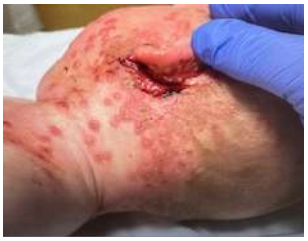
Neonatal rashes: the good, the bad, and the ugly.



Vita Boyar, MD,CPE,FAAP,CWSP
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1

I have nothing to disclose as pertaining to this presentation

2

Functions of Skin

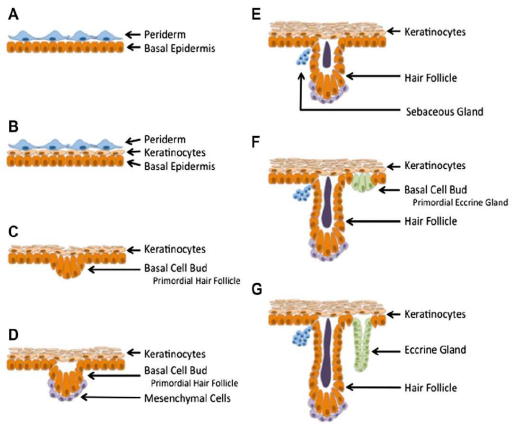
- Growth and nutrition of embryo
- Serves as barrier against infection and protects internal organs
- Plays major role in thermoregulation and storage of fat
- Regulates insensible water loss, also secretes electrolytes & water
- Provides tactile sensory input and sensations of touch, pressure, temperature, pain & itch
- Regulates microbiome, influences skin-gut-brain axis

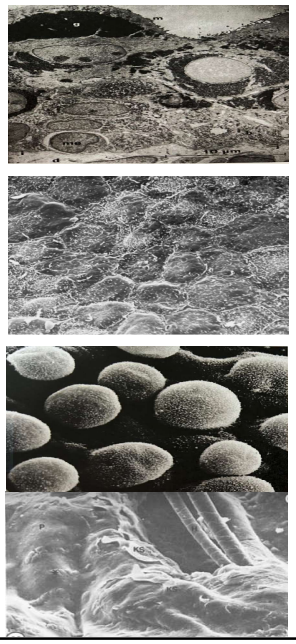
Barrier	Roles	Effectors
Permeability	Prevents excess water loss, harmful chemicals, allergens, and microbial pathogens; Maintains body temperature	Components of skin structure
Antimicrobial	Protects against multiple pathogens, *e.g*, Gram-positive and Gram-negative bacteria, fungi, and some viruses	Acidic pH (<5.5); Sphingoid bases; Innate immune elements, including antimicrobial peptides
Antioxidant	Protects skin from oxidative stress	α-/γ-tocopherol Vitamin C and E Certain flavonoids
UV	Protects skin from UV light-mediated DNA damage, and oxidative stress	Urocanic acid Structure components, including sphingolipids

Park 2015

3

Skin development

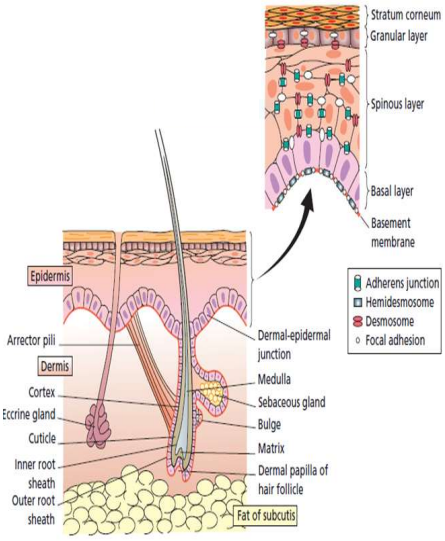


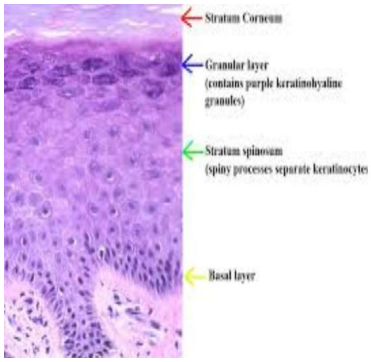


Holbrook et al., JID.;1975
Kind et al., 2013;McGrath et al., Textbook of Dermatology.2010

4

Skin: Epidermis





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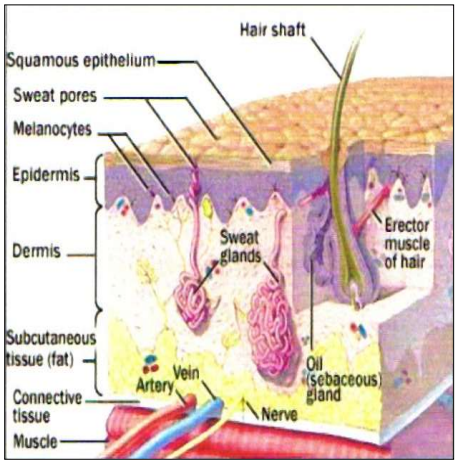
Skin--Dermis



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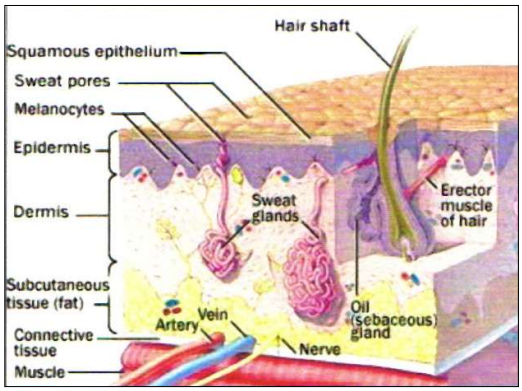
Skin--SQ

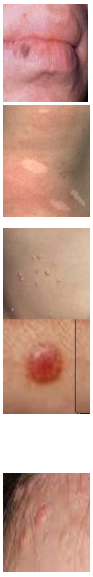


7

Assessment of Skin

Definitions to describe skin lesions

- Macule: pigmented, flat spot that is visible but not palpable. If more than 1 cm-patch.
- Papule: solid, elevated, palpable lesion, with distinct borders < 1 cm in size
- Plaque: solid, elevated, palpable lesion, with distinct borders > 2 cm in size
- Nodule: a solid lesion, elevated with depth, up to 2 cm in size

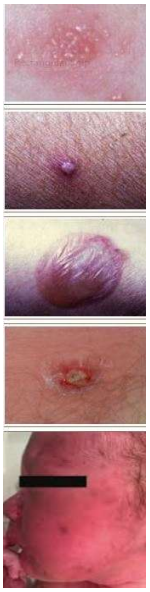


8

Assessment of Skin

Definitions cont.

- Tumor: solid lesion, elevated with depth > 2 cm is size.
- Vesicle: elevated lesion or blister filled with serous
- fluid and < 1 cm in diameter.
- Bulla: fluid filled lesion larger that 1 cm.
- Pustule: a vesicle filled with cloudy or purulent fluid.
- Petechiae: subepidermal hemorrhages, pinpoint in size, that do not blanch.

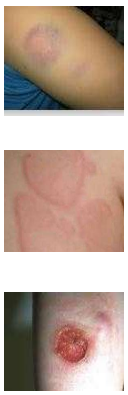


9

Assessment of Skin

Definitions cont.

- Ecchymosis: a large area of subepidermal hemorrhage.
- Wheal: area of edema in the upper dermis, creating a palpable, slightly raised lesion.
- Ulcer: erosion of skin with damage of the epidermis into the dermis.

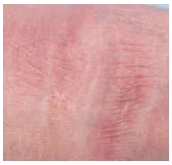
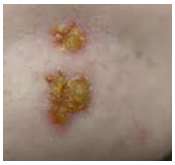
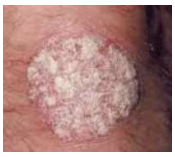


10

Assessment of Skin

Definitions cont.

- Atrophy: The skin surface is depressed because of thinning or absence of the dermis or subcutaneous fat. (atrophic scar, fat necrosis, anetoderma)
- Crusting: Represents dried exudates of plasma combined with the blister roof, which sits on the surface of the skin after acute dermatitis. (impetigo , contact dermatitis)
- Scale: Whitish plates present on the skin surface. (psoriasis, ichthyosis)

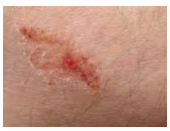




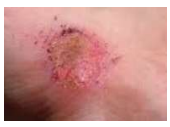
11

Assessment of Skin

Definitions cont.

- Excoriation: Depressions in the skin with a complete removal of the epidermis , exposing a broad section of red dermis. (atopic dermatitis)
- Fissure: Linear, wedge-shaped cracks in the epidermis extending down to the dermis and narrowing at the base. (warts)
- Erosion: Moist , circumscribed, slightly depressed areas representing a blister base with the roof of the blister removed. (burns , dermatitis)





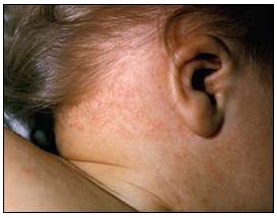
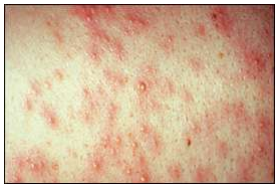
12

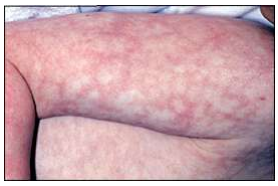
Classification of Skin Disorders in Infancy

1. Transient dermatoses
2. Common Congenital Malformations of Skin
3. Birthmarks
4. Infections
   - Viral infections
   - Bacterial infections
   - Fungal infections
5. Infestations
6. Genodermatosis
7. Neurocutaneous disorders
8. Metabolic & nutritional dermatoses
9. Cutaneous manifestations of systemic diseases
10. Miscellaneous conditions

13

Common neonatal skin finding



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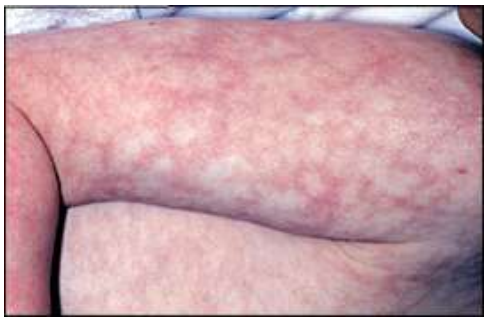
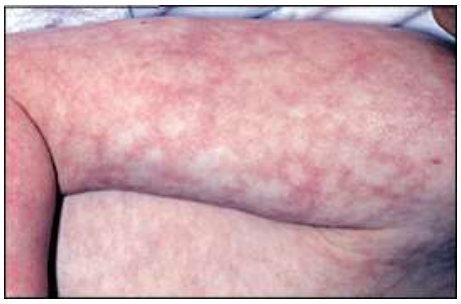


15

Cutis Marmorata

- Cutis marmorata is a reticulated mottling of the skin that symmetrically involves the trunk and extremities.
- It is caused by a vascular response to cold and generally resolves when the skin is warmed.
- Past 6 mo can be a marker for hypothyroidism, Tr18, Tr21, Cornelia de Lange



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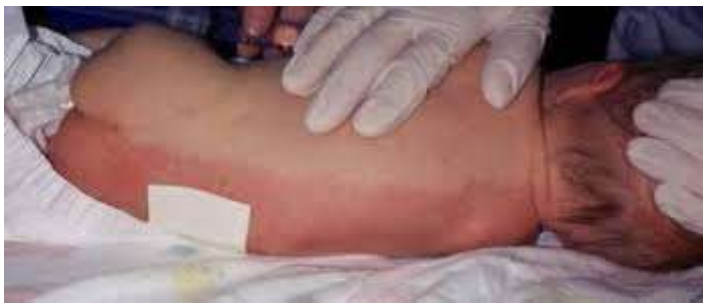

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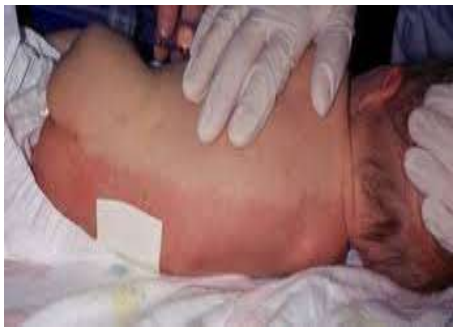
Harlequin Color change

- Harlequin color change occurs when the newborn lies on his or her side. Erythema of the dependent side of the body with simultaneous blanching of the contralateral side.
- The color change develops suddenly and persists for 30 seconds to 20 minutes. It resolves with increased muscle activity or crying. This phenomenon affects up to 10%FT.
- It occurs most commonly during the 2-5 day of life and may continue for up to three weeks.
- Harlequin color change is thought to be caused by immaturity of the hypothalamic center that controls the dilation of peripheral blood vessels.



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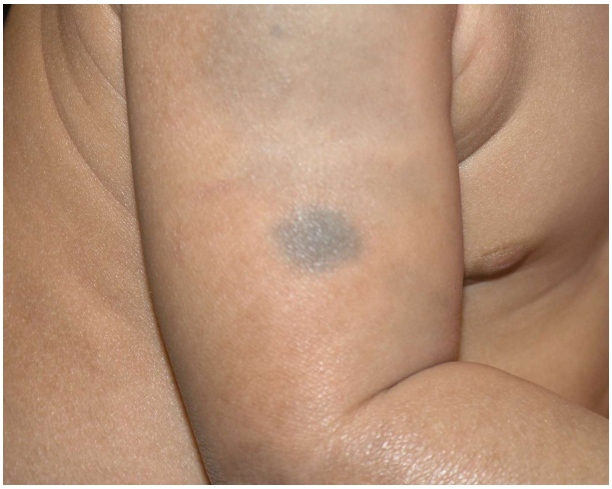

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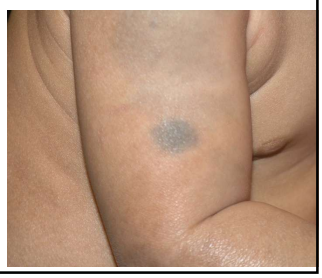
Mongolian Spot

- Flat, slate-gray to bluish-black, poorly circumscribed macules/patches
- Most commonly located over the lumbosacral area and buttocks
- Usually fade by 7 years of age



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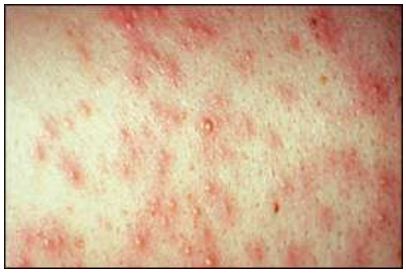
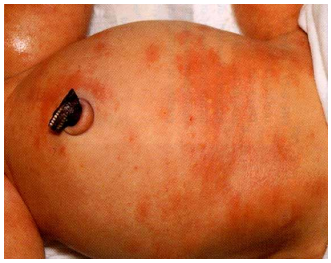
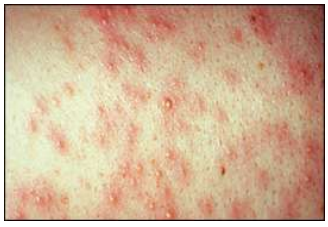


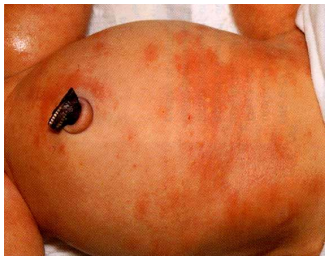


21

Erythema Toxicum Neonatorum

- Most common pustular eruption in newborns. Incidence 40 -70%.
- Erythematous, 2- to 3-mm macules and papules that evolve into pustules.
- Each pustule is surrounded by a blotchy area of erythema, leading to what is classically described as a "flea-bitten" appearance. Lesions usually occur on the face, trunk, and proximal extremities. Palms and soles are spared
- Pustules contain eosinophils/ neutrophils
- Etiology of ET is not known. Lesions generally fade over five to seven days, but they may recur for several weeks.





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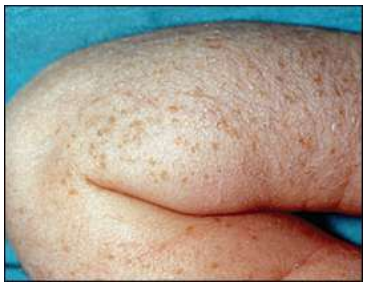
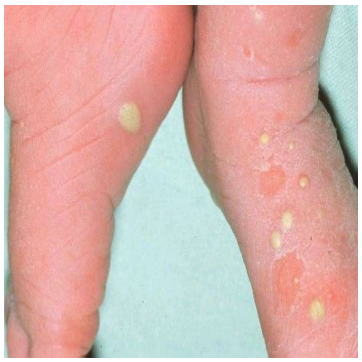
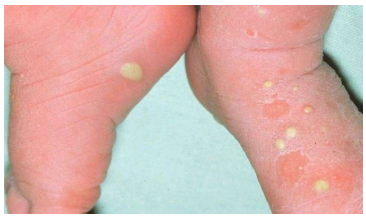




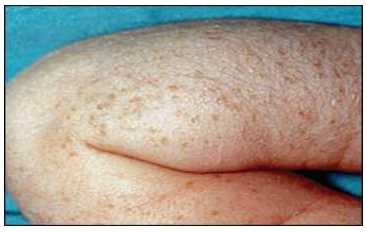
23

Transient Neonatal Pustular Melanosis

- Vesiculopustular rash that occurs in 5 % of AA newborns, but in less than 1 % of Caucasian.
- No surrounding erythema
- Lesions rupture easily, leaving a collarette of scale and a pigmented macule that fades over three to four weeks. All areas of the body may be affected, including palms and soles.



- Gram, Wright, or Giemsa staining of the pustular contents will show polymorphic neutrophils and, occasionally, eosinophils



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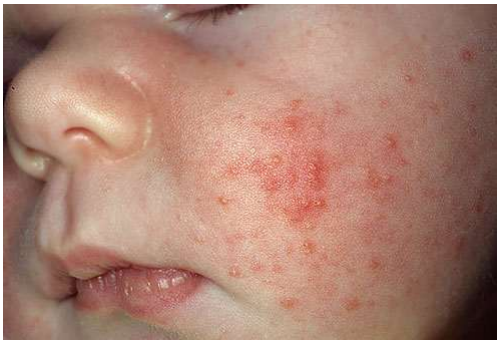
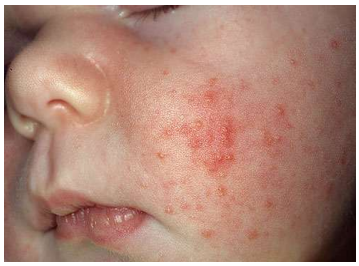


25

Acne Neonatorum

- Up to 20 % of newborns.
- It typically consists of closed comedones on the forehead, nose, and cheeks, although other locations are possible. Open comedones, inflammatory papules, and pustules can also develop.
- Neonatal acne is thought to result from stimulation of sebaceous glands by maternal or infant androgens.
- Lesions resolve spontaneously within four months without scarring.
- Treatment generally is not indicated, but infants can be treated with a 2.5% benzoyl peroxide lotion if lesions are extensive and persist for several months.
- Severe, unrelenting neonatal acne accompanied by other signs of hyper-androgenism should prompt an investigation for adrenal cortical hyperplasia, virilizing tumors, or underlying endocrinopathies



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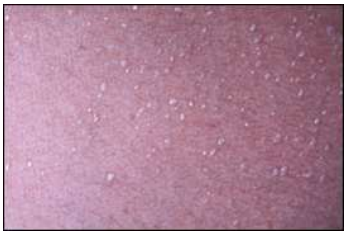
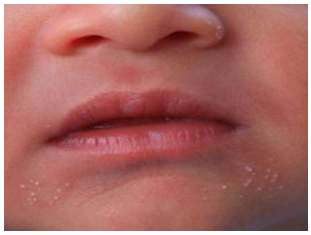
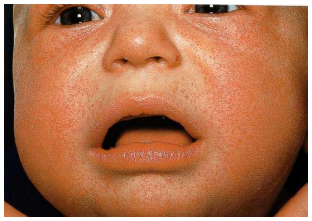






27

Milia/Miliaria

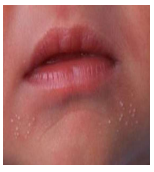
2-mm pearly white or yellow papules caused by retention of keratin within the dermis. ~50%

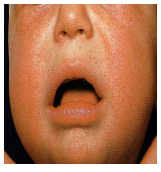
Forehead, cheeks, nose, and chin, but they may also occur on the upper trunk, limbs, penis, or mucous membranes.

Miliaria results from sweat retention caused by partial closure of eccrine structures. Both result from immaturity of skin structures.~40%

Miliaria crystallina is caused by superficial eccrine duct obstruction at the SC level. It consists of 1- to 2-mm vesicles without surrounding erythema, most commonly on the head, neck, axillae and trunk. Each vesicle evolves, with rupture followed by desquamation, and may persist for hours to days

Miliaria rubra (heat rash) is caused by a deeper level of sweat gland obstruction. Small erythematous papules and vesicles, usually occurring on covered portions of the skin.





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DD of pustular eruptions

Table 3. Causes of pustular neonatal eruptions

Cause	Age	Investigations
Infectious		
• Bacterial: *Staphylococcus aureus, Streptococcus pyogenes, Hemophilus influenzae, Escherichia coli, Klebsiella pneumoniae,* pseudomonas, listeria		Swab MCS, systemic work-up
• Syphilis (palmoplantar changes)		Darkfield microscopy serology, X-ray
• Viral: herpes simplex virus, herpes varicella-zoster cytomegalovirus, AIDS • Fungal: candida, pityrosporum • Parasitic: scabies	First 6 weeks	Tzanck/IF/PCR/ culture, urine sediment, serology Swab MCS
Reactive		
• Miliaria	First weeks	Smear for stains – variable
• Transient neonatal pustular melanosis	Day 0	– neutrophils
• Erythema toxicum	Day 1–3	– eosinophils
• Eosinophilic folliculitis	First year	– eosinophils
• Acne	First year	– neutrophils
• Acropustulosis	Hours to 6 weeks	– neutrophils (+/– eosinophils)
Infiltrate		
• Histiocytosis • Incontinentia pigmenti		Histology – histiocytes – eosinophilic spongiosis
MCS = microscopy, culture, sensitivity; IF = immunofluorescence; PCR = polymerase chain reaction		

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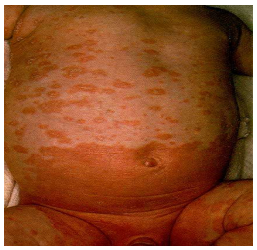
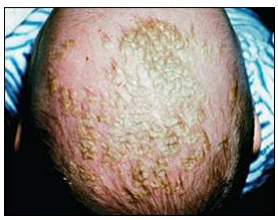
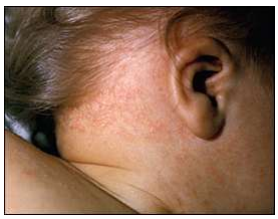

30

Seborrheic Dermatitis

Petrolatum/ dimethicone	**Apply daily**	**May soften scales, facilitating removal with soft brush**
Tar-containing shampoo	**Use several times per week**	**Use when baby shampoo has failed Safe, but potentially irritating**
Ketoconazole 2% cream or 2% shampoo	**Cream: apply to scalp three times weekly Shampoo: lather, leave on for three minutes, then rinse. Use three times weekly**	**Small trial showed no systemic drug levels or change in liver function after one month of use**
Hydrocortisone 1% cream	**Apply every other day or daily**	**Limit surface area to reduce risk of systemic absorption and adrenal suppression. Especially effective for rash in flexural areas**

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American Academy of Pediatrics
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Diagnosis and Management of Infantile Hemangioma

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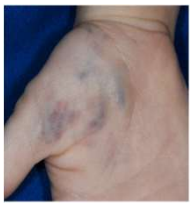
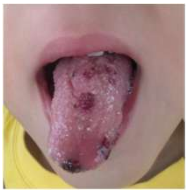
the SECTION ON DERMATOLOGY, SECTION ON OTOLARYNGOLOGY–HEAD AND NECK SURGERY, and SECTION ON PLASTIC SURGERY

TABLE 1 Classification of Cutaneous Vascular Anomalies, 2014

Vascular malformations
Venous malformations
Lymphatic malformations
Capillary malformations
Arteriovenous malformations and fistulae
Mixed (combined) malformations
Vascular tumors
Benign
Infantile hemangioma (IH)
Congenital hemangioma (rapidly involuting [RICH]; non-involuting [NICH])
Lobulated capillary hemangiomas (LCH) (pyogenic granuloma)*
Tufted angioma (TA)
Others
Locally aggressive
Kaposiform hemangioendothelioma (KHE)
Kaposi sarcoma
Others
Malignant
Angiosarcoma
Others

Adapted from the International Society for the Study of Vascular Anomalies, 2014, ref 1 (issva.org/classification).
*Reactive proliferating vascular lesion





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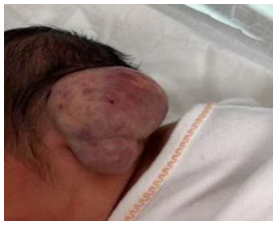
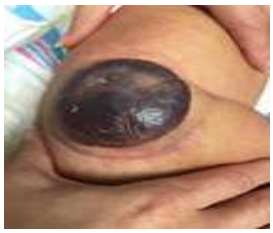
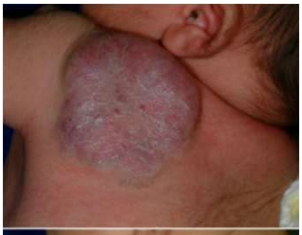
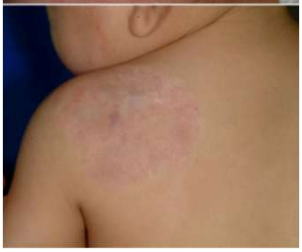
Congenital hemangioma









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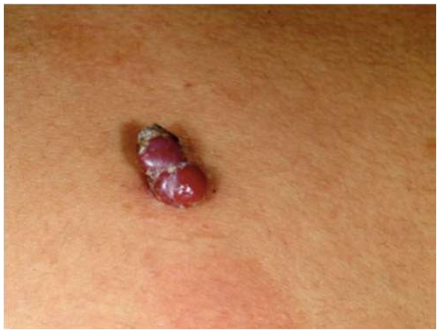
Pyogenic granuloma



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Kaposiform hemangioendothelioma
Tufted angioma

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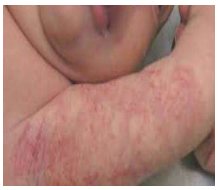
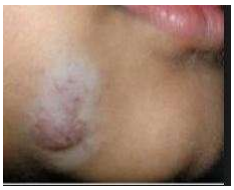
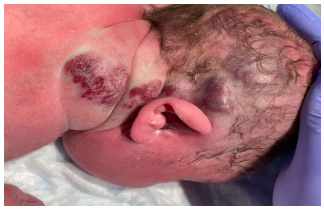
Infantile Hemangioma



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PHACE

Large facial infantile hemangioma

CNS defects– Dandy-Walker, posterior fossa malformations/ abn cerebrovascular arterial malformation

Cardiovascular, including CoA

Ophthalmologic

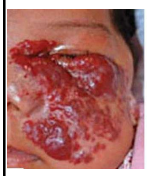
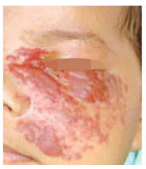
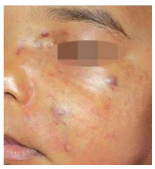

TABLE 3 Consensus Diagnostic Criteria for PHACE Syndrome

Organ System	Major Criteria	Minor Criteria
Cerebrovascular	Anomaly of major cerebral arteries Dysplasia[a] of the large cerebral arteries[a] Arterial stenosis or occlusion with or without moyamoya collaterals Absence or moderate-severe hypoplasia of the large cerebral arteries Aberrant origin or course of the large cerebral arteries[b] Persistent trigeminal artery Saccular aneurysms of any cerebral arteries	Persistent embryonic artery other than trigeminal artery Proatlantal intersegmental artery (types 1 and 2) Primitive hypoglossal artery Primitive otic artery
Structural brain	Posterior fossa anomaly Dandy-Walker complex or unilateral/bilateral cerebellar hypoplasia/dysplasia	Enhancing extraaxial lesion with features consistent with intracranial hemangioma Midline anomaly[c] Neuronal migration disorder[d]
Cardiovascular	Aortic arch anomaly Coarctation of aorta Dysplasia[a] Aneurysm Aberrant origin of the subclavian artery with or without a vascular ring	Ventricular septal defect Right aortic arch (double aortic arch)
Ocular	Posterior segment abnormality Persistent hyperplastic primary vitreous Persistent fetal vasculature Retinal vascular anomalies Morning glory disc anomaly Optic nerve hypoplasia Coloboma Peripapillary staphyloma	Anterior segment abnormality Microphthalmia Sclerocornea Coloboma Cataracts
Ventral or midline	Sternal defect Sternal cleft Supraumbilical raphe Sternal defects	Hypopituitarism Ectopic thyroid

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Segmental IH with large liver hemangioma

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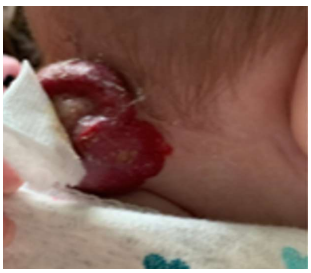
Complications



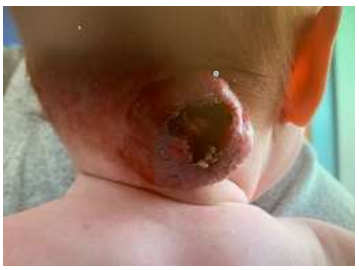


TABLE 4 Treatment Options in the Management of Ulcerated IH

Wound Care	Adjuvant Therapies
Dressings	Antimicrobials
White petrolatum–impregnated gauze	Metronidazole gel
Nonadherent dressings (eg, Mepitel [Mölnlycke Health Care; Gothenburg, Sweden], Telfa [Covidien/Medtronic; Minneapolis, MN])	Mupirocin, gentamicin, bacitracin ointment
Hydrocolloid dressings (eg, DuoDERM [ConvaTec; Luxembourg])	Pain control
Topical agents	Topical
White petrolatum, Aquaphor [Beiersdorf Inc.; Hamburg, Germany], Silver sulfadiazine (Silvadene; Monarch Pharmaceuticals; Bristol, TN)	Anesthetics (eg, lidocaine, benzocaine)
	Oral
	Acetaminophen with or without narcotics
	Other
	Becaplermin gel
	Topical timolol
	PDL
	Early excision
	Oral propranolol or steroids

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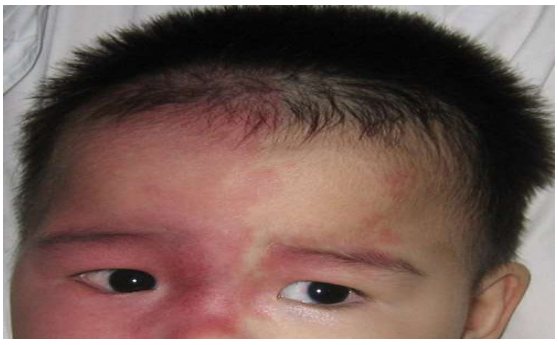

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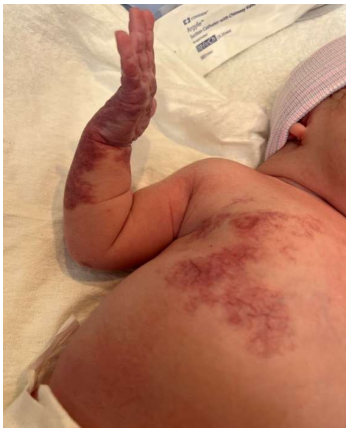
Port Wine Stain



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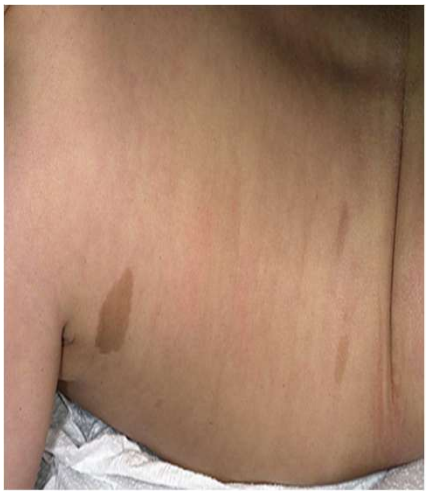

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Café-Au-Lait spot

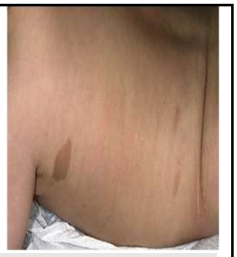

Table 1 Diagnostic criteria for neurofibromatosis 1 (NF1)

(NIH consensus development conference 1988)[3]

- 6 or more café au lait macules (>0.5 cm in children or >1.5 cm in adults)
- 2 or more cutaneous/subcutaneous neurofibromas or one plexiform neurofibroma
- Axillary or groin freckling
- Optic pathway glioma
- 2 or more Lisch nodules (iris hamartomas seen on slit lamp examination)
- Bony dysplasia (sphenoid wing dysplasia, bowing of long bone ± pseudarthrosis)
- First degree relative with NF1

Table 4 Frequency and age of onset of major clinical manifestations of neurofibromatosis 1

Clinical manifestation	Frequency (%)	Age of onset
Café au lait patches	>99	Birth to 12 y
Skin-fold freckling	85	3 y to adolescence
Lisch nodules	90–95	>3 y
Cutaneous neurofibromas	>99	>7 y (usually late adolescence)
Plexiform neurofibromas	30 (visible) –50 (on imaging)	Birth to 18 y
Disfiguring facial plexiform neurofibromas	3–5	Birth to 5 y
Malignant peripheral nerve sheath tumour	2–5 (8–13% lifetime risk)	5–75 y
Scoliosis	10	Birth to 18 y
Scoliosis requiring surgery	5	Birth to 18 y
Pseudarthrosis of tibia	2	Birth to 3 y
Renal artery stenosis	2	Lifelong
Phaeochromocytoma	2	>10 y
Severe cognitive impairment (IQ <70)	4–8	Birth
Learning problems	30–60	Birth
Epilepsy	6–7	Lifelong
Optic pathway glioma	15 (only 5% symptomatic)	Birth to 7 y (up to 30 y)
Cerebral gliomas	2–3	Lifelong
Sphenoid wing dysplasia	<1	Congenital
Aqueduct stenosis	1.5	Lifelong

Table 2 Differential diagnosis of neurofibromatosis 1 (NF1)[10 18–24]

Other forms of neurofibromatosis
- Segmental/mosaic NF1
- Watson syndrome
- Autosomal dominant multiple café au lait patches alone (some allelic with NF1)
- Neurofibromatosis 2
- Schwannomatosis

Other conditions with café au lait patches
- McCune–Albright syndrome
- DNA repair syndromes
- Homozygosity for one of the genes causing hereditary non-polyposis cancer of the colon.

Conditions with pigmented macules confused with NF1
- LEOPARD syndrome
- Neurocutaneous melanosis
- Peutz–Jeghers syndrome
- Piebaldism

Localised overgrowth syndromes
- Klippel–Trenauny–Weber syndrome
- Proteus syndrome

Conditions causing tumours confused with neurofibromas
- Lipomatosis
- Banayan–Riley–Ruvalcuba syndrome
- Fibromatoses
- Multiple endocrine neoplasia type 2B

Ferner R et al, 2006

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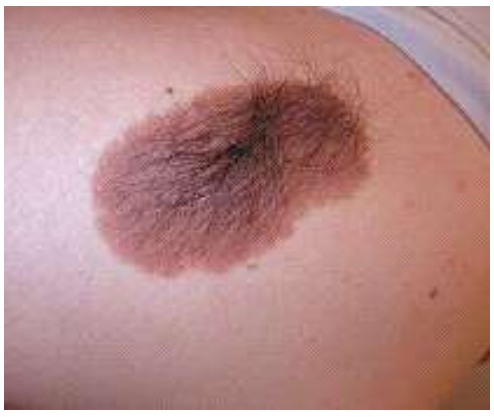

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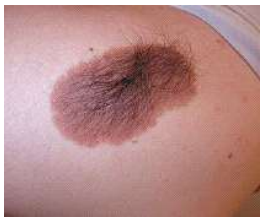
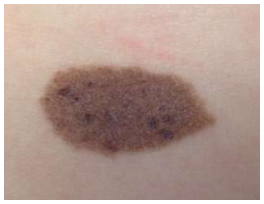
Congenital Melanocytic Nevi

TABLE 1 Authors' Management Recommendations for Children With CMN

Section	Subsection	Statement
Skin care and specialty management		
General skin care	Bathing	[a]Bathe with water alone or with a nonsoap cleanser[b] at least 2 to 3 times per week followed by the application of a bland emollient.[c]
	Xerosis and pruritus	[a]Apply bland, thick emollients (creams or ointments with minimal or no fragrances or preservatives) for chronic management and low- to mid-potency topical corticosteroids twice daily as needed for acute eczematous flares.
	Skin fragility/wound healing	[a]Cleanse ulcerations or erosions with soap or a nonsoap cleanser and water and apply petroleum jelly or bland ointment and a bandage. [a]Consider hydrocolloid or foam dressings, which are adherent yet easily removable and gentle on skin. Consider wound cultures or biopsy for nonhealing wounds.
	Hypohidrosis/anhidrosis	Counsel on avoidance of overheating and use of cooling techniques.
	Photoprotection	Follow standard recommendations regarding sunscreen, hats, protective clothing, seeking shade, avoiding sun during peak hours.
Specialty care and comorbidities	Dermatology referral: small or medium CMN	[a]Unless there are clinical concerns (color variation, nodules, symptoms, or location), referral can be delayed or deferred to the primary care provider.
	Dermatology referral: large, giant, or multiple CMN	All of these patients should be referred to dermatology.
	Physical examination: CMN palpation	Palpate CMN with elevated melanoma risk at every visit.
	Physical examination: Lymph nodes	Palpate lymph nodes of patients at higher risk for melanoma. [a]Clinical context, imaging, and biopsy, when needed, differentiate benign and malignant lymph node enlargement.
	Frequency and timing of dermatology office visits	[a]Determined by location and characteristics of the nevus, patient's age, parental concerns, and medical comorbidities. [a]Follow larger, multiple, and changing nevi closely during infancy or times of expected nevus change, such as puberty, because of increased melanoma risk and need for family counseling; visits every 3 months may be appropriate. [a]After the first year of life, in the absence of particular concerns, visit frequency is gradually decreased. Eventually a minimum of a yearly dermatologist evaluation may be appropriate for large, giant, and multiple CMN or smaller CMN with concerning features.
	Changes and growths within CMN	[a]Between visits, patients and/or caregivers should visually inspect and palpate CMN and notify their physician of any concerning changes (rapid growth, bleeding, pain, development of a lump or nodule, or ulceration). These changes require prompt evaluation, preferably by a dermatologist.
	Neural melanosis screening and monitoring	[a]Solitary small, medium, and large CMN are low risk for NCM and MRI screening is not recommended unless signs or symptoms are elicited during examination. [a]Patients with multiple medium CMN, ≥10 "satellite" lesions, and giant CMN are at higher risk for NCM and should undergo screening MRI. [a]Early MRI screening, with neither contrast nor anesthesia, of the brain and spine in infants with risk for NCM decreases procedure risks for the infant and can provide useful clinical information. Children with neurologic symptoms should undergo MRI to evaluate for neural melanosis and other CNS abnormalities.
Surgery and procedures		
Surgery	All nevi	The decision for procedural interventions or removal of a CMN is complicated by numerous factors, including family preference, the size and location of the nevus, patient age, overall health, and prognosis if NCM or melanoma is present. Detailed risk and benefit discussions are required.
Other procedures	Laser	Pigment-specific ablative lasers, curettage, and dermabrasion can be considered, but they may be associated with adverse outcomes, including obscuring clinical evaluation for melanoma and frequent pigment recurrence.
	Hair removal	When hair removal is desired, shaving, waxing, threading, chemical depilation, electrolysis, or trimming are low risk.
Patient and family support	Family support	Provide prompt support and reliable information about CMN and skin care.





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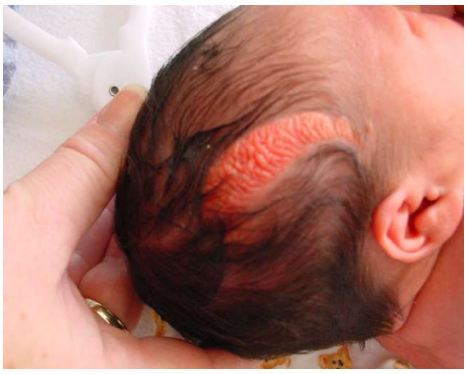

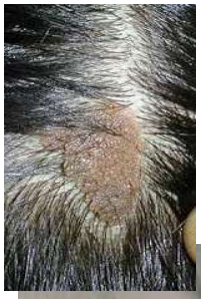

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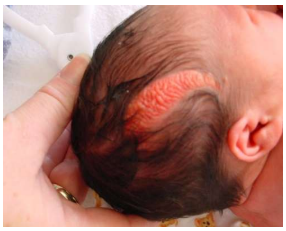
Epidermal nevus/ Jadassohn's Sebaceous nevus

- Overgrowth of mature epidermal cells, hair follicle, sebaceous glands
- Curvilinear or straight, follow lines of Blaschko.
- SN-(overgrowth of sebaceous glands) may enlarge at puberty under androgenic stimulation.
- Basal Cell Carcinoma-- 10-20%



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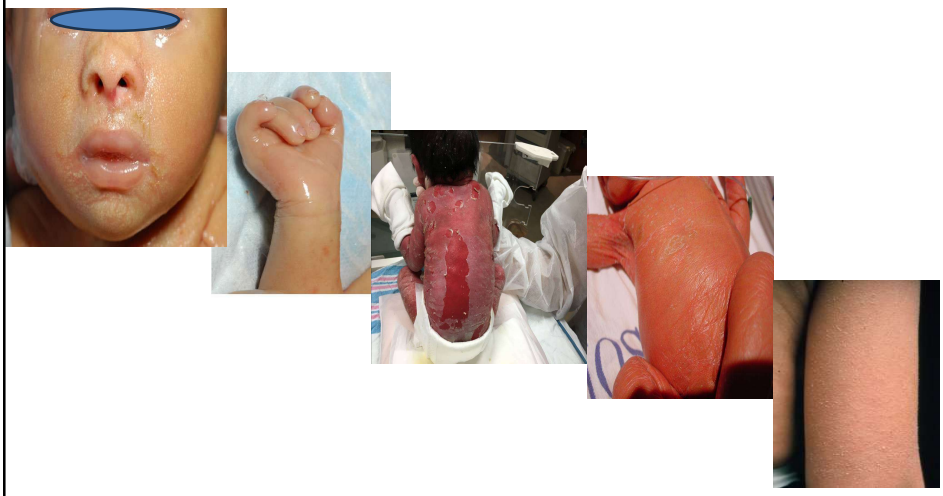
Genodermatosis



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Disorders of Abnormal Keratinization

Ichthyoses

Keratosis pilaris

Keratosis follicularis

Palmoplantar Keratoderma

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Ichthyosis

- Derived from Greek word *ichthys meaning fish*
- Primary ichthyoses are a collection of heterogeneous inherited disorders featuring excessive non-inflammatory scaling of skin surfaces
- There is dysfunction with skin keratinization and exfoliation of the horny skin layer
- Scales vary in size, color and location on the body

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Non syndromic ichthyosis

Harlequin Ichthyoses
Ichthyosis vulgaris
X-linked recessive Ichthyosis
Lamellar Ichthyosis
Congenital Ichthyosiform erythroderma
Epidermolytic Hyperkeratosis

Syndromic ichthyosis

Sjögren-Larsson syndrome
Netherton syndrome
KID syndrome
Refsum syndrome
Rud syndrome

Table 48-1 Summary of Ichthyoses

Disease	Inheritance	Defective Protein(s)
Ichthyosis vulgaris	AD	Filaggrin
X-linked ichthyosis	XLR	Steroid sulfatase
Lamellar ichthyosis	AR	Transglutaminase 1
NBCIE	AR	Transglutaminase 1; ALOX12B; ALOXE3; CGI58
Bullous congenital ichthyosiform erythroderma	AD	Keratin 1; keratin 10
Harlequin fetus	AR	ABCA12
Sjögren-Larsson syndrome	AR	Fatty aldehyde dehydrogenase
Refsum syndrome	AR	Phytanoyl-CoA hydroxylase
Conradi-Hunermann syndrome	XLD	Emopamil binding protein
CHILD syndrome	XLD	NSDHL (NAD(P)H steroid dehydrogenase-like protein)
Netherton syndrome	AR	LEKTI (lymphoepithelial Kazal-type–related inhibitor)
Erythrokeratodermia variabilis	AD	Connexin 31, connexin 30.3
KID syndrome	AD	Connexin 26

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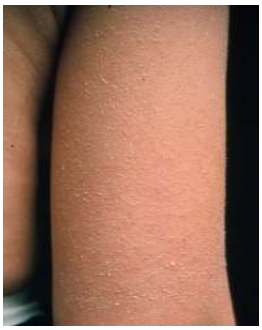

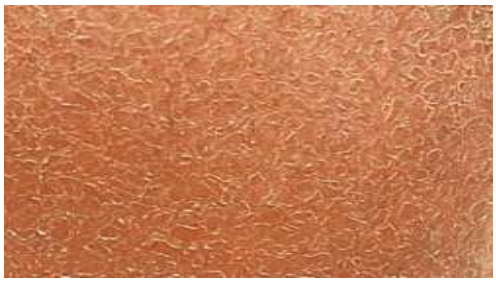

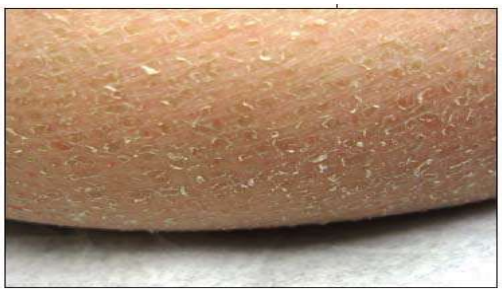

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Ichthyosis vulgaris

- Autosomal dominant and MC of ichthyosis
- Mutation in gene coding for the Filaggrin protein
- Mildest form with main symptoms skin dryness and scaling on extensor surfaces of trunk and extremities
- Onset: first months of life to early childhood
- Subsided by adulthood

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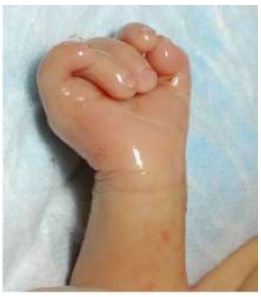
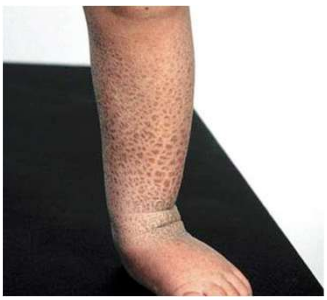

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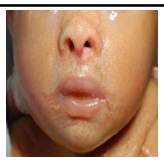
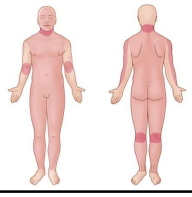
X-linked Ichthyosis



- Rare condition with x linked recessive pattern; therefore, primary males affected
- Lack of steroid sulfatase enzyme resulting in accumulation of cholesterol sulfate in horny cells of the skin with delayed exfoliation and hyperkeratosis
- Presents at birth or within 3 months of life
- Clinical Features
  - Mildly thickened granular and suprabasal cell layers
  - Adherent scaling over scalp, preauricular skin, posterior neck with sparing of palms and soles
  - Scales more evident as child ages appearing dirty yellow or brown



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X-linked Ichthyosis

- Prolong labor
- IUGR
- Renal agenesis
- Corneal opacity
- Testicular cancers

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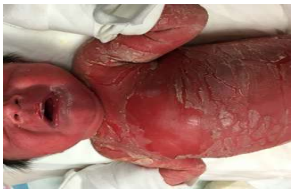
Congenital Ichthyosiform Erythroderma

- Autosomal recessive
- Decreased B-Glucosidase in epidermis
- Clinical features
  - Scaly dry skin
  - Tight clear sheath sheds in first few weeks resulting in red skin like appearance with fine white scales
  - Ectropion
  - Eclabium



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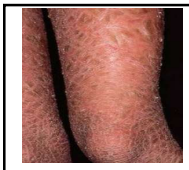
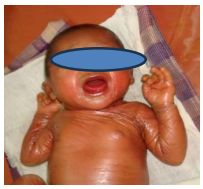


Lamellar Ichthyosis



- Autosomal recessive
- Incidence: 1:200,000
- Mutation in TGM1 gene, coding for transglutaminase-1
- Clinical Features
  - Collodion baby phenotype at birth
  - General of localized plate-like large dark brown scales
  - Ectropion, eclabium
  - Scarring alopecia
  - Palmoplantar keratoderma
  - No puritis or erythroderma

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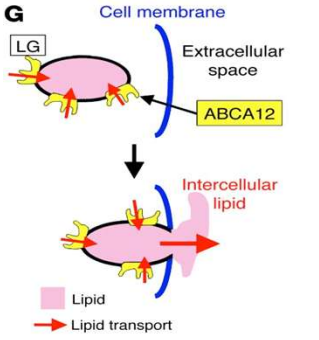
Harlequin Ichthyosis

- Harlequin ichthyosis (HI) is a rare, severe form of congenital ichthyosis (AR)
- HI is caused by a mutation in *ABCA12*, a lipid transporter adenosine triphosphate binding protein
- *ABCA12* functions at the level of the epidermis to facilitate the delivery of lipid glucosylceramides into lamellar granules which are then deposited in extracellular space of the stratum corneum
- Less damaging mutations in *ABCA12* cause milder forms of disease such as lamellar ichthyosis



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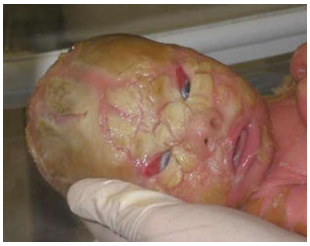
Clinical Presentation

- Rudimentary ears
- Nasal hypoplasia
- Hypoplasia or necrosis of digits
- Pseudo contractures of the extremities from thick scales
- AGA 35 weeks
- Ectropion/eclabium



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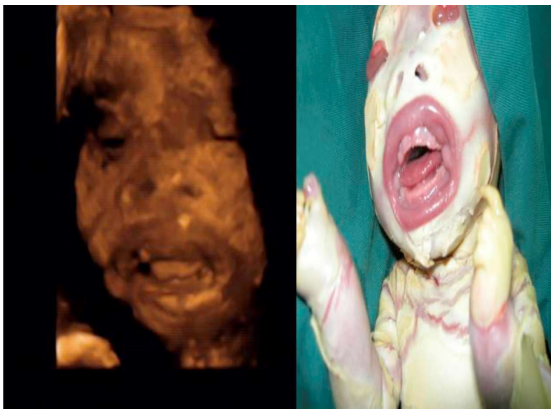
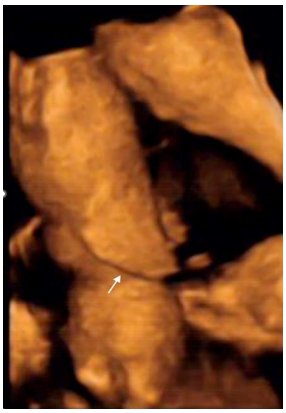
Prenatal US





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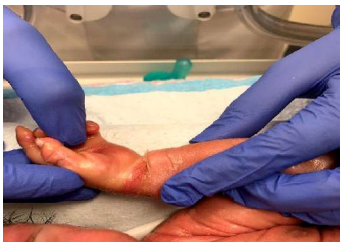
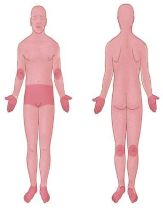
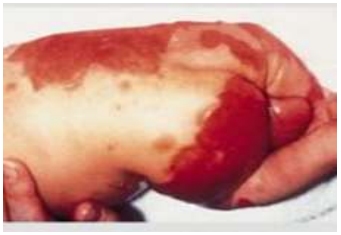
Epidermolytic Hyperkeratosis

Defect in the cytoskeleton (intermediate filament) of supra-basal cells keratin 1 and keratin 10,leading to abnormal keratin fiber formation, cytoskeleton distortion, and epidermal blistering, leading to secondary thickening of the horny and supra-basal cell layers
and degeneration of the granular layer.







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		Ichthyosis vulgaris	X-linked ichthyosis	Bullous congenital ichthyosiform erythroderma (BCIE)	Nonbullous congenital ichthyosiform erythroderma (NBCIE), lamellar ichthyosis	Harlequin ichthyosis
Frequency		Common	Uncommon	Rare	Rare	Very rare
Inheritance pattern		SD (semidominant)	XR	AD	AR	AR
Age of onset		Babyhood, infancy	At birth or early after birth	At birth or early after birth	At birth	At birth
Skin symptom	Site	Extremities, trunk (back > abdomen), intertriginous sites, extensor surface > flexor surface	Abdomen > back, intertriginous sites, extensor surface = flexor surface	Whole body	Whole body	Whole body
	Form	Fine scales	Large, dark brown scales	Severe hyperkeratosis	Flushing, fine or dark brown (NBCIE) large scales (lamellar ichthyosis)	Markedly thick hyperkeratosis, deep fissures, ectropion
Pathology		Hyperkeratosis, thinned granular cell layer	Hyperkeratosis, almost normal granular cell layer	Degeneration of granular cell layer	Hyperkeratosis (with or without parakeratosis)	Severe hyperkeratosis
Causative gene		Filaggrin (FLG)	Steroid sulfatase	Keratin 1 or keratin 10	Transglutaminase 1 in some cases	ABCA12

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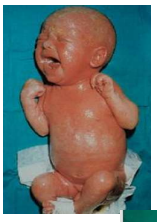
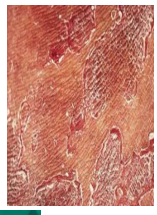
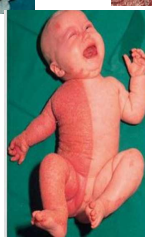
- Netherton Syndrome

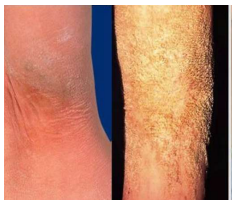


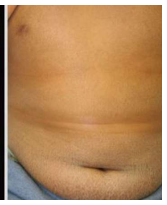


- CHILD Syndrome



- Sjogren Larsen Syndrome





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Management

Practice Guideline > Br J Dermatol. 2025 Jun 20;193(1):16-27. doi: 10.1093/bjd/ljaf076.

Management of congenital ichthyoses: guidelines of care: Part one: 2024 update

Management of congenital ichthyoses: guidelines of care: Part two: 2024 update FREE

Juliette Mazereeuw-Hautier ✉ , Amy S Paller , Edel O'Toole , Isabelle Dreyfus , Christine Bodemer , Masashi Akiyama , Andrea Diociaiuti , Maya El Hachem , Judith Fischer , Rogelio Gonzalez-Sarmiento ... Show more
Author Notes

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https://doi.org/10.1093/bjd/ljaf077
Published: 07 April 2025 **Article history**

TABLE 3 Monitoring Parameters in HI

Complete blood count
Electrolytes: Na, K, Cl, Mg, P, CO_2, glucose, calcium
Kidney function: blood urea nitrogen, creatinine, urine output
Liver function[a]
Lipid levels[a]
Total protein, albumin and prealbumin
Daily weights
Skin surface cultures daily × 1 wk and weekly while in intensive care
Blood cultures[b]
Vitamin D level[a]

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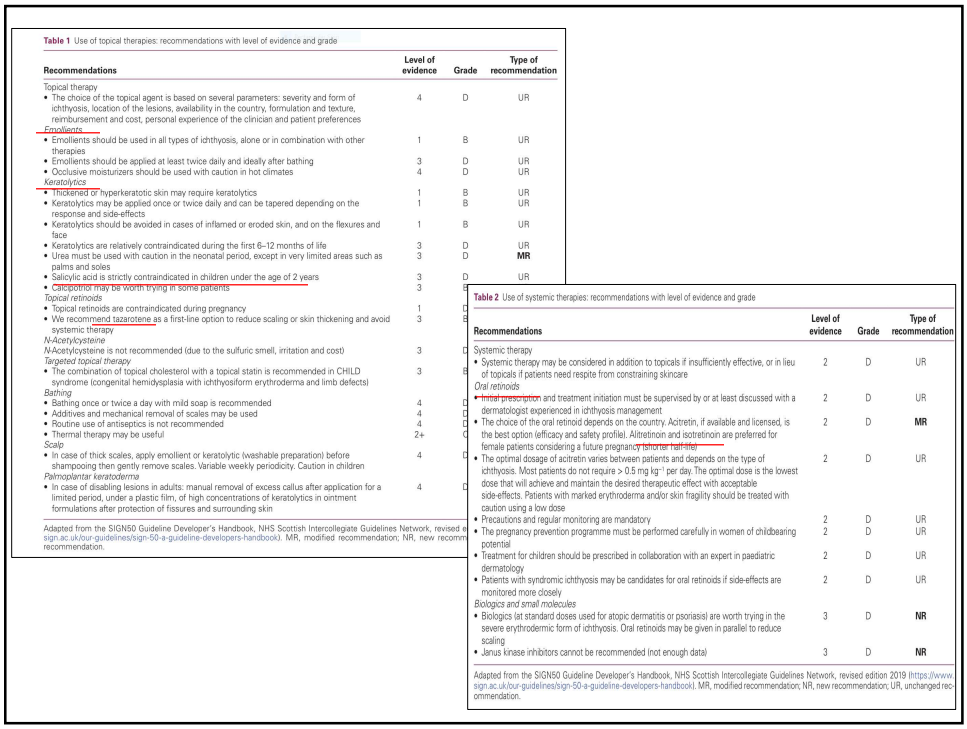

Table 1 Use of topical therapies: recommendations with level of evidence and grade

Recommendations	Level of evidence	Grade	Type of recommendation
Topical therapy			
• The choice of the topical agent is based on several parameters: severity and form of ichthyosis, location of the lesions, availability in the country, formulation and texture, reimbursement and cost, personal experience of the clinician and patient preferences	4	D	UR
Emollients			
• Emollients should be used in all types of ichthyosis, alone or in combination with other therapies	1	B	UR
• Emollients should be applied at least twice daily and ideally after bathing	3	D	UR
• Occlusive moisturizers should be used with caution in hot climates	4	D	UR
Keratolytics			
• Thickened or hyperkeratotic skin may require keratolytics	1	B	UR
• Keratolytics may be applied once or twice daily and can be tapered depending on the response and side-effects	1	B	UR
• Keratolytics should be avoided in cases of inflamed or eroded skin, and on the flexures and face	1	B	UR
• Keratolytics are relatively contraindicated during the first 6–12 months of life	3	D	UR
• Urea must be used with caution in the neonatal period, except in very limited areas such as palms and soles	3	D	**MR**
• Salicylic acid is strictly contraindicated in children under the age of 2 years	3	D	UR
• Calcipotriol may be worth trying in some patients	3		
Topical retinoids			
• Topical retinoids are contraindicated during pregnancy	1		
• We recommend tazarotene as a first-line option to reduce scaling or skin thickening and avoid systemic therapy	3		
N-Acetylcysteine			
N-Acetylcysteine is not recommended (due to the sulfuric smell, irritation and cost)	3		
Targeted topical therapy			
• The combination of topical cholesterol with a topical statin is recommended in CHILD syndrome (congenital hemidysplasia with ichthyosiform erythroderma and limb defects)	3		
Bathing			
• Bathing once or twice a day with mild soap is recommended	4		
• Additives and mechanical removal of scales may be used	4		
• Routine use of antiseptics is not recommended	4		
• Thermal therapy may be useful	2+		
Scalp			
• In case of thick scales, apply emollient or keratolytic (washable preparation) before shampooing then gently remove scales. Variable weekly periodicity. Caution in children	4		
Palmoplantar keratoderma			
• In case of disabling lesions in adults: manual removal of excess callus after application for a limited period, under a plastic film, of high concentrations of keratolytics in ointment formulations after protection of fissures and surrounding skin	4		

Adapted from the SIGN50 Guideline Developer's Handbook, NHS Scottish Intercollegiate Guidelines Network, revised e
sign.ac.uk/our-guidelines/sign-50-a-guideline-developers-handbook). MR, modified recommendation; NR, new recomm
recommendation.

Table 2 Use of systemic therapies: recommendations with level of evidence and grade

Recommendations	Level of evidence	Grade	Type of recommendation
Systemic therapy			
• Systemic therapy may be considered in addition to topicals if insufficiently effective, or in lieu of topicals if patients need respite from constraining skincare	2	D	UR
Oral retinoids			
• Initial prescription and treatment initiation must be supervised by or at least discussed with a dermatologist experienced in ichthyosis management	2	D	UR
• The choice of the oral retinoid depends on the country. Acitretin, if available and licensed, is the best option (efficacy and safety profile). Alitretinoin and isotretinoin are preferred for female patients considering a future pregnancy (shorter half-life)	2	D	**MR**
• The optimal dosage of acitretin varies between patients and depends on the type of ichthyosis. Most patients do not require > 0.5 mg kg^{-1} per day. The optimal dose is the lowest dose that will achieve and maintain the desired therapeutic effect with acceptable side-effects. Patients with marked erythroderma and/or skin fragility should be treated with caution using a low dose	2	D	UR
• Precautions and regular monitoring are mandatory	2	D	UR
• The pregnancy prevention programme must be performed carefully in women of childbearing potential	2	D	UR
• Treatment for children should be prescribed in collaboration with an expert in paediatric dermatology	2	D	UR
• Patients with syndromic ichthyosis may be candidates for oral retinoids if side-effects are monitored more closely	2	D	UR
Biologics and small molecules			
• Biologics (at standard doses used for atopic dermatitis or psoriasis) are worth trying in the severe erythrodermic form of ichthyosis. Oral retinoids may be given in parallel to reduce scaling	3	D	**NR**
• Janus kinase inhibitors cannot be recommended (not enough data)	3	D	**NR**

Adapted from the SIGN50 Guideline Developer's Handbook, NHS Scottish Intercollegiate Guidelines Network, revised edition 2019 (https://www.sign.ac.uk/our-guidelines/sign-50-a-guideline-developers-handbook). MR, modified recommendation; NR, new recommendation; UR, unchanged recommendation.

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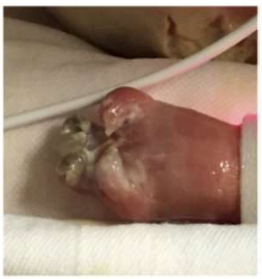
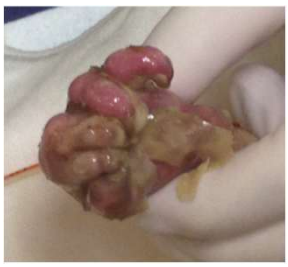
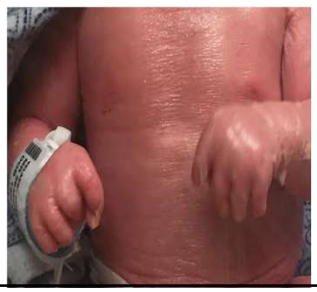
Fasciotomy







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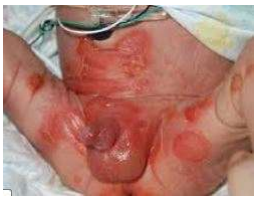
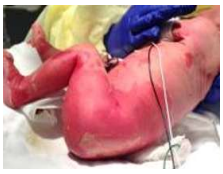
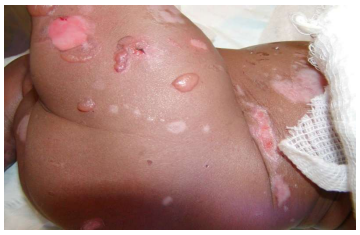


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Differential Diagnosis of Blisters/Erosions

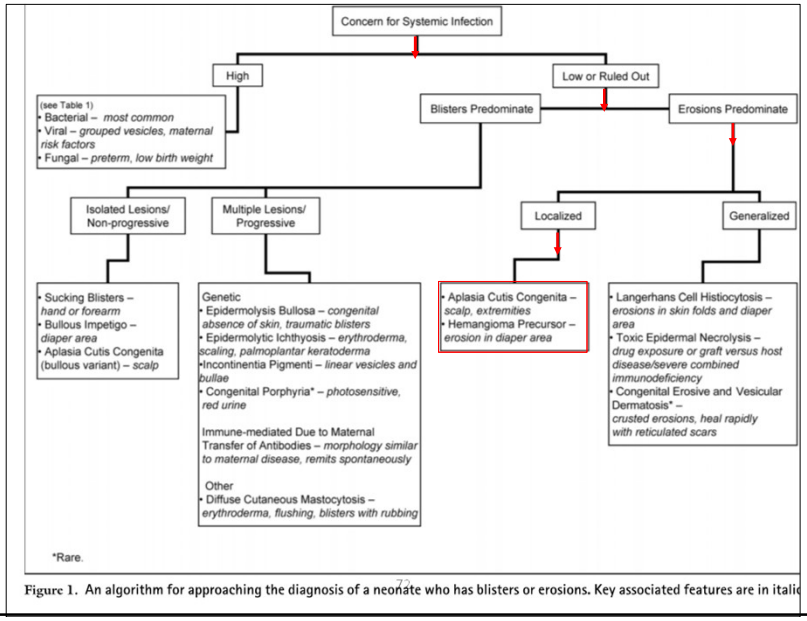

Figure 1. An algorithm for approaching the diagnosis of a neonate who has blisters or erosions. Key associated features are in italic

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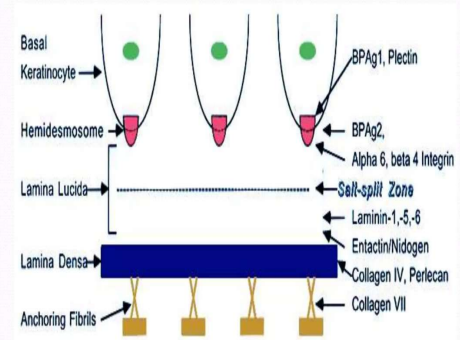
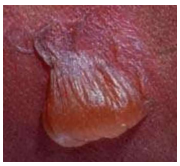
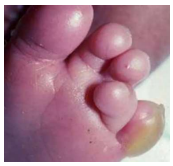
EB-disorders of dermal-epidermal junction

Epidermolysis bullosa simplex
Intradermal blister, above BM. Often confined to hands & feet.

Junctional Epidermolysis bullosa
Blister develops within the BM, often fatal.
Involves respiratory
tract, GI

Dystrophic Epidermolysis bullosa
Blister between BM and dermal papilla

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Other features

- Nail dystrophy
- Milia
- Atrophic scarring
- Exuberant granulation tissue
- Keratoderma of palms/ soles
- Dyspigmentation
- Decreased/ absence hair
- Hypo/hyper hydrosis

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Prevention of further trauma

- No adhesives/tape
- Avoid alcohol-based product, CHG, betadine
- Treat as skin tear
- Silicon Contact layer
- Telfa
- Rolled gauze, Cling
- Silicon foam

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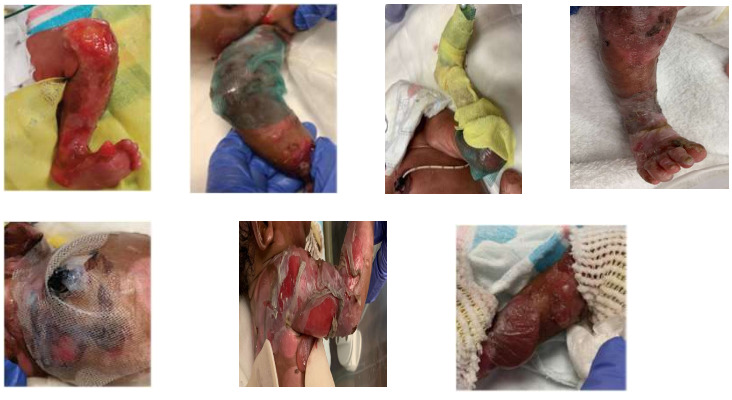
Epidermolysis Bullosa



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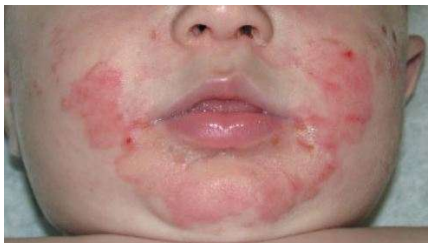
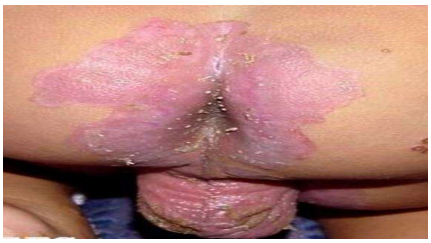
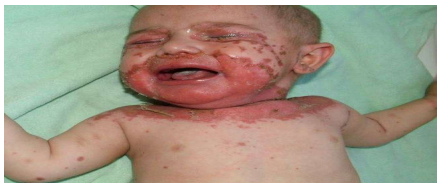
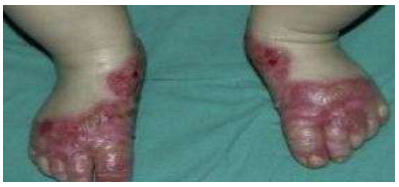

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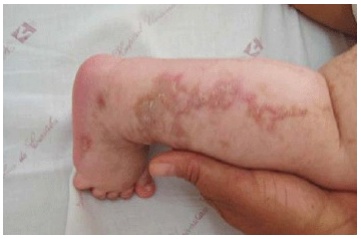
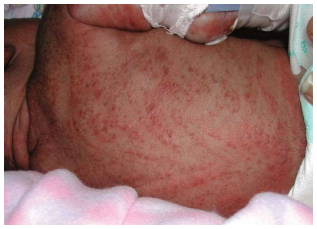
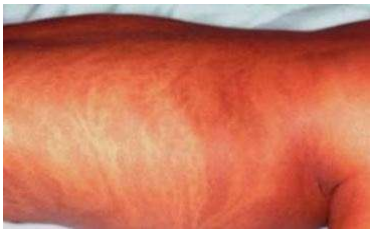
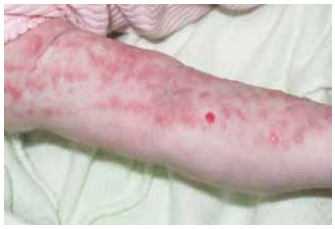

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Table 4. Causes of vesicular neonatal eruptions

Cause	Investigations
Infectious	
• Bullous impetigo	Tzanck smear, blister roof histology, microscopy, culture, sensitivity (MCS)
• Syphilis	Darkfield microscopy serology X-ray
• Herpes simplex • Varicella	Tzanck smear, polymerase chain reaction, immunofluorescence
• Candida	Culture MCS
Infiltrate	
• Langerhans cell histiocytosis • Bullous mastocytosis (Figure 8)	Histology Plus giemsa/toluidine blue
Immune mediated	
• Dermatitis herpetiformis • Epidermolysis bullosa acquisita • Bullous systemic lupus erythematosus • Linear IgA bullous dermatosis • Bullous pemphigoid • Herpes gestationis • Pemphigus vulgaris	Histology Plus direct and indirect immuofluorescence
Child abuse	
Toxic epidermal necrolysis	
Hereditable	
• Epidermolysis bullosa • Incontinentia pigmenti • Goltz syndrome • Porphyrias	Histology Plus electron microscopy, immunofluorescence mapping, gene testing

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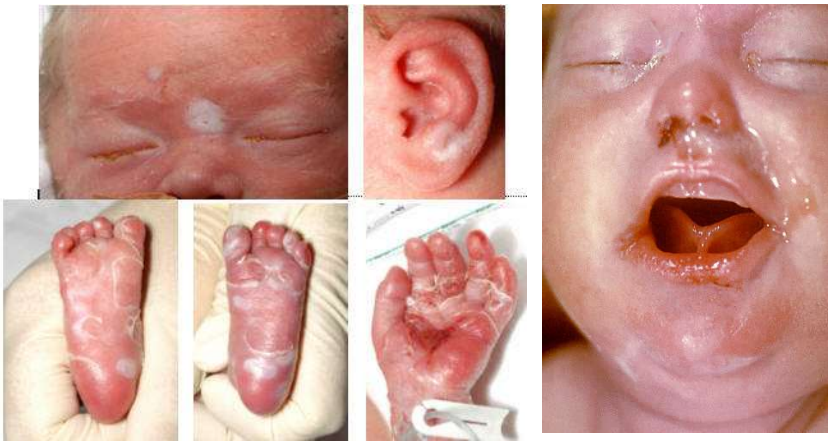

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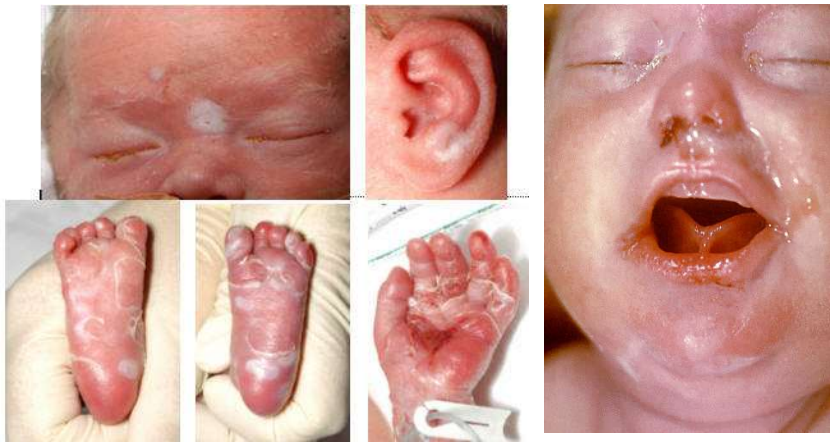
Congenital Syphilis



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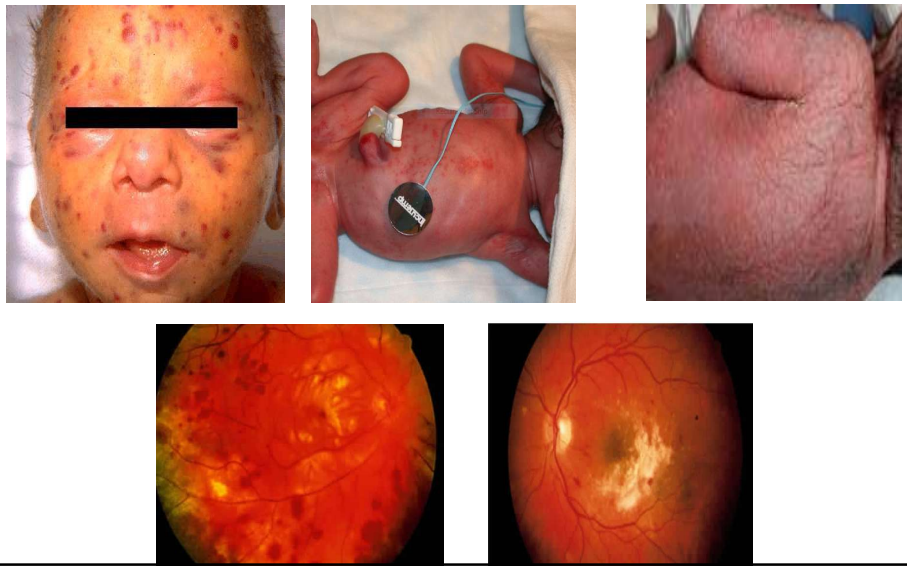

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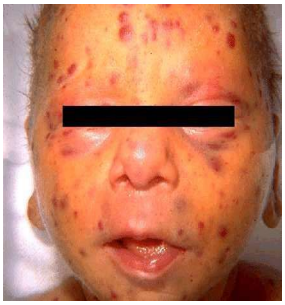
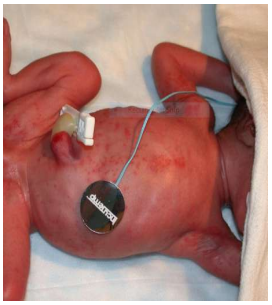
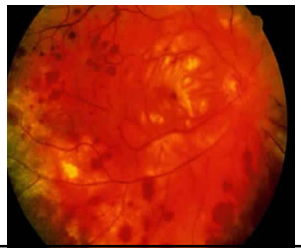
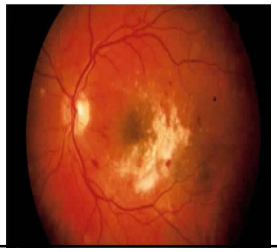
Congenital Rubella or CMV or Toxoplasma

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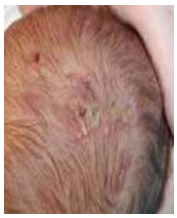
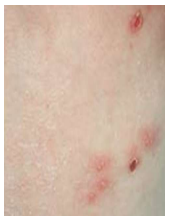

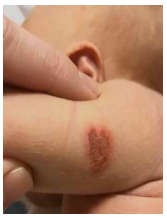

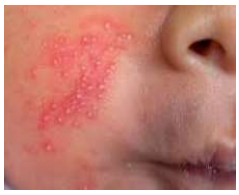
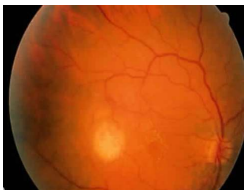

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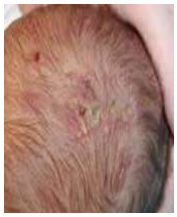
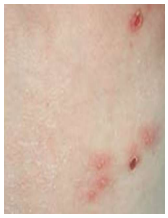
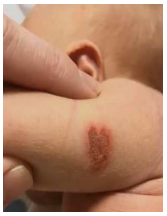
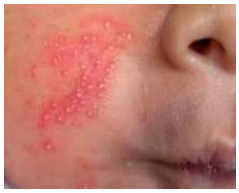
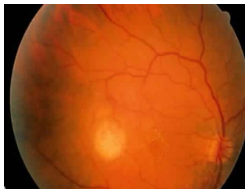
Herpes Simplex



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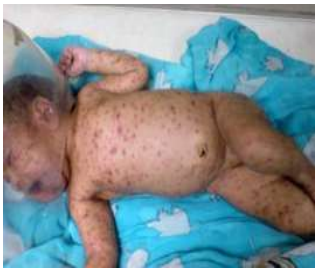
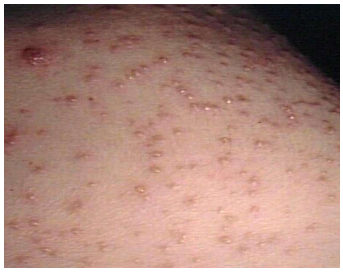
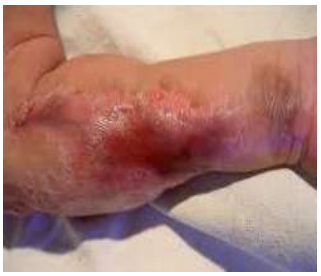
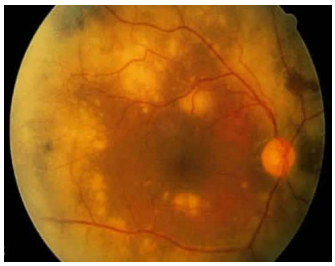

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Neonatal Varicella

- Early exposure in utero during 1st trimester(<20wk) can lead to neonatal varicella syndrome:
  - Cicatrical skin scarring, limb hypoplasia
  - Neurologic abnormalities: microcephaly, cortical atrophy, seizures, MR
  - Ocular abnormalities: chorioretinitis, microphthalmia &cataract
  - Renal abnormalities: hydroureter & hydronephrosis
  - CNS: neurogenic bladder, swallowing dysfunction, aspiration pneumonia
- Late exposure in 3rd trimester increases the risk of baby acquiring the disease during the neonatal period (the closer to delivery, the higher the risk)
- Vesicles usually develop over 1st 3-10 days of life
- Dissemination can lead to pneumonitis, encephalitis, purpura with hemorrhage, hypotension, and death
- If newborn at risk, should consider Varicella-zoster immune globulin or IVIG
- Start acyclovir early if lesions are suspicious for varicella
- Confirm diagnosis with DFA or PCR of lesion

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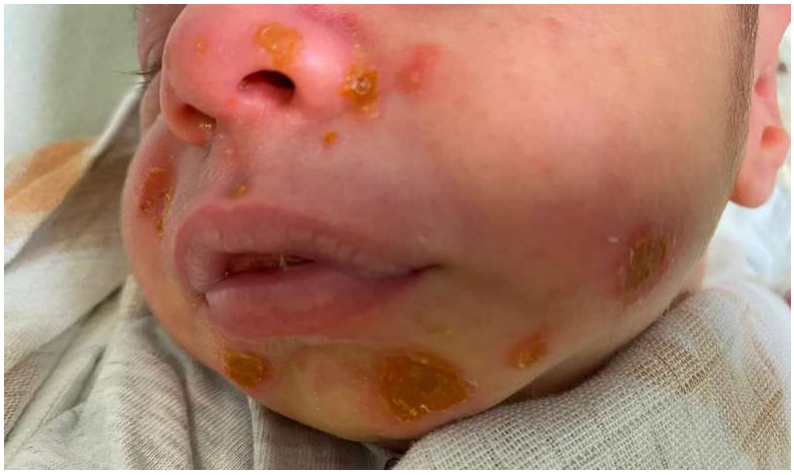

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Bacterial infections: Impetigo

- Most common skin infection in children
- Nonbullous I:subcorneal portion of epidermis(SA, GAS, Strep pyogenesis)
- Bullous I: (SA, phage group 2– exfoliative/ epidermolytic toxins A or B->epidermolysis->blister formation. Localized form SSSS

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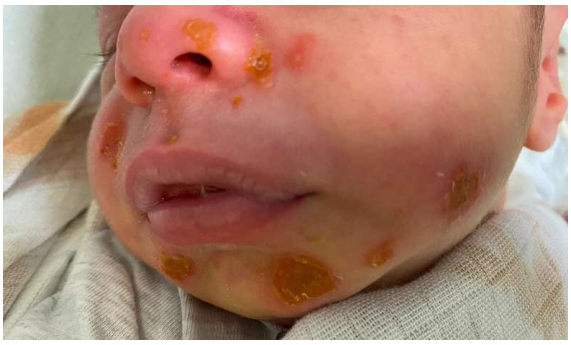

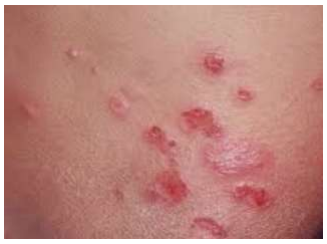

Culture from vesicle fluid

Differential Diagnosis:
HSV
Varicella
Enterovirus
Syphilis
CCC
Listeriosis
Scabies
ETN
TNPM
IP
Pemphigus

90

Treatment

- Topical mupirocin
- Systemic Abx: resistant to cleavage by penicillinases and cover Strep and SA, MRSA
- Cephalexin, Cloxacillin, Dicloxacillin
- Clindamycin , but MRSA R on the rise
- Other cephalosporins and Augmentin, but R to MRSA
- IV: oxacillin, nafcillin.
  - Vanco.
  - Clindamycin- decreases epidermolytic toxin production
  - Linezolid
- Mortality up to 40%

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antibiotics

MDPI

Review

Staphylococcal Infections and Neonatal Skin: Data from Literature and Suggestions for the Clinical Management from Four Challenging Patients

Domenico Umberto De Rose [1], Flaminia Pugnaloni [1], Ludovica Martini [1], Iliana Bersani [1], Maria Paola Ronchetti [1], Andrea Diociaiuti [2], May El Hachem [2], Andrea Dotta [1] and Cinzia Auriti [1,*]

Term Neonates		Preterm Neonatesor Small-for-Gestational-Age Neonates (<2500 g)
Without Systemic Findings	With Systemic Findings (Fever or Low Temperature, Ill-Appearance, Poor Feeding …)	
Topical antibiotic therapy for 7–10 days (e.g., fusidic acid),with at least 20 days of close follow-up	Intravenous therapy for 5–7 days (e.g., ampicillin)	Intravenous therapy for 5–7 days (e.g., ampicillin)
	In case of >15% of the community, *S. aureus* isolates are MRSA. An empiric intravenous coverage for MRSA should be considered (e.g., vancomycin, teicoplanin, linezolid or clindamycin)	

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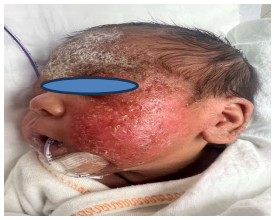
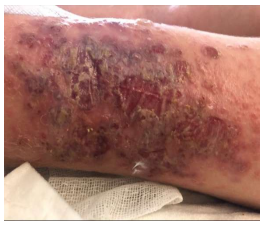
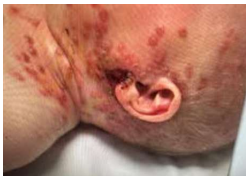
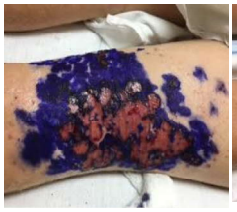
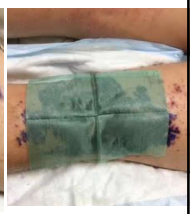
Superinfection

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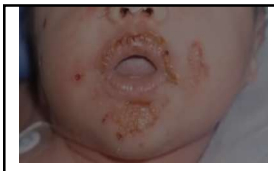
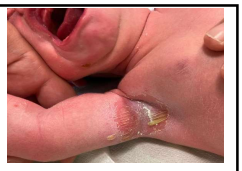


SSSS



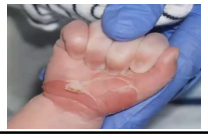
Lesions with diffuse erythematous rash, tender skin, discomfort, + Nikolsky sign

No mucous membranes

Most caused by MSSA, but initial antibiotics should cover MRSA

SA releasing serine protease exfoliative ETA and ETB.

Do not culture skin lesions as injury is caused by the toxins. May culture 1ry focus, such as nasopharynx, umbilicus. Blood cx typically negative.

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SSSS

CDC Case Definition for SSSS	
Clinical Criteria	- Temperature > 38.9 °C - Diffuse macular erythroderma - Desquamation, 1 to 2 weeks after onset, particularly palmoplantar - Hypotension for age - Multisystem involvement with three or more of the following: Gastrointestinal Muscular Renal Hepatic Hematologic Central nervous system
Laboratory Criteria	Negative test results for the following (if obtained): - Throat, cerebrospinal fluid, blood cultures (although blood may be positive for *S. aureus*) - Serological tests for other micro-organisms (HSV, measles, or others)
✓ Probable" disease: laboratory criteria + 4 out of 5 clinical criteria ✓ Confirmed" disease: laboratory criteria + all 5 clinical criteria (unless patient dies before desquamation)	

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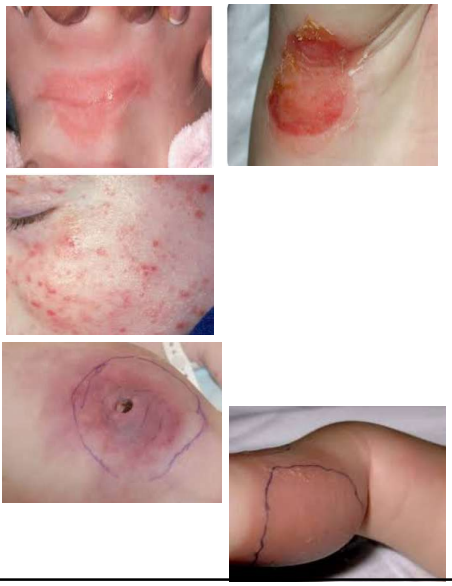
Bacterial Infections

- Intertrigo
- Folliculitis
- Funisitis/ Omphalitis
- Cellulitis



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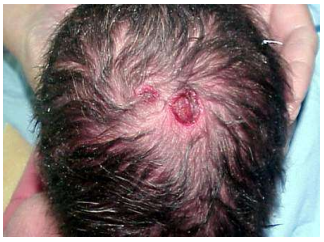

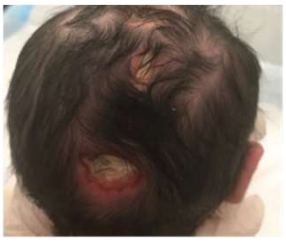

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Aplasia Cutis Congenita

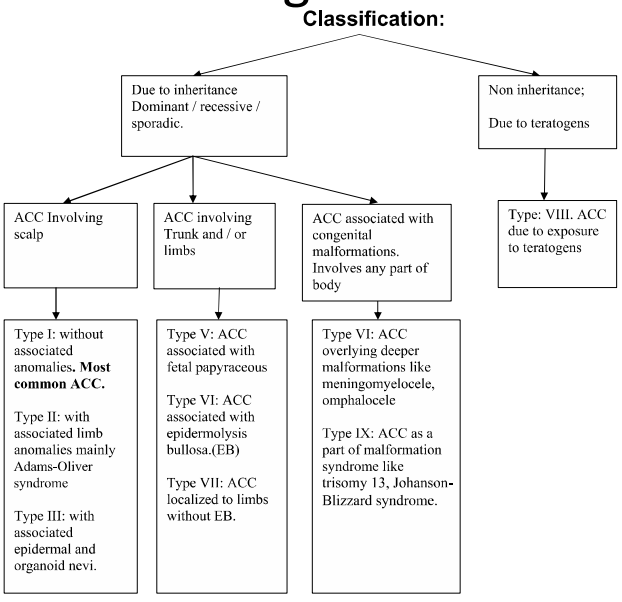
Table 1. **Conditions Associated With ACC**

Syndromes/genetic diseases
- AOS
- Johanson–Blizzard syndrome
- Setleis syndrome
- Focal dermal hypoplasia
- Trisomy 13
- Chromosome 4p-
- Epidermolysis bullosa
- Ectodermal dysplasia
- 46 XY gonadal dysgenesis
- Oculo–cerebro–cutaneous syndrome
- Epidermal nevus syndrome
- SCALP syndrome

Malformations
- CNS: meningocele, spinal dysraphism
- Congenital heart defects
- Omphalocele
- Tracheo–esophageal fistula
- Cleft lip and palate

Teratogens
- Herpes simplex virus
- Congenital varicella zoster virus infection
- Methimazole

Other
- Amniotic band sequence



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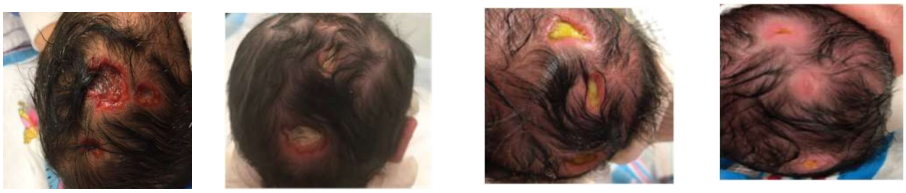
Aplasia Curis Congenita



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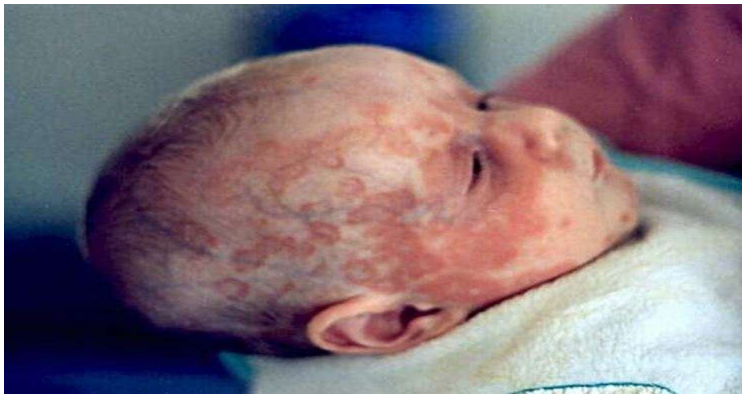

100

Neonatal Lupus Erythematosus

- Annular erythematous plaques with a central scale. Periorbital redness ”owl-eye” appearance.
- Transplacentally acquired ssA (Ro) and ssB (La) Ab is thought to play role in pathogenesis
- May be triggered or exacerbated by sun exposure
- Associated with heart block, hepatosplenomegaly, anemia, leukopenia, thrombocytopenia, and/or lymphadenopathy
- Except for cardiac involvement, usually resolves in 6-12 months
- May need topical steroids, rarely requires systemic steroids
- At delivery 50% of mothers are asymptomatic.
- Most useful test-fluorescent ANA , positive in >90%

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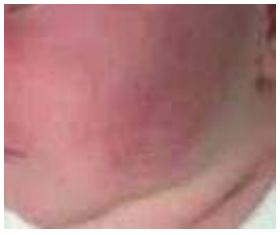

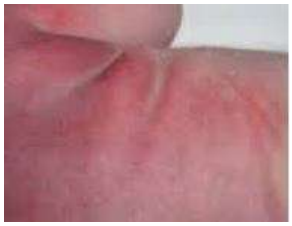

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SFNN

- Exact pathogenesis is not known
- Hypothermia is a common antecedent. The brown fat of neonates has a greater ratio of saturated palmitic acid to unsaturated oleic acid. Palmitic acid has a higher melting point than oleic acid, making it more susceptible to solidification and crystallization in response to lowered temperature
- Cold or stress-induced injury to immature fat cells results in the development of solidification and necrosis. A granulomatous infiltrate forms, which may lead to life-threatening hypercalcemia.
- Increased levels of 1-alpha hydroxylase...promotes the conversion of 25-OH-D3 to its active form 1,25 OH 2D3 →increases intestinal absorption of calcium, potentially leading to hypercalcemia.
- Elevated levels of prostaglandin E2 (PGE2), ?/elevated Ca.
- Rh factor incompatibility, meconium aspiration, placenta previa, umbilical cord prolapse, anoxia, seizures, preeclampsia, maternal cocaine abuse, local pressure trauma, gestational diabetes, maternal use of calcium antagonists during pregnancy, familial dyslipidemia, and a family history of thrombophilia, maternal hypercoagulable(Pr C deficiency and antiphospholipid syndrome).

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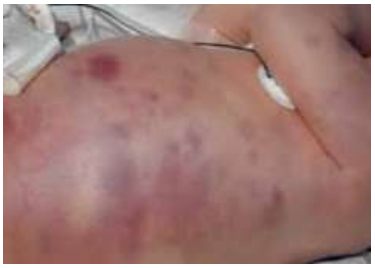

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