits the transmission of passage of water, electrolytes, and various substances as well as energy stored as fat and the synthesis of vitamin D. The skin is critical to thermoregulatory homeostasis and impacts the maintenance of euthermia through an intricate process of capillary dilatation and restriction, as well as the regulation of moisture. This chapter reviews embryologic development, lists the primary functions, explores the anatomic layers and their physiologic functions, discusses genetic influences, and outlines common neonatal skin problems.

TIMELINE OF ORGAN DEVELOPMENT

The skin is embryologically derived from two separate origins. The epidermis, or the superficial layer, originates from the ectoderm, whereas the deeper layer, known as the *dermis*, arises from the mesenchyme (Sadler, 2015). The following is an overview of embryologic development of the skin and its derivatives. It is important to remember that studying the details of skin-layer-specific maturation with the use of visual aids may create the false perception of spaciousness. Rather, we encourage students and clinicians to be mindful of the fact that the five major layers of the skin are tightly connected and account for, on average, 0.9 mm (premature infants) to 1.2 mm (term infants) of depth (Bolender & Kaplan, 2017).

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Epidermis

Embryonic Period. The epidermis arises from the embryonic ectoderm (neural crest; Figure 12.1). During week 4 of gestation, a single layer of ectodermal cells appears. Between weeks 4 and 6 of gestation, these cells stratify into peridermal (outermost) and basal (innermost) layers (Bolender & Kaplan, 2017; Carlson, 2014; Moore, Persaud, & Torchia, 2016). The periderm protects the developing epidermis from amniotic fluid and manages glucose uptake. The periderm thereby begins a cyclic process of cellular generation, keratinization, and exfoliation. Simultaneously, the lower basal layer begins synthesizing skin cells (Moore et al., 2016). Around week 4, the sebaceous glands begin to form and mammary ridges begin to appear. Melanocytes start appearing in the basal layer from weeks 5 to 8 of gestation. The ectodermal cells begin to form ridges around week 6 and, by week 8, as epidermal mammary ridges begin to disappear.

Fetal Period. The early fetal period is marked by epidermal differentiation into a three-layered structure, which begins between weeks 8 and 11 of gestation. Proliferation and maturation of basal layer keratinocytes proliferate to form the spinous cell layer between the basal layer and the periderm (Figure 12.2). The lowest basal layer (stratum germinativum) increases production of cells and assumes the role of germinal matrix for cellular synthesis. The rapid synthesis and upward migration of new skin cells exceeds the turnover rate of normally expiring peridermal cells and gives rise to an intermediate skin layer (Bolognia, Schaffer, & Cerroni, 2018). Periderm, spinous cells (two layers), basal cells, desmosomes, hair follicles, and hair bulb mesenchymal cells of the hair bulb appear between weeks 12 and 16 of gestation. There are six to eight basal layers for each periderm layer, and the upper spinous cells flatten from weeks 14 to 17 of gestation (Visscher & Narendran, 2014).

Basal layer cellular proliferation also projects in a downward direction, toward the deeper mesenchyme (dermis). This gives rise to epidermal ridges, or invaginations, that resemble U-shaped curves. By week 15 of gestation, these ridges give rise to touch pads and grooves at the hands and feet (Moore et al., 2016). These grooves develop curves and whorls by week 35 of gestation, bestowing a unique fingerprint to the infant; abnormal matriculation of the pads and grooves are commonly observed among individuals with trisomy 21 (Moore et al., 2016).

By week 16 to 23 of gestation, the five epidermal layers are evident (Table 12.1). These layers are both thick and thin, uniquely equipped with a complement of follicles, arrector muscles, sebaceous glands, and sweat glands (Table 12.2; Moore et al., 2016; Sadler, 2015). Polygon-shaped cells, composed of keratin, appear in the interfollicular regions and hair follicles. At 18 to 19 weeks of gestation, the stratum corneum (SC) can be seen around the hair follicle. By week 21, it can be seen along the hair canal. This demonstrates the important role of the hair follicle in epidermal barrier development. The terminally differentiated outermost layer, or SC, can be seen at week 23, but may be only a few layers thick. Periderm is no longer observed around week 23. By week 26, the epidermis is fully keratinized, composed of (a) one basal layer, (b) two to three spinous layers, (c) a granular layer containing keratohyalin granules, and (d) five to six layers of SC. The interfollicular epidermis cornifies programmatically from head (initially, week 23) to toe and dorsal–ventral (week 25, abdomen) across the developing infant (Visscher & Narendran, 2014). Cornification of the appendages and trunk usually begins between weeks 24 and 26 of gestation and continues throughout gestation. The time for complete maturation of the neonatal epidermal barrier, to achieve structure and function comparable to adults, is currently unknown (Visscher & Narendran, 2014).

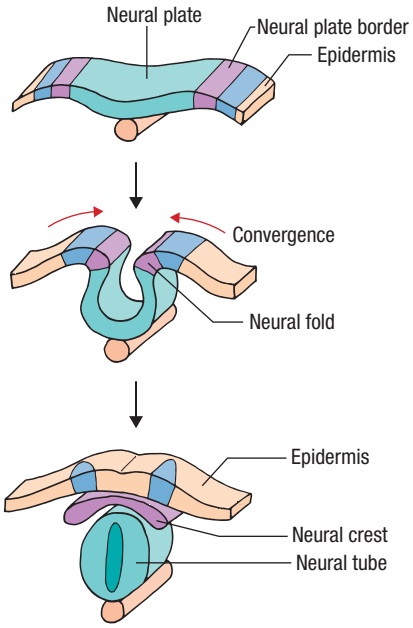


Figure 12.1 Origin of the epidermis.

Dermis and Hypodermis

Embryonic Period. The origin of the dermis is shared between the neural crest and mesoderm (Carlson, 2014). Dermal mesenchyme that comprise the face and scalp arise from the neural crest. Dermal mesenchyme of the

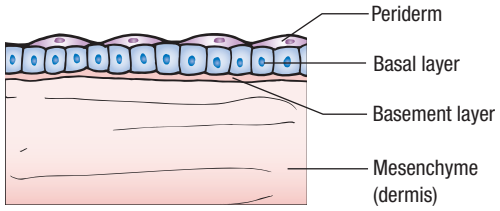
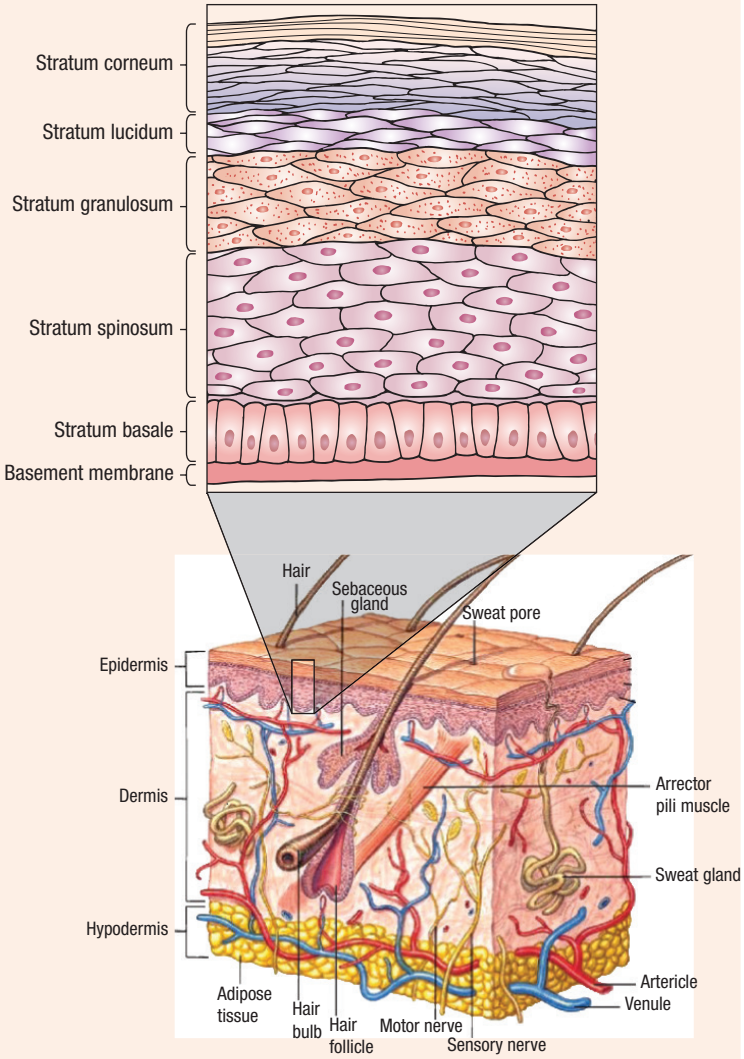


Figure 12.2 Early layers of the epidermis.

TABLE 12.1 The Epidermis

Epidermal Sublayer	Composition and Function	Visual Description
Corneum *Outermost layer*	• *Composition*: On average, 16 layers composed of nonviable cells known as corneocytes consisting of water-retaining keratin proteins and a highly structured cell envelope to provide strength. • *Function*: Barrier to external agents and transepidermal water loss and containing antimicrobial proteins.	
Granulosum and lucidum	• *Composition*: Consists of 3–5 cell layers with the lucindum present only in skin of palms and soles; keratinocytes at this stage contain keratohyalin granules • *Function*: Keratohyalin granule proteins aggregate keratin proteins and move the cells toward the stratum corneum	
Spinosum	• *Composition*: 8–10 layers of keratinocytes with tonofibrils and Langerhans cells • *Function*: Formation of keratinocytes begins here; keratins are synthesized; intermediate filaments form to strengthen cells and connect to desmosomes; initiates cell-mediated immune response	
Basal *Deepest layer*	• *Composition*: Single germinal cell layer of proliferating and stem keratinocytes and melanocytes (pigment cells) • *Function*: Melanocytes produce melanin pigmentation to protect the living cells from solar radiation damage	

NOTE: This information is based on normal adult skin values. Comparable data for premature and full-term infant skin is currently incomplete.

Sources: Carlson, B. M. (2014). *Human embryology and developmental biology* (5th ed., pp. 156–192). Philadelphia, PA: Elsevier/Saunders; Leung, A., Balaji, S., & Keswani, S. G. (2013). Biology and function of fetal and pediatric skin. *Facial Plastic Surgery Clinics of North America*, *21*(1), 1–6. doi:10.1016/j.fsc.2012.10.001; Moore, K. L., Persaud, T. V. N., & Torchia, M. G. (2016). Integumentary system. *The developing human: Clinically oriented embryology* (10th ed., pp. 437–455). Philadelphia, PA: Elsevier.

back arises from the embryonic somite. In addition, the dermal mesenchyme associated with the appendages and trunk (ventral) arise from the lateral plate mesoderm. No rationale for this phenomenon exists. Primitive dermal cells can be seen during the latter end of the embryonic period of development (week 8 of gestation); however, they are not active until the early fetal period of development (Figure 12.3).

TABLE 12.2 Features of Epidermal Skin Thickness

	Thick Skin Layer (*Hands, Feet*)	Thin Skin Layer (*All Areas Except Hands and Feet*)
Follicles	NO	YES
Arrector Muscles	NO	YES
Sebaceous Glands	NO	YES
Sweat Glands	YES	YES

Source: Moore, K. L., Persaud, T. V. N., & Torchia, M. G. (2016). *The developing human: Clinically oriented embryology* (10th ed., pp. 437–455). Philadelphia, PA.: Elsevier.

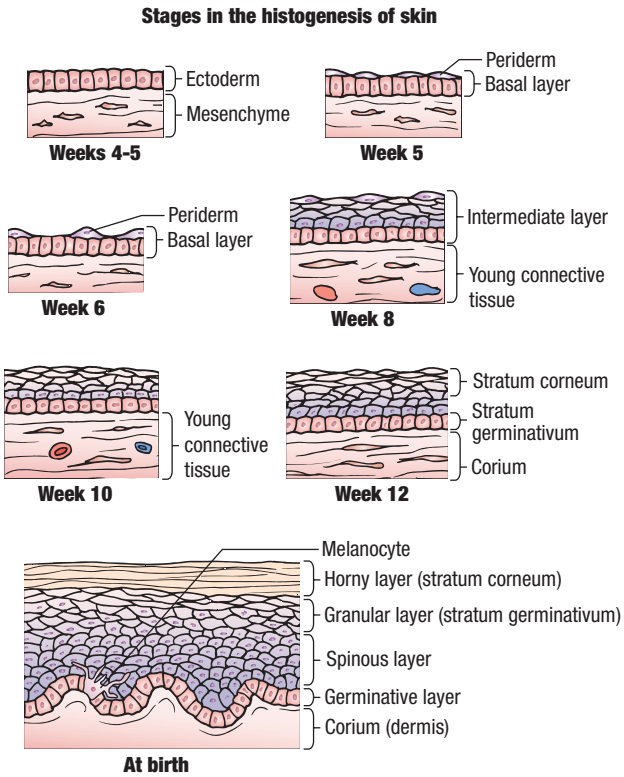


Figure 12.3 Stages of histogenesis of the skin.

Fetal Period. Proliferation commences early into the fetal period, as the dermis subdivides into its two primary layers, the (a) dermal papillae and (b) reticular layer. Although the previously described epidermal cells invade the topmost layer of the dermis, creating epidermal ridges, the dermis reciprocates by developing rounded, fingerlike extensions (papillae) that project upward and into the epidermal ridges. This marks the genesis of the *dermal papillae* (papillary layer), the most superficial layer of the dermis. Papillae permit the proliferation of primitive blood vessels and the matriculation of afferent sensory nerves. This process of vascular proliferation directs the differentiation of primitive capillaries into arterioles and arteries, whereas others become veins (Table 12.3). The *reticular layer*, which lies below the papillary layer, thereby begins to form. Collagen fibers arranged in parallel ranks and lymphatic meshes, which drain into larger lymphatic vessels, comprise this layer of the dermis.

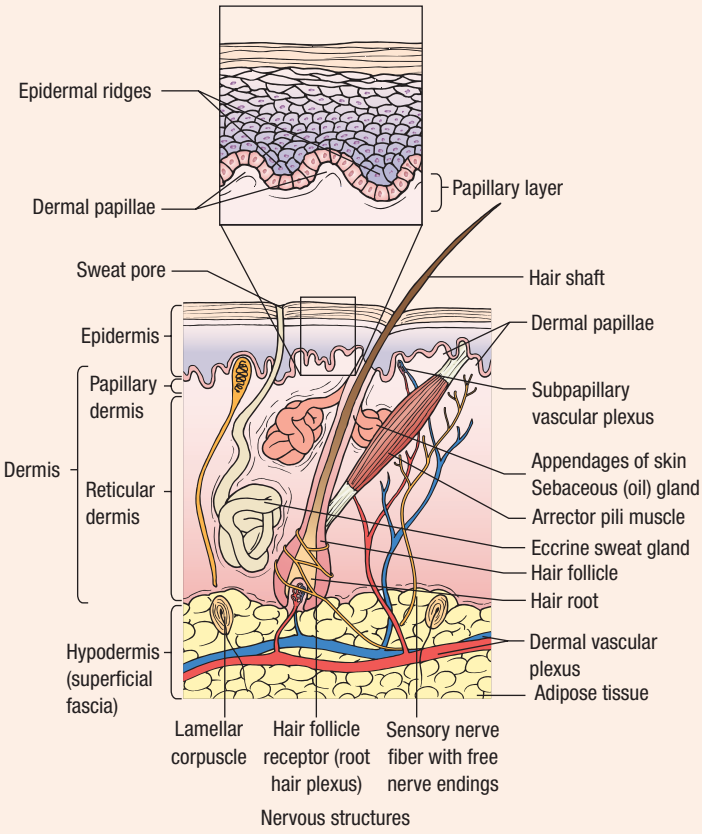
Evidence of the hypodermis can be seen between weeks 7 and 9 of gestation, as distinct from the dermis. Fibroblasts, adipose cells, and macrophages comprise this layer of the skin and have been observed using electron microscopes beginning with week 22 of gestation (Bolognia et al., 2018; Schoenwolf, Bleyl, Brauer, & Francis-West, 2015). From this period through birth, the dermis shifts from a well-hydrated and cellular-dense structure to a thicker, more fibrous structure (Bolognia et al., 2018).

Hair

Embryonic Period. Hair is derived from the surface ectoderm (Carlson, 2014). In fact, dermal-to-epidermal signaling is responsible for follicle formation. The dermis modulates a process of epidermal thickening, which forms hair placode cells within the basal layer of the epidermis. These placodes are observed by the end of week 11 of gestation and participate in the formation of the dermal papillary layer (Bolender & Kaplan, 2017). The placodes interact with genes, including Sonic hedgehog (*SHH*), wingless type (*WNT*), bone morphogenic proteins (*BMPs*), and fibroblast growth factor (*FGF*), which signals further downward movement and differentiation. This movement pushes the placodes deeper while carving a canal for the future expression of hairs.

Fetal Period. By week 12 of gestation, the keratinocytes of the placode reach the dermis and the germinal matrix and hair formation is established. Peripheral cells along

TABLE 12.3 The Dermis and Hypodermis

Dermal Sublayer	Composition and Function	Visual Description
Papillary	• *Composition*: Vasculature and afferent nerves • *Function*: Renders vascular and sensory (afferent) nervous innervation	
Reticular	• *Composition*: Collagen fibers, lymphatic meshes • *Function*: Contain loosely organized collagen fibers	
Hypodermis	• *Location*: Innermost layer of the skin • *Composition*: Fibroblasts, adipose cells and collagen fibers, and macrophages • *Function*: Insulation and shock absorption; renders vascular and sensory (afferent) nervous innervation	

Source: Vandergriff, T. W. (2018). Anatomy and physiology. In J. Bolognia, J. V. Schaffer, & L. Cerroni (Eds.), *Dermatology* (4th ed., pp. 44–55). Philadelphia, PA: Elsevier.

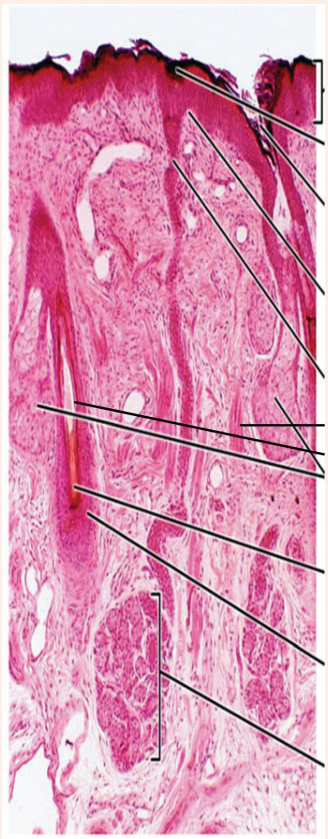
the hair shaft take on a cuboidal shape and give rise to the epithelial hair sheath. This hair sheath bulges, allowing innervation of arrector pili muscles and sebaceous glands. By week 14 of gestation, the base of the follicle is properly situated within the papillary layer. The hair canal is fully formed by week 21 of gestation (Bolender & Kaplan, 2017). The proliferation of hair begins as cells are pushed upward by the arrector muscles, keratinized, and expressed. In fact, contraction of the arrector muscles elicits the "goose bump" response (Moore et al., 2016).

Hair first appears on the surface of the fetus, in particular along the regions of the eyebrow and upper lip. The majority of body hair is visible by week 20 of gestation. Over time, several cycles of hair proliferation and shedding occur during intrauterine development; hair that is shed can be found within the amniotic fluid (Bolender & Kaplan, 2017; Moore et al., 2016). The first fine and downy hair that appears along the embryo's body, and is particularly abundant among premature infants, is termed *lanugo* (Table 12.4; Sadler, 2015).

Nails

The nails are derived from the surface ectoderm (Carlson, 2014). The fingernails are first to develop, beginning during early fetal development (weeks 9 and 10 of gestation) as thickenings in the epidermal layer (Bolender & Kaplan, 2017; Moore et al., 2016). The toenails follow in a similar fashion and begin matriculating within 4 weeks of the fingernails (Moore et al., 2016).

TABLE 12.4 The Hair and Glands

Visual Description	Hair and Glands	Primary Function
	Epidermis Sweat pore Hair follicle Dermis Duct of eccrine gland Arrector pili Hair sheath Sebaceous glands Hair shaft Dermal papillae (hair root) Eccrine gland	• The *epidermis* is the outermost layer of the skin. • The *sweat pore* is an opening through which sweat emerges on the surface of the skin (not functional in neonates). • Each hair is made of a hair shaft, hair sheath, and root. The *hair shaft* contains the keratinized fibers that appear as a single hair. The *hair sheath* surrounds the hair shaft and connects to the sebaceous glands. The body's hair serves to protect the skin. • The *duct of the eccrine gland* is a conduit through which sweat rises from the eccrine gland to the surface of the skin (not fully functional in neonates). • Connected to each hair is a tiny muscle known as the *arrector pili* muscle that contracts in response to cool temperatures or emotions, such as fear, causing the hair to stand on end. • The *sebaceous glands* are attached to each hair and secrete an oily sebum. This lipid-based substance functions to provide an epidermal permeability barrier as well as structure and differentiation, signal skin-specific hormones, transport antioxidants to the skin's surface, and offer protection from ultraviolet radiation. • The *hair root*, or *dermal papilla*, is fed by tiny blood vessels and is responsible for thermoregulation. • The *eccrine glands* are found over a majority of the body and are secretory glands that are under psychological and thermal control through sympathetic (cholinergic) nerve fibers. Eccrine glands secrete sweat containing chloride, lactic acid, fatty acids, urea, glycoproteins, and mucopolysaccharides.

Source: Vandergriff, T. W. (2018). Anatomy and physiology. In J. Bolognia, J. V. Schaffer, & L. Cerroni. (Eds.). *Dermatology* (4th ed., pp. 44–55). Philadelphia, PA: Elsevier.

Nails reach the fingertips by 32 weeks of gestation and the distal edges of the toes by week 36 of gestation (Moore et al., 2016; Sadler, 2015).

Glands

The glands (sebaceous, sweat, apocrine, mammary, lacrimal, and salivary) are derived from the surface ectoderm (Carlson, 2014). The skin contains several types of glands, including sebaceous, sweat, and mammary glands. Each has a distinct developmental timeline, location, and function.

Sebaceous Glands. Sebaceous glands are found only where hair grows and are directly connected to the hair's sheath. These are, at first, solid, hemispherical protuberances on the posterior surfaces of the hair pegs. The sebaceous glands are formed from the epidermal cells and begin to develop between weeks 13 and 14 of gestation (Niemann & Horsley, 2012). Sebaceous glands are well developed and generally large at term. Yet, after birth, the size rapidly diminishes, and only after puberty do they once again enlarge to become functional.

Sweat Glands. There are two primary types of sweat glands: eccrine and apocrine; each type of gland is located within the dermal layer. Eccrine glands reside over most of the body, with the exception of the lips and external ear canals, and are derived as buds from the basal layer of the epidermis (Cui & Schlessinger, 2015). These glands begin to form between weeks 28 (palmoplantar region) and 35 (rest of body) of gestation (Cui & Schlessinger, 2015). Apocrine glands reside within the axillae and external genitalia (Sadler, 2015). These glands

form during early adolescence, commensurate with the onset of puberty.

Mammary Glands. Mammary glands are adapted sweat glands that first appear during week 4 of gestation as bilateral buds of thickened epidermis (Moore et al., 2016). These buds are commonly referred to as *mammary ridges* or *crests*. By the end of week 5 of gestation, the mammary crests penetrate the underlying mesenchyme and form 16 to 24 sprouts, which give rise to the mammary buds. Mammary buds undergo a progressive process of canalization and form lactiferous ducts. By term, up to 20 lobes of breast tissue have formed, each affixed with one lactiferous duct (Javed & Lteif, 2013; Moore et al., 2016; Sadler, 2015). Further differentiation of the buds gives rise to the glands, located at the tips of each mammary bud. The glands are well established by week 24 of gestation and breast tissue is evident on physical examination (Javed & Lteif, 2013). Although the term neonate is affixed with lactiferous ducts at birth, the breasts are devoid of milk-releasing alveoli.

Nipples

Nipple formation also begins during late fetal development. The epidermis invaginates within the pectoral region at the fourth intercostal space on the chest region, forming a pit. Abnormal positioning yields supernumerary nipples, which are observed in 2% to 5% of newborns (Javed & Lteif, 2013). These pits give rise to each nipple, which often remain below the level of the epidermis for several weeks into postnatal life. During this time, connective tissue infiltrates the surrounding area and raises the nipple to a position above the level of the epidermis. During puberty, females will undergo progressive breast development, whereas male breasts remain in their primitive form across the life span (Moore et al., 2016).

DEVELOPMENTAL PHYSIOLOGY

The skin, or integumentary system, is the largest organ in the body and serves multiple functions, including barrier protection, thermoregulation, sensation, and metabolic functions. Through its anatomic construct and physiologic function, the skin resists infection and offers immunosurveillance, an acid mantle, antioxidant function, and protection from ultraviolet light (Visscher, Adam, Brink, & Odio, 2015). We offer a discussion of the core functions of the skin, which serves as an expansion of core concepts discussed within Chapter 9.

Barrier Protection

The epidermal barrier forms as a result of a well-orchestrated progression that culminates in the formation of flattened, cornified keratinocytes. The keratinocytes are imbedded within a sophisticated bilayer lipid matrix, connected together by specialized structures called *desmosomes*. This outermost barrier provides protection from chemicals and irritants as well as physical dangers and mechanical trauma (Mancini & Lawley, 2015). At birth, this role becomes immediately crucial, as the fetus transitions from the hospitable environment provided by the womb to a cold, dry, and microorganism-filled atmosphere (Hoath & Shah, 2017).

Skin barrier function is typically effective among infants born at or beyond 37 weeks of gestation, yet immature among infants born at less than 37 weeks of gestation. As with other organ systems, skin barrier function increases with advancing gestational age (GA). Well-developed skin is affixed with a thick epidermis and SC; these layers offer physical barrier function (Mancini & Lawley, 2015). In contrast, the skin of premature infants is affixed with fewer cornified layers, resulting in reduced barrier function, an increased risk for the penetration of exogenous materials and pathogens, transepidermal water loss (TEWL), and mechanical injuries (skin tears; Visscher et al., 2015). TEWL decreases with maturation of the SC, which among premature infants occurs between 2 to 9 weeks postnatal age; complete acid mantle formation may require additional months. Time required for epidermal maturation among infants less than 28 weeks GA is unknown (Visscher & Narendran, 2014).

Thermoregulation

The skin also participates in postnatal thermoregulation, a function that was unnecessary before birth and largely performed by the placenta. Maintaining optimal body core temperature (37°C or 98°F–99°F), or thermoregulation, involves balancing heat loss and production. The majority of thermoreceptors are located at the face, neck, and shoulder region; activation elicits a thermoregulatory response that involves increased caloric expenditures. Thermoregulatory function is modulated through a complex series of neurogenic, myogenic, and metabolic processes; collectively, these processes regulate vasomotor tone within the dermis. Neurogenic and myogenic processes trigger the constriction or expansion of blood vessels. This controls blood flow and determines whether heat is dispelled or conserved.

Heat production, or *thermogenesis*, is modulated through oxidative metabolism as regulated by the thyroid gland, nonshivering thermogenesis, muscle flexion, and peripheral vasoconstriction. Oxidative metabolism involves the mobilization of glucose, fats, and proteins. Nonshivering thermogenesis involves the metabolism of brown fat; this offers limited thermogenesis as brown fat accounts for approximately 4% to 10% of total adipose tissue among term infants (Mancini & Lawley, 2015). Premature infants possess reduced brown fat and glycogen stores. In fact, brown adipose tissue is often not generated until 26 to 30 weeks of gestation. In addition,

premature infants possess a reduced capacity to remain in a flexed position (to prevent heat loss through increased surface area exposure to colder temperatures), as well as reduced ability to mobilize existing brown adipose tissue.

Thermolysis refers to the loss of heat. Infants born at less than 38 weeks of gestation are at increased risk for heat loss. Heat loss can occur by way of (a) conduction, (b) convection, (c) radiation, and (d) evaporation. *Conduction* involves heat lost through direct contact with a cold surface, such as a cold blanket or neonatal scale. *Convection* involves heat lost from cooler air flowing over the body's surface, such as from an air-conditioning vent. *Radiation* is electromagnetic heat lost from heat radiating toward a cooler surface, which does not come into direct contact with the neonates' skin. Examples include a cold exterior window or the walls of an isolette. *Evaporation* is the final mechanism of heat loss and can be the result of bathing, birth, and sweating. Evaporation involves heat lost through wet skin.

Neurosensory Function

Skin contains both somatic sensory and sympathetic autonomic nerve fibers (Figure 12.4). These fibers function to innervate with arrector pili muscles, cutaneous blood vessels, and sweat glands. They serve as receptors for touch, pain, temperature, itch, and mechanical stimuli (Mancini & Lawley, 2015). Each stimulus provides the brain with afferent information that the brain translates into an efferent response. At the level of the skin, responses may include "goose bumps" or mottling. Thus, evidence of central nervous system maturation and responses to stimuli at the skin depend on sensory input received during the immediate postnatal period (Hoath & Shah, 2017).

Glandular Function

As mentioned earlier, the skin contains glands, including apocrine, eccrine, mammary, and sebaceous glands. The apocrine glands are secretory glands found within the face, axilla, and pubic region. These glands open solely into hair follicles, develop during puberty, and are under thermal control by way of sympathetic (adrenergic) nerve fibers (Schaller & Plewig, 2018). Sweat, a by-product of the apocrine glands, is composed of lipids, proteins, and pheromones. Typically, once children reach puberty, the bacterial breakdown of sweat produces foul odors.

The eccrine glands are also sweat glands and are found throughout the body. The highest density of eccrine glands is noted in the palms of the hands and soles of the feet. Eccrine sweat glands are composed of a secretory coil and a duct (located in the lower dermis), as well as subcutaneous tissue. Components of eccrine sweat include water, sodium, chloride, potassium, urea, lactate, ammonia, antimicrobial peptides, cytokines, and immunoglobulins (Schaller & Plewig, 2018). *Eccrine glands* are innervated by the sympathetic nervous system. Pharmacologic stimulation or emotional or thermal stress stimulates the secretion of acetylcholine, which activates eccrine activity (Mancini & Lawley, 2015). Among neonates, eccrine activity manifests as thermal

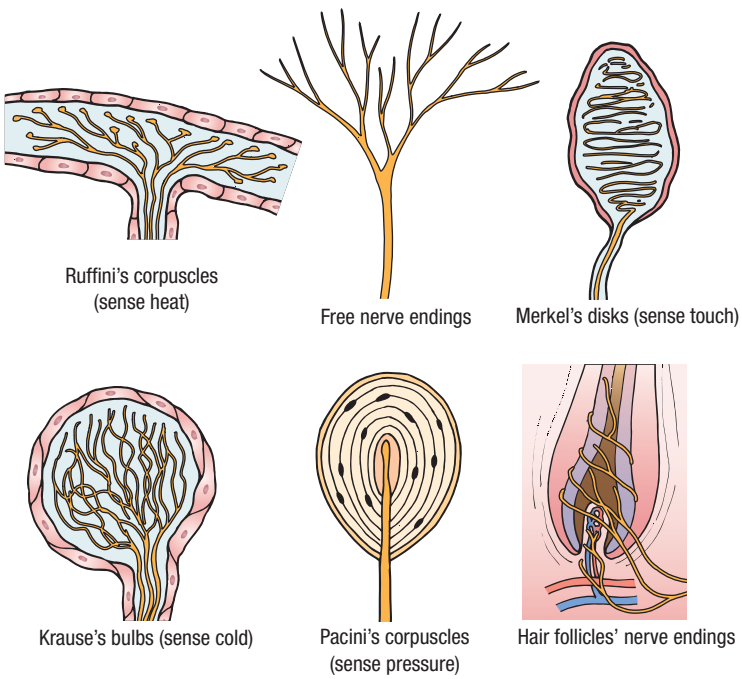


Figure 12.4 Depiction of the cutaneous nerve endings.

and emotional sweating. The core temperature required to induce neonatal sweating is approximately 37.2°C (Mancini & Lawley, 2015). This is typically immature among premature neonates and is a process that matures over time among all neonates. *Mammary glands* are found in the breast tissue. These glands have no secretory tissue at birth. At puberty, increased circulating estrogen and progesterone stimulate the lactiferous ducts to form alveoli and secretory cells primarily for milk production (Sadler, 2015). *Sebaceous glands* are numerous at birth. During fetal development, secretions from the sebaceous glands contribute to vernix formation. This early sebaceous gland activity is modulated by maternal hormonal (androgen) influences. After birth, maternal hormone concentrations wane; however, residual hormonal influence may trigger continued sebaceous activity, which manifests as scalp flaking, or cradle cap. Once this transient phenomenon subsides, physiologic function of the sebaceous glands is not observed until puberty.

Vernix

During the last trimester vernix caseosa, a whiteish pastelike substance, begins to coat fetal skin from head to toe and back to front (Visscher et al., 2015). The cells in vernix may originate from the hair follicles, suggesting that vernix is "extruded" out through the hair shaft onto the skin surface initially around the hair and spreading over the entire surface as gestation progresses (Sadler, 2015). Vernix is primarily composed of sebaceous gland secretions and desquamated SC cells and provides physical protection from maceration by amniotic fluid and enzymes due to its hydrophobic lipids. Vernix also influences the antimicrobial function of the skin by (a) lowering the pH of the skin's surface, and (b) providing hydration and lipids for further formation of the cutaneous layers (Visscher et al., 2015). Each of these aforementioned functions is enhanced by allowing vernix to remain in place at least 6 hours after birth (Visscher et al., 2015). Clinicians are encouraged to delay the first postnatal bath, as appropriate.

Histological Function

Although an investigation into cell-mediated skin function of the skin may seem like a daunting task, it is particularly significant for the neonatal clinician. Neonates, specifically premature neonates, depend on their skin for barrier protection against surface pathogens. In order to achieve this functional status, certain cells must matriculate into the epidermis.

Skin Coloration. Beginning with the second month of gestational development, primitive epidermal neural crest cells migrate from the dermis into the epidermis. This stimulates the synthesis of melanocytes. Under the influence of *WNT* signaling pathways, skin pigment granules are synthesized. These processes modulate melanin production and skin coloring, which is known to be influenced by ethnicity (Moore et al., 2016). Darker skin coloration is associated with earlier production of melanocytes and an increased number of pigment granules per cell (Carlson, 2014; Moore et al., 2016).

Immune Response. Toward the end of the first trimester, Langerhans cells migrate from the bone marrow to the stratum germinativum. These cells participate in cell-mediated immune responses to pathogens that persistently attempt to penetrate the skin barrier. The quantity of Langerhans cells increases across gestational development, with the most significant amount of proliferation noted during the third trimester. As such, infants born prematurely are often affixed with a significantly reduced number of Langerhans cells, which reduces the skin's ability to protect the body from antigens (Carlson, 2014).

GENETIC INFLUENCES

There are certain hereditary disorders that manifest with noteworthy dermatologic aberrations. Here, we review some common genetic disorders and their associated dermatologic findings.

Noonan Syndrome

Noonan syndrome is one of a group of related autosomal dominant inherited disorders, collectively known as the *RASopathies* caused by a mutation in the genes of the RAS/MAPK pathway. In addition to Noonan syndrome, the RASopathies include cardiofaciocutaneous syndrome, Costello syndrome, neurofibromatosis 1, and Legius syndrome. Noonan syndrome affects one in every 1,000 to 2,500 births (National Institutes of Health [NIH], 2018c; Roberts, Allanson, Tartaglia, & Gelb, 2013). Heterozygous mutations in the genes affect the *RAS/MAPK* (mitogen-activated protein kinase) signaling pathway, most commonly isolated at the *PTPN11* gene (75%). This disrupts normal cellular proliferation, differentiation, and migration (Bertola et al., 2014). Common skin-related manifestations include a deep groove at the philtrum, webbing of the skin of the neck, and a low posterior hairline. Abnormal synthesis and secretion of growth hormone may implicate the aforementioned manifestations, as well as stunt overall growth and development.

Neurofibromatosis (Type 1)

Neurofibromatosis type 1 (NF1) is the more common form of autosomal dominant neurofibromatosis, with an estimated incidence of one in every 3,000 to 4,000 individuals (Paulus, Koronowska, & Fölster-Holst, 2017; NIH, 2018b). Germline mutations in the *NF1* gene (involved in the RAS/MAPK pathway) overstimulate the RAS signaling activity, which alters normal keratinocyte

differentiation (Peltonen, Kallionpää, & Peltonen, 2017). Therefore, although NF1 is commonly characterized by the growth of tumors on the nerves, this disease can also affect the skin. Common skin-related manifestations include cutaneous neurofibromas, café-au-lait lesions (infancy), freckles (childhood), and palpable neurofibromas (noncancerous tumors) that manifest under the skin; these tumors often present in adulthood.

Waardenburg Syndrome

Waardenburg syndrome is an autosomal dominant auditory-pigmentary syndrome. The incidence is estimated at one in every 40,000 individuals (NIH, 2018e). Mutations in several genes, including *PAX3*, *EDN3*, *EDNRB*, and *SOX10*, impose alterations in melanocyte production. Four types of Waardenburg syndrome are reported; type 1 and 2 are associated with alterations to skin and hair pigmentation. Skin-related manifestations include a white forelock and cutaneous hypochromia. The clinical picture is quite striking. It is interesting to note that 2% to 5% of all cases of congenital hearing loss are also attributed to Waardenburg syndrome (type 1 and 2; NIH, 2018e).

Localized Hypotrichosis

Localized autosomal recessive hypotrichosis is characterized by sparse hair on the scalp beginning in infancy. The global incidence is unknown; however, an incidence of one in every 10,000 individuals is reported among Japanese infants, as this condition prevails among the Japanese population (NIH, 2018a). Males and females are equally affected. Mutations in the *LIPH*, *LPAR6*, and *DSG4* genes alter the normal synthesis and proliferation of the hair and also may contribute to epidermal dysfunction. Common skin-related manifestations of hypotrichosis may include erythema, pruritis, or coarse, dry skin. At birth, scalp hair ranges from sparse and tightly curled whorls of hair to thin hair, which typically gradually decreases as the infant ages. A decreased complement of eyebrows, eyelashes, and axillary hair has also been reported (Basit, Khan, & Ahmad, 2015).

Sturge–Weber Syndrome

Sturge–Weber syndrome is a congenital neurocutaneous disorder that affects one in every 20,000 to 50,000 individuals (NIH, 2018d). It commonly manifests during infancy as a triad of three classic features: (a) port-wine stains, usually located to the cutaneous distribution of the first branch of the trigeminal nerve; (b) a leptomeningeal venous malformation; and (c) glaucoma (Jnah, Newberry, & Robertson, 2017). Life-span implications do not relate to the skin. Rather, affected individuals may suffer visual disturbances (associated with choroidal hemangiomas), intellectual disabilities (secondary to seizures or leptomeningeal angiomas), and hemiparesis (NIH, 2018d).

Epidermolysis Bullosa

Epidermolysis bullosa (EB) refers to a group of heterogeneous diseases that may affect the epidermis, dermal–epidermal junction, and dermis (Jnah et al., 2017; Moore et al., 2016). Current evidence suggests that EB affects 19.6 per 1 million individuals (Fine, 2016). The four major types of EB are (a) EB simplex (most common; 1/30,000–50,000 infants), (b) junctional EB, (c) dystrophic EB, and (d) Kindler syndrome (rarest; 250 cases worldwide); at least 39 subtypes have been reported (Table 12.5; Fine & Mellerio, 2018). At present, 14 distinct structural genes representing more than 1,000 different mutations are linked etiologically to EB and affect at least 19 different structural proteins (Fine & Mellerio, 2018; Gonzalez, 2013). The degree (severity) of gene mutation directly affects protein synthesis and disease severity.

In 2014, seeking to foster continuity in the use of nomenclature and diagnostics, the National Epidermolysis Bullosa Registry proposed a revised classification system. Patients are currently classified by major type of EB, phenotype (severity and distribution of lesions), mode of transmission, site of cleavage, protein involvement, gene involvement, and type of mutation. Terminology used to describe disease distribution and severity would be limited to *localized*, *generalized other*, and *generalized severe*, as opposed to prior use of vague eponyms (Fine et al., 2014).

Clinical manifestations vary in the newborn period; however, *skin fragility and blistering are consistent findings across all types and subtypes of EB* (Figure 12.5). EB simplex usually manifests with small and localized blisters. Junctional and dystrophic EB, most notably the recessive forms, involve deeper blisters that may implicate a larger surface area (Jnah et al., 2017). Blisters are termed

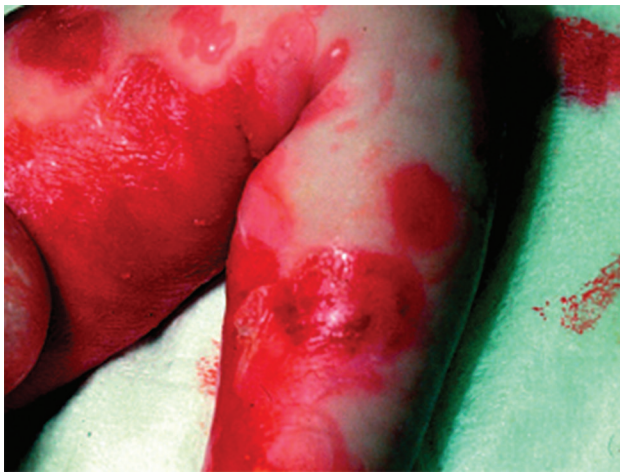


Figure 12.5 Denudation and erosion as a result of blistering in an infant with epidermolysis bullosa.

Source: Antaya, R. J., & Robinson, D. M. (2010). Blisters and pustules in the newborn. *Pediatric Annuals*, *39*, 635–645. doi:10.3928/00904481-20100922-01

TABLE 12.5 Epidermolysis Bullosa: Inheritance Pattern, Level of Skin Cleavage, and Affected Proteins

	Inheritance Pattern	Level of Skin Cleavage	Common Proteins
EB simplex	Autosomal dominant[a]	Intraepidermal (*basal and basal epidermis*)	Keratins 5 and 14 Plectin Dystonin Plakophillin-1 Desmoplakin
Junctional EB	Autosomal recessive	Intralamina lucida (*basement membrane*)	Laminin-332 Collagen XVII α6β64 integrin
Dystrophic EB	Autosomal dominant *and* Autosomal recessive	Sublamina densa (*dermis*)	Collagen VII
Kindler syndrome	Autosomal recessive	Multiple points	Kindlin-1

[a]Most forms of EB simplex are autosomal dominant, with the exception of suprabasilar types and forms with muscular dystrophy or pyloric atresia.

EB, epidermolysis bullosa.

Source: Gonzalez, M. E. (2013). Evaluation and treatment of the newborn with epidermolysis bullosa. *Seminars in Perinatology*, *37*, 32–39. doi:10.1053/j.semperi.2012.11.004

a *congenital localized absence of skin (CLAS)*; the classic appearance is a red, shiny blister with clearly defined margins (Fine & Mellerio, 2018). Infants who do not manifest with intrauterine-acquired blisters will develop them in the postnatal period, often secondary to friction imposed during the birth process. Blisters are composed of serous or hemorrhagic fluid; many heal without scarring, yet the breach in the skin barrier increases the risk for nosocomial infection during the birth hospitalization and later bacterial infections. Other consequences of EB include transepidermal water loss and fluid and electrolyte imbalances.

The care of EB extends across the life span and may involve rigorous and frequent dressing changes, rehospitalizations, recurrent infections, dehydration, or poor nutrition secondary to oral or esophageal blistering. Activity restrictions are common in order to reduce high-friction blistering. Affected children and adults are at risk for psychosocial disturbances due to disfigurement (Adni, Martin, & Mudge, 2012).

MATERNAL HEALTH INFLUENCES

Maternal health issues can influence fetal skin development and function. In particular, maternal autoimmune disorders, infectious diseases, and nutritional deficits can implicate fetal and neonatal skin. We discuss the effect of maternal lupus infection and nutritional deficits on the developing skin. The effect of maternal viral infections, when acquired by the fetus or neonate, is presented later in this chapter.

Maternal Systemic Lupus Erythematosus and the Fetus and Neonate

Mothers with anti-Ro/SSA and/or anti-La/SSB antibodies are at increased risk for giving birth to infants with neonatal lupus, an autoimmune disease that occurs in approximately 10% of infants whose mothers test positive for systemic lupus erythematosus (SLE). Common clinical manifestations of neonatal lupus include dermatologic, cardiac, and hepatic abnormalities (Bermas & Smith, 2018). Specific to the skin, cutaneous lesions may present at birth, but often appear within the first few weeks of life. Erythematous or polycystic plaques appear mainly on the scalp, neck, or face, but similar plaques may appear on the trunk or extremities. This dermatitis resembles the rash of subacute cutaneous lupus erythematosus rather than the malar rash of SLE. Periorbital erythema, referred to as *raccoon eye* or *owl eye*, is a very common characteristic (Figure 12.6). Bullous lesions may be seen on the soles of the feet. Besides the dermatologic signs, the most serious complication of neonatal lupus that all clinicians should be mindful of is complete heart block (Lun Hon & Leung, 2012). Children with neonatal lupus have an excellent long-term outcome when only skin lesions are present. The cutaneous lesions usually disappear by 6 months of age (Lun Hon & Leung, 2012).

Maternal Nutritional Deficits

Biotin Deficiency. Biotin deficiency is a rare nutritional disorder, more often observed in poorly developed countries. Biotin is a water-soluble vitamin, generally classified as a B-complex vitamin. Genetic disorders, such as

biotinidase deficiency, multiple carboxylase deficiency, and holocarboxylase synthetase deficiency, can lead to inborn or late-onset forms of biotin deficiency (National Organization of Rare Disorders, 2017). In all cases, dietary, genetic, or otherwise, supplementation with biotin is the primary method of treatment.

Pregnancy alters biotin catabolism and, despite a regular biotin intake, approximately 50% of pregnant women in the United States are recognized as marginally biotin deficient (Zempleni, Wijeratne, & Hassan, 2009). Signs and symptoms of neonatal biotin deficiency include red, patchy rashes near the mouth (erythematous periorofacial macular rash), fine and brittle hair, alopecia, anemia, birth defects, seborrheic dermatitis, and fungal infections. Fortunately, biotin supplements are readily available within the United States, and when prenatal care is pursued and continued throughout pregnancy, biotin deficiency is typically averted.

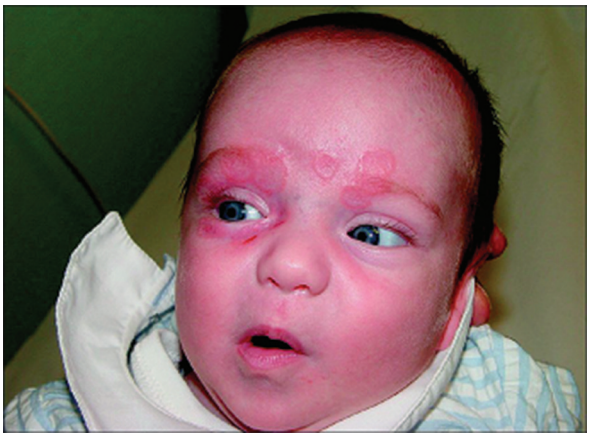


Figure 12.6 Cutaneous neonatal lupus erythematosus.

NOTE: "Racoon eye" appearance is noted over the right periorbital area. Customary erythematous annular plaques are seen over the glabella, along with central atrophy.

Source: Jaka, A., Zubizarreta, J., Ormaechea, N., & Tuneu, A. (2012). Cutaneous neonatal lupus erythematosus. *Indian Journal of Dermatology Venereology & Leprology, 78*(6), 775. Retrieved from http://www.ijdvl.com/text.asp?2012/78/6/775/102396

COMMON PROBLEMS WITH IMPLICATIONS ACROSS THE LIFE SPAN

The skin is a critical interface between the body and environment. This layer differentiates between "self" and "nonself." In fact, maternal–infant bonding is, in large part, a complex dynamic interaction between skin surfaces. Cutaneous characteristics are routinely used as determinants of gestational age. Pathologic processes visible on the skin surface range from general signs of systemic

TABLE 12.6 Common Dermatological Terms

	Brief Description	Examples of Association(s)	Primary or Secondary
Cicatricial	Fibrous and contracted scar tissue	Congenital VZV	Primary
Crusted ulcerations	Crusted skin lesions composed of dried exudate (blood, pus, or other serous or serosanguinous fluid) found on the epidermal layer of the skin	Trauma, viral/infectious etiologies, genetic or congenital syndromes, or vascular or other malformations	Secondary
Erythema	Redness of the skin that can occur in one or more locations and cover a small to large volume of surface area of the skin	Erythema toxicum, periumbilical erythema (omphalitis or funusitis), erythema multiforme, and staphylococcal scalded skin syndrome	Secondary
Exanthem	Widespread rash	Toxoplasmosis, HSV	Primary
Fissures	Linear breaches at the skin surface, resulting in an often painful separation of the epidermal layer	Keratodermas, eczema	Secondary
Scaling	Heaping of the stratum corneum with resultant shedding upon exfoliation	Ichthyosis, seborrheic dermatitis	Secondary
Scarring	Permanent, fibrotic alteration in skin integrity incurred as a result of trauma or tissue injury	Congenitally acquired infections, epidermolysis bullosa, infantile acne	Secondary

HSV, herpes simplex virus; VZV, varicella zoster virus.

Source: Jnah, A., Newberry, D., & Bell Robertson, T. (2017). Dermatology cases. In S. Bellini & M.J. Beaulieu (Eds.), *Neonatal advanced practice nursing: A case-based approach* (pp. 217–218). New York: Springer.

dysfunction to clinical evidence of specific diseases. Table 12.6 presents a list of common dermatology-specific terms and associated definitions. Readers should refer to this table while studying the common problems described in this final section of the chapter.

Transient Cutaneous Lesions

A number of benign and transient skin lesions are commonly observed in a normal newborn nursery population. It is important for the clinician to distinguish such transient lesions from cutaneous manifestations associated with life-threatening diseases. A precise description of primary and secondary skin cutaneous lesions forms the basis for understanding the skin pathology. Tables 12.7 and 12.8 describe the basic lesional morphology of infant skin with associated clinical exemplars.

Acrocyanosis. Acrocyanosis is one of the most common and typically transient cutaneous blood flow abnormalities, caused by reduced capillary reperfusion to the hands and feet. Reduced perfusion may be secondary to vasomotor immaturity, or caused by vasoconstriction secondary to cold temperatures (Maguiness & Garzon, 2015). Common clinical manifestations include a bluish color to the hands and feet. Because this phenomenon commonly self-resolves within 24 to 48 hours after birth and is not typically a primary or sole indicator of a congenital heart lesion, it is considered a benign finding (Jnah et al., 2017).

Sebaceous Gland Hyperplasia and Milia. These two conditions are presented in a side-by-side manner because they are easily confused in the clinical setting. Sebaceous gland hyperplasia is reported in approximately 20% to 40% of well-appearing newborns, with recent reports indicating occurrences of 89% (Haveri & Inamadar, 2014). The enlarged glands manifest secondary to increased sebum secretion at birth, likely due to maternal levels of the androgen dehydroepiandrosterone (via the placenta; Brzezinski & Chiriac, 2015). Defining

TABLE 12.7 Primary Cutaneous Lesions

Type	Description	Clinical Examples
Abscess	Same as a pustule but >1 cm in size	Pyodermas
Bulla	Same as a vesicle but >1 cm in size	Sucking blisters Epidermolysis bullosa Bullous impetigo
Nodule	A circumscribed, elevated, solid lesion with depth, up to 2 cm in size	Neuroblastoma
Macule	A circumscribed, flat lesion with color change, up to 1 cm in size; by definition, they are not palpable	Café-au-lait spots Capillary ectasias
Papule	A circumscribed, elevated, solid lesion, <1 cm in size; elevation may be accentuated with oblique lighting	Milia
Patch	Same as macule but >1 cm in size	Mongolian spots Nevus simplex
Plaque	A circumscribed, elevated, plateau-like, solid lesion, >1 cm in size	Nevus sebaceous
Pustule	A circumscribed, elevated lesion filled within purulent fluid, <1 cm in size	Neonatal pustular melanosis Erythema toxicum neonatorum Infantile acropustulosis
Tumor	Same as a nodule but >2 cm in size	Hemangioma Rhabdomyosarcoma
Vesicle	A circumscribed, elevated, fluid-filled lesion up to 1 cm in size	Herpes simplex virus Varicella zoster virus Miliaria crystalline
Wheal	A circumscribed, elevated, edematous, often evanescent lesion, caused by accumulation of fluid within the dermis	Urticaria Bite reactions Drug eruptions

Source: Modified from Yan, A. C., Kim, H. J. & Honig P. J., (2015). Lesional morphology and assessment. In L. F. Eichenfield, I. J. Frieden, E. F. Mathes, & A. L. Zaenglein (Eds.), *Neonatal and infant dermatology* (3rd ed., pp. 24–35). Philadelphia, PA: Elsevier Saunders.

TABLE 12.8 Secondary Cutaneous Lesions*

Type	Description	Clinical Examples
Atrophy	Localized diminution of skin. *Epidermal atrophy* results in a translucent epidermis with increased wrinkling, whereas *dermal atrophy* results in depression of the skin with retained skin markings. Use of topical steroids can result in epidermal atrophy, whereas intralesional steroids may result in dermal atrophy.	Aplasia cutis congenita Intrauterine scarring Focal dermal hypoplasia
Crust	Results from dried exudates overlying an impaired epidermis. Can be composed of serum, blood, or pus.	Epidermolysis bullosa Impetigo
Erosion	Intraepithelial loss of epidermis. Heals without scarring.	Herpes simplex
Fissure	Linear, often painful break within the skin surface, as a result of excessive xerosis.	Inherited keratodermas Eczema (hands, feet)
Lichenification	Thickening of the epidermis with exaggeration of normal skin markings caused by chronic scratching or rubbing.	Sucking blister Atopic dermatitis
Scale	Results from increased shedding or accumulation of stratum corneum as a result of abnormal keratinization and exfoliation. Can be subdivided further into pityriasiform (branny, delicate), psoriasiform (thick, white, and adherent), and ichthyosiform (fish scale–like).	Ichthyoses Postmaturity desquamation Seborrheic dermatitis
Scar	Permanent fibrotic skin changes that develop as a consequence of tissue injury. In utero scarring can occur as a result of certain infections or amniocentesis or postnatally from a variety of external factors.	Congenital varicella Aplasia cutis congenita
Ulcer	Full-thickness loss of the epidermis with damage into the dermis. Will heal with scarring.	Ulcerated hemangiomas Aplasia cutis congenita

*Lesions arise as characteristic modifications of primary lesions through environmental interaction (e.g., drying) or subject interaction (e.g., scratching).

Source: Modified from Yan, A. C., Kim, H. J., & Honig P. J. (2015). Lesional morphology and assessment. In L. F. Eichenfield, I. J. Frieden, E. F. Mathes, & A. L. Zaenglein (Eds.), *Neonatal and infant dermatology* (3rd ed., pp. 24–35). Philadelphia, PA: Elsevier Saunders.

characteristics include yellow-white papules with swelling of the sebaceous glands (Figure 12.7). These papules are often clustered together into small groupings, often located on the nose or midface region (Lucky, 2015).

On the contrary, milia are characterized as white cysts measuring approximately 1 mm in diameter. Milia are typically scattered over the cheeks, forehead, nose, and nasolabial folds. They may be few or numerous, but they frequently occur in clusters. Because all of these cysts exfoliate or involute spontaneously within the first few weeks of life, they are considered a benign finding.

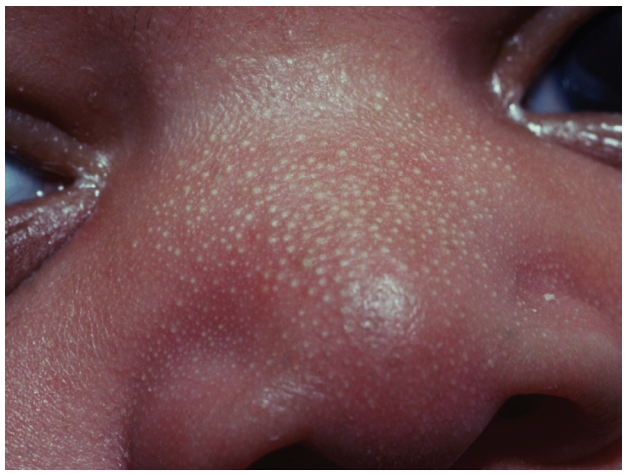


Figure 12.7 Sebaceous gland hyperplasia.

Source: Image appears with permission of VisualDx.

Pigmentary Abnormalities

The melanocyte system of the newborn skin usually is not mature at birth. As a result, all babies, regardless of racial pigmentation, may look lighter than their parents at birth. Within the first few weeks, pigmentation becomes more evident because melanin production has been stimulated by exposure to the postnatal environment.

Albinism. Albinism (e.g., complete albinism, oculocutaneous albinism), which occurs in all races, has an incidence of one per 17,000 individuals in the United States; the phenotypic picture is caused by an autosomal recessive gene. Several forms of this disorder have been delineated, including albinism type 1 and type 2 (Chan & Tay, 2015).

The biochemical defect responsible for oculocutaneous albinism type 1 is a deficiency of tyrosinase, the enzyme responsible for converting tyrosine to dopamine, an early step in the formulation of melanin. Structurally, the melanosomes appear to be normal. In oculocutaneous albinism type 2, however, mutations in the *OCA2* gene affect function of a melanosomal protein. Both conditions reduce melanin synthesis and yield reduced pigmentation.

Clinical manifestations include markedly reduced skin pigment, yellow or white hair, pink pupils, gray irises, photophobia, and cutaneous photosensitivity. Among African American infants, the skin may be tan, the hair may have a yellow or orange color, and freckles can appear upon exposure to light (Wright, Norval, & Hertle, 2015). Over the lifetime, reduced pigmentation and associated increased susceptibility to ultraviolet radiation can result in elastosis, actinic keratoses, and skin cancers including squamous cell carcinoma, basal cell carcinoma, and melanoma (Figure 12.8).

Café-au-Lait Macules. Café-au-lait macules are flat, pigmented macules with distinct borders that may be present in the newborn infant. The macules are light brown in Caucasians and dark brown in African Americans (Marcoux et al., 2011). Lesions are commonly seen on the trunk in older children, and over the buttocks in newborns (Price & Marghoob, 2015; Figure 12.9).

The pathogenesis involves an accumulation of melanin within the epidermis. Because the macules may be associated with several syndromes, including neurofibromatosis type 1, Leopard syndrome, Russell–Silver syndrome, and tuberous sclerosis, a differential diagnosis is recommended based on size and number (single versus multiple; Taieb, Ezzedine, & Morice-Picard, 2014). *Lesions that are larger than 0.5 cm in diameter and more than six in number, especially when accompanied by "freckling" in the flexures, strongly suggest neurofibromatosis, a disorder characterized by mutations of the* NF1 *gene.* The *NF1* gene makes neurofibromin, a protein that regulates cell growth and prevents tumor formation. In neurofibromatosis, neurofibromin is deficient, thereby allowing tumors to grow along nerves in various locations. Patients with tuberous sclerosis also may have café-au-lait spots that are identical in appearance to those of neurofibromatosis, but they are usually accompanied by white macules.

Clinical manifestations may include axillary freckles, which actually represent tiny café-au-lait macules. Café-au-lait spots are usually the first cutaneous lesions to appear in a patient with neurofibromatosis, but additional genetic and clinical investigations are required to establish a diagnosis. Café-au-lait macules may change size, and even increase over the first few years of life, but they do not spontaneously resolve. Because these skin lesions persist, they may be cosmetically problematic as the child ages. Lesions associated with neurofibromatosis incur additional life-span issues addressed in prior chapters of this textbook, which include neurological or cognitive difficulties and/or tumor formation.

Congenital Melanocytic Nevi, Small to Intermediate. Congenital melanocytic (pigmented) nevi present at birth or within the first few months of life. Small nevi (<1.5 cm) are seen in 1% to 2% of newborns and intermediate nevi (1.5 to 20 cm) in 0.6% (Price & Marghoob, 2015). These skin lesions are believed to arise due to mutations in *NRAS* and *BRAF* genes. The mutations provoke an abnormal proliferation of cells with a melanocytic phenotype, which nest together in the epidermis; at least three melanocytic cells touch the dermis or other tissues (Roh, Eliades, Gupta, & Tsao, 2015). Clinical manifestations of small nevi are flat and light- to dark- brown lesions, often with variegated color or speckling and an accentuated epidermal surface ridge pattern. These lesions vary in site, size, and number, but most often are solitary. Melanocytic nevi may be malignant and should be monitored diligently from birth through adulthood (Figure 12.10A).

Figure 12.8 Albinism.

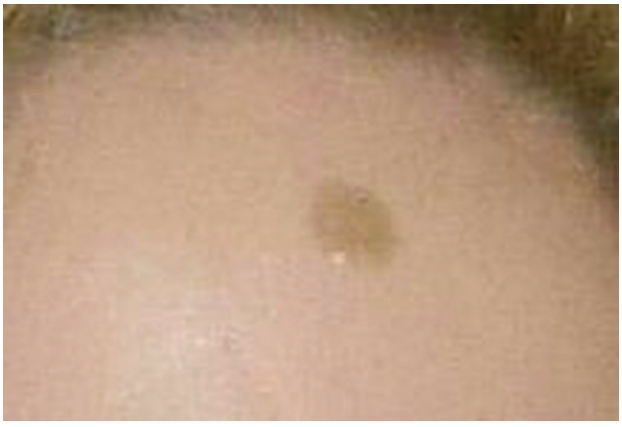
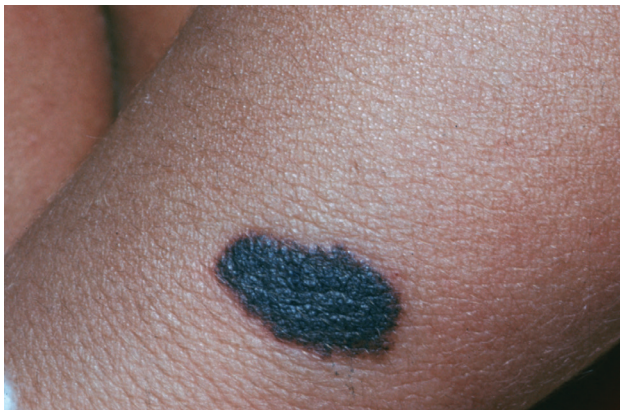


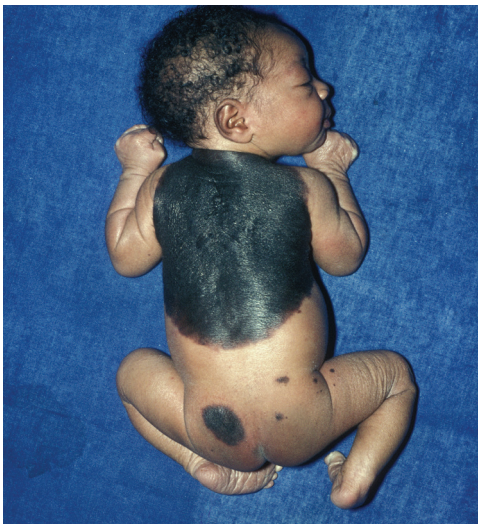
Figure 12.9 Café-au-lait macules.

Source: Bellini, S., & Beaulieu, M. J. (Eds.). (2017). *Neonatal advanced practice nursing: A case-based learning approach*. New York, NY: Springer Publishing.

Congenital Melanocytic Nevi, Large. The occurrence of large nevi is less than 0.02%. The giant (>20 cm) nevus is associated with a lifetime risk for malignant transformation, and melanoma is estimated to occur in 6% to 8% of affected individuals (Price & Marghoob, 2015). The onset of melanoma in utero has been reported. These nevi may occupy 15% to 35% of the body surface, most commonly involving the trunk. The pigmentation often is variegated from light brown to black. The affected skin may be smooth, nodular, or leathery in consistency. Prominent hypertrichosis is often present. Almost invariably, numerous satellite nevi coexist elsewhere on the body. Leptomeningeal melanocytosis has been documented in some of these patients, and this complication may manifest as seizures. Because of the significant incidence of malignant transformation, the hideous deformity, and the intense pruritus that may accompany them, it is desirable, when feasible, to excise these lesions surgically as soon as possible (Figure 12.10B).



(A)



(B)

Figure 12.10 Congenital melanocytic nevi: (A) small to intermediate; (B) large.

Source: (A) Image appears with permission of VisualDx.

Nevus Anemicus. Nevus anemicus is a congenital vascular anomaly that occurs in about 1% to 2% of individuals, and typically yields lesions that measure 5 to 10 cm in diameter (Kolb & Krishnamurthy, 2017). These lesions present as permanently pale, mottled lesions located on the trunk. The cause is believed to be secondary to a heightened response to the effects of catecholamines (adrenaline noradrenaline). For that reason, the nevus is best characterized as a pharmacologic abnormality, rather than an anatomic one. The lesions appear hypopigmented, but contain normal amounts of pigment. Pallor results from increased local reactivity to catecholamines, which provokes vasoconstriction and subsequent pallor. When rubbed, the lesion does not redden like the surrounding skin. These lesions do not spontaneously resolve and, therefore, may impose cosmetic issues over time.

Pigmentary Lesions

Erythema Toxicum. Erythema toxicum is a benign and self-limited inflammatory reaction that usually manifests within the first 24 to 72 hours of life; new lesions may appear until 2 to 3 weeks of age (Monteagudo, Labandeira, Cabanillas, Acevedo, & Toribio, 2012). The disorder is more common among term than premature infants, which suggests that the inflammatory reaction requires mature skin. The pathogenesis involves skin reactions to elevated concentrations of IL-8, LI1, eotaxin, and psoriasin, further supporting the inflammatory etiology for this type of transient lesion (Monteagudo et al., 2012). Lesions may be firm, 1 mm to 3 mm in diameter, pale yellow to white, and manifest as papules or pustules that sit on an erythematous base resembling flea bites. They may also manifest as erythematous macules as large as 3 cm in diameter. Individual lesions are fleeting, often lasting only a matter of hours. They may be found on any area of the body, but only rarely to the palms and soles. They are asymptomatic with no related systemic involvement. A microscopic examination of a Wright- or

Figure 12.11 Erythema toxicum.

Source: © David Gee/Alamy Stock Photo

Giemsa-stained smear of the pustule contents will yield numerous eosinophils; Gram stains are negative for bacteria and cultures are sterile. Spontaneous resolution occurs in 6 days to 2 weeks (Figure 12.11).

Transient Neonatal Pustular Melanosis. Transient neonatal pustular melanosis is a distinctive eruption that consists of three types of lesions. First-stage lesions are small, superficial vesiculopustules with little or no surrounding erythema (Ghosh, 2015). These rapidly progress to the second stage, which consists of collarettes of scale or scale crust surrounding a hyperpigmented macule (third stage). All three types of lesions may be present at birth, but the macules are observed more frequently. The lesions may be profuse or sparse and occur on most body surfaces, including the palms, soles, and scalp. Sites of predilection are the forehead, submental area, anterior neck, and lower back. The pathophysiology is not well understood. Cultures and Gram stains of smears prepared from intact pustules are typically devoid of organisms; however, increased neutrophil counts have been observed (Reginatto, Muller, Peruzzo, & Cestari, 2017). Pustules typically disappear within 48 hours of onset, whereas the hyperpigmented macules may persist for as long as 3 months. The disorder is benign and transient (Figure 12.12).

Harlequin Color Change. Harlequin color change is a transient phenomenon observed in the immediate neonatal period, commonly noticed among low-birth-weight infants. The pathophysiology is attributed to a temporary imbalance in the autonomic regulatory mechanism of the cutaneous vessels; there are no accompanying vital sign changes (Figure 12.13; Khemani, Ali, Karim, & Yezdan, 2017). The dependent side of the body becomes intensely red, the upper side pales, and a sharp, vertical line of demarcation appears down the trunk (midline). The episodes can be observed during the first 3 weeks of life and are of no pathologic significance.

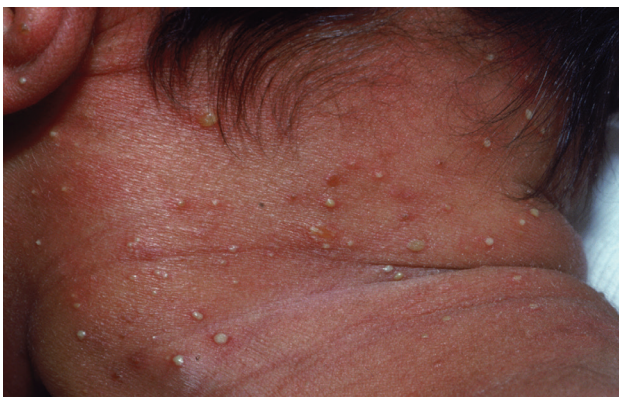


Figure 12.12 Transient neonatal pustular melanosis.

Source: Image appears with permission of VisualDx.

Miliaria. Miliaria is a skin eruption that results from eccrine sweat duct obstruction. This leads to sweat retention (Engür, Türkmen, & Şavk, 2013; Hölzle & Kligman, 1978). Three clinical presentations are observed: (a) superficial thin-walled vesicles without inflammation (i.e., miliaria crystalline); (b) small, erythematous, grouped papules (i.e., miliaria rubra); and (c) nonerythematous pustules (i.e., miliaria pustulosis). The eruption most frequently develops in the intertriginous areas and over the face and scalp. It is exacerbated by exposure to a warm and humid environment. Rapid resolution occurs when the infant is placed in a cooler environment. A Wright-stained smear of vesicular lesions demonstrates only few squamous cells or lymphocytes. In a seminal controlled study, *Staphylococcus epidermidis* produced miliaria but *S. hameolyticus, S. hominis, S. cohnii, S. saprophyticus*, and *S. simulans* did not (Mowad, McGinley, Foglia, & Leyden, 1995). The condition resolves spontaneously (Figure 12.14).

Mongolian Spot. The most frequently encountered pigmented lesion is the Mongolian spot (dermal melanosis), which occurs in 90% to 100% of African American and Asian infants, 50% in Hispanic infants, and less frequently (less than 10%) among Caucasian infants (Gupta & Thappa, 2013). The pathophysiology relates to the excessive accumulation and delayed disappearance of melanocytes in varying numbers. Although most of these lesions are found in the lumbosacral area, they can occur at other sites. The pigmentation is macular and gray-blue, lacks a sharp border, and may span a diameter of 10 cm or more. Most of these lesions gradually disappear during the first

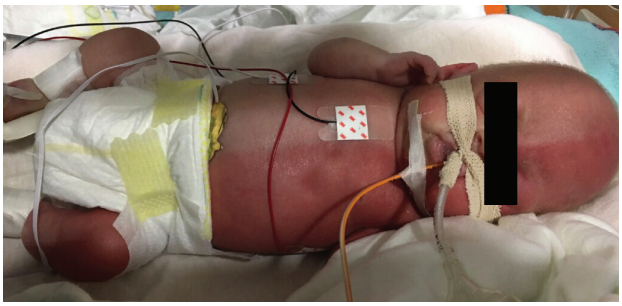


Figure 12.13 Harlequin color change.

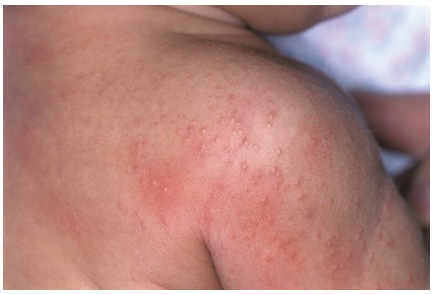


Figure 12.14 Miliaria.

Source: ISM/MedicalImages.com.

few years of life, but aberrant lesions in unusual sites are more likely to persist. There is some indication that they are associated with metabolism disorders or neurocristopathies (Figure 12.15).

Neonatal Acne. Neonatal acne occurs in up to 20% of newborns, and is more common among males (Yeo & Ormerod, 2014). Increased sebaceous secretions, secondary to maternal and neonatal androgens, and colonization of the sebaceous glands by the yeast *Malassezia furfur* are implicated in its pathogenesis (Friedlander, Baldwin, Mancini, Yan, & Eichenfeld, 2011).

Neonatal acne presents as small, red papules and pustules on the face, usually within the first weeks of life. Unlike in adolescence, comedones and cysts are usually absent. The lesions are asymptomatic and resolve spontaneously without scarring over several weeks. The clinical significance lies in differentiating this rash from infections, excluding virilization as its underlying cause, and potential implication of severe acne in adolescence.

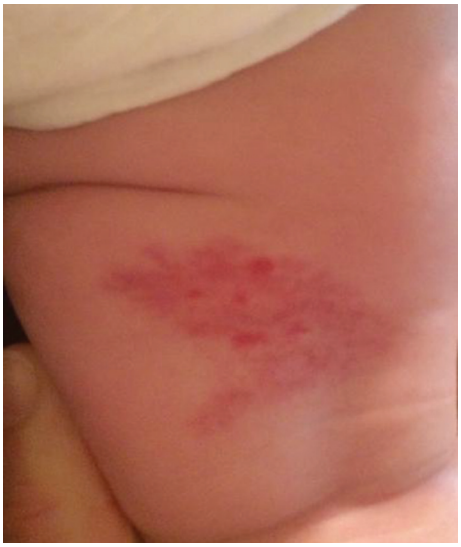
Nevus Simplex (Salmon Patch). The nevus simplex (stork bite) is the most common neonatal cutaneous lesion, and is present in up to 80% of normal newborns (Kanada, Merin, Munden, & Friedlander, 2012). Stork bites manifest as a result of distended dermal capillaries and blanch when compressed. The lesions are transient and typically manifest within the first 72 hours of life (Reginatto, DeVilla, et al., 2017). Clinicians will commonly note their central location and symmetric presentation; lesions typically appear at the nape of the neck, eyelids, and glabella. In a prospective study of affected infants, most of the facial lesions had faded by 1 year of age, but those on the neck were more persistent (Reginatto, DeVilla, et al., 2017). Surveys of adults confirm the persistence of the nuchal lesions in approximately 25% of affected individuals (Figure 12.16).

Disorders of Cornification: The Scaly Baby

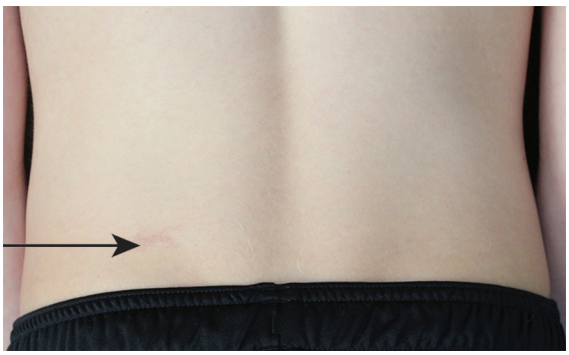
The most common and benign cause for excessive scaling is attributed to physiologic desquamation (normal term infants) and dysmaturity (postmature and small-for-gestational-age infants), neither of which have long-term sequelae. Less common causes include the congenital ichthyoses and the ectodermal dysplasias, both of which are chronic, heritable disorders (Craiglow, 2013; Foley, Paller, & Irvine, 2015). In the normal infant with accentuated physiologic scaling and the dysmature infant,

Figure 12.15 Mongolian spot.

Source: Bellini, S., & Beaulieu, M. J. (Eds.). (2017). Neonatal advanced practice nursing: A case-based learning approach. New York, NY: Springer Publishing.



(A)



(B)

Figure 12.16 (A) Nevus simplex (salmon patch) on 2-month-old infant. (B) A faded salmon patch on a 13-year-old child.

Source: (A) Image courtesy of Elizabeth Carmac, MSN, NNP-BC; (B) image courtesy of Amy Jnah, DNP, NNP-BC.

desquamation is a transient phenomenon. The integument continues to serve its intended protective function. In contrast, the infant with congenital ichthyosis may exhibit impaired barrier function and incur a heightened risk for secondary infections.

Ichthyoses. *Ichthyosis* refers to a complex and often confusing plethora of conditions characterized by disorders of cornification with or without systemic symptoms (Craiglow, 2013; Foley et al., 2015). Ichthyosis is a genetic disorder, characterized by mutations in the genes that produce keratin (i.e., *KRT1, KRT2*, or *KRT10*), which disrupt normal skin barrier formation (Vahlquist, Fischer, & Törmä, 2018). The major clinical phenotypes in the newborn of ichthyoses are enumerated in the "Genetic Influences" section of this chapter (**Figure 12.17**). Clinical manifestations during the neonatal period include isolated scaling, scaling with erythroderma, a collodion membrane, or thickened plates of harlequin ichthyosis. Although rare, early recognition is critical. Ichthyosis compromises the skin barrier, which increases the risk for secondary infection and increased penetration of irritants.

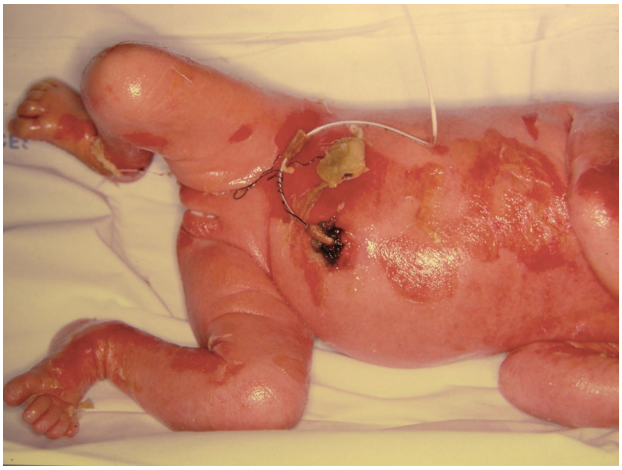


Figure 12.17 Ichthyoses.

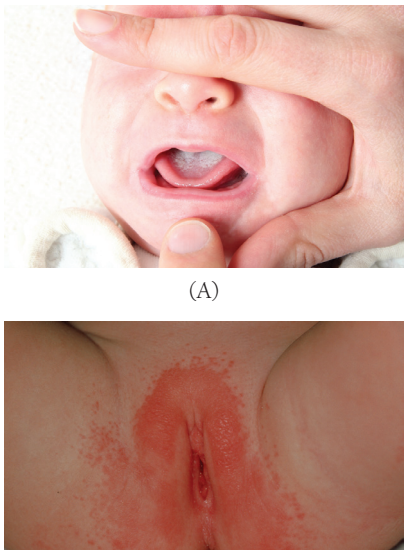
Source: Waikato District Health Board/DermNet New Zealand

Infectious Etiologies

Candidiasis. Candidiasis is an infection caused by *Candida*, a species of yeast. The incidence of confirmed cases ranges from 2% to 28% in U.S. NICUs (Benjamin et al., 2010). Among extremely premature infants (<1000 g), the incidence ranges from 4% to 8% and the mortality risk is 30% (Kelly, Benjamin, Daniel, & Smith, 2015). Fecal contamination is the usual source of the organism in candidal dermatitis. *Candida* species are commensal organisms commonly found in the gastrointestinal and female genital tracts. Roughly 33% of healthcare workers in NICUs test positive for *Candida* on routine surveillance cultures, and up to 40% of women are positive for *Candida* at the time of delivery (Filippidi et al.. 2014).

Rarely, cutaneous candidiasis is congenitally acquired as a result of vertical (ascending) infection from a vaginal or cervical focus. Affected infants usually manifest with pustules to the palms and soles, and occasionally, nail dystrophy. Candidiasis in the first 4 weeks of life is more common, usually benign, and typically localized to the oral cavity (thrush) or diaper area (**Figure 12.18A, B**). The lesions of thrush are detectable as creamy-white patches of friable material on the buccal mucosa, gums, palate, and tongue. Early cutaneous lesions consist of erythematous papules and vesicopustules that become confluent, forming a moist, erosive, scaly dermatitis surrounded by satellite pustules.

In contrast to acquired cutaneous candidiasis, congenital candidiasis has lesions at nonflexural sites (K. Chen, Chien, Chen, & Chiu, 2016). Distinctive yellow-white papules on the umbilical cord and placenta represent



(A)

(B)

Figure 12.18 Candidiasis. (A) White, curd-like patch to the buccal mucosa, consistent with early stages of oral thrush. (B) Red, shiny rash with satellite lesions located within diaper region, consistent with candida diaper rash.

Sources: (A) Shutterstock/riopatuca; (B) Dr P. Marazzi/Science Source

Candida granulomas. *C. albicans* may be demonstrable on histologic examination of these tissues and may be cultured from the amniotic fluid. Although *Candida* infection is usually localized to skin, infants who weigh less than 1,500 g are at risk for systemic infections. Additional risk factors for disseminated candidiasis include central-line placement, invasive mechanical ventilation, broad-spectrum antibiotic exposure, and the provision of intravenous parenteral nutrition.

Congenital Syphilis. Congenital syphilis occurs as a result of vertical transmission of *Treponema pallidum*. Sixty percent of infants with congenital syphilis are asymptomatic at birth. Clinical manifestations include erythematous vesicles or bullae atop a polished base (macule with erythematous halo); lesions located on the palms and soles are pathognomonic (**Figure 12.19**; Tsimis & Sheffield, 2017). Skin lesions may be accompanied by hepatosplenomegaly, periostitis of long bones, snuffles, and iritis. If undiagnosed, the symptoms persist or worsen. Diagnosis is confirmed through nontreponemal antibody titers (Heston & Arnold, 2018).

Herpes Simplex Virus. Herpes simplex virus (HSV) infection is one of the most common causes for vesicular rashes in the neonatal period (Howard & Frieden, 2015). The virus may be acquired in utero or during the perinatal period. Intrauterine infection typically presents with vesicles at birth, or within the first 24 hours of life. An inconspicuous cutaneous lesion heralds the onset of severe systemic infection. The vesicular eruption may be widespread or even bullous, resembling epidermolysis bullosa (**Figure 12.20**). Vesicles may also present on the torso or buttocks, especially with a breech presentation. Rarely, congenital scars are present.

HSV infection acquired during the perinatal period is often limited to the skin, eyes, and mouth; disseminated infection is possible. Cutaneous lesions usually manifest during the second week of life, concurrent with or after nonspecific systemic signs and symptoms. Typically, the vesicles measure 1 mm to 3 mm in diameter and are usually noted on the scalp or face. Rarely, pustules, erosions, or oral ulcerations appear as isolated manifestations.

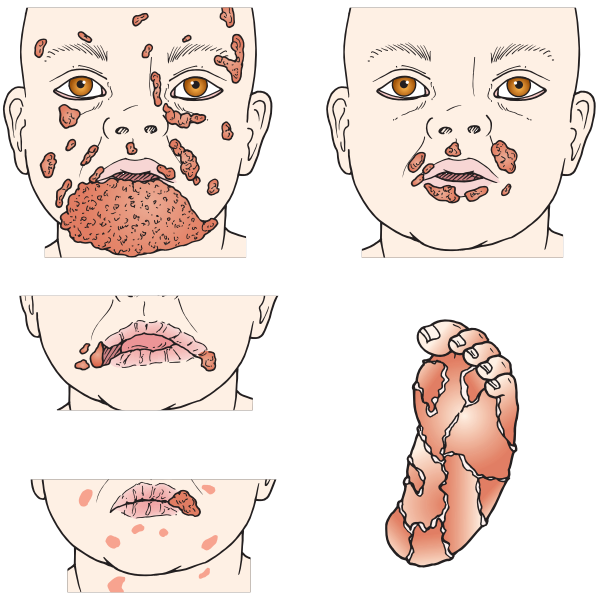


Figure 12.19 Congenital syphilis.

Staphylococcal Infection and Impetigo. Superficial skin infections caused by *Staphylococcus aureus* are a concern because of the increase in community acquired *Methicillin-resistant Staphylococcus aureus (MRSA)*. The *S. aureus* organism disrupts the host immune response by mechanisms that include isolation of host antibodies, the formation of a polysaccharide biofilm, and prevention of chemotaxis of leukocytes (Tong et al., 2015). Infections range from localized bullous impetigo to generalized cutaneous involvement with systemic illness. In contrast to congenital blistering diseases, which are often present at birth, skin infections with *S. aureus* usually develop after the first few days of life (Newnam, 2016). Lesions may be bullous, crusted, or pustular; typical lesions are small vesicles or pustules, or large, fragile bullae filled with clear, turbid, or purulent fluid. They rupture easily, leaving red, moist, denuded areas often with a superficial varnish-like crust (**Figure 12.21 A, B**; Nguyen, Wang, Eichenfield, & Barrio, 2016). Although they may develop anywhere on the body, the blisters and

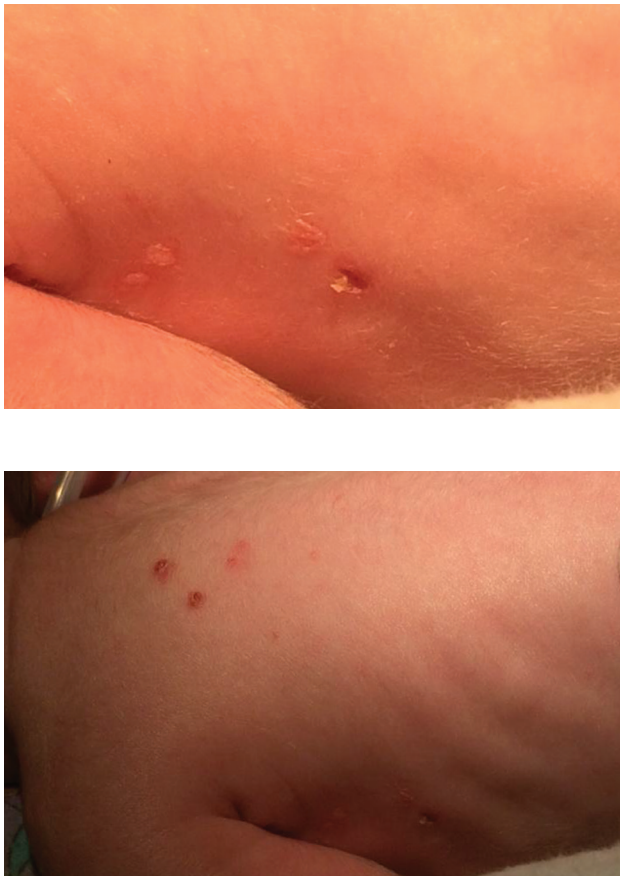


Figure 12.20 Herpes simplex virus.

Source: Bellini, S., & Beaulieu, M. J. (Eds.). (2017). Neonatal advanced practice nursing: A case-based learning approach. New York, NY: Springer Publishing.

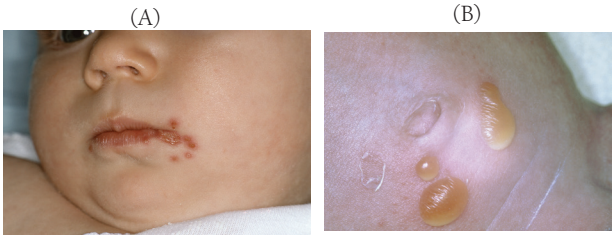


Figure 12.21 (A) Infant with perioral impetigo, an acute contagious staphylococcal or streptococcal skin disease that presents as vesicles or pustules, and yellowish crusts. (B) Bullish impetigo, a staphylococcal or streptococcal skin infection which begins as a red patch, followed by the formation of large and fragile pustules that join together and form crusty, yellow-colored blisters (bullae). May present around axilla or periumbilical area.

Sources: (A) ISM/MedicalImages.com; (B) © SPL/Science Source

pustules commonly occur on the diaper area, axillae, and periumbilical skin.

Staphylococcal Scalded Skin Syndrome. Staphylococcal scalded skin syndrome (SSSS) is a blistering skin disorder. Premature infants are at increased risk for SSSS due to a lack of maternal antitoxin antibodies. The infecting organism is *S. aureus*, usually a group 2 phage type, although other phage types occasionally have been incriminated. These organisms produce exotoxins (e.g., exfoliatin) that exert proteolytic activity on desmoglein-1, a molecule found within the desmosomes of keratinocytes responsible for the cutaneous manifestations (Hennigan & Riley, 2016). The release of the endotoxins (epidermolytic toxin A and B) provokes widespread epidermal necrolysis with severe bullous eruptions. The bullous eruptions usually present between days 3 and 7 of life. Denudation and blister formation characteristically occur after gentle rubbing of the skin, which is referred to as *Nikolsky's sign*. Histologic examination of the skin shows a striking absence of inflammatory infiltrate. Infants are typically febrile, irritable, and exhibit marked cutaneous tenderness. Crusting around the mouth and eyes results in atypical facies. Conjunctivitis is common, along with hyperemia of the mucous membranes, but oral ulcerations do not occur.

Vascular Anomalies: Vascular Malformations and Vascular Tumors

Arteriovenous Malformations. Arteriovenous malformations (AVMs) are a more aggressive type of simple malformation. They are composed of malformed arteries, veins, and capillaries; direct arteriovenous communications result in arteriovenous shunting (Wassef et al., 2015). The incidence is estimated to be 0.001% within northern European geographies. AVMs arise due to a mutation in the *RASA1* gene, which normally directs cell proliferation and migration (Weitz et al., 2015). Lesions are large, red, warm, and painful and exhibit pulsations, thrills, or a bruit. Rarely, AVMs present as ulcerated and bleeding lesions or with high output congestive cardiac failure. AVMs may remain quiescent through early childhood, and display sudden growth at puberty or following a local trauma. A high recurrence risk is reported (Richter & Suen, 2010).

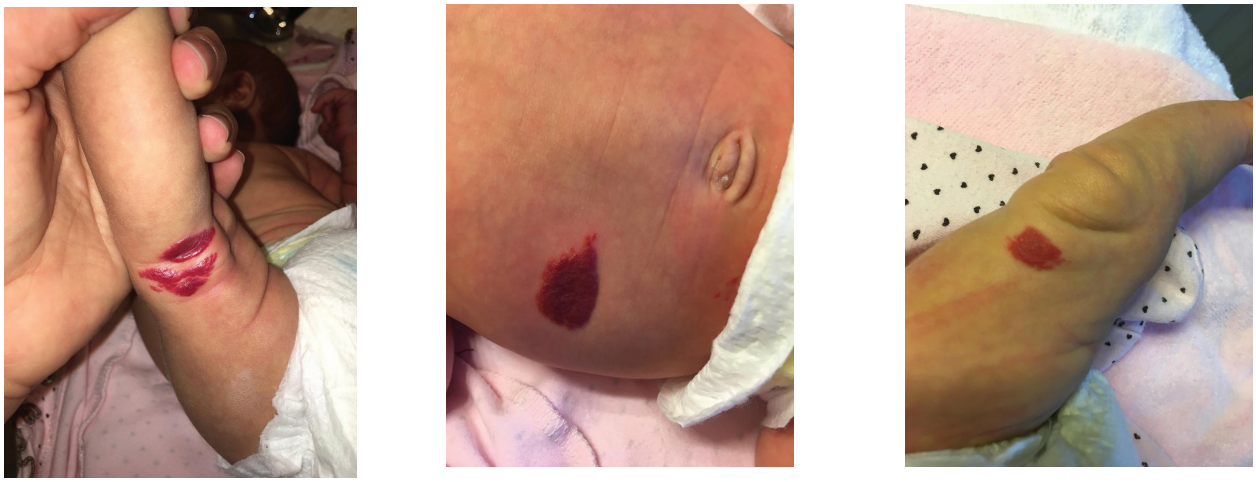
Epidermal Nevi. Epidermal nevi occur among one to three of every 1,000 newborns (Brandling-Bennett & Morel, 2010). *RAS* gene mutations have been implicated in the formation of this skin lesion, which provoke overgrowth of keratinocytes (Hafner et al., 2012; Prendiville, 2015). Variations in size, clinical appearance, histologic characteristics, and evolution are reported. Lesions occurring in sites normally rich in sebaceous glands (e.g., scalp) may appear similar to sebaceous nevi, whereas others found in areas where the epidermis is thick (e.g., elbow) appear wart-like.

The most common type of epidermal nevus in the newborn infant is the sebaceous nevus, a hairless, papillomatous, yellow or pink, slightly elevated plaque on the scalp, forehead, or face (Prendiville, 2015). These lesions have a characteristic oval or lancet shape. Because a significant incidence of basal cell epitheliomas occurs in these lesions after puberty, they should be surgically removed.

Hemangiomas. Hemangiomas are the most common soft tissue tumors of infancy, occurring in approximately 4% and 10% of infants and children, respectively (Kanada et al., 2012). These are benign vascular neoplasms that undergo rapid endothelial cell proliferation shortly after birth, stabilize, and then slowly involute with diminishing cellular activity and fibrous fatty deposition for up to 5 to 7 years (Shah et al., 2016).

Infantile hemangiomas (IH) are subclassified as focal, multifocal, segmental, and indeterminate, depending on their morphology, extent, or distribution (Wassef et al., 2015). IH are characterized by a growth phase, marked endothelial proliferation, and hypercellularity, followed by an involutional phase. IH that lie deeper in the skin are soft, warm masses with a slightly bluish discoloration. Frequently, IH have superficial and deep components. They range from a few millimeters to several centimeters in diameter and usually are solitary; up to 20% of infants display multiple lesions (Figure 12.22). Generally, superficial IH reach their maximal size by 6 to 8 months, but deep hemangiomas may proliferate for 12 to 14 months or, rarely, up to 2 years. MRI and ultrasonography are the preferred imaging methods and should be considered when lesions are detected on the scalp, orbits, airways, or are found in groups of five or more.

Despite the benign nature of most cutaneous hemangiomas, a significant number cause functional compromise or permanent disfigurement. Approximately 65% of hemangiomas are on the head and neck. Even with treatment, half



(A) (B) (C)

Figure 12.22 Images of a female newborn with five focal cutaneous hemangiomas (four shown here: [A] two lesions to the right leg; [B] lesion to the right abdomen; and [C] lesion to the left thigh). Further examination revealed normal thyroid function and an absence of associated hepatic hemangiomas.

of hemangiomas located on the lip, eyelid, nose, cheek, or glabella require surgical treatment (Brennan, Waner, & O, 2017). Nasal tip, lip, and parotid hemangiomas are notorious for slow involution, and very large superficial facial hemangiomas often leave disfiguring scarring. Ulceration, the most frequent complication, can be excruciatingly painful and carries the risk of infection, hemorrhage, and scarring. Occasionally, hemangiomas manifest as congenital ulcerations with only a very small rim of typical hemangioma, making the diagnosis difficult.

Periorbital hemangiomas and hemangiomas that involve the ear pose considerable risk to vision, hearing, and speech. Multiple cutaneous (i.e., diffuse hemangiomatosis) and large facial hemangiomas may be associated with visceral hemangiomas. Due to the potential for visceral hemangiomas, additional evaluations including ultrasounds and/or MRI may be warranted (Friedland, Ben Amitai, & Zvulunov, 2017; Reimer & Hoeger, 2016). Subglottic hemangiomas manifest with hoarseness and stridor, and progression to respiratory failure may be rapid. Approximately 50% of these infants have associated cutaneous hemangiomas. Any "noisy breathing" by an infant with a cutaneous hemangioma involving the chin, lips, mandibular region, and neck warrants direct visualization of the airway. Sixty percent of young infants with extensive facial hemangiomas in the "beard" distribution develop symptomatic airway hemangiomas.

The presence of an extensive cervicofacial hemangioma may indicate PHACE syndrome, where the hemangioma is associated with other anomalies; P = posterior fossa (possible abnormal structures in the brain, especially the cerebellum), H = hemangioma, A = arterial (possible brain artery abnormalities), C = cardiac (possible abnormalities of the great vessels of the heart), and E = eyes (possible eye anomalies). This syndrome has a marked female predominance (9:1) and is thought to represent a developmental field defect that occurs between weeks 8 and 10 of gestation. Lumbosacral hemangiomas may be markers for occult spinal dysraphism and anorectal and urogenital anomalies.

Congenital hemangiomas are relatively uncommon, present fully grown at birth, and either undergo rapid involution (RICH: rapidly involuting congenital hemangioma) or persist into adulthood (NICH: noninvoluting congenital hemangioma). Congenital hemangiomas that resolve rapidly often leave pronounced atrophic skin changes in their wake.

Most hemangiomas require "active nonintervention" coupled with a careful discussion of the natural history of the lesions and photographic documentation of involution (Blei & Guarini, 2014; T. S. Chen, Eichenfield, & Friedlander, 2013; Maguiness & Garzon, 2015). Up to 40% of children develop complications requiring intervention. Ulceration is the most common complication, but other problems include bleeding, airway or visual axis obstruction, cosmetic disfigurement, and high-output cardiac failure (Blei & Guarini, 2014; T. S. Chen et al., 2013; Maguiness & Garzon, 2015).

Kaposiform hemangioendothelioma (Kasabach–Merritt phenomenon), a complication of a rapidly enlarging vascular lesion, is characterized by hemolytic anemia, thrombocytopenia, and coagulopathy. These massive tumors are usually a deep red-blue color, firm, grow rapidly, have no sex predilection, tend to proliferate for a longer period (2 to 5 years), and have a different histologic pattern than other hemangiomas.

Most patients with Kasabach–Merritt phenomenon manifest with proliferative vascular tumors, usually kaposiform hemangioendotheliomas or tufted angiomas (Maguiness & Garzon, 2015). The Kasabach–Merritt phenomenon carries a significant mortality risk.

Lymphangiomas. Lymphangiomas are congenital hamartomatous malformations composed of dilated lymph channels that are lined by normal lymphatic endothelium (Maguiness & Garzon, 2015). Fetal skin and subcutaneous tissues are involved in this malformation that affects 1.1 to 5.3 of every 10,000 births (Ersoy, Oztas, Saridogan, Ozler, & Danisman, 2016). These malformations may be observed prenatally via ultrasound, may be superficial or deep, and are often associated with anomalies of the regional lymphatic vessels (Figure 12.23).

Milroy primary congenital lymphedema may present at birth and often affects the dorsal aspects of the feet. This autosomal dominant condition arises from a congenital dysgenesis of the lymphatic microvessels secondary to mutation in the *FLT4* (*VEGFR3*) gene. This condition is rarely associated with significant complications.

Simple and deep lymphangiomas, as well as cystic hygromas, may present at birth or during infancy. Simple lymphangiomas appear as solitary, skin-colored, dermal or subcutaneous nodules. After trauma, they may exude serous fluid. On occasion, these lesions have been associated with more extensive lymphatic involvement. Alternatively, deep lymphangiomas are more diffuse and consist of large, cystic dilations of lymphatics in the dermis, subcutaneous tissue, and intermuscular septa. Cystic hygroma is a benign, multilocular tumor usually found in the neck region. These tumors tend to increase in size.

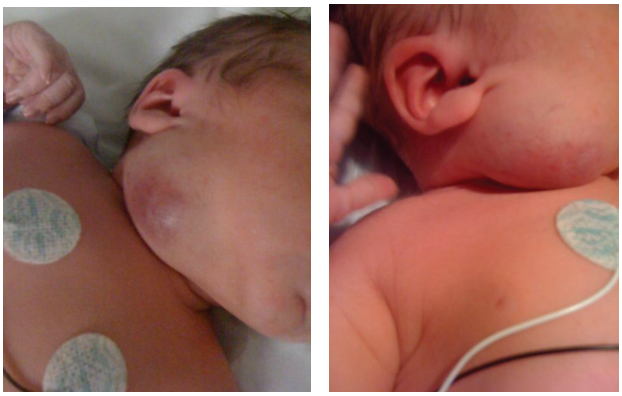


Figure 12.23 Lymphatic malformation ("cystic hygroma") present at birth.

Source: Bellini, S., & Beaulieu, M. J. (Eds.). (2017). *Neonatal advanced practice nursing: A case-based learning approach*. New York, NY: Springer Publishing.

Lymphangioma circumscriptum is probably the most common type of lymphangioma and may be present at birth or appear in early childhood. Areas of predilection are the oral mucosa, proximal limbs, and flexures. This malformation consists of clustered, small, thick-walled vesicles resembling frog spawn; it is often skin colored but may have a red or purple cast because of the presence of blood mixed with lymph in the vesicles.

Port-Wine Stain. Port-wine stains are capillary malformations that are almost always present at birth and should be considered permanent developmental defects (Maguiness & Garzon, 2015). They occur in 0.3% of neonates (Bae, Ng, & Geronemus, 2016). These lesions may span a few millimeters in diameter or cover extensive areas, but facial lesions are the most common (Figure 12.24). They do not proliferate after birth, but may appear to increase in size with the growth of the child. Port-wine stains are sharply demarcated and flat during infancy, but with time develop a pebbly or slightly thickened surface and frequently darken. Most port-wine stains occur as isolated defects; occasionally, these lesions may be associated with ocular defects or certain vascular malformation syndromes.

Inflammatory Diseases of the Skin

Several inflammatory skin conditions may occur in the neonate. Irritant contact dermatitis and seborrheic dermatitis are the most frequently encountered (Cordoro & Schulman, 2015; Tom & Eichenfield, 2015). They may be difficult to distinguish because their clinical features have a significant degree of overlap.

Irritant Contact Dermatitis. Primary irritant contact dermatitis (as opposed to allergic contact dermatitis) is probably the most common exogenous cause for

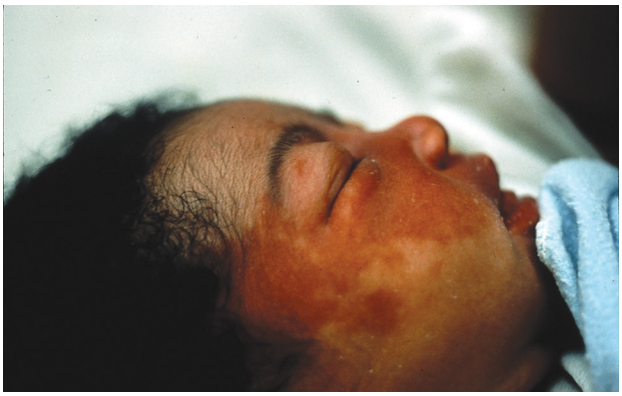


Figure 12.24 Port wine nevus.

Source: Clark, D. A. (2000). *Atlas of Neonatology*. Philadelphia, PA: Saunders.

dermatitis in the newborn. Irritant contact dermatitis is generally a result of penetration of external agents, or iatrogenic causes, via a damaged or underdeveloped SC. External agents may disrupt the SC barrier by way of hydration or alteration of the lipid bilayer structure. Irritants penetrate into the epidermis causing inflammation, cytokine release, and acceleration of barrier repair (Visscher et al., 2015). The distribution of the eruption varies somewhat, depending on the precipitating agent. The principal irritants in diaper dermatitis are fecal enzymes, skin maceration, friction, high pH, and prolonged contact with urine and feces (Figure 12.25; Atherton, 2016). Detergent bubble bath, antiseptic proprietary agents, and soap zealously used to clean the perianal area may cause acute eczematous diaper dermatitis, which may become generalized. Obtaining precise information about what has been applied to the skin and how it has been applied is imperative in making an accurate diagnosis.

Seborrheic Dermatitis. Seborrheic dermatitis affects as many as 10% of neonates. It typically occurs on the scalp but may develop on the face, neck, and in the diaper area (Cohen, 2017). Seborrheic dermatitis is characterized by greasy, nonpruritic scaling associated with patchy redness, fissuring, and occasional weeping, usually involving the scalp, ears, axillary, and perineal folds (Figure 12.26). The yeast *Malassezia* is believed to contribute to the pathophysiology. There is controversy about whether seborrheic dermatitis is a distinct entity or presages the advent of atopic dermatitis. Some infants never progress beyond the seborrheic phase of the dermatitis, which in its classic form rarely is seen in the first month of life. Cradle cap is a minor variant of seborrheic dermatitis.

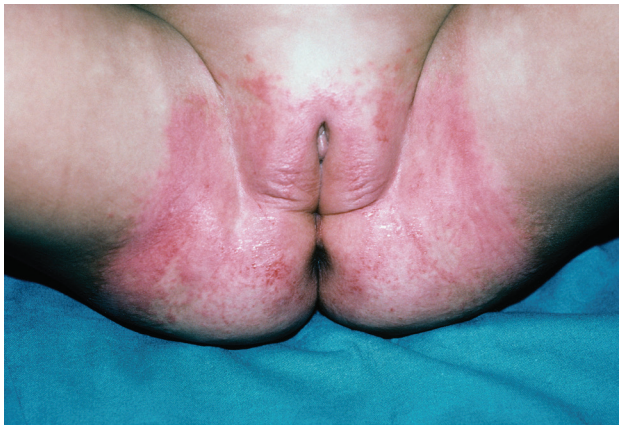


Figure 12.25 Irritant contact dermatitis.

Source: © Dr. Ken Greer/Visuals Unlimited, Inc.

Other Skin Disorders

Sucking Blisters. Sucking blisters present in 0.4% of neonates (Aydin, Hakan, Zenciroglu, & Demirol, 2013). They are benign, fluid-filled erosions on the skin surface secondary to in utero fetal sucking maneuvers. Episodic or short-term sucking produces a soft and fluid-filled blister, whereas chronic sucking may increase the likelihood for postnatal calluses (Figure 12.27). Asymmetric or irregular borders are common and, unlike infectious blisters, these are often limited to one blister in a specific location. As such, these blisters often present on the hands, lips, or inside the mouth (Bruckner & O'Regan, 2015).

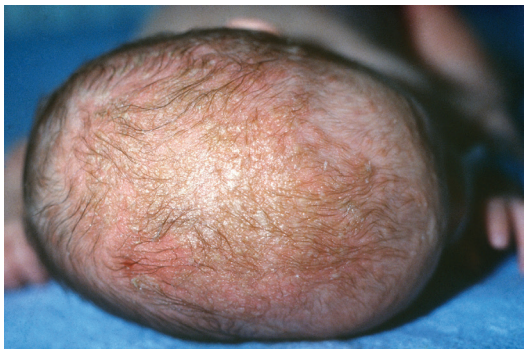


Figure 12.26 Infant with scales on the scalp, consistent with seborrheic dermatitis. ("cradle cap")

Source: Biophoto Associates/Science Source

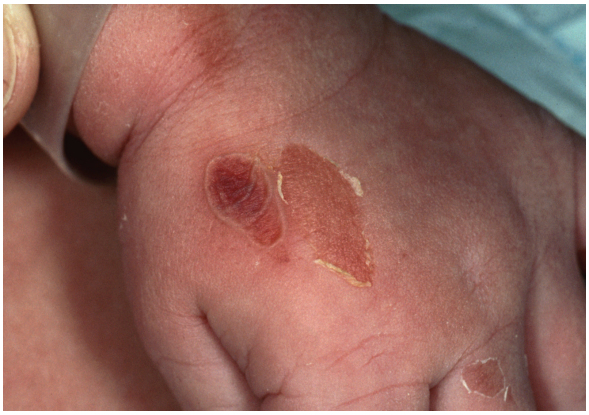


Figure 12.27 Evidence of sucking blister to left hand, which presented at birth.

Source: Image appears with permission of VisualDx

CONCLUSION

The skin is the largest organ in the body and plays vital roles in protection, thermoregulation, and communication with the environment. Understanding its embryologic origins is important. Genetic and maternal influences should be explored. Finally, accurate visual diagnosis is key to uncovering neonatal skin conditions.

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LEARNING TOOLS AND RESOURCES

Podcast

Neonatal Skin and Innate Immunity: Differences Between the Term and Preterm Infant

Rani Delaney, Lauren Fraser, Maryellen Lane, and Melissa Bauserman

Discussion Prompts

1. Discuss the purpose and derivatives of vernix. How might the presence or absence of vernix implicate newborn skin?
2. Identify and discuss the major issues for the premature infant as a result of underdeveloped skin.
3. What is the most common neonatal skin condition? Correlate the etiology with your understanding of the physiology of the skin.
4. Describe the difference between a vascular malformation and a vascular tumor in neonates.
5. Describe the causes and appearance of Candida infections.

Advice From the Authors

"You are learning to be a neonatal detective. Your patients cannot tell you what is wrong. You must seek out the clues through assessment, diagnostics, labs, thorough history, and chart review. Pathophysiology is the bedrock of understanding diseases, syndromes, and congenital abnormalities. If you can understand the pathogenesis of your patient's disorder(s), then moving forward to diagnosis and treatment will be more seamless. Use the keen observation skills you have developed as a bedside nurse. Assessment is primarily observation. Gather information as you walk up to the bedside and begin your differential diagnosis list from there."

–Leigh Ann Cates-McGlinn, PhD, APRN, NNP-BC, RRT-NPS, CHSE

"This book is very unique in that it will help the learner in various didactic methods. Not all of us learn at the same pace or in a certain way. This textbook is structured to assist the student learner to understand concepts in various ways and to enhance your learning. The book will not only help you in understanding neonatal concepts in order to pass certification, but will also assist you in becoming a lifelong learner."

–Rebecca Chuffo Davila, DNP, APRN, NNP-BC, FAANP

"A keen understanding of the structure and function of the epidermal barrier is invaluable in evaluating, diagnosing, and determining the etiology of observed cutaneous conditions. As such, it forms the basis for treatment planning. Many neonatal skin 'conditions' have common features. A differential approach to diagnosis is warranted. Conditions, such as irritant contact dermatitis, may occur as a result of standard infant care practices, for example, use of tapes and adhesives, and may be exacerbated in prematurely born infants. Strategies to minimize iatrogenic effects are necessary."

–Marty Visscher, PhD, MEd, CPI

"It is crucial to familiarize and understand the skin-specific basic lesion (morphology) and its associated definition. This will help with accurate description of the lesion, which will assist you in making the correct differential diagnosis. Remember that the common, benign, and transient lesions occur more often than the severe pathological skin conditions. Ruling out infectious causes for the skin lesion is critical and a priority as you can avoid its widespread dissemination. The goal of treatment is to first do no harm or worsen the condition. Recognize and avoid all iatrogenic injuries."

–Vivek Narendran, MD, MRCP(UK), MBA

Mind Maps

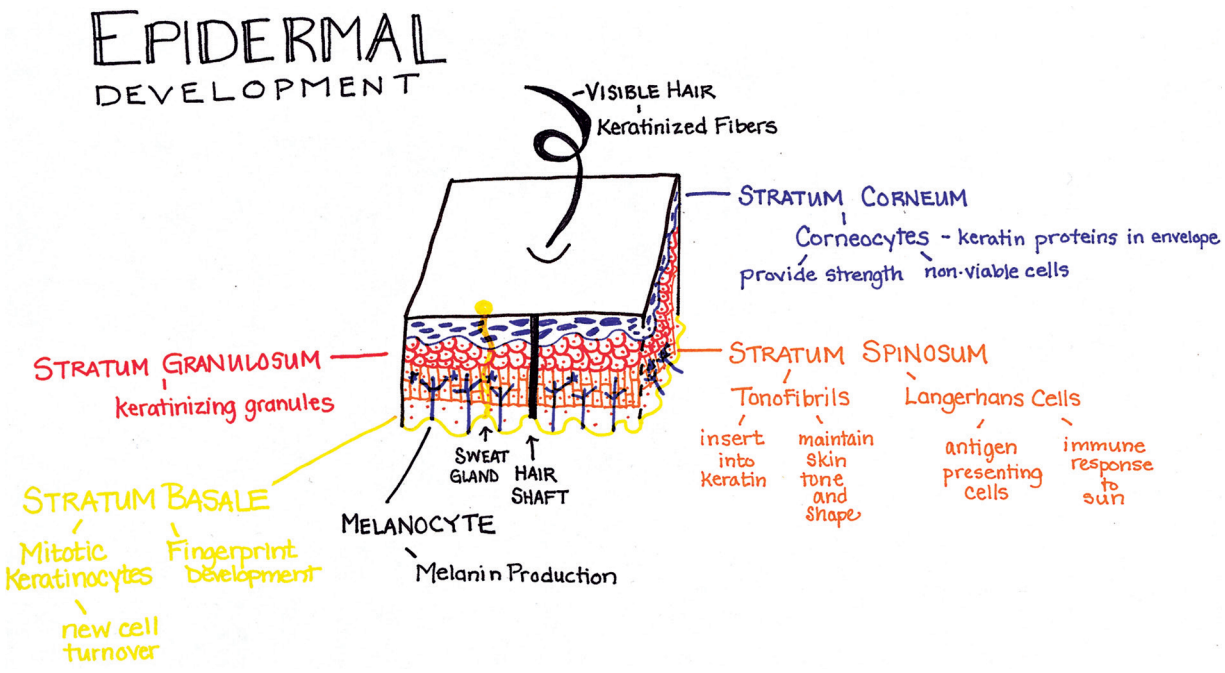
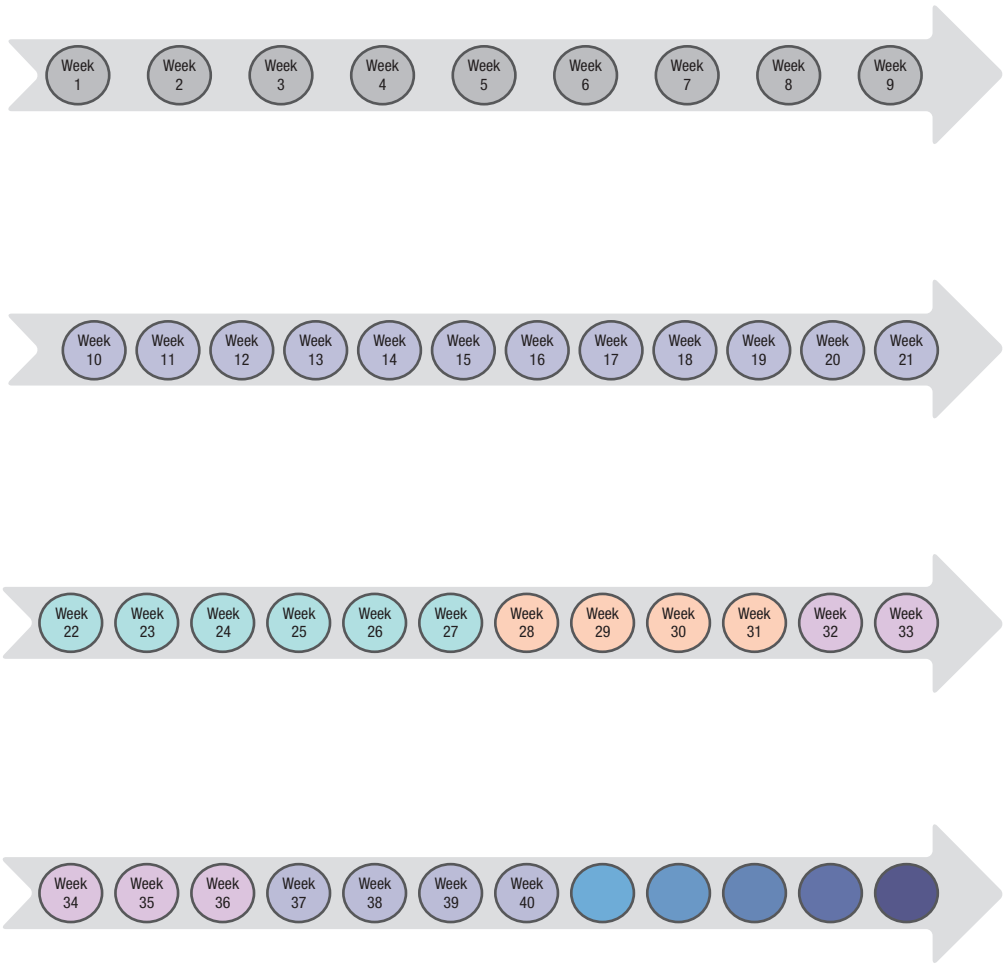


Image credit: Amanda Dawkins, BSN, RN

Note: This mind map reflects one student's interpretation of a portion of one or more concepts addressed in this chapter. Readers should regard the mind maps woven throughout this textbook as examples of multi-sensory study tools that can be developed to encourage conceptual understanding. Readers are encouraged to develop their own unique mind maps in consultation with academic faculty or clinical preceptors.

TIMELINE OF ORGAN DEVELOPMENT



NOTE:
Placement of common problems is meant to offer visual/conceptual perspective on the timing of onset of these commonly reported malformations. Variation exists across the literature.

LEGEND
<22 – 27 6/7 weeks = extremely preterm
28 – 31 6/7 weeks = very preterm
32 – 36 6/7 weeks = late/moderate preterm
37 – 40 weeks = term

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