Neonatal Dermatology: The Normal, the Common, and the Serious

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Practice Gap

Rashes are commonly encountered in neonates; all pediatric clinicians should be aware of common neonatal dermatologic conditions and recognize severe conditions that require referral.

Abstract

The objective of this review is to help practitioners of neonatal and pediatric medicine become more familiar with diagnosing and managing neonatal skin conditions. This article will discuss normal neonatal skin care and benign and common rashes, as well as some of the serious dermatologic conditions that require specialists for further evaluation and/or treatment.

Objectives After completing this article, readers should be able to:

1. Recognize benign neonatal rashes and lesions and describe the management of these skin conditions.
2. Recognize serious neonatal rashes and lesions that require consultation with a pediatric dermatologist.

NEONATAL SKIN AND BARRIER FUNCTION

Neonatal skin is thinner and more fragile than adult skin. (1)(2) This leaves the neonate more vulnerable to transepidermal water loss and injury from heat, irritants, and mechanical trauma. Newborn skin also has a limited spectrum of skin flora and natural skin microbiome, which puts neonates at potentially higher risk for colonization of pathogens. (3) As the skin of the newborn matures, the barrier function will also improve because of increased skin thickness, skin tension, and better developed pigmentary, as well as adnexal structures. (4)

Importantly, infants have an increased body surface area–to–body mass ratio compared with older children and adults. This becomes important in percutaneous absorption of substances via skin exposure and their subsequent systemic effects, especially in premature infants. Some examples of reported topical agents with risk of toxicity in newborns include neomycin, which may cause neural deafness; isopropyl alcohol, which may cause cutaneous hemorrhagic necrosis;

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and topical steroids, which can lead to skin atrophy and adrenal suppression. (1) Other possible common exposures and potential systemic risks for toxicity in neonates are listed in Table 1.

The natural skin barrier in premature neonates is even more fragile than their term counterparts. The epidermis in premature skin is about half the thickness of mature skin, and the cell anchoring structures are not as abundant as in mature skin. This leads to increased permeability of the skin, which can potentially cause concerns for fluid loss, electrolyte imbalance, thermoregulation, and increased risk of systemic toxicity via cutaneous exposure. (5)(6) Extremely premature infants therefore need to be in a humid and temperature-regulated environment during early life to minimize these risks. Preterm infant skin usually matures within 2 to 3 weeks after birth.

NORMAL SKIN FINDINGS IN THE NEONATE

Vernix Caseosa

During the final trimester of pregnancy, the fetus develops a white, watery biofilm known as "vernix caseosa." As a neonate transitions from the intrauterine to extrauterine environment, the vernix serves as a barrier to prevent water loss and helps improve thermoregulation, moisturization, and immunity. (7) Because the vernix starts forming around 28 weeks' gestation and peaks at 33 to 37 weeks' gestation, it may not be fully formed in a preterm infant. (5)(8)(9) The vernix should not be removed immediately after birth as noted in studies showing that vernix retention improves skin hydration, lowers skin pH, and decreases skin inflammation as well as risk of infection. (10) In term infants, the vernix starts to desquamate approximately 3 days after birth but may take up to 2 to 3 weeks in preterm infants.

Transient Vascular Phenomena

During the first few weeks of age, cold stress can lead to physiologic acrocyanosis or cutis marmorata because of immature neurologic and vascular regulation. Acrocyanosis refers to bluish skin discoloration of the hands and feet without associated edema. Cutis marmorata is a reticulated or "lacelike" vascular change (Fig, A) that appears with cold and resolves with warming of the newborn. Cutis marmorata in neonates is considered physiologic and does not warrant an evaluation. However, vascular change that does not resolve with warming of the skin or persists beyond the neonatal period warrants further evaluation by specialists. Persistent cutis marmorata can be seen in children with trisomy 21 syndrome, Cornelia de Lange syndrome, and homocystinuria. The differential diagnosis for cutis marmorata in an otherwise healthy child includes cutis marmorata telangiectatica congenita, which may be associated with other findings such as limb hypo- or hyperplasia, as well as additional syndromic or nonsyndromic vascular anomalies. (9)

Congenital Dermal Melanocytosis

Congenital dermal melanocytosis consists of congenital macules or patches that are gray or blue and most commonly located in the lumbosacral region of full-term infants of color (Fig, B). Affected neonates do not require treatment

TABLE 1. **Potential Percutaneous Exposures in Neonates**

COMPOUND	EXPOSURE	TOXICITY RISKS
Alcohol	Skin antiseptic	Cutaneous hemorrhagic necrosis, elevated blood alcohol
Benzocaine	Topical anesthetic	Methemoglobinemia
Boric acid	Baby powder	Vomiting, diarrhea, erythroderma, seizures, death
Corticosteroids	Topical agents (anti-inflammatory)	Skin atrophy, striae, adrenal suppression
Iodine	Topical antiseptic	Hypothyroidism
Lidocaine	Topical anesthetic	Petechiae, seizures
Neomycin	Topical antibiotic	Neural deafness
Silver sulfadiazine	Topical antibiotic	Kernicterus, agranulocytosis, argyria
Triple dye	Topical antiseptic	Ulceration, skin necrosis, vomiting, diarrhea
Urea	Keratolytic emollient	Uremia

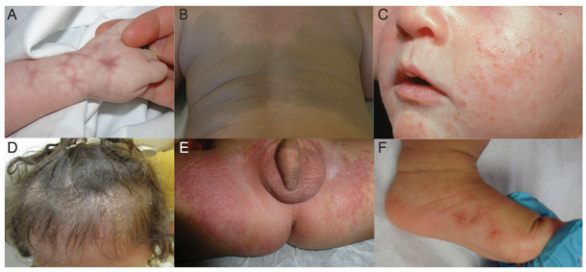

Figure. Typical presentation of common neonatal dermatological conditions. A. Cutis marmorata. B. Congenital dermal melanocytosis. C. Neonatal acne. D. Seborrheic dermatitis. E. Diaper dermatitis. F. Scabies.

and the pigmentation often fades by 3 to 6 years of age. Extensive dermal melanocytosis, however, does warrant a thorough evaluation to rule out an association with syndromes such as phakomatosis pigmentovascularis and mucopolysaccharide disorders. (11)

Sebaceous Hyperplasia

Sebaceous hyperplasia presents as 1- to 2-mm yellow papules over the nose, cheeks, and scalp of term infants. (12)(13) It is caused by maternal or endogenous androgenic stimulation of the sebaceous gland and generally resolves by 6 months of age. (4) In contrast to milia, which are discrete and solitary lesions, the papules of sebaceous hyperplasia tend to be grouped together into plaques. (2) Sebaceous hyperplasia is a physiologic phenomenon of the newborn and no treatment is needed.

BENIGN LUMPS, BUMPS, AND PITS OF THE NEWBORN

Variants of Epidermal Inclusion Cyst in the Newborn: Milia, Epstein Pearls, Foreskin Cysts

Milia are common, self-limited, small inclusion cysts filled with keratin. Neonatal milia appear as 1- to 3-mm yellow or white papules distributed over the forehead, face, and chin. Though not needed for diagnosis, gentle unroofing of a single lesion using a no. 11 blade or an 18-gauge needle can confirm diagnosis of milia and will also allow for extraction of the keratinous debris. Milia typically self-resolve over several months. Numerous, persistent, or unusual distribution of milia should raise concern for associated syndromes such as epidermolysis bullosa. Skin fragility, however, would be an obvious finding in those children. (14)(15)

Newborns often have milia on the mucosa as well, which are known as "Epstein pearls," on the palate, and Bohn nodules, on the gum margins. (16) These asymptomatic lesions spontaneously rupture in the first few weeks to months of age, and usually do not require treatment. (1)(16)(17)

Foreskin cysts and perineal median raphe cysts, however, are epidermal inclusion cysts that appear on the foreskin of the penis and ventral surface of scrotum. Although these lesions tend to be larger than milia of the head and neck, they are benign and usually do not require treatment. (2)

Dimpling

Dimpling of the skin is commonly seen over bony prominences, such as the elbow, knee, acromion, and sacral region. (18) These depressions, deep pits, or creases may be seen in healthy infants but they may also be associated with spinal cord anomalies; toxoplasmosis, other (syphilis, varicella-zoster, parvovirus B19), rubella, cytomegalovirus, and herpes (TORCH) infections, or genetic syndromes. Therefore, large, deep, or multiple lesions, especially when present along the midline, will need additional investigations such as imaging studies to rule out developmental anomalies. (19)(20)(21)

Umbilical Granulomas

Umbilical granulomas are formed from excessive granulation tissue of the umbilical cord because of moisture and low-grade bacterial colonization of the umbilicus. These commonly form in the first few weeks of age, which is the period during which the cord normally dries, separates, and forms a scar. They appear as friable grayish-pink papules on the umbilical stump with a velvety texture. (2) In contrast to umbilical polyps that represent a developmental abnormality and require surgical intervention, umbilical granulomas can be treated with silver nitrate or isopropyl alcohol. (4)

IATROGENIC SKIN FINDINGS IN NEWBORNS AFTER BIRTH

A detailed maternal obstetric history, such as history of amniocentesis, should be obtained whenever pits or dimples are seen on the skin of a newborn. (1) In addition, fetal scalp monitoring can cause ulceration, bleeding, sterile abscess, or infection. (22) Vacuum delivery and forceps-assisted deliveries can also cause localized injuries such as edema, cephalohematoma, and skull fracture. (23) It is important to differentiate between these localized, self-resolving injuries from inborn conditions such as aplasia cutis congenita (a congenital defect of scalp characterized by localized absence of the epidermis, dermis, and possibly subcutaneous tissues). (24) Aplasia cutis congenita may be associated with underlying cranial or cerebrovascular

defects. A previous study found that the anatomic location of the lesion (vertex or midline), positive hair collar sign, presence of vascular stains, and nodules were strong indicators of extracutaneous involvement, and thus warranted a referral to neurosurgery. (25) Anetoderma of prematurity refers to loss of cutaneous tissue and permanent scarring with depressions at the sites of cardiac electrode placement. (24)(26)(27)(28)

Multiple heel sticks can result in nodular deposits of calcium at the site of repeated needle injury for blood collection. Initially, these lesions resemble milia but over the course of a few months, they calcify, forming a white, hard nodule. These benign lesions may last 18 to 30 months but usually resolve spontaneously as the contents migrate to the surface and extrude. (1) Calcinosis cutis can form at the site of electrode placement on the chest and scalp as well. If these lesions are painful or otherwise bothersome, a referral to a dermatologist for removal of the lesion may be helpful.

COMMON BENIGN RASHES: TRANSIENT ERUPTIONS OF THE NEWBORN

Erythema Toxicum Neonatorum

Erythema toxicum neonatorum is a common neonatal rash. It usually appears on the second or third day after birth but may develop within the first 24 hours after birth and as late as 2 to 3 weeks of age. It begins as 2- to 3-mm erythematous papules that may evolve to pustules. Lesions are on a broad erythematous base, described as having a "flea-bitten" appearance. Erythema toxicum commonly involves the face, trunk, and proximal extremities. Diagnosis is made clinically or on Wright stain showing the presence of eosinophils in pustules. Up to 15% to 20% of affected infants may also have transient systemic eosinophilia, which can be diagnostically useful when a child has extensive lesions. (29) It usually resolves spontaneously within 5 to 7 days among most neonates.

Transient Neonatal Pustular Melanosis

Transient neonatal pustular melanosis is an eruption that generally occurs in infants with darker skin. (30) It presents in otherwise healthy neonates during the first few days after birth as asymptomatic, superficial, sterile pustules that rupture easily. Ruptured lesions may leave behind a collarette of fine white scale, which then evolve into hyperpigmented macules. These remnant lesions resolve in weeks to months. Wright-stained smears of the pustules characteristically demonstrate the presence of neutrophils instead of eosinophils, as in erythema toxicum neonatorum. The etiology of this condition is unknown. (31) Widespread lesions can appear concerning, but no treatment is necessary.

Neonatal and Infantile Acne

Neonatal acne may appear at birth or in early infancy, consisting of open or closed comedones, papules, pustules, and rarely cysts (Fig, C). (9) Maternal and endogenous androgens have been implicated in the pathogenesis of neonatal acne, and overgrowth of the *Malassezia* (formerly known as *Pityrosporum*) species also may play a role. Although neonatal acne has an earlier onset and resolves by 3 months of age, infantile acne can develop anytime thereafter in the first year after birth. Both neonatal and infantile acne typically do not require treatment because they are self-resolving conditions. However, in more severe cases, topical acne treatments including antibiotics and low concentration of benzoyl peroxide may be used to reduce inflammation and prevent scarring. (9) Dermatologists may consider oral medication, such as erythromycin or even isotretinoin, on rare occasions, to treat severe cases. For these children, evaluation to rule out congenital adrenal dysplasia or hyperandrogenism should be considered. (2)(9)

Neonatal Cephalic Pustulosis

Neonatal cephalic pustulosis is an eruption of the face and scalp that may present similarly to acne but typically lacks comedones. Pustules begin to develop between 5 and 30 days of age. The exact cause of this cutaneous eruption is unclear but is thought to be associated with *Malassezia* colonization. Giemsa stain of pustules usually reveals yeast and neutrophils. (11)(18)(32)

Neonatal cephalic pustulosis is a self-limiting condition but can be treated with ketoconazole-containing shampoo or topical 2% ketoconazole cream in combination with low-potency topical steroids. (4)(11)

Seborrheic Dermatitis

Seborrheic dermatitis commonly affects the scalp, also termed "cradle cap." Infants can also have generalized involvement of the face, postauricular areas, chest, abdomen, and intertriginous creases, including the diaper area and axillae. Seborrheic dermatitis usually appears between 2 and 10 weeks of age and appears as salmon-colored patches with greasy, yellow scale (Fig, D). (33) When intertriginous areas are involved, fissuring and maceration can be seen, especially in the neck or diaper areas. Overgrowth of *Malassezia furfur* (formerly *Pityrosporum ovale*) has been implicated in the development of seborrheic dermatitis. Mild cases are self-limited and resolve within weeks to months

without treatment. Emollients, gentle combing, and frequent gentle washing are recommended. Ketoconazole shampoo or cream or low-potency topical steroids may also be used. (4) If exudate is present in intertriginous areas, a secondary infection or colonization should be suspected and bacterial or fungal culture can be considered.

In the neonatal period, seborrheic dermatitis can overlap with atopic dermatitis and it can often be difficult to distinguish. It is also important to note that patients with seborrheic dermatitis have a higher incidence of atopic dermatitis later in life, suggesting that early priming of the immune system may play a role in the development of atopic dermatitis. A prior study found that 49% of infants with atopic dermatitis had a history of infantile seborrheic dermatitis. (34)

Miliaria

Miliaria refers to skin eruptions caused by obstruction of the eccrine ducts as a result of thermal stress and frequently develop in the first few weeks after birth. Lesions manifest differently depending on the depth of the eccrine gland obstruction. Miliaria crystallina occurs when the duct is blocked just below the stratum corneum, manifesting as superficial clear vesicles with no surrounding skin inflammation. Obstruction in the midepidermis results in formation of clusters of pinpoint erythematous papules and pustules seen in miliaria rubra, whereas the deep-seated papulopustular lesions found in miliaria profunda occur when the eccrine duct ruptures at the dermal-epidermal junction. Surrounding skin erythema and pruritus are often associated with miliaria rubra and profunda. Management is symptomatic and includes cooling measures and avoiding excessive bundling. (4) Low-potency topical steroids can be used for symptomatic relief.

Acropustulosis of Infancy

Acropustulosis of infancy presents as pruritic, recurrent pustules, concentrated on the palms and soles that can begin anytime between birth and 2 years of age. Before making a diagnosis of acropustulosis, it is important to rule out other vesicular eruptions, and more specifically scabies infestation (discussed later herein). Preceding scabies infestation has been described in association with acropustulosis of infancy. (35)(36) Diagnosis of acropustulosis is clinical, but mineral oil preparation is helpful to exclude scabies infection. Obtaining a thorough history of possible exposure at home could be helpful in making the diagnosis, as well. Typically, acropustulosis requires therapy because of intense pruritus that may last for 1 to 2 years. Although the first line of treatment is mid- to high-potency topical steroids, empiric treatment for scabies infestation is often used as well. Antihistamines can be used for symptomatic relief, and treatment of recalcitrant cases with topical or oral dapsone has been reported. (35)(37)

DIAPER DERMATITIS: A CLINICAL PRESENTATION OF A BROAD SPECTRUM OF DISEASES

Diaper dermatitis (Fig, E) is one of the most common skin complaints of infancy. The differential diagnosis can be broad and management may be challenging. Common causes of diaper dermatitis include: 1) frictional dermatitis, 2) irritant contact dermatitis, and 3) candidiasis. These common causes, as well other conditions that can present as cutaneous eruptions in the diaper area and warrant additional diagnostic evaluation, are detailed in Table 2.

RASHES NOT TO BE MISSED IN NEWBORNS

Blueberry Muffin Baby: TORCH Infections and Leukemia Cutis

The TORCH infections refer to a group of serious congenital neonatal infections consisting of toxoplasmosis, other (syphilis, varicella-zoster, parvovirus B19), rubella, cytomegalovirus, and herpes infection. The most striking skin finding of these infections is the "blueberry muffin" rash. Blueberry muffin lesions refer to an eruption of violaceous (blue-red) infiltrative papules and nodules present at birth that represent extramedullary hematopoiesis. Blueberry muffin lesions can also be seen in neoplastic and other fetal disorders but are the most distinct cutaneous feature of viral TORCH infections. The rashes associated with these infections, as well as associated findings with each infection are summarized in Table 3. Some of these infections are explained in greater detail later on in this review. (33)(38)(39)

Leukemia cutis refers to the cutaneous manifestation of an underlying hematologic malignancy, usually of systemic myeloblastic leukemia. (40) It may manifest in newborns similarly to the TORCH infections with the characteristic blueberry muffin baby rash because of its extramedullary hematopoiesis. (41) Congenital infections, such as those described here, should, however, be ruled out before diagnosis. A number of diagnoses on the differential present similarly, therefore, sometimes a biopsy may be needed to confirm the diagnosis. (42) Leukemia cutis is also described later in the section on malignant skin disorders of the newborn.

TABLE 2. **Causes and Mimickers of Diaper Dermatitis**

CLINICAL CONDITION	CAUSE	SKIN FINDINGS	MANAGEMENT
Frictional or chafing dermatitis	Friction from diaper against skin and repeated wet to dry cycles	Mild erythema and scaling in areas of friction of inner thighs, buttocks, abdomen, and genitalia; skinfolds are often spared	Decrease friction Ensure diapers are well-fitting Generous use of barrier cream or ointment (zinc oxide and petrolatum-based formulations)
Irritant contact dermatitis	Prolonged contact with feces and urine in damp diaper; or sensitivity to chemicals in cleansing agents or other skin care products	Well-demarcated erythematous patches with papules on convex areas with sparing of the inguinal and intergluteal folds (where contact with irritant is limited)	Frequent diaper change Gentle cleansing with water or wash cloth, can use mineral oil if patient has adherent feces Use of barrier cream or ointment (zinc oxide and petrolatum-based formulations) Low-potency topical steroids if symptomatic
Candida diaper dermatitis	Overgrowth of *Candida* species (part of normal skin flora)	Groups with papules, pustules, "satellite lesions" with or without confluent erythema	Topical antifungal formulation (ie, nystatin, clotrimazole, econazole, miconazole) in addition to barrier protection Gentle cleansing Low-potency topical steroids may be needed should there be concurrent inflammation and pruritus
Candida intertrigo	Overgrowth of *Candida* species in flexural areas that are prone to heat and moisture	Erythematous macerated plaques with satellite lesions, pustules, and erosions in flexural areas	Topical antifungal formulation (ie, nystatin, clotrimazole, econazole, miconazole)
Seborrheic dermatitis	Colonization with *Pityrosporum* may be the trigger	Salmon-colored, greasy plaques with a yellowish scale in intertriginous areas May involve the scalp, face, neck, chest, postauricular, or flexural areas	Mild antifungal cream such as 2% ketoconazole cream Low-potency topical steroids may be used in combination Reduce moisture accumulation Barrier protection is crucial
Inverse psoriasis	Chronic, immune-mediated inflammatory disease	Sharply demarcated erythematous plaque (with or without scale, as moisture of the diaper area may mask the scale); often involving the skinfolds	Topical anti-inflammatory formulations such as mild steroids, vitamin D analogs, or topical calcineurin inhibitors (off label)
Granuloma gluteale infantum	Robust inflammatory reaction, in response to chronic irritation, inflammation or candida infection (often associated with frequent stools)	Purple-red papules and nodules on the skin of the groin, lower abdomen, or inner thighs	Prevention of the underlying irritation Use of barrier cream or ointment (zinc oxide and petrolatum-based formulations)
Acrodermatitis enteropathica	Zinc deficiency Caused by a mutation in intestinal zinc-specific transporter*	Mimics a severe irritant contact dermatitis Eroded or crusted, erythematous patches and plaques involving diaper area (especially the skin folds), perioral area, as well as extensors of upper and lower extremities Triad of diarrhea, failure to thrive, and alopecia may be present; immune suppression and neurologic changes may occur in severe deficiency	Zinc supplementation Potent topical steroid

Continued

TABLE 2. (Continued)

CLINICAL CONDITION	CAUSE	SKIN FINDINGS	MANAGEMENT
Langerhans cell histiocytosis	Multisystem disease affecting bone, liver, lung, and the central nervous system 50% have activating mutations in BRAF proto-oncogene (9)	Mimics seborrheic dermatitis in the intertriginous area of the diaper, axillae, and retroauricular scalp as erythematous papules and patches with superficial erosions and crust Red-brown purpuric erosive and crusted papules on body may be present Lymphadenopathy	Skin biopsy to confirm presence of Langerhans cells and referral to pediatric oncologist Skin-limited disease may be observed or treated with topical steroids

**Breast milk provides an alternative zinc-binding protein for infants and thus the disorder does not present until breastfeeding ceases.*

Varicella Zoster Virus (VZV): Congenital, Neonatal, and Infantile Infection

Congenital or fetal varicella syndrome refers to an infection seen in neonates born to women who contract primary infection from VZV exposure in the first 20 weeks of gestation. This is rare because of universal varicella vaccination programs. Thus, most women have acquired immunity to VZV by the time they become pregnant. In rare instances in which pregnant women acquire VZV before 20 weeks of gestation, the newborn will have congenital varicella syndrome at birth. (43)(44)

Congenital varicella syndrome presents as red macules, vesicles, or scarring in a dermatomal distribution. The skin findings may be associated with a spectrum of extracutaneous findings including limb hypoplasia, ophthalmic findings, neurologic findings, and other organ defects. (45) Examples of ophthalmic manifestations include microphthalmia and chorioretinitis, whereas neurologic defects may include cortical atrophy, microcephaly, or encephalitis. Gastrointestinal, genitourinary, and cardiovascular abnormalities have also been reported. (46) Mortality rate (up to 30% fatality within the first few months of age in patients with congenital varicella syndrome) is high in patients with disseminated infection. (43)(44)(45)(46)

Neonatal varicella syndrome refers to an infection found in neonates who acquire VZV in the last few weeks of pregnancy or the first few days after birth. Depending on the timing of contraction of the infection, the clinical manifestations in a newborn may range from a mild limited skin disease to severe disseminated infection with a high mortality rate. When the mother acquires VZV infection between 5 days before or 2 days after delivery, there is not enough time for transfer of maternal IgG antibodies to protect the newborn. Because of lack of innate immunity, severe infection may present with disseminated erythematous papules, vesicles, and erosions along with pneumonia, hepatitis, meningoencephalitis, coagulopathy, and a mortality rate of around 30%. Therefore, all infants born to women who contracted VZV between 5 days before and 2 days after delivery are candidates for aggressive treatment with varicella zoster immune globulin in addition to intravenous acyclovir. (47)

Infantile herpes zoster refers to infection secondary to reactivation of VZV. Infantile zoster appears as small erythematous papules or crusted vesicles in a dermatomal pattern. Infantile herpes zoster typically has a benign course with an excellent prognosis. Symptomatic therapy and antiviral treatment are recommended. (48)

Herpes Simplex Virus (HSV): Congenital, Perinatal, and Postnatal Infection

HSV infection occurs in up to 1 in 3,000 live births and may occur 1) congenitally or in utero (least common), 2) during labor (most common), or 3) postnatally. (2) In utero infections happen either via ascending genital infection or transplacentally. Infection during labor through an infected birth canal (perinatal transmission) is the most common way of exposure and occurs via genital secretions or active genital herpetic lesions at the time of delivery. Newborns may also acquire HSV postnatally via hospital or household contact. (49)(50)

Herpes infection in neonates and infants can vary from mild to severe with neurologic sequalae or even death. Congenital (in utero) herpes presents with skin lesions at birth or within 12 hours after birth and has devastating consequences, including abnormal brain findings, such as hemorrhagic encephalitis usually involving the temporal lobes. Neonatal HSV, on the other hand, can have variable

TABLE 3. **TORCH Infections and Associated Findings**

INFECTION	CUTANEOUS FINDINGS	ASSOCIATED FINDINGS
Toxoplasmosis (protozoan *Toxoplasma gondii*)	Diffused vascular papules; "Blueberry muffin" rash	Stillbirth or prematurity Intellectual disability, seizures, blindness
Other		
Syphilis (spirochete *Treponema pallidum)*	Cutaneous findings are seen in one-third to one-half of affected infants and may be varied Most common presentation is diffuse papulosquamous eruption involving palms and soles (similar to secondary syphilis in older patients) Red and fissured palms and soles	Stillbirth, hydrops fetalis, premature delivery, low birthweight, and small size for gestational age (38) Rhinitis (snuffles) usually first sign Treatment: Parenteral penicillin G
Varicella-zoster	See text	Greatest risk in infection is acquired before 20 weeks of gestation
Parvovirus B19 (the same virus that causes erythema infectiosum/Fifth disease/ "slapped cheek disease")	Skin findings are not a major feature of this infection in neonates, blueberry muffin lesions have been described	Anemia, hydrops fetalis, intrauterine fetal death
Rubella	Diffuse vascular papules; blueberry muffin rash	Classic triad of congenital cataracts, deafness, and cardiac defects
Cytomegalovirus (most common intrauterine infection in the United States) (33)(39)	Jaundice, petechiae, purpura, generalized maculopapular eruption, and blueberry muffin rash	Hydrops, intrauterine growth restriction, microcephaly, chorioretinitis, ventriculomegaly and cerebral calcifications, prematurity, hepatosplenomegaly, deafness, pneumonitis
Herpes	See text	Meningoencephalitis

presentations, in order of incidence: 1) localized to the skin, eyes, or mouth (also known as "skin-eyes-mouth disease"), 2) central nervous system (CNS) infection, or 3) disseminated disease with disseminated intravascular coagulation, as well as liver and respiratory involvement.

HSV skin lesions appear as small 2- to 4-mm vesicles with surrounding erythema. Because of the potentially devastating consequences of CNS infection with HSV, any newborn seen with vesicular lesions should raise suspicion for HSV, and thus, be isolated with contact precautions, fully evaluated for signs of systemic infection, and empirically treated with intravenous antiviral therapy.

Bacterial Infections: Impetigo and Staphylococcal Scalded Skin Syndrome

Impetigo, classified as nonbullous and bullous types, is a common superficial skin infection that can be caused by streptococci or staphylococci. Most lesions of impetigo are described as nonbullous eczema, hallmarked by a honey-colored crust. The yellow crust is formed by rupture of thin superficial vesicles. In contrast, bullous impetigo, which is caused by exfoliative toxin (same toxin involved in staphylococcal scalded skin syndrome [SSSS]), appears as flaccid blisters or shallow erosions covered with a collarette of scale (remnants of the blister roof).

Treatment of impetigo depends on the clinical presentation and risk of systemic spread of infection, potentially leading to pneumonia or sepsis. Most limited presentations can be treated with topical antibiotics. Mupirocin remains the topical treatment of choice because of its broad-spectrum gram-positive coverage (including in most cases of methicillin-resistant *Staphyloccus aureus*) and has a low potential for contact dermatitis. (51)(52)(53)(54) Severe or widespread impetigo requires oral or intravenous antibiotics with coverage for both streptococci and staphylococci. It is best practice to obtain a bacterial culture specimen before starting oral antibiotics.

SSSS is caused by the exfoliating toxin of group II staphylococci, leading to widespread blistering and desquamation of the skin. (55) SSSS presents with exquisite tenderness of the skin, generalized macular erythema with a wrinkled appearance, and sheetlike superficial desquamation that develops over 2 to 5 days of onset. A positive Nikolsky sign may also be seen. Patients with SSSS should be treated promptly with antibiotics. Clindamycin is often selected as therapy to reduce protein toxin production. Isolation precautions should also be taken to prevent the spread of infection. Infants usually recover in 10 to 14 days without scarring or long-term complications. However, potential complications can include excessive fluid loss, electrolyte imbalance, temperature dysregulation, or infection/sepsis because of extensive skin erosion. Inpatient admission and close monitoring should be considered based on the extent of skin involvement.

Fungal Infections: Candida Infection

All newborns are susceptible to candida infection, which commonly presents as oral candidiasis, diaper candidiasis, or intertrigo. These superficial infections are readily treatable with topical antifungals. However, candida infections are most concerning in premature and immunocompromised infants who are at risk for more severe infections, such as systemic candidiasis with respiratory symptoms, hyperglycemia, temperature instability, hypotension, urinary tract infection, meningitis, and candida septicemia. (56)(57)

Newborns have 2 clinical presentations of candida infection: congenital candidiasis, presenting at birth or within the first few days after birth, and neonatal candidiasis, acquired after the first week of age. Congenital candidiasis is usually acquired in utero from women with a history of candida vulvovaginitis. (58) It may be associated with premature labor, chorioamnionitis, or a serious systemic infection, especially in premature or low-birthweight neonates. (59) Congenital candidiasis usually presents initially as diffuse erythema with or without erythematous papules and pustules. Occasionally, bullae may present on the back, extremities, and skin folds. Interestingly, the diaper area is usually spared, and oral thrush is not present. Evolving pustules on the palms and soles can be a diagnostic clue, and nail abnormalities may be present at birth. (5)

Neonatal candidiasis is acquired during passage through an infected birth canal, or as a result of invasive procedures that interrupt the skin barrier. Clinically, it can present as localized disease, such as oral thrush or diaper dermatitis, or as systemic infection. The common presentation for neonatal candidiasis includes a diaper rash with intense erythema and satellite vesicles or pustules. Oral thrush and intertrigo are also common presentations.

Candida infection can be diagnosed with a smear of the pustules using potassium hydroxide. Microscopic examination shows spores and pseudohyphae. A culture specimen for speciation is often obtained for children with systemic infection or localized infection that has failed treatment. An evaluation of premature and low-birthweight neonates with possible disseminated systemic disease should include fungal cultures of the blood, urine, airway, and cerebrospinal fluid. Treatment of systemic candidiasis requires parenteral antifungal therapy.

Infestations of the Skin: Scabies

Scabies is caused by the *Sarcoptes scabiei* mite that lives in burrowed tunnels within the epidermis. It is usually transmitted by direct human contact with an infected person. Less commonly, scabies may also be transmitted from bedding and clothing, because mites do not survive more than 24 hours off the human body. In infants, scabies has a different clinical presentation than in adults or older children. In addition to the typical burrows, it usually presents as vesicles and crusted papules on the head, palms, soles, axillae, genitals, and scalp because of infants' lack of dexterity to scratch these areas (Fig, F). Therefore, diagnosis of scabies should be considered in any infant with a widespread vesicular and papular rash including the palms, soles, and scalp. Diagnosis can be made by scraping a burrow or a fresh papule and examining the smear with mineral oil for identification of mites, eggs, or feces. Treatment with topical permethrin cream is approved by the Food and Drug Administration for infants older than 2 months but is also usually used off-label in newborns. Unlike treatment in older individuals, the scalp should be treated in infants with scabies. Sulfur 6% is also safe to use; however, this treatment has to be compounded at a local pharmacy. (9)(60) It is important to treat household contacts simultaneously as well. Infants may also develop a hypersensitivity response known as scabies nodules that may persist for several months. (1) The presence of Langerhans cells in these nodules may create confusion and lead to misdiagnosis of Langerhans cell histiocytosis, resulting in an unnecessary evaluation or even treatment.

Autoimmune Skin Disease in the Newborn: Neonatal Lupus

Neonatal lupus, the most common cause of congenital heart block, presents as erythematous plaques with central scaling and atrophy. These characteristic annular lesions often present around the periorbital area, cheek, and forehead,

which may subsequently spread to the trunk and extremities. The cutaneous manifestations of neonatal lupus may be treated with low- to medium-potency topical corticosteroids but typically spontaneously resolve by 6 to 12 months of age as maternal autoantibodies are cleared. (61) Adequate sun protection is recommended, as residue dyspigmentation or skin atrophy may occur. Hepatobiliary disease associated with NLE is not uncommon and therefore may require surveillance. CNS involvement has been reported, but the risk is low.

MALIGNANT SKIN DISEASE IN NEWBORNS

Langerhans Cell Histiocytosis

Langerhans cell histiocytosis (LCH) may present as a seborrheic dermatitis-like rash in the intertriginous areas, including the diaper region. LCH is a dendritic cell proliferative disorder that may present as a multisystem disease with extracutaneous manifestations affecting the bone, viscera, and CNS. Skin is an organ that is commonly affected during the early phase of LCH, and on morphologic examination, is often recognized as clusters of hemorrhagic and crusted papules involving the skin folds. Tissue biopsy is necessary for definitive diagnosis of LCH, and a systemic evaluation is recommended. (62)(63) Of note, a history of scabies exposure should be obtained from parents of infants with localized Langerhans cell neoplasms.

Leukemia Cutis

Cutaneous manifestations of an underlying hematologic malignancy are often seen in newborns. It is reported that leukemia cutis may be the initial presenting symptom in 50% of neonates with leukemia. (64)(65) It manifests as infiltrative papules or plaques resulting from extramedullary hematopoiesis. (41) Skin biopsy with special immunoperoxidase stain can provide a timely diagnosis so that referral to hematology/oncology can be made as early as possible.

Neuroblastoma

Neuroblastoma (NB) is the most common neonatal malignancy. (66) In the metastatic form, neuroblastoma may present as multiple bluish nodules with a characteristic blanch response to palpation. Its presentation has put the rash among the differential diagnoses for the blueberry muffin baby presentation. (67)

CONCLUSION

In summary, newborns can develop many benign rashes that are easily diagnosable and treatable by neonatologists and primary care physicians. We hope that this review will help clinicians identify some of the more serious skin eruptions that warrant a prompt referral to a specialist.

American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Know the cutaneous manifestations of severe candidiasis.
- Know the cutaneous manifestations of herpes simplex and varicella zoster.
- Know the cutaneous and laboratory manifestations of scalded skin syndrome.
- Know the development of the human skin and understand the differences between preterm and full-term skin.
- Know the potential toxicity of various drugs applied topically to newborn skin, including antiseptics, lidocaine, and mydriatic agents.
- Know the treatment of scalded skin syndrome.
- Know the pathogenesis and cutaneous manifestations of CMV.
- Know the etiology and cutaneous manifestations of common neonatal skin lesions, including erythema toxicum, neonatal pustular melanosis, and neonatal acne.
- Know the management of common neonatal dermatoses, including diaper dermatitis.
- Know the cutaneous manifestations of neonatal lupus erythematosus.

References

1. Paller A, Mancini AJ, Hurwitz S. *Hurwitz Clinical Pediatric Dermatology*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2011
2. Eichenfield LF, Frieden IJ, Mathes EF, Zaenglein AL. *Neonatal and Infant Dermatology*. 3rd ed. Philadelphia, PA: Elsevier; 2014
3. Schoch JJ, Monir RL, Satcher KG, Harris J, Triplett E, Neu J. The infantile cutaneous microbiome: a review. *Pediatr Dermatol*. 2019;36(5):574–580
4. Cohen BA. *Pediatric Dermatology*. 4th ed. Philadelphia, PA: Elsevier; 2013
5. Darmstadt GL, Dinulos JG. Neonatal skin care. *Pediatr Clin North Am*. 2000;47(4):757–782
6. Mathes E, Williams M. *Skin of the Premature Infant in Neonatal and Infant Dermatology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2015:36–45

7. Singh G, Archana G. Unraveling the mystery of vernix caseosa. *Indian J Dermatol*. 2008;53(2):54–60
8. Lund CH, Osborne JW, Kuller J, Lane AT, Lott JW, Raines DA. Neonatal skin care: clinical outcomes of the AWHONN/NANN evidence-based clinical practice guideline. Association of Women's Health, Obstetric and Neonatal Nurses and the National Association of Neonatal Nurses. *J Obstet Gynecol Neonatal Nurs*. 2001;30(1):41–51
9. Teng JMC, Marqueling AL, Benjamin LT. *Therapy in Pediatric Dermatology: Management of Pediatric Skin Disease*. New York, NY: Springer; 2017
10. Visscher MO, Narendran V, Pickens WL, et al. Vernix caseosa in neonatal adaptation. *J Perinatol*. 2005;25(7):440–446
11. Rybojad M, Moraillon I, Ogier de Baulny H, Prigent F, Morel P. Extensive Mongolian spot related to Hurler disease [in French]. *Ann Dermatol Venereol*. 1999;126(1):35–37
12. Nanda A, Kaur S, Bhakoo ON, Dhall K. Survey of cutaneous lesions in Indian newborns. *Pediatr Dermatol*. 1989;6(1):39–42
13. Rivers JK, Frederiksen PC, Dibdin C. A prevalence survey of dermatoses in the Australian neonate. *J Am Acad Dermatol*. 1990;23(1):77–81
14. Berk DR, Bayliss SJ. Milia: a review and classification. *J Am Acad Dermatol*. 2008;59(6):1050–1063
15. Rapelanoro R, Mortureux P, Couprie B, Maleville J, Taïeb A. Neonatal *Malassezia furfur* pustulosis. *Arch Dermatol*. 1996;132(2):190–193
16. Cambiaghi S, Gelmetti C. Bohn's nodules. *Int J Dermatol*. 2005;44(9):753–754
17. Weston WL, Lane AT, Morelli JG. *Color Textbook of Pediatric Dermatology*. Philadelphia, PA: Mosby Elsevier; 2007:224–227
18. Samlaska CP. Congenital supraspinous fossae. *J Am Acad Dermatol*. 1991;25(6 pt 1):1078–1079
19. Bruce S, Duffy JO, Wolf JE Jr. Skin dimpling associated with midtrimester amniocentesis. *Pediatr Dermatol*. 1984;2(2):140–142
20. Wilson P, Hayes E, Barber A, Lohr J. Screening for spinal dysraphisms in newborns with sacral dimples. *Clin Pediatr (Phila)*. 2016;55(11):1064–1070
21. Albert GW. Spine ultrasounds should not be routinely performed for patients with simple sacral dimples. *Acta Paediatr*. 2016;105(8):890–894
22. Okada DM, Chow AW, Bruce VT. Neonatal scalp abscess and fetal monitoring: factors associated with infection. *Am J Obstet Gynecol*. 1977;129(2):185–189
23. Simonson C, Barlow P, Dehennin N, et al. Neonatal complications of vacuum-assisted delivery. *Obstet Gynecol*. 2007;109(3):626–633
24. Prizant TL, Lucky AW, Frieden IJ, Burton PS, Suarez SM. Spontaneous atrophic patches in extremely premature infants: anetoderma of prematurity. *Arch Dermatol*. 1996;132(6):671–674
25. Patel DP, Castelo-Soccio L, Yan AC. Aplasia cutis congenita: evaluation of signs suggesting extracutaneous involvement. *Pediatr Dermatol*. 2018;35(1):e59–e61
26. Boyle RJ, Oh W. Erythema following transcutaneous PO2 monitoring. *Pediatrics*. 1980;65(2):333–334
27. Golden SM. Skin craters: a complication of transcutaneous oxygen monitoring. *Pediatrics*. 1981;67(4):514–516
28. Colditz PB, Dunster KR, Joy GJ, Robertson IM. Anetoderma of prematurity in association with electrocardiographic electrodes. *J Am Acad Dermatol*. 1999;41(3 pt 1):479–481
29. Chang MWOS. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, eds. *Fitzpatrick's Dermatology in General Medicine*. 7th ed. New York, NY: McGraw Hill; 2008;1:935–954
30. Behne MJ, Barry NP, Hanson KM, et al. Neonatal development of the stratum corneum pH gradient: localization and mechanisms leading to emergence of optimal barrier function. *J Invest Dermatol*. 2003;120(6):998–1006
31. Reginatto FP, Villa DD, Cestari TF. Benign skin disease with pustules in the newborn. *An Bras Dermatol*. 2016;91(2):124–134
32. Niamba P, Weill FX, Sarlangue J, Labrèze C, Couprie B, Taïeh A. Is common neonatal cephalic pustulosis (neonatal acne) triggered by *Malassezia* sympodialis? *Arch Dermatol*. 1998;134(8):995–998
33. Foley P, Zuo Y, Plunkett A, Merlin K, Marks R. The frequency of common skin conditions in preschool-aged children in Australia: seborrheic dermatitis and pityriasis capitis (cradle cap). *Arch Dermatol*. 2003;139(3):318–322
34. Moises-Alfaro CB, Caceres-Rios HW, Rueda M, Velazquez-Acosta A, Ruiz-Maldonado R. Are infantile seborrheic and atopic dermatitis clinical variants of the same disease? *Int J Dermatol*. 2002;41(6):349–351
35. Mancini AJ, Frieden IJ, Paller AS. Infantile acropustulosis revisited: history of scabies and response to topical corticosteroids. *Pediatr Dermatol*. 1998;15(5):337–341
36. Elpern DJ. Infantile acropustulosis and antecedent scabies. *J Am Acad Dermatol*. 1984;11(5 Pt 1):895–896
37. Kahn G, Rywlin AM. Acropustulosis of infancy. *Arch Dermatol*. 1979;115(7):831–833
38. Lago EG, Vaccari A, Fiori RM. Clinical features and follow-up of congenital syphilis. *Sex Transm Dis*. 2013;40(2):85–94
39. Bristow BN, O'Keefe KA, Shafir SC, Sorvillo FJ. Congenital cytomegalovirus mortality in the United States, 1990-2006. *PLoS Negl Trop Dis*. 2011;5(4):e1140
40. Handler MZ, Schwartz RA. Neonatal leukaemia cutis. *J Eur Acad Dermatol Venereol*. 2015;29(10):1884–1889
41. Cho-Vega JH, Medeiros LJ, Prieto VG, Vega F. Leukemia cutis. *Am J Clin Pathol*. 2008;129(1):130–142
42. Jandali S, Kirschner RE. Congenital leukemia cutis presenting as multiple violaceous lesions in a newborn. *Ann Plast Surg*. 2011;66(3):310–312
43. Schleiss MR. Antiviral therapy of congenital cytomegalovirus infection. *Semin Pediatr Infect Dis*. 2005;16(1):50–59
44. Harger JH, Ernest JM, Thurnau GR, et al; National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. Frequency of congenital varicella syndrome in a prospective cohort of 347 pregnant women. *Obstet Gynecol*. 2002;100(2):260–265
45. Birthistle K, Carrington D. Fetal varicella syndrome--a reappraisal of the literature. A review prepared for the UK Advisory Group on Chickenpox on behalf of the British Society for the Study of Infection. *J Infect*. 1998;36(suppl 1):25–29
46. Sauerbrei A, Wutzler P. The congenital varicella syndrome. *J Perinatol*. 2000;20(8 Pt 1):548–554
47. Pickering LK, Baker CJ, Kimberlin DW, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. Itasca, IL: American Academy of Pediatrics; 2012
48. Kakourou T, Theodoridou M, Mostrou G, Syriopoulou V, Papadogeorgaki H, Constantopoulos A. Herpes zoster in children. *J Am Acad Dermatol*. 1998;39(2 pt 1):207–210

49. Komorous JM, Wheeler CE, Briggaman RA, Caro I. Intrauterine herpes simplex infections. *Arch Dermatol*. 1977;113(7):918–922
50. Francis DP, Herrmann KL, MacMahon JR, Chavigny KH, Sanderlin KC. Nosocomial and maternally acquired herpesvirus hominis infections: a report of four fatal cases in neonates. *Am J Dis Child*. 1975;129(8):889–893
51. Wannamaker LW. Differences between streptococcal infections of the throat and of the skin. I. *N Engl J Med*. 1970;282(1):23–31
52. Zomorrodi A, Wald ER. Ecthyma gangrenosum: considerations in a previously healthy child. *Pediatr Infect Dis J*. 2002;21(12):1161–1164
53. Mull CC, Scarfone RJ, Conway D. Ecthyma gangrenosum as a manifestation of Pseudomonas sepsis in a previously healthy child. *Ann Emerg Med*. 2000;36(4):383–387
54. Ross EV, Cooke LM, Overstreet KA, Buttolph GD, Blair MA. Treatment of pseudofolliculitis barbae in very dark skin with a long pulse Nd:YAG laser. *J Natl Med Assoc*. 2002;94(10):888–893
55. Shwayder T, Akland T. Neonatal skin barrier: structure, function, and disorders. *Dermatol Ther*. 2005;18(2):87–103
56. Woodruff CA, Hebert AA. Neonatal primary cutaneous aspergillosis: case report and review of the literature. *Pediatr Dermatol*. 2002;19(5):439–444
57. Krallis N, Tzioras S, Giapros V, et al. Congenital candidiasis caused by different Candida species in a dizygotic pregnancy. *Pediatr Infect Dis J*. 2006;25(10):958–959
58. Chen C-J, Weng Y-H, Su L-H, Huang Y-C. Molecular evidence of congenital candidiasis associated with maternal candidal vaginitis. *Pediatr Infect Dis J*. 2006;25(7):655–656
59. Ito F, Okubo T, Yasuo T, et al. Premature delivery due to intrauterine Candida infection that caused neonatal congenital cutaneous candidiasis: a case report. *J Obstet Gynaecol Res*. 2013;39(1):341–343
60. Strong M, Johnstone P. Interventions for treating scabies. *Cochrane Database Syst Rev*. 2007;(3):CD000320. doi: 10.1002/14651858.CD000320.pub2 PubMed
61. Vanoni F, Lava SAG, Fossali EF, et al. Neonatal systemic lupus erythematosus syndrome: a comprehensive review. *Clin Rev Allergy Immunol*. 2017;53(3):469–476
62. Grana N. Langerhans cell histiocytosis. *Cancer Contr*. 2014;21(4):328–334
63. Monsereenusorn C, Rodriguez-Galindo C. Clinical characteristics and treatment of Langerhans cell histiocytosis. *Hematol Oncol Clin North Am*. 2015;29(5):853–873
64. Bas Suárez MP, López Brito J, Santana Reyes C, Gresa Muñoz M, Diaz Pulido R, Lodos Rojas JC. Congenital acute lymphoblastic leukemia: a two-case report and a review of the literature. *Eur J Pediatr*. 2011;170(4):531–534
65. Bresters D, Reus ACW, Veerman AJP, van Wering ER, van der Does-van den Berg A, Kaspers GJL. Congenital leukaemia: the Dutch experience and review of the literature. *Br J Haematol*. 2002;117(3):513–524
66. Mondì V, Piersigilli F, Salvatori G, Auriti C. The skin as an early expression of malignancies in the neonatal age: a review of the literature and a case series. *BioMed Res Int*. 2015;2015:809406
67. Mehta V, Balachandran C, Lonikar V. Blueberry muffin baby: a pictoral differential diagnosis. *Dermatol Online J*. 2008;14(2):8