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# Neonatal Dermatologic Challenges

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## IMPORTANT POINTS

1. The differential diagnosis of vesiculopustular rashes in the neonatal period is extensive, with more than 30 diverse, yet clinically similar, conditions. It is essential to separate the diseases into four basic categories: mild noninfectious and infectious diseases and potentially serious, life-threatening infectious and noninfectious processes.
2. Potentially life-threatening infections can have a banal clinical appearance, whereas self-limited dermatoses can be widespread and clinically dramatic. Signs and symptoms of systemic involvement should be noted and acted upon.
3. Various combinations of primary lesions (vesicles, bullae, and pustules) and secondary changes (erosions, ulcerations, and crusting) are seen. Because pathognomonic morphology or distribution of lesions often is not evident, laboratory testing is required to make the correct diagnosis.
4. Due to the heterogeneity of clinical findings seen with vesiculopustular rashes in the neonate, a detailed maternal, obstetric, and family history as well as a complete physical examination of the neonate are essential.
5. The potential negative consequences of initiating inappropriate therapy includes delayed diagnosis due to the creation of atypical presentations, spread of infectious agents, increased morbidity from prolonged illness, and toxicity created by invasive diagnostic tests and therapies.

## Introduction

Medicine is both an art and a science, and there is no more critical situation for the two to blend as in the evaluation of the newborn who has a vesiculopustular rash. Does the patient appear healthy or toxic? Life-threatening conditions can look innocuous, whereas self-limited rashes that do not need therapy can become generalized and appear dramatic! More than 30 conditions are included in the differential diagnosis, and there is no place for “shot-gun” approaches with their inherent dangers.

Signs and symptoms can be deceiving, or at the very least misleading. Primary lesions (vesicles, bullae, or pustules) often are hidden in a sea of secondary changes (erosions, ulcerations, or crusting). Classic presentations, such as grouped vesicular lesions of a herpes simplex infection, might not be apparent. It

is essential to be aware of the diverse range of possibilities to formulate an organized, comprehensive plan of attack.

Infections always should be considered first. If the initial evaluation (ie, special stains) does not yield the diagnosis and an infectious etiology is strongly suspected, appropriate therapy should be initiated pending the results of confirmatory tests. In many cases, a laboratory evaluation is essential to ferret out the correct diagnosis quickly.

Special testing (Tables 1 and 2), such as Gram stain; Tzanck (Giemsa/Wright); potassium hydroxide (KOH); and scabies preparations, cultures, and skin biopsies, are routine. Although expertise is needed to perform and interpret the special stains, a diagnosis can be made in a matter of minutes. Certain infections, such as herpes simplex, must have cultures taken within a critical time frame or false-negative results may be reported. In a confusing situation, skin biopsies should be considered and often can assure the diagnosis when the clinical picture is equivocal. Potential pitfalls with a skin biopsy include not choosing a repre-

sentative lesion to sample or not having a dermatopathologist read the slide. Newer and more sophisticated diagnostic tests are available (Table 3).

Polymerase chain reaction amplification (PCR) is a very sensitive test that detects viruses and other organisms that are either slow growing, difficult to grow, or not present in significant amounts to be identified. PCR methodology is extremely sensitive, with a quick turnaround time. In the neonate, organisms identified most commonly with PCR include herpes simplex virus (HSV), varicella, cytomegalovirus, *Chlamydia trachomatis*, and syphilis.

False-positive and false-negative results occur for all diagnostic procedures, and there will be particular confusion with overlap syndromes, such as transient neonatal pustular melanosis together with erythema toxicum neonatorum. When in doubt, a dermatology consultation is prudent. A dermatologist who likes to deal with children and has experience with neonates is preferable.

The history should not begin at parturition but at conception. The maternal, obstetrical, and family histories are all important. Does the mother have a history of any skin or mucous membrane diseases or infections? A history of genital herpes, vaginal yeast infection, venereal disease, drug abuse, or prostitution could point to an infectious etiology. Results of maternal serology for syphilis and human immunodeficiency virus (HIV) should be

**TABLE 1. Algorithm to Evaluate Primary or Secondary Lesions**

- Fluid: Gram stain, C+S plus herpes simplex virus culture or polymerase chain reaction
- Roof of lesion: KOH
- Base of lesion: Tzanck
- Scabies preparation
- Skin biopsy

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**TABLE 2. Common Laboratory Techniques for Vesicular and Pustular Lesions**

**KOH Stain for Fungi and Yeast**

- Place scales or skin scraping on glass slide and cover with coverslip
- Add KOH from side of coverslip to cover entire area
- Heat gently; do not boil
- Examine slide for pseudohyphae and spores

**Tzanck Preparation for:**

- White blood cell morphology of neonatal pustular disorders—eosinophils in erythema toxicum neonatorum, eosinophilic pustular folliculitis, and incontinentia pigmenti; neutrophils in transient neonatal pustular melanosis, acropustulosis of infancy, and candidiasis
- Acantholysis; pemphigus
- Multinucleated giant cells: herpes simplex, varicella/zoster
- Epidermal cell morphology: staphylococcal scalded skin syndrome and toxic epidermal necrolysis

**Giemsa Method**

- Place scraping of base of lesion on glass slide
- Air-dry slide
- Flood with methyl alcohol for 1 minute, then drain off alcohol and dry
- Add approximately 15 drops of Giemsa stain and leave for 1 min
- Add approximately 30 drops of water and continue staining
- Drain off and wash with water

**Wright Stain**

- Place scraping of base of lesion on glass slide
- Air-dry slide
- Add stain and leave for 3 min
- Add equal amount of water and leave for another 3 min
- Drain off and wash with water

**Gram Stain for Bacteria: Quick Method**

- Place fluid from lesion on glass slide
- Air-dry slide; then heat-fix by passing through flame once or twice
- Cover with gentian violet, then wash
- Cover with Gram's iodine, then wash
- Decolorize with 95% alcohol until no more gentian violet is extracted
- Cover with safranin; then wash

**Scabies Preparation**

- Gently scrape intact vesicles, papules, or burrows with a #15 blade coated with immersion oil\*
- Place on slide with a cover slip
- Scan on low power for mites, eggs, or stool

*\*Sample as many primary lesions as possible; the more lesions sampled, the greater the chance of having a positive scabies preparation.*

other family members have an itchy rash, it is essential to perform a scabies scraping on the patient who presents at 3 weeks with widespread papulovesicular lesions.

A comprehensive skin examination (head to toe) should be performed on every patient; to be complete, it includes checking of mucous membranes, hair, and nails. Try to identify primary lesions (vesicles, bullae, pustules), secondary changes (erosions, ulcerations), and secondary infection (bullae and honey-colored crusting of *Staphylococcus aureus* and *Streptococcus pyogenes*). Secondary infection is very common and can be overlooked easily. The time frame in terms of hours, days, or weeks after birth that the rash began, as well as the birth history, often are helpful in narrowing the differential diagnosis.

Our approach to classification of vesiculopustular eruptions is to employ four primary categories: noninfectious, usually benign; noninfectious, potentially serious; mildly infectious; and serious, potentially life-threatening infections (Tables 4–7).

**Noninfectious: Not Serious**

**NEONATAL ACNE**

Neonatal acne can be seen in up to 20% of newborns. It is characterized by the presence and predominance of follicular comedones (blocked hair follicles). Whiteheads are 1- to 3-mm skin-colored to whitish-typical acne location on the face (Fig. 1). Erythematous papules and pustules also can be found on the face, trunk, and proximal upper extremities.

The diagnosis is made by recognizing the primary lesions (comedones) and classic acne distribution on the face. Miliaria rubra, bacterial and yeast (*Pityrosporum*) infections, and seborrheic dermatitis should be considered in the differential diagnosis.

Typically, neonatal acne is self-limited, mild, and disappears within the first 6 months of life. Moderate-to-severe and persistent cases require therapy to prevent scarring.

known. Is there a history of primary bullous or autoimmune disease that could be passed transplacentally to the neonate?

In the obstetric history, was there any maternal illness, surgery, fever, or rashes? Intrauterine monitoring could be the source of infection such as HSV or create skin changes that

imitate aplasia cutis congenita. Was maternal fever, illness, or skin lesions present at the time of delivery?

A family history of chronic blistering suggests the diagnosis of epidermolysis bullosa. Siblings who have thick patches of dry skin and blistering could indicate epidermolytic hyperkeratosis. If several

**TABLE 3. Laboratory Tests Available to Diagnose Infectious Causes of Vesiculopustular Rashes in the Neonate**

INFECTIOUS	CONVENTIONAL CULTURE	SEROLOGIC	PCR*	OTHER
<b>Bacterial Infections</b>				
• <i>Chlamydia trachomatis</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
• <i>Escherichia coli</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
• <i>Haemophilus influenzae</i>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>
• <i>Klebsiella pneumoniae</i>	<input type="checkbox"/>			<input type="checkbox"/>
• <i>Listeria monocytogenes</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
• <i>Pseudomonas aeruginosa</i>	<input type="checkbox"/>			<input type="checkbox"/>
• <i>Staphylococcus aureus</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
• <i>Streptococcus</i> (group A and B beta-hemolytic)	<input type="checkbox"/>	A rapid group A strep screen is available	<input type="checkbox"/>	<input type="checkbox"/>
• Congenital syphilis		<input type="checkbox"/>	<input type="checkbox"/>	Dark field microscopy
• Scalded skin syndrome	<input type="checkbox"/>			Frozen section blister roof
<b>Fungal Infections</b>				
• Candidiasis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Histopathology
• <i>Aspergillus flavus</i>	<input type="checkbox"/>	<input type="checkbox"/>		Histopathology
<b>Viral Infections</b>				
• Herpes simplex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Tzanck preparation
• Fetal and neonatal varicella	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Tzanck preparation
• Cytomegalovirus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
• Enterovirus	<input type="checkbox"/>		<input type="checkbox"/>	

We want to thank Steven J. Melnick, MD, PhD, Miami, FL, for preparing this table.

\* Polymerase chain reaction.

Treatment of the neonate is topical, as with older patients, keeping in mind that the skin of infants is more



FIGURE 1. Neonatal acne (courtesy of Ron Hansen, MD).

susceptible to the irritant effects of topical anti-acne medications.

**BEST TEST:** Comedo extraction

**DIAGNOSTIC PEARL:** It looks like teenage acne

#### ACROPUSTULOSIS OF INFANCY (AI)

A history of severely pruritic vesiculopustular discrete and confluent acral lesions, recurring in crops every 2 to 4 weeks, is almost pathognomonic of AI. Seen in fewer than 1% of the population, there is a slightly increased incidence in African-American males. It begins any time from birth through the first year of life; remission usually occurs spontaneously within 1 to 2 years.

The 1- to 3-mm red papules change within a 24-hour period into papulovesicular and vesiculopustular lesions. Scaling, postinflammatory

hyperpigmentation, and signs of secondary infection commonly are encountered. Localized predominantly on the hands and feet, lesions also can be found elsewhere on the body (Figs. 2 and 3). The children often appear irritable and restless because of the severely pruritic nature of this dermatosis. Eosinophilia is common. The etiology and pathogenesis of AI are unknown. Antecedent scabies has been reported in some but not all cases.

To confirm a clinical impression of AI, special stains and a skin biopsy can be performed. The Gram stain, KOH, and Tzanck preparations typically show many neutrophils, some eosinophils, but no bacteria or yeast. It is important to rule out scabies with a negative scabies scraping.

**TABLE 4. Noninfectious:  
Not Serious**

• Acne—neonatal
• Acropustulosis of infancy (AI)
• Allergic contact dermatitis
• Eosinophilic pustular folliculitis (EPF)
• Erythema toxicum neonatorum (ETN)
• Miliaria crystallina, rubra, pustulosa
• Sucking blisters
• Transient neonatal pustular melanosis (TNPM)

**TABLE 5. Noninfectious:  
Potentially Serious**

• Acrodermatitis enteropathica
• Amniotic band syndrome
• Aplasia cutis congenita
• Bart syndrome
• Behçet disease
• Congenital erosive and vesicular dermatosis
• Congenital self-healing histiocytosis
• Ectodermal dysplasias
• Epidermolysis bullosa
• Epidermolytic hyperkeratosis
• Erythropoietic porphyria
• Herpes gestationis
• Hyperimmunoglobulin E syndrome
• Incontinentia pigmenti
• Mastocytosis
• Pemphigus vulgaris
• Perinatal and neonatal trauma
• Pustular psoriasis
• Transient bullous dermolysis
• Toxic epidermal necrolysis (TEN)

Symptomatic treatment with anti-histamines and low-potency topical steroids is the first approach. This regimen often is not adequate, however, and moderate-to-potent topical steroids may be used cautiously. Both local and systemic side effects can occur with the use of stronger steroid preparations. Toxicity also can be seen with long-term use of low-potency topical corticosteroids. Dapsone in a daily dose of 2 mg/kg has been used by others; however, we have never found that regimen to be necessary. In time, the disease runs its course.

**BEST TEST:** Tzanck preparation

**DIAGNOSTIC PEARL:** Recurrent acral neutrophilic pustules suggest AI

**ALLERGIC CONTACT DERMATITIS**

Uncommon, yet underdiagnosed, allergic contact dermatitis can be seen during the first month of life. A history of ear piercing (earlobe dermatitis) or well-circumscribed red areas under metal pajama snaps is strong evidence of nickel allergy. Other potential causes of allergic contact dermatitis in neonates include fragrances found in soaps and body lotions, rubber in the elastic of diaper products, or topical medications containing antihistamines or neomycin. Sensitization and dermatitis can occur in as few as 10 days.

The physical examination may show well-demarcated vesicular or vesiculobullous lesions on erythematous, edematous skin. HSV and staphylococcal infections should be ruled out. A clinical impression can be confirmed with a skin biopsy and patch testing. Allergic contact dermatitis is a type IV hypersensitivity reaction; it is important to be aware that these patients can have life-threatening, concomitant type I immediate reactions to the same allergens (ie, rubber).

Identifying the allergen by history or via patch testing and then avoiding the identified allergens will result in a cure within 1 to 2 weeks. Mild to mid-potency topical steroids and antihistamines can hasten the healing process.

**BEST TEST:** Patch test

**TABLE 6. Infectious:  
Mild**

• <i>Candida</i> —neonatal
• Impetigo neonatorum
• Scabies

**TABLE 7. Infectious:  
Serious**

**Bacterial**

- *Chlamydia trachomatis*
- *Escherichia coli*
- *Haemophilus influenzae*
- *Klebsiella pneumoniae*
- *Listeria monocytogenes*
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus* (sepsis, scalded skin syndrome)
- *Streptococcus* (group A and B beta-hemolytic)
- Syphilis—congenital

**Fungal**

- *Aspergillus flavus*
- Candidiasis—congenital\*

**Viral**

- Cytomegalovirus (CMV)
- Enteroviruses\*\*
- Fetal and neonatal varicella
- Herpes simplex

*\*In preterm or immunocompromised neonates.*

*\*\*Enteroviruses can cause vesicular lesions in older children and are a theoretic cause in neonates if other signs of enteroviral infection are present.*

**DIAGNOSTIC PEARL:** If ear lobe dermatitis, think nickel hypersensitivity

**EOSINOPHILIC PUSTULAR FOLLICULITIS (EPF)**

EPF rarely presents during the first month of life. The majority of reported cases are seen in male patients and begin any time from birth through the first year. Crops of pruritic, crusted, 1- to 3-mm papules, vesicles, and pustules on a red base recur every 2 to 4 weeks for 2 to 3 years, sometimes forming annular and circinate patterns. Located primarily on the scalp and



*FIGURE 2. Acropustulosis of infancy with recurrent crops of pruritic vesiculopustular lesions on the palms (courtesy of Ron Hansen, MD).*



*FIGURE 3. Typical AI lesions on the soles of the feet (courtesy of Ron Hansen, MD).*



*FIGURE 4. Eosinophilic pustular folliculitis with recurrent, pruritic, excoriated, vesiculopustular lesions on the face.*

face (Fig. 4), lesions also can be found on the trunk and extremities. The etiology is unknown. There are no signs and symptoms of systemic involvement other than recurring peripheral eosinophilia and leukocytosis, which are common.

Erythema toxicum neonatorum (ETN) is included in the differential diagnosis, and some authors feel that EPF may represent a persistent form of ETN. The two are easily separated by the evanescence of ETN and the recurrences and persistence of EPF. Staphylococcal infection, seborrheic dermatitis, miliaria rubra, and scabies also should be included in the differential diagnosis.

A Tzanck preparation, Gram stain, and KOH of a pustule will show eosinophils without bacteria or yeast. Variable improvement is possible with the use of topical steroids and systemic antibiotics. Erythromycin has been used more frequently with apparent (anecdotal) greater success than other antibiotics.

**BEST TEST:** Tzanck preparation

**DIAGNOSTIC PEARL:** Recurring crops of vesiculopustular lesions on the face and scalp

#### **ERYTHEMA TOXICUM NEONATORUM (ETN)**

Most macular, vesiculopustular rashes in the neonatal period should suggest this condition; it is seen in 20% to 60% of term infants weighing more than 2,500 g. Conversely, it is rare in preterm infants weighing

less than 2,500 g. Serious conditions also must be considered in a preterm infant who has the clinical appearance of ETN.

Classically, lesions ranging in size from a few millimeters to several centimeters begin within the first 24 to 72 hours of life. Combinations of erythematous macules, papules, wheals, vesicles, and pustules are seen (Fig. 5). The distinctive feature of ETN is the evanescent waxing and waning appearance of the rash. Individual lesions often disappear within 1 to 2 days, and the rash usually remits completely within 1 week. However, persistence of the process has been reported. The etiology and pathogenesis of this common dermatosis are unknown. Babies thrive, having no apparent systemic involvement other than occasional peripheral eosinophilia.

Transient neonatal pustular melanosis (TNPM) could confuse the diagnosis; some cases of typical clinical and laboratory TNPM coexist with ETN. Other conditions to be considered in the differential diagnosis include HSV and *S aureus* infections, congenital candidiasis, miliaria rubra, incontinentia pigmenti, and EPF. The Tzanck preparation shows eosinophils in ETN. Reassurance that the rash will soon fade is the only therapy needed.

**BEST TEST:** Tzanck preparation  
**DIAGNOSTIC PEARL:** If rash is evanescent and pustules are eosinophilic, think ETN

#### **MILIARIA**

Four types of miliaria are seen equally in male and female patients of all races: miliaria crystallina, miliaria rubra (prickly heat), miliaria pustulosa (a variant of miliaria rubra), and miliaria profunda. The incidence of miliaria is greatest in the first few weeks of life because a relative immaturity of the eccrine ducts favors closure of the pores and retention of sweat. Miliaria crystallina and rubra are the most common forms seen in the neonatal period. Excessive warming in incubators, fevers, occlusive clothing, dressings, or devices could be precipitating factors.

Myriads of 1- to 2-mm grouped, monomorphic, easily ruptured vesicles on otherwise normal appearing skin are typical of miliaria crystallina (Fig. 6). Diffuse scaling can be seen with older lesions. Miliaria rubra is characterized by discrete and confluent tiny, scaly, erythematous papules or papulovesicular lesions (Fig. 7). Miliaria pustulosa consists of distinct superficial pustules in a patient who has other lesions of miliaria rubra, and miliaria profunda represents deep blockage of pores. The distribution of lesions can be generalized, favoring intertriginous areas and skin covered by clothing. The diagnosis often is suggested by the typical clinical presentation, but scabies and folliculitis should be ruled out.

The most important aspect of treatment is to reverse the environ-



FIGURE 5. Evanescent rash seen with erythema toxicum neonatorum (ETN) (courtesy of Ron Hansen, MD).



FIGURE 6. Myriads of monomorphous-appearing clear vesicles seen with miliaria crystallina (courtesy of Ron Hansen, MD).



FIGURE 7. Miliaria rubra (courtesy of Ron Hansen, MD).

mental conditions that cause excessive sweating and occlusion. Air conditioning, cooling soaks, and baths should be curative.

**BEST TEST:** Clinical cooling. If in doubt, biopsy.

**DIAGNOSTIC PEARL:** History of high ambient temperature and humidity

#### SUCKING BLISTERS

Reportedly seen in 1 in 250 births, sucking blisters seem to us to be rarer. Bullae are found most commonly on the thumb, index finger, and dorsum of the dominant hand or wrist. Continued sucking causes the bullae to collapse and erosions to form. The lack of bullae elsewhere may help to rule out many potentially serious conditions.

Sucking blisters usually are diagnosed by clinical appearance in characteristic locations. The bullae disappear when the baby begins to feed.

**BEST TEST:** Hand sucking noticed on ultrasonography

**DIAGNOSTIC PEARL:** Self-limits with regular feeding

#### TRANSIENT NEONATAL PUSTULAR MELANOSIS (TNPM)

This is one of the vesiculopustular rashes in the neonate that has distinctive clinical features that allow separation from other dermatoses included in the differential diagnosis. These features include well-demarcated 2- to 3-mm hyper-

pigmented macules, in addition to pustular lesions of the same size (Fig. 8).

TNPM is a common condition seen in 2% to 5% of full-term African-American newborns and in fewer than 1% of full-term caucasian babies. Males and females are affected equally. At birth, lesions are seen at different stages of evolution, ranging in number from a solitary lesion to a florid distribution. Vesicles typically become pustules that rupture within a few days, leaving hyperpigmented well-circumscribed macules with a collarette of scale. This is followed by a purely macular hyperpigmentation that fades spontaneously within a few months. The vesiculopustular phase could be

entirely in utero, with only the final macular stage visible in the newborn. Babies appear healthy, with no signs of systemic toxicity. ETN, AI, miliaria rubra, and infectious processes should be included in the differential diagnosis. Congenital candidiasis and syphilis can have similar-appearing widespread lesions that also involve the palms and soles, as can be seen in TNPM. The Tzanck-preparation, Gram stain, and KOH will show a predominance of neutrophils without evidence of bacteria or yeast. Because the condition is asymptomatic and self-limited, therapy is not needed.

**BEST TEST:** Tzanck preparation  
**DIAGNOSTIC PEARL:** Pustules and brown macules present at birth



FIGURE 8. Classic dyschromia seen with transient neonatal pustular melanosis (TNPM) (courtesy of Ron Hansen, MD).



FIGURE 9. Linear lesions following Blaschko lines seen with incontinentia pigmenti (courtesy of Ron Hansen, MD).



FIGURE 10. Severe, potentially life-threatening bullae and erosions with epidermolysis bullosa (courtesy of Ron Hansen, MD).



FIGURE 11. Bullous mastocytosis.



FIGURE 12. Congenital candidiasis with nonspecific lesions in which KOH preparation is required (courtesy of Ron Hansen, MD).

### Noninfectious: Potentially Serious

Serious dermatoses rarely occur; however, red flags should go up in several situations. Characteristic clinical presentations, such as linear streaks of erythematous papules and vesicles, can be seen with incontinentia pigmenti (Fig. 9). The history should address whether other family members have lifelong debilitating widespread dermatoses. Bullae and erosions point to a diagnosis of epidermolysis bullosa (Fig. 10) or bullous ichthyosis.

Signs and symptoms of systemic illness also raise the possibility of serious disease. For example, sharply demarcated scaly plaques, vesicles, and bullae in a periorificial and acral distribution in conjunction with diarrhea and failure to thrive suggest acrodermatitis enteropathica, and a serum zinc level should be obtained. Serious developmental defects, such as hypoplasia of the skin, with hair and nail dystrophy and blistering, are seen with ectodermal dysplasia syndromes.

A rash that responds poorly to treatment also is of concern. Persistent erosions with scaly atrophic plaques that do not clear with topical steroids in conjunction with cardiac symptomatology point to a diagnosis of neonatal lupus erythematosus. If there is diffuse infiltration of the skin with erythema and bullae on physical examination, special stains should be performed so that mast

cells associated with bullous mastocytosis are not missed (Fig. 11).

Time is of the essence in these situations, and it is essential to be aware of the more serious noninfectious causes of vesiculopustular dermatosis that can present in neonates. Appropriate diagnostic procedures should be performed in a timely fashion, patients should be monitored for potentially life-threatening events, and specific therapies should be initiated. Consultations with other specialists often are advisable and should be based on symptomatology.

### Infectious: Mild

#### CANDIDIASIS

There are two forms of candidal infection in the neonatal period that affect males and females equally. Congenital candidiasis is an in utero acquired infection that is seen in fewer than 1% of newborns. Neonatal candidiasis, which is acquired by delivery through an infected birth canal, is seen in 4% to 5% of neonates. By definition, congenital lesions are present at birth, whereas neonatal disease usually begins after the first week of life. Commonly, there is a past or present maternal history of a vaginal yeast infection.

Congenital infection is characterized by pustular and vesiculopustular lesions that progress to a drying exfoliative stage and often clear

spontaneously within a few weeks (Fig. 12). The process can be mild, moderate, or severe, with lesions found anywhere, including the nails, oral mucosa (thrush), palms, and soles. The differential diagnosis includes bacterial infections, HSV, erythema toxicum, miliaria pustulosa, and TNPM.

The hallmark of neonatal disease is a vivid, beefy red, glazed, weeping dermatitis in the genital area. The lesions are well-demarcated, with raised borders, a collarette of scale, and erythematous papules and/or vesiculopustular satellite lesions at the periphery. Diseases that may simulate this presentation of neonatal candidiasis include seborrheic dermatitis, psoriasis, contact dermatitis, nonspecific intertrigo, acrodermatitis enteropathica, and Letterer-Siwe disease.

Both types of candidiasis can be diagnosed with a KOH preparation, which shows budding yeasts and pseudohyphae. A positive fungus culture demonstrates white mucoid growth, usually within 48 to 72 hours.

Topical therapy with anticandidal creams is indicated in most cases. Preparations that also contain strong topical steroids are contraindicated in intertriginous areas. The skin is extremely thin in these areas and vulnerable to local side effects such as atrophy, as well as systemic absorption with potential long-term serious side effects such as suppression of the HPA axis.

The prognosis is excellent for the majority of cases of congenital candidiasis, but systemic involvement must be considered in the following clinical situations: prematurity with low birthweight, respiratory distress, or pneumonia; sepsis; immunodeficient states (HIV); or previous treatment with broad-spectrum antibiotics.

**BEST TEST:** KOH

**DIAGNOSTIC PEARL:** When in doubt, KOH

### IMPETIGO NEONATORUM

At birth the skin is sterile. Organisms are acquired during delivery, from fomites, or from people. Up to 40% of newborns can be colonized with *S aureus*, not only in the anterior nares but also in the genital area. *S aureus* and, to a lesser degree, streptococcal species are the most common causes of uncomplicated superficial pyodermas. A carriage state can be a source of recurrent infection in the child or be responsible for infection in others. Conversely, hospital personnel or family members often are the cause of infection in the neonate.

Impetigo neonatorum can begin as early as the second or third day of life or any time within the neonatal period and is a very common cause of vesicles and pustules. The spectrum of disease provoked by exfoliative exotoxins ranges from bullous impetigo to the scalded skin syndrome. Organisms that do not produce exotoxins only form localized lesions. Lesions can be few or many and favor moist opposing sur-

faces (kissing lesions), such as the groin, axilla, neck, and umbilicus. The typical presentation is vesicles, pustules, and/or bullae on normal to erythematous skin (Fig. 13). Bullae are tense, rupture easily, and leave red, glazed, oozing areas. Spreading peripherally and clearing centrally, a collarette of scale and satellite lesions usually are evident. The classic honey-colored crusting may be present, as well as fever and adenopathy.

Gram stain shows Gram-positive cocci in clusters, with neutrophils. Culture and sensitivities are important guides to therapy because of the rapidly increasing emergence of methicillin-resistant and erythromycin-resistant strains of *S aureus*.

The differential diagnosis includes congenital candidiasis, ETN, and TNPM. If large bullae are present, primary bullous disorders should be considered.

When the disease is localized, mupirocin ointment can be used for treatment. However, because neonates are susceptible to developing widespread disease, systemic therapy usually is indicated. Strict isolation restrictions are important to prevent spread to others.

**BEST TEST:** Gram stain

**DIAGNOSTIC PEARL:** A glazed erosion with "cigarette paper" collarette of scale

### SCABIES

Often called the great imitator, scabies can be the easiest or most diffi-

cult diagnosis to make. When the diagnosis is missed, scabies can be spread rapidly to many people.

Neonatal scabies is possible because the incubation period is from 3 to 6 weeks. Children never are born with scabies, and a history of an itchy rash in hospital personnel or close family members is a very helpful clue.

In the neonatal period, scabies is characterized by a greater number of papulovesicular and nodular lesions, eczematization, and secondary infection, often with widespread distribution of lesions on the head, neck, scalp, palms, and soles (Figs. 14 and 15). When topical and systemic steroids are misused, much of the symptomatology improves, but the infectivity does not change, creating atypical presentations that have been referred to as "scabies incognito." Neonates can appear irritable or placid, feed poorly, and fail to thrive until proper therapy is initiated.

To make a definitive diagnosis, the female itch mite *Sarcoptes scabiei* eggs and/or stool should be identified in a scabies scraping. Mineral oil or KOH can be used to perform this test; we prefer mineral oil. The majority of the rash is a hypersensitivity reaction to the mites, which usually are found in relatively small numbers. Therefore, even with a negative scabies scraping, if there is a positive history and clinical picture, therapy should be initiated as soon as possible. Erythematous papules and burrows yield



FIGURE 13. Bullous impetigo.



FIGURE 14. Classic diffuse rash seen with scabies (courtesy of Ron Hansen, MD).



FIGURE 15. Scabies with scalp involvement is the norm in the neonate (courtesy of Ron Hansen, MD).

the greatest positive results when searching for evidence of infestation. The differential diagnosis of scabies includes AI, other mite infestations, impetigo, miliaria rubra, and serious bacterial infections.

With an apparent rise in the number of lindane-resistant cases and the potential for central nervous system toxicity (ie, seizures), permethrin 5% cream has become the treatment of choice. It has been approved by the Food and Drug Administration for use in children as young as 2 months of age, and it has been our experience that it is both safe and effective to use in the neonatal period. Secondary bacterial infection is common and should be looked for and treated.

**BEST TEST:** Scabies preparation

**DIAGNOSTIC PEARL:** An itchy family

### Infectious: Potentially Serious

Serious infections that can affect the neonate and create vesiculopustular or bullous lesions are divided into bacterial, fungal, and viral etiologies. Some rarely encountered, potentially life-threatening bacterial infections include *Listeria monocytogenes*, *Chlamydia trachomatis*, *Escherichia coli*, *Haemophilus influenzae*, *Pseudomonas* species, and syphilis. In certain situations congenital candidiasis can become disseminated. Viral infections that have potentially significant morbidity and mortality include cytomegalovirus, enteroviruses, HSV, and varicella.

An aggressive evaluation is indicated when there is evidence of serious systemic involvement, such as hyperthermia, hypothermia, irritability, failure to thrive, respiratory distress, meningeal signs, lethargy, history of maternal infections, maternal fever, or premature labor. Extreme prematurity, immunosuppressed states, or congenital abnormalities also predispose the neonate to serious infections. A classic presentation of a herpes simplex infection



**FIGURE 16.** Grouped vesicular lesions and widespread herpetiform ulcers in neonatal herpes simplex infection (courtesy of Ron Hansen, MD).

includes grouped vesicles, crusts, and erosions on erythematous skin (Fig. 16). Positive serology for syphilis should be sought in a sick neonate who has a clinical picture with bullous lesions on the palms and soles. As a general rule, infections should be considered first in neonates who present with vesiculopustular or bullous lesions.

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### PIR QUIZ

- The presence of eosinophils in a Tzanck preparation of a vesicular skin lesion from an infant is seen with:
  - Acne.
  - Erythema toxicum neonatorum.
  - Herpes simplex infection.
  - Impetigo.
  - Transient neonatal pustular melanosis.
- Erythema toxicum neonatorum and transient neonatal pustular melanosis share which one of the following features?
  - Evanescence that disappears in 1 to 2 days.
  - Lack of systemic symptoms.
  - More common in African-American infants.
  - Presence of hyperpigmented macules.
  - Tzanck preparation shows neutrophils.
- Which one of the following statements about scabies infection in infants is true?
  - The diagnosis should not be made if the scabies scraping is negative.
  - Eczematization and secondary infection are common.
  - Lesions do not clear with use of topical steroids.
  - Lesions may be present at birth.
  - The rash does not occur on the head or face.
- Neonatal candidiasis may be confused clinically with:
  - Acrodermatitis enteropathica.
  - Incontinentia pigmenti.
  - Miliaria rubra.
  - Neonatal acne.
  - Scabies.

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