An infant has a port-wine stain on the face. His parents are concerned about the appearance of the lesion and request advice about available treatments.

Of the following, the modality that offers the BEST cosmetic palliation is

1. cryosurgery
2. excision and grafting
3. pulsed dye laser
4. radiation therapy
5. systemic corticosteroid therapy

You selected 3, the correct answer is 3.

Port-wine stains (PWS) are permanent vascular malformations that are present at birth in 0.3% of infants. Lesions may occur anywhere on the body, but most often they are located on the face. Over time, PWS on the face darken, often develop vascular nodules that bleed, and may cause overgrowth of tissue. Several studies indicate, not surprisingly, that facial PWS frequently are a source of emotional distress.

Most experts agree that the treatment of choice for a patient who has significant facial PWS is therapy with a pulsed dye laser. The majority of children experience a reduction in the size of the PWS following treatment and a few will have complete resolution. Factors that affect the treatment outcome include the location and size of the lesion and the age at which therapy was begun. Treatment-related reductions in PWS size appear to be greatest when a lesion is located on the central forehead, followed in order by those on the peripheral face (e.g., lateral forehead, cheeks, temples, jaws and chin), central face (e.g., nose, upper lip, and fatty cheeks), and those that are mixed in location. Smaller lesions are more likely to diminish in size and become lighter after treatment than larger lesions. In one study, children who had lesions smaller than 20 cm² had a mean reduction in PWS size of 60%, and 32% achieved complete resolution. In contrast, children who had larger PWS had a mean size reduction of only 41%, and none had complete resolution. Finally, early treatment appears to be associated with the best outcome. When laser treatment was initiated during the first year of life, one group of investigators documented a mean PWS size reduction of 65% and complete resolution in 32% of treated infants. In contrast, those who began treatment between 2 and 6 years of age had a mean PWS size reduction of 54%, and only 17% achieved complete clearance.

Other treatment modalities, such as cryosurgery, radiation therapy, or excision and grafting, are not indicated for the child described in the vignette. Although systemic corticosteroids may be effective in the treatment of infants who have hemangiomas that threaten vital structures, they are of no value in the management of PWS.

References


Nguyen CM, Yohn JJ, Huff C, Weston WL, Morelli JG. Facial port wine stains in childhood: prediction of the rate of improvement as a function of the age of the
patient, size and location of the port wine stain and the number of treatments with the pulsed dye (585 nm) laser. Br J Dermatol. 1998;138:821-825


Content Specification(s)
Recognize, diagnose, and manage Port wine stain
An African-American newborn has pustules without surrounding erythema on the trunk and forehead and small (2 mm) hyperpigmented macules, some of which have peripheral scale.

Of the following, the MOST appropriate management is to

- administer acyclovir intravenously
- administer cephalexin orally
- advise no therapy
- apply mupirocin topically
- apply nystatin topically

You selected 4, the correct answer is 3.

One disorder that commonly affects African-American newborns is transient neonatal pustular melanosis, a condition of unknown cause that begins in utero. It is characterized by pustules and small (two to three mm) hyperpigmented macules that are present at birth. The macules have peripheral scale that represents the remnant of a pustule roof. Although the clinical diagnosis usually is straightforward, if there is uncertainty, a Gram or Wright stain of the pustule contents will reveal polymorphonuclear neutrophils without organisms. If indicated, a bacterial, viral, or fungal culture may be performed to exclude other causes. No treatment is required; pustules resolve within 5 days, with hyperpigmented macules persisting for up to 3 months.

A number of other disorders can produce pustules or vesicles in the neonatal period. Cutaneous herpes simplex virus infection is characterized by the presence of clustered vesicles on an erythematous base. Due to the risk of associated central nervous system or disseminated infection, affected infants merit careful evaluation and treatment with acyclovir parenterally. Folliculitis due to Staphylococcus aureus results in pustules that have a surrounding rim of erythema. Depending on the extent of infection, topical mupirocin, oral cephalaxin, or other appropriate antibiotic may be employed. Parenteral therapy is warranted if infants exhibit signs of bacterial sepsis. Cutaneous candidiasis causes diffuse scaling and erythema or erythematous papules and pustules. It may be present at birth (congenital) or appear days to weeks following delivery (acquired). Treatment with a topical antiyeast preparation (eg, nystatin) is indicated.

References:

Article

Content Specification(s):
Understand how to recognize, diagnose and manage hyperpigmentation, including Café au lait spots, Peutz-Jeghers syndrome, giant hairy nevus, incontinentia pigiamenti, and pigmented nevi
A newborn has a **violaceous patch** involving the face, including the upper and lower eyelids.

Of the following, the MOST likely associated finding is

- **1.** arrhythmias
- **2.** consumptive coagulopathy
- **3.** glaucoma
- **4.** polycystic kidney disease
- **5.** renovascular hypertension

You selected **4**, the correct answer is **3**.

The infant described in the vignette has a facial port-wine stain (PWS), a permanent vascular malformation that is present at birth in 0.3% of infants. Although a PWS may be located anywhere on the body and usually is an isolated finding, its presence on the face raises concern about Sturge-Weber syndrome (SWS). The risk of SWS is greatest if the PWS involves both the upper and lower eyelids (the distribution of the first and second branches, respectively, of the trigeminal nerve), is bilateral, or involves the distribution of all three branches of the trigeminal nerve, as seen in the figure.

In children who have SWS, the vascular malformation involves not only the skin, but the ipsilateral leptomeningeal vessels, particularly those in the parieto-occipital region. Altered blood flow in these vessels produces ischemia that, in turn, may cause seizures or contralateral hemiparesis. The vascular malformation also may involve the ipsilateral eye. Abnormalities of the episcleral vessels may lead to glaucoma; involvement of choroidal vessels may cause retinal detachment.

A number of disorders characterized by cutaneous abnormalities have associated systemic complications, but these do not occur in SWS. Children who have tuberous sclerosis may have cardiac rhabdomyomas (that may cause mechanical obstruction, heart failure, or arrhythmias) or hamartomas or multiple cysts of the kidneys (that may cause pain, hemorrhage, or renal failure). Kasabach-Merritt syndrome is characterized by a large, atypical hemangioma (actually a hemangioepithelioma) that may trap platelets and cause consumptive coagulopathy. Finally, renovascular hypertension may occur in individuals who have neurofibromatosis type 1.

**References:**


**Content specifications:**

- Know how to diagnose Port wine stain
- Know how to diagnose Sturge-Weber syndrome
A 3,800-g infant is born to a primiparous woman following a vertex vaginal delivery at 37 weeks of estimated gestational age. The obstetric history is significant for trapping of the fetal head in the maternal pelvis. The delivery is assisted with mid-forceps and vacuum extraction. On the second day after birth, the infant has an enlarging, fluctuant mass with bruised skin on the posterior aspect of the head.

Of the following, the MOST likely cause of the mass in this infant is:

1. caput succedaneum
2. cephalhematoma
3. epidural hemorrhage
4. subarachnoid hemorrhage
5. subgaleal hemorrhage

You selected 2, the correct answer is 5.

The clinical circumstances surrounding the birth of the large infant to the primiparous woman described in the vignette are conducive to birth trauma. Cranial hemorrhage due to birth trauma varies in location, progression, and clinical manifestations. The hemorrhage is classified as extracranial or intracranial based on the affected tissue plane between the skin and the brain. The extracranial hemorrhage includes caput succedaneum, cephalhematoma, and subgaleal hemorrhage. The intracranial hemorrhage includes epidural hemorrhage, subdural hematoma, and subarachnoid hemorrhage. The infant described in the vignette has clinical features that are consistent with the diagnosis of subgaleal hemorrhage.

Subgaleal hemorrhage refers to hemorrhage beneath the aponeurosis covering the scalp and connecting the frontal and occipital components of the occipito-frontalis muscle. Blood may spread beneath the entire scalp and into the subcutaneous tissue of the posterior neck. A subgaleal hematoma typically presents as a firm, fluctuant mass that initially increases in size after birth and resolves over 2 to 3 weeks. The hemorrhage is associated with vacuum extraction and is attributed to linear skull fracture, suture diastasis, or parietal bone fragmentation that often accompanies the hemorrhage. Management includes observation of the infant for blood loss, consumption coagulopathy, and hyperbilirubinemia.

Caput succedaneum refers to hemorrhagic edema of the skin and the subcutaneous tissue covering the presenting part of the head during vaginal delivery. The swelling is soft and pitting, crosses suture lines, and resolves without an initial increase in size over the first few days after birth. Blood loss and consumption coagulopathy are rare. Management involves expectant observation and monitoring of the infant for hyperbilirubinemia.

Cephalhematoma refers to hemorrhage in the plane between the bone and the periosteum on the outer surface of the skull. A cephalhematoma typically presents as a well-circumscribed, firm mass overlying the skull and confined by cranial sutures. The mass usually increases in size after birth before resolving over a few weeks. Calcification within the hematoma may result in a hard skull protuberance that may require months of skull growth and remodeling for resolution. Most cephalhematomas are unilateral and located over the parietal bone. The
hemorrhage is associated with forceps extraction and is attributed to shearing forces that separate the periosteum from the bone. An underlying linear skull fracture is detected in 10% to 25% of cases of cephalhematoma. No specific treatment is indicated other than observation and monitoring of the infant for blood loss, consumption coagulopathy, and hyperbilirubinemia. Rarely, a cephalhematoma may become infected, resulting in meningitis or osteomyelitis, which warrants treatment.

Epidural hemorrhage refers to hemorrhage in the plane between the bone and the periosteum on the inner surface of the skull. It represents the intracranial analog of a cephalhematoma, which is a frequent accompaniment. An epidural hematoma is not clinically evident as a mass because of its intracranial location. However, symptoms and signs of increased intracranial pressure, such as a bulging anterior fontanelle, may develop within the first few hours after birth. Seizures are common. Signs of uncal herniation, such as a fixed and dilated pupil on the ipsilateral side, may occur. The diagnosis is confirmed by demonstration of a convex, lentiform lesion on computed tomography. When accompanied by a linear skull fracture with overriding of the fracture segments, the epidural hemorrhage is attributed to tearing of branches of the middle meningeal artery or a large venous sinus. Although the hemorrhage most often resolves spontaneously, surgical evacuation may become necessary with the development of increased intracranial pressure or compression of the underlying brain. Medical management includes observation and monitoring of the infant for blood loss, consumption coagulopathy, and hyperbilirubinemia.

Subarachnoid hemorrhage refers to hemorrhage within the subarachnoid space between the arachnoid mater and the pia mater. It is termed primary subarachnoid hemorrhage when the hemorrhage is not due to extension from a subdural, intraparenchymal, or intraventricular hemorrhage. Moreover, the primary designation excludes subarachnoid blood resulting from a structural vascular lesion, such as an aneurysm or an arteriovenous malformation, tumor, coagulopathy, or hemorrhagic infarction. The clinical manifestations of primary subarachnoid hemorrhage are determined by the extent of the hemorrhage. In most cases that involve minor degrees of hemorrhage, infants exhibit minimal or no symptoms and signs. With moderate degrees of hemorrhage, infants have seizures that typically manifest on the second day after birth. These infants appear well and healthy in the interictal period. In rare cases of massive hemorrhage, the infants experience a catastrophic deterioration in clinical status and a rapidly fatal course. The suspicion of subarachnoid hemorrhage is raised by the findings of an elevated erythrocyte count and an elevated protein concentration in the cerebrospinal fluid. The diagnosis is confirmed by demonstration of increased attenuation located most prominently over the cerebral convexities and in the posterior fossa. The source of bleeding in primary subarachnoid hemorrhage is believed to be vascular channels derived from the involuting anastomoses between leptomeningeal arteries or bridging veins within the subarachnoid space. No specific treatment is indicated in most cases, especially those that have minor degrees of hemorrhage. In others, the treatment includes control of symptoms, such as seizures; monitoring for blood loss, consumption coagulopathy, and hyperbilirubinemia; and treatment of complications, such as posthemorrhagic hydrocephalus.

References:


Hartley JB, Burnett CW. An inquiry into the causation and characteristics of cephalohematoma. Br J Radiol. 1944;17:33


Content Specifications:

Understand the pathogenesis, clinical and radiographic features, diagnosis, management, and outcome associated with subarachnoid hemorrhage

Understand the diagnosis, clinical and radiographic features of extracranial hemorrhage, including cephalhematoma and subgaleal hemorrhage

Understand the management and outcomes of extracranial hemorrhage, including cephalhematoma and subgaleal hemorrhage
You are asked to see an infant who has a bilateral port wine stain (Figure 1) on the upper right side of the face. The parents request advice on removing the lesion.

Of the following, your BEST recommendation is

1. an explanation that there is no effective therapy
2. consecutive cryotherapy treatments
3. repeated dermabrasion treatments
4. sequential pulsed dye laser treatments
5. staged surgical excision

You selected 3, the correct answer is 1.

Port wine stain (PWS) (also called nevus flammeus (NF) or dermal capillary malformation or venulocapillary malformation) occurs among 0.3-0.5% of newborns in the United States. PWS is the most common type of vascular malformation. The name derives from the dark red color that develops as the lesions mature. PWS must be differentiated from nevus flammeus neonatorum which applies to telangiectatic areas on the glabella, nose, upper lip, eyelids and/or occipital area of the scalp. These lesions go by terms such as salmon patch, stork bite, angel kiss, nevus simplex, NF nuchae, medial telangiectatic nevus, and medial NF. These conditions occur more commonly, affecting 42% of white and 31% of black infants. With the exception of the occipital lesions, these lesions lighten and resolve in the first two years of life. In contrast, PWS grows commensurate with the child and shows no tendency to involute.

The vascular-specific (585-nm) pulsed (450-msec) dye laser (Figure 2) is the treatment of choice for port wine stains. The procedure is relatively painless when topical anesthetics are used, and adverse effects are minimal. The response of the lesions to treatment depends on the age of the patient at initiation of therapy and the size of the port wine stain. Treatment in the first year of life, beginning as early as the second week of life, may elicit a better response although some studies showed no benefit to very early treatment.

Younger patients who have small lesions are more likely to experience complete removal.

For patients who have facial port wine stains, the possibility of the Sturge-Weber syndrome should be considered. The Sturge-Weber syndrome (leptomeningeal angiomatosis) is the association of a PWS involving the facial portion (V-1 branch) of the trigeminal nerve with central nervous system vascular malformations involving the ipsilateral leptomeninges. Approximately 8% of port wine stains involving a unilateral V-1 (first branch of the trigeminal nerve) dermatome are associated with ocular or central nervous system involvement. The risk triples if the V-1 involvement is bilateral. Individuals with SWS may have involvement of the V-2 (maxillary) and/or V-3 (mandibular) branches, but involvement of V-2 or V-3 without V-1 involvement is not consistent with SWS. NF or PWS affecting an extremity (85% leg) with associated varicose veins and ipsilateral tissue hypertrophy occurs in the Klippel-Trenaunay syndrome. PWS may be seen also in Parkes-Weber, Cobb, and Wyburn-Mason syndromes.

Cryotherapy is inappropriate for the patient described in the vignette because of the recognized complications of postoperative pain, hypopigmentation, atrophic scarring, and inadvertent nerve injury. Both dermabrasion and surgical excision involve the inherent risk of significant scarring and infection. None of these treatments is appropriate for PWS.
References:


Content specification:

Know how to manage port wine stain
A 31-week-gestation African-American female infant is admitted from the delivery room for tachypnea and retractions. Physical examination is also remarkable for appropriate growth for gestational age and for widespread vesicles and pustules that involve the forehead, palms, and soles. No microcephaly, hepatosplenomegaly, or petechiae are present. The infant’s mother had a cerclage placed at the 19th week of pregnancy for premature cervical dilation. During the last three weeks, she also was treated for syphilis and chlamydia.

Of the following, the disorder MOST likely to cause this infant's skin manifestations is:

- congenital candidiasis
- congenital syphilis
- erythema toxicum
- infantile acropustulosis
- neonatal pustular melanosis

You selected 3, the correct answer is 1.

There are many causes for vesicles, pustules, and blisters of the skin in neonates. These vesiculopustular and blistering diseases may be infectious, transient, or uncommon congenital disorders (Table 1 and 2). These types of lesions on the palms and soles of infants at birth are relatively uncommon.

Congenital candidiasis is an uncommon condition acquired in utero or during delivery. Risk factors include cervical sutures (ie, cerclage), retained intrauterine device, prematurity, and maternal vaginal candidiasis. A generalized skin eruption may be present, in addition to systemic manifestations involving the blood, lung, meninges, and urinary tract. The skin lesions range from erythematous papules, diffuse erythema (especially in preterm infants), vesicopustules and bullae to a fine scaling rash. Most frequently, a fine erythematous papular rash presents and then evolves into a more pustular and scaly eruption. Any area of the skin may be involved including the palms and soles; this distribution differentiates the skin lesions from that of erythema toxicum and miliaria. Although congenital candidiasis is unusual, the rare presentation of infantile acropustulosis at birth makes congenital candidiasis more likely the cause for the skin lesions in the infant in the vignette. However, other diagnostic testing may be required to differentiate from intrauterine herpes simplex, pustular miliaria rubra, and neonatal pustular melanosis.

Congenital syphilis may present with blistering and ulcerations of the skin, although these skin lesions only occur in 3% of cases. Bullae, not vesicles or pustules as in the infant in the vignette, often are located on the palms, soles, knees, and abdomen. Furthermore, these bullae often are superimposed on dusky, hemorrhagic, or erythematous skin. Bullous lesions on the hands and feet at birth also may be due to congenital candidiasis, infantile acropustulosis and epidermolysis bullosa (Table 2). Additional testing may be required to make this differentiation.

Erythema toxicum is a common skin finding in neonates, with most cases involving term infants and presenting 24 to 48 hours after birth. Erythema toxicum may present with varying combinations of erythematous macules, wheals, papules, and pustules. Occasionally, vesicular lesions appear and subsequently become pustular. The face often is the first site where lesions are found; lesions also may be found on the trunk, buttocks, and proximal extremities. Erythema toxicum rarely appears at birth, in preterm infants, or on the palms and soles. It is
unlikely to cause the skin lesions in the infant in this vignette.

Infantile acropustulosis rarely is found at birth. The cause for this disorder is unknown. It presents as pruritic vesiculopustules on the hands and feet, usually during the first weeks and months after birth. Recurrent crops of lesions lasting 5 to 10 days characterize the disorder. The lesions evolve by flattening, developing scales, and leaving a hyperpigmented macule. Intense pruritus with irritability accompany the lesions. Infantile acropustulosis usually is not widespread and usually does not present at birth; it is unlikely to cause the skin disorder in the infant in the vignette.

Neonatal pustular melanosis is a relatively common skin disorder that presents at birth. Term infants usually are affected, and lesions are almost always present after birth. The skin lesions include pustules without underlying erythema, ruptured pustules with a surrounding collaret of scale, and hyperpigmented macules without scale. All of these lesions may be present at the same time. The lesions may be 1 mm to 10 mm in diameter, although most are 2 mm to 3 mm. Any site on the skin may be affected, including the palms and soles. Most common sites include the forehead, neck, back, and behind the ears. The infant in the vignette is preterm and does not have the mixture of lesions often found with neonatal pustular melanosis.

References:


Content Specifications:

Understand the etiology and differential diagnosis of bullous skin lesions

Understand the cutaneous and laboratory manifestations of congenital syphilis

Understand the cutaneous and laboratory manifestations of severe candidiasis

Know the etiology and cutaneous manifestations of nonpruritic skin lesions
### Table 1

**Vesiculopustular Diseases Presenting at Birth**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Skin morphology</th>
<th>Skin distribution</th>
<th>Clinical caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group B streptococcus</td>
<td>Vesicles, bullae, erosions, honey-crusted lesions</td>
<td>Any area</td>
<td>Pneumonia, bacteremia, meningitis</td>
</tr>
<tr>
<td><em>Haemophilus influenza</em></td>
<td>Vesicles, crusted areas</td>
<td>Any area</td>
<td>Bacteremia, meningitis</td>
</tr>
<tr>
<td>Congenital candidiasis</td>
<td>Erythema, small papules and pustules</td>
<td>Any area; palms and soles often involved</td>
<td>Prematurity, foreign body in cervix</td>
</tr>
<tr>
<td>Intrauterine herpes simplex</td>
<td>Vesicles, pustules, erosions, scars, areas of missing skin</td>
<td>Any area, often scalp</td>
<td>Low birthweight, microcephaly, chorioretinitis</td>
</tr>
<tr>
<td>Neonatal varicella</td>
<td>Vesicles on erythematous base</td>
<td>Generalized</td>
<td>Maternal primary varicella 7 days before to 2 days after delivery</td>
</tr>
<tr>
<td><strong>Transient skin lesions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythema toxicum neonatorum</td>
<td>Erythematous macules, papules, pustules, wheals</td>
<td>Any area except palms and soles</td>
<td>Term infants, unusual in preterm infants</td>
</tr>
<tr>
<td>Neonatal pustular melanosis</td>
<td>Pustules without erythema; collarettes of scale; hyperpigmented macules</td>
<td>Any area; often on forehead, ears, back, fingers and toes</td>
<td>Term infants, more common in black infants</td>
</tr>
<tr>
<td>Miliaria crystallina</td>
<td>Fragile vesicles without erythema</td>
<td>Forehead, upper trunk and arms</td>
<td>Occasional history of overwarming or fever</td>
</tr>
<tr>
<td><strong>Uncommon causes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infantile acropustulosis</td>
<td>Vesicles and pustules</td>
<td>Hands and feet, occasionally elsewhere</td>
<td>Pruritus, recurrent crops</td>
</tr>
<tr>
<td>Eosinophilic pustular folliculitis</td>
<td>Pustules</td>
<td>Scalp and face; occasionally trunk or extremities</td>
<td>Pruritus, recurrent crops</td>
</tr>
<tr>
<td>Congenital self-healing histiocytosis</td>
<td>Vesicles, crusts, papules, nodules, petechiae</td>
<td>Any area</td>
<td>Rarely mucosal or extracutaneous sites</td>
</tr>
<tr>
<td>Incontinentia pigmenti</td>
<td>Vesicles, hyperkeratosis in linear arrays</td>
<td>Trunk, scalp or extremities</td>
<td>Extracutaneous involvement of eye, teeth, nervous system, development</td>
</tr>
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Close
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<td>Group B streptococcus</td>
<td>Vesicles, bullae, erosions, honey-crusted lesions</td>
<td>Any area</td>
<td>Pneumonia, bacteremia, meningitis</td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>Bullae or erosions</td>
<td>Hands, feet and perioral</td>
<td>Lack of prenatal care, hepatosplenomegaly, bony lesions</td>
</tr>
<tr>
<td>Intrauterine herpes simplex</td>
<td>Vesicles, pustules, widespread erosions, scars, areas of missing skin</td>
<td>Any area, especially scalp</td>
<td>Low birthweight, microcephaly, chorioretinitis</td>
</tr>
<tr>
<td>Fetal varicella</td>
<td>Scarring, limb hypoplasia, erosions</td>
<td>Any area, especially extremities</td>
<td>Maternal varicella in first trimester</td>
</tr>
<tr>
<td><strong>Transient lesions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucking blisters</td>
<td>Flaccid bullae or linear erosion, occasionally 2 symmetric lesions</td>
<td>Fingers, wrists, occasionally foot</td>
<td></td>
</tr>
<tr>
<td>Perinatal trauma/iatrogenic</td>
<td>Erosions, ulcerations</td>
<td>Cause-specific</td>
<td>Perinatal history of monitoring, prolonged labor and/or vacuum or forceps delivery</td>
</tr>
<tr>
<td><strong>Uncommon causes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidermolysis bullosa</td>
<td>Bullae and skin fragility</td>
<td>Focal or widespread, often on hands, feet, other sites of friction or trauma</td>
<td>Pain, irritability and difficulty feeding; extracutaneous findings in eye, respiratory tract, or gastrointestinal system</td>
</tr>
<tr>
<td>Mastocytosis</td>
<td>Nodules with wheal or bullae, blisters</td>
<td>Focal or generalized</td>
<td>Hives, flushing, irritability, sudden pallor, diarrhea</td>
</tr>
<tr>
<td>Maternal bullous disease</td>
<td>Tense or flaccid bullae</td>
<td>Generalized</td>
<td>Maternal history of blistering disease</td>
</tr>
<tr>
<td>Intrauterine epidermal necrosis</td>
<td>Erosions and ulceration without vesicles or pustules</td>
<td>Generalized, mucus membranes spared</td>
<td>Prematurity, rapid mortality</td>
</tr>
<tr>
<td>Condition</td>
<td>Lesion</td>
<td>Distribution</td>
<td>Additional Features</td>
</tr>
<tr>
<td>------------------------------------------------</td>
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</tr>
<tr>
<td>Congenital erosive and vesicular dermatosis</td>
<td>Erosions, vesicles, crusts, erythematous areas</td>
<td>Generalized, usually sparing face, palms and soles</td>
<td>Prematurity, occasionally collodion membrane, transparent skin, reticulated vascular pattern</td>
</tr>
<tr>
<td>Restrictive dermopathy</td>
<td>Rigid, tense skin with erosions, linear ulcerations</td>
<td>Generalized</td>
<td>Joint contractures, micrognathia, natal teeth</td>
</tr>
<tr>
<td>Aplasia cutis congenita</td>
<td>Bullae or erosions</td>
<td>Scalp or face</td>
<td>Extracutaneous manifestations of the nervous system, chromosomes, limb-reduction abnormalities</td>
</tr>
<tr>
<td>Absent dermal ridges and congenital milia syndrome</td>
<td>Bullae</td>
<td>Fingers, soles</td>
<td>Absent dermal ridge patterns, multiple milia, autosomal dominant</td>
</tr>
</tbody>
</table>
An infant born at 35 weeks’ gestation, is transferred to your care. Striking physical examination findings include shiny, tight, thickened skin that is membranelike, with emerging cracks and moist fissures. The facial skin is taut and has pulled the mouth into an O shape, and the eyelids are everted. The hands and feet are edematous and have contractures (Figure 1).

Figure 1: Collodion baby with bilaterally everted eyelids (ectropion) and contracted lip (eclabion). Membrane is cracked in places, revealing moist erythematous skin.

Of the following, the MOST appropriate initial management for this newborn's skin is:

1. application of keratolytic agents
2. application of topical emollients
3. comfort care only, because this condition is lethal
4. manual débridement of the membrane
5. no therapy indicated, because spontaneous resolution expected

You selected 5, the correct answer is 2.
The infant in this vignette presents with features characteristic of the collodion baby. At birth, an oiled-parchment-like membrane of thick hyperkeratotic epidermis encases the infant, with underlying yellowish erythematous skin. Taut facial skin everts the eyelids (ectropion) and fixates the lip in an O shape or fish-mouth configuration (eclabium). Similarly, the nose is flattened, the pinnae are malformed, and hair may be absent or perforate the membrane (Figures 1 and 2).

Figure 1: Collodion baby with bilaterally everted eyelids (ectropion) and contracted lip (eclabion). Membrane is cracked in places, revealing moist erythematous skin.

Circumferential constriction results in peripheral edema and contractures of the hands and feet.

The term collodion baby describes a phenotype common to several disorders of cornification. Nearly two thirds of collodion babies have either classic lamellar ichthyosis or
nonbullous congenital ichthyosiform erythroderma. Less common disorders presenting with a collodion membrane include autosomal dominant lamellar ichthyosis, trichothiodystrophy, recessive X-linked ichthyosis, neonatal Gaucher's disease, neutral lipid storage disease, and Sjögren-Larsson syndrome (Table).

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Incidence</th>
<th>Inheritance</th>
<th>Mutation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamellar ichthyosis</td>
<td>1:300,000</td>
<td>Usually autosomal recessive</td>
<td>Transglutaminase I</td>
<td>Large, platelike scales</td>
</tr>
<tr>
<td>Nonbullous congenital ichthyosiform erythroderma</td>
<td>1:300,000</td>
<td>Autosomal recessive</td>
<td>Lipoxygenases</td>
<td>Fine, white scaling, overlying erythema</td>
</tr>
<tr>
<td>Recessive X-linked ichthyosis</td>
<td>1:6,000 males</td>
<td>X-linked recessive</td>
<td>Steroid sulfatase</td>
<td>Only 17% present at birth; accumulation of cholesterol sulfate may be measured in plasma</td>
</tr>
<tr>
<td>Neutral lipid storage disease (Dorfman-Chanarin syndrome)</td>
<td>Rare, less than 100 described cases</td>
<td>Autosomal recessive</td>
<td>Disruption of recycling of triacylglycerol to diacylglycerol</td>
<td>Lamellar ichthyosis phenotype; decreased sulfur content in hair</td>
</tr>
<tr>
<td>Trichothiodystrophy</td>
<td>Rare</td>
<td>Autosomal recessive</td>
<td>Unknown; decreased DNA repair levels</td>
<td>Lamellar ichthyosis phenotype; decreased sulfur content in hair</td>
</tr>
<tr>
<td>Gaucher's disease</td>
<td>1:100,000</td>
<td>Autosomal recessive</td>
<td>Lysosomal b-glucocerebrosidase</td>
<td>Hepatosplenomegaly and neurologic symptoms</td>
</tr>
<tr>
<td>Sjögren-Larsson syndrome</td>
<td>&lt;1:100,000</td>
<td>Autosomal recessive</td>
<td>Fatty aldehyde dehydrogenase</td>
<td>Only rarely presents as collodion baby; ichthyosis, mental deficiency, and spasticity</td>
</tr>
</tbody>
</table>
Harlequin ichthyosis, a rare (fewer than 100 described cases) and generally lethal form of congenital skin thickening, does not present with a collodion membrane.

Postnatally, the collodion membrane splits to reveal moist fissures and eventually peels off, though only to re-form in most cases. By several months after birth, the characteristic clinical features of the underlying skin disorder emerge and the diagnosis can be confirmed with skin biopsy. The membrane sheds, with apparently normal skin, in 5% of cases.

The molecular basis for many of the congenital ichthyosiform disorders is known and prenatal diagnosis with analysis of fetal DNA may be possible. In lamellar ichthyosis, mutations in the transglutaminase-1 gene on chromosome 14q11 account for 50% of the cases.

Fluid and electrolyte balance, thermoregulation, nutritional support, and infection prevention are key elements of the initial treatment of the collodion baby. Although markedly thickened, the stratum corneum is a poor barrier and allows excessive transcutaneous fluid and electrolyte loss to occur. The collodion baby has increased metabolic requirements and is at risk for hypernatremic dehydration. The eclabium interferes with the ability to suckle, and intravenous nutritional support is often initially needed. The risk of systemic infection is high and antibiotic coverage should be initiated at first suspicion. Temperature instability is managed with a humidified isolette, with care to avoid hyperpyrexia as well. Initially, pain may be considerable and the use of narcotic agents is indicated.

The shedding of the membrane occurs over the first month, and can be facilitated by the liberal application of topical emollients, which also retard water loss and soften the stratum corneum (Figure 3).

Manual débridement of scales should be avoided. The poor skin barrier of the collodion baby increases the risk of systemic toxicity with topical keratolytic agents such as salicylic acid and tretinoin, and their use in the newborn is discouraged. However, topical keratolytic agents, oral retinoids, and topical
Steroids are important in the long-term treatment of older infants and children. Over time, the ectropion and eclabium resolve, but artificial tears may be indicated to avoid corneal injury.

The long-term prognosis for the collodion baby is influenced by the underlying skin disorder. In the newborn period, with attention to thermoregulation, fluid management, and early treatment of infection, survival is the rule. Classic lamellar ichthyosis persists throughout the affected individual's lifetime as a severe and unremitting scaling skin disorder. Heat intolerance, due to obstructed sweat ducts by plates of scale, and cutaneous infections are common morbidities. Nonbullous congenital ichthyosiform erythroderma is similarly lifelong, but manifests with much milder symptoms.

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References:


American Board of Pediatrics Content Specification(s):

Know how to diagnose and manage ichthyosis
A 15-day-old male infant who had been born at 28 weeks' gestation developed several painful red macules and a hemorrhagic bulla on his right thigh. The macules varied in size from 1.5 to 3.0 cm in diameter. Within 12 hours, the macules vesiculated, some with hemorrhage, and ulcerated (Figures 1 and 2).

The skin surrounding the ulcers was bright pink. The ulcers then developed a necrotic, black, depressed appearance and the centers became encrusted. Culture specimens of the blood, urine, cerebrospinal fluid, and vesicles were obtained and broad-spectrum antibiotics were initiated. A biopsy of the ulcer showed a vasculitis with few inflammatory cells. Edema, hemorrhage, and necrosis were found surrounding the veins and some arteries. Bacteria were seen in the perivascular tissue and vessel walls. As the skin lesions evolved, the infant also developed shock requiring vigorous fluid resuscitation, mechanical ventilation, and vasopressor support.

Of the following, the organism MOST often associated with the skin lesions described for this infant is:

- Candida albicans
The skin of the newborn infant serves as a physical and immunologic barrier to invasion by infectious organisms. During and following birth, the infant is quickly colonized by organisms found on the cervix, vagina, and skin of caregivers. The initial colonization occurs on the umbilicus, genitalia, groin, and abdomen, and spreads rapidly to other surfaces and mucous membranes. The organisms most often found during initial colonization are *Staphylococcus epidermidis*, diphtheroids, and gram-negative enteric organisms. Subsequently, organisms present in the environment, such as *Staphylococcus aureus*, group B streptococci, and other gram-negative microbes, also appear.

The intact skin protects the infant from microbial invasion. The presence of vernix caseosa (shed epithelial cells, sebum, and hair) at birth and stratum corneum physically block movement of microbes into the deeper layers of the skin and blood vessels. Breach of skin barriers, as seen during phlebotomy or placement of intravascular catheters, facilitates microbial penetration.

The skin immune system is composed of cellular components (keratinocytes, antigen-presenting cells, monocytes, macrophages, granulocytes, mast cells, lymphocytes, and endothelial cells) and humeral components (antimicrobial peptides, complement proteins, immunoglobulins, cytokines, and prostaglandins). Langerhans cells are antigen-presenting cells unique to the skin. Microorganisms bind to Langerhans cells and are presented to cellular immune components for processing and killing.

Microbial infections of the skin may be manifest as a maculopapular rash, vesicles, pustules, bullae, abscesses, cellulitis, impetigo, erythema multiforme, and petechiae or purpura. Lesions characteristic of a single organism are unusual because each of the aforementioned manifestations of skin infections can be caused by several different microorganisms. An exception to this generality are the ecthyma gangrenosum lesions found in the infant in the vignette.

Ecthyma gangrenosum occurs in 2% to 6% of infections caused by *Pseudomonas aeruginosa*. Although *Pseudomonas* is the predominant cause for ecthyma gangrenosum, other organisms such as group B streptococcus, *Aeromonas hydrophilia*, *Enterobacter* species, *Escherichia coli*, *Proteus* species, *Pseudomonas cepacia*, *Serratia marcescens*, *Xanthomonas maltophilia*, *Aspergillus* species, mucorales, and *Candida albicans* have been infrequently associated with this lesion.

*Pseudomonas* infection often occurs in patients with suppressed immune systems. The organism may be spread hematogenously or by direct inoculation of the skin. As described for the infant in the vignette, the lesion usually begins as a painful red or purpuric macule that centrally vesiculates or becomes pustular. Bullae may also form. Surrounding tissues are pink or violaceous. The lesion quickly ulcerates, develops raised edges, and becomes necrotic in the center. A black, crusted eschar covers an erythematous base that microscopically is characterized by a vasculitis, especially the veins. The ecthyma gangrenosum lesions are caused by production of enzymes and proteases (especially elastase but also gelatinase, collagenase, lecithinase, neutral and alkaline protease, cytoxin, and phospholipase C), endotoxin, and exotoxins A and S. The lesions are characteristically devoid of inflammatory
cells. *Pseudomonas* organisms may be found in the adventitia and media of the dermal veins. Culture of the base of these lesions, not the exudate or eschar, is necessary to determine the microbial source of infection. The presence of ecthyma gangrenosum generally indicates treatment with anti-*Pseudomonas* antibiotic agents.

Skin lesions associated with *C. albicans* vary in presentation and include diffuse erythema with or without pustules (especially congenital and systemic candidiasis), diffuse maculopapular lesions, cutaneous abscesses at insertion sites of intravascular lines, confluent red and scaly plaques with adjacent red satellite lesions in skin creases of the groin, axilla, and neck, and rarely, as ecchymoses and necrosis (ecthyma gangrenosum). Crusting of lesions and desquamation may follow these presenting lesions. All body surfaces may be involved including the palms, soles, and face in the diffuse skin disorders (ie, congenital and systemic forms) caused by *C. albicans*.

Of note, congenital and local forms of candidiasis can be treated with topical agents alone (nystatin, gentian violet, natifine, terbinafine). Recurrent lesions may require oral fluconazole or itraconazole. If systemically ill, intravenous treatment with amphotericin B for 14 to 21 days may be needed. Intravenous fluconazole is also effective for *C. albicans* but other *Candida* species are often resistant; amphotericin B is the usual drug of choice for infections caused by non-*C. albicans* species. 5-Fluorocytosine, a pyrimidine antimetabolite that penetrates the blood brain barrier, acts synergistically with amphotericin B against fungal pathogens such as *Cryptococcus* and *Candida* species.

*Staphylococcus aureus* is a frequent cause for skin infections. Superficial infections (such as impetigo and bacterial folliculitis), cutaneous and subcutaneous abscesses (such as breast and scalp abscesses), nonnecrotizing subcutaneous infections (such as funisitis and omphalitis), necrotizing subcutaneous infections (such as necrotizing fasciitis), and toxin-mediated disorders (staphylococcal scalded skin syndrome) may be caused by *S. aureus*. Ecthyma gangrenosum is rarely caused by *S. aureus* and, when associated, it most often presents late in the course of necrotizing fasciitis.

Infection caused by *Streptococcus agalactiae*, or group B streptococcus, is rarely accompanied by skin manifestations. Cellulitis is the most frequently encountered skin disorder, occurs more often with late-onset disease, and has a predilection for facial and submandibular skin. Impetigo, cutaneous and subcutaneous abscesses, erythema nodosum–like lesions, necrotizing fasciitis, and purpura fulminans have been reported with group B streptococcus. Ecthyma gangrenosum is rarely caused by group B streptococcus.

*Treponema pallidum*, the spirochete that causes syphilis, is responsible for a wide variety of skin manifestations in congenitally infected infants. At birth, fewer than half of all infected infants have skin lesions. Lesions include papulosquamous plaques, erythematous macules, hemorrhagic vesicles and bullae (pemphigus syphiliticus), annular lesions, and polymorphous rashes. The palms, plantar surfaces of the feet, perioral skin, and anogenital region are common sites for lesions to be found. Snuffles (syphilitic rhinitis) may be the first sign of congenital syphilis and begins as a clear nasal discharge that becomes profuse, chronic, and hemorrhagic. Papules and plaques at the mucocutaneous junctions of the nose, mouth, and anus are highly infectious (condyloma lata) and, if chronic, lead to rhagades. Bullae resembling the early lesions that develop into ecthyma gangrenosum are infrequently found in infants with congenital syphilis. The bullae form on an erythematous base and after rupturing, maceration occurs, and a crusty exudate appears.

**References:**


**American Board of Pediatrics Content Specification(s):**

Understand the causes and differential diagnosis of infections of the skin and mucous membranes

Understand the clinical and laboratory features of infections of the skin and mucous membranes

Understand the clinical manifestations of group B streptococcal infections

Understand the clinical manifestation and diagnostic criteria of neonatal infections with *Staphylococcus aureus* and *Staphylococcus epidermidis*

Understand the clinical manifestations and diagnostic criteria of perinatal infections with *Treponema pallidum*

Understand the clinical manifestations of neonatal infections with *Candida*, coccidiodomycosis, cryptococcus, histoplasmosis, and *Malassezia*

Recognize the cutaneous and laboratory manifestations of congenital syphilis

Recognize the cutaneous and laboratory manifestations of severe candidiasis

Know the treatment of severe candidiasis

Know the etiology and cutaneous manifestations of nonpurpuric skin lesions
A term infant presents with a rash (Figure). He is clinically stable without cardiopulmonary distress. The infant was born after an uncomplicated pregnancy and labor. The family history is negative for bleeding disorders.

Of the following, the histopathologic finding that is MOST likely to be present in these skin lesions is:

1. extramedullary hematopoiesis
2. Langerhans cell histiocytes
3. mononuclear infiltrate
4. neuroblastoma cells
5. venous malformations

You selected 1, the correct answer is 1.

Blueberry muffin skin lesions in newborn infants, like those depicted in the infant in the vignette, are most often associated with extramedullary hematopoiesis. Histologically, the lesions consist of poorly circumscribed collections of nucleated and nonnucleated red blood cells, mostly confined to the dermis with extension into the subcutaneous tissue. Myeloid precursors may be present but are few in number.

Extramedullary hematopoiesis in skin lesions, or dermal erythropoiesis, is most commonly associated with infectious or hematologic disorders (Table).
Intrauterine anemia appears to be a common factor for some of the causes of dermal erythropoiesis. The skin lesions are frequently mistaken to be “hemorrhagic-purpuric” in nature when, in fact, they consist of erythroid progenitors and cells. The lesions typically are 2 to 7 mm in diameter with the larger being circular and raised 1 to 2 mm above skin level. The larger lesions may be firm and vary from dark blue to dark magenta. Smaller lesions are frequently macular, ranging in color from dark red to pale grey–purple to copper brown. The skin lesions fade over 3 to 6 weeks. Of interest, dermal erythropoiesis occurs normally in the undifferentiated mesenchyme of the skin until about the fifth fetal month. Thereafter, erythropoiesis in the dermis disappears.

Langerhans cells are unique to the skin and serve as dendritic cells that take up and present antigens (such as bacteria) to macrophages and other effector cells for destruction and disposal. Histologically, lesions consist of a dense dermal infiltrate of large histiocytic cells that have eosinophilic cytoplasm, kidney-shaped nuclei, and, on electron microscopy, Birbeck granules (pentalaminar layers of cell membranes that look like a tennis racket).

Langerhans cell histiocytosis has replaced the terms histiocytosis X, eosinophilic granuloma, Hand-Schuller-Christian disease, Letterer-Siwe disease, and congenital self-healing reticulohistiocytosis (Hashimoto Pritzker variant). Although a rare disorder in infants, the diagnosis is considered when more common causes for blueberry muffin skin lesions are absent. Skin lesions may be generalized, multiple, and, in 25% of cases, solitary. The skin lesions appear as 2- to 10-mm yellow to brown papules or nodules. The nodules may be pseudovesicular, involve central ulceration, and resemble neonatal blistering disorders. Skin lesions resolve spontaneously during the first weeks after birth in the congenital self-healing

Table. Blueberry Muffin Skin Lesions: Differential Diagnosis*

<table>
<thead>
<tr>
<th>Extra-remullary hemato/erythropoiesis</th>
<th>Infections</th>
<th>Congenital infections:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Toxoplasmosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Syphilis</td>
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<tr>
<td></td>
<td></td>
<td>Parvovirus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Coxsackie B2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rubella</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Herpes simplex virus</td>
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<tr>
<td></td>
<td></td>
<td>Sepsis</td>
</tr>
<tr>
<td></td>
<td>Hematologic disorders</td>
<td>Twin-twin transfusion syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fetomaternal hemorrhage</td>
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<tr>
<td></td>
<td></td>
<td>Intrauterine intracranial hemorrhage</td>
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<tr>
<td></td>
<td></td>
<td>Hemolytic disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hereditary spherocytosis</td>
</tr>
<tr>
<td></td>
<td>Glycogen storage diseases†</td>
<td>Gaucher disease type 2 (acute neuropathic form)</td>
</tr>
</tbody>
</table>

Neoplasia
- Congenital leukemia
- Solid tumor metastases
- Neuroblastoma
- Rhabdomyosarcoma

Histocytoses (Langerhans cell histiocytoses)
- Hemangioendotheliomatosis
- Multifocal lymphangioendotheliomatosis
- Blue rubber bleb nevus syndrome
- Glomangiomomas (glomerueneous malformations)

Vascular
- Hemangiomatosis

* Adapted from Holland and colleagues (2005).
† Personal communication, WA Engle, MD, August 15, 2007.
reticulohistiocytosis/Langerhans cell histiocytosis disorder that is frequently found in neonatal cases. Other lesions are erythematous and appear vascular, similar to lesions of hemangiomatosis and blue rubber bleb nevus syndrome. Langerhans cell histiocytosis also appears as eczematous or hemorrhagic scaling lesions. The prognosis with these disorders varies considerably from a self-limited disease to a life-threatening multisystem disorder.

Mononuclear infiltration of the skin characterizes infants with congenital monocytic leukemia. Congenital leukemia is the second most common malignancy during infancy (41 cases per million infants), second only to neuroblastoma (65 cases per million infants). Myelogenous leukemia is nine times more prevalent than lymphocytic leukemia. The lesion of leukemia cutis is characterized as a dense diffuse pleomorphic mononuclear cell infiltrate below an intact but atrophic overlying epidermis. Myeloperoxidase is present in myelogenous leukemic cells and is responsible for a green color when skin lesions are compressed. Multiple 2- to 50-mm firm, erythematous, violaceous to blue papules or nodules typify leukemia cutis with early lesions being macular. Although the face and neck are commonly involved, lesions may be generalized. Survival with congenital leukemia is 20% to 30% with the presence of chromosomal abnormalities of tumor cells indicating a particularly poor prognosis. Spontaneous remissions have also been reported, but relapse within weeks to 10 years may occur in more than half the cases.

Neuroblastoma originates from neural crest cells of the adrenal medulla and sympathetic ganglia. Histologic examination of skin lesions demonstrates uniform small neuroblastoma cells with hyperchromatic round nuclei, frequent rosettes, and numerous mitoses. Necrosis, calcification, and fibrovascular septa are also found.

Skin metastases in neuroblastoma are found in about one third of neonatal cases; this is 10 times more frequent than at other ages at presentation. Neonatal cases, on the other hand, rarely have bone marrow involvement. The skin lesions are usually firm, skin-colored, or bluish nodules. When compressed, the nodules blanch for 30 to 60 minutes because of the presence of catecholamines. Periorbital ecchymoses (“raccoon eyes”) and heterochromia irides from disruption of sympathetic innervations of the iris are unusual presentations that are indicative of neuroblastoma. The prognosis with neuroblastoma during infancy (5-year survival rate, 80%) is better than found at later presentations (5-year survival rate, 45%). The stage IV-S subgroup of neuroblastoma involves the liver, skin, and bone marrow; spontaneous remission is common and overall survival is greater than 90%.

Histologic examination may show venous malformations in the skin lesions of the blue rubber bleb nevus syndrome. Large irregular blood-filled vascular spaces that are lined by a thin layer of endothelial cells are found in the deep dermis and subcutis. This is a rare disorder in newborn infants but the abnormal vascular lesions often are present at the time of birth. The skin lesions have a variable morphologic appearance. The most characteristic lesion is a 1- to 50-mm dark blue-purple, soft, rubbery, easily compressible sac that wrinkles when compressed and refills when released (blue rubber nipple). Although lesions are generalized, the feet, other limbs, trunk, and face are most frequently involved. There may be hundreds of lesions in the skin. The gastrointestinal organs may be involved and bleeding may cause iron deficiency beginning in infancy. More severe bleeding may occur in the gastrointestinal and other involved organ systems (liver, spleen, thyroid, eyes, peritoneum, pleura, respiratory tract, muscle, bone, thymus, pancreas, retroperitoneum, genitourinary tract, parotid gland, and central nervous system). Chronic bleeding may require iron and blood replacement.

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References:


**American Board of Pediatrics Content Specification(s):**

- Identify the clinical and laboratory features of congenital leukemia
- Recognize the cutaneous and laboratory manifestations of CMV
- Recognize the cutaneous and laboratory manifestations of rubella
- Recognize the cutaneous and laboratory manifestations of Langerhans cell histiocytosis
- Know the etiology and cutaneous manifestations of nonpurpuric skin lesions
- Recognize the clinical and laboratory features of neuroblastoma in the newborn
March: Question 6

A 35-week-gestation female infant with symmetrical growth restriction is born via vaginal delivery to a 21-year-old woman with polyhydramnios. The infant has large bullous lesions over her hands, feet, and knees. Her nails are normal. She has areas of denuded skin on the abdominal and chest walls, several of which have atrophic bases with increased vascularity (Figure 1 and Figure 2).

The mother denies skin rashes or infections during her pregnancy, and no one in the family has a history of skin disorders. Vital signs are normal. A complete blood count is normal.

Of the following, the statement that MOST accurately relates to the family of skin disorders affecting this neonate is that:

1. Clinical features will establish the subtype and prognosis
2. Growth restriction is common among neonates with the dominant subtype
3. Mortality is more common among dominant subtypes
4. Oral mucosal involvement is an ominous prognostic sign
5. Pyloric atresia may occur in the recessive subtype of this disorder

You selected 5, the correct answer is 5.

Do you want to add anything to your Learning Plan?
(You must be an AAP member or PediaLink® Learning Center Subscriber to use this feature.)
Epidermolysis bullosa (EB) encompasses a heterogeneous group of dermatoses characterized by blistering of the skin and often, extracutaneous manifestations. EB is classified into three general categories: intraepidermal or simplex subtypes comprising 92% of cases, junctional subtypes comprising 1% of cases, and subepidermal or dystrophic subtypes comprising 5% of cases. About 2% of cases remain unclassified. All forms present with blisters after minor trauma and heat. Because the milder simplex type often goes unreported and is the most common form of EB, the exact incidence is unknown. The occurrence estimate from the National Epidermolysis Bullosa Registry is around 50 cases per 1 million births.

Subtypes of EB result from various inherited defects of the proteins that maintain skin integrity. Molecular genetic studies among EB variants have demonstrated mutations in at least 10 distinct genes that encode for eight structural proteins of the cutaneous basement membrane. These structural proteins form a link from the basal epithelial cells across the basement membrane to the underlying dermis. When one of these proteins is altered by a mutation, as in EB, weakness in the structural chain will lead to mechanical fragility. Clinical phenotypes vary according to the region within the skin where the defective protein is expressed and at the depth at which blistering occurs (Figure 3).

Recently a revised classification system for inherited EB was developed which reflects the molecular basis of EB as well as clinical, epidemiologic, and laboratory data (Table 1).
AD = autosomal dominant; AR = autosomal recessive; DEB = dystrophic epidermolysis bullosa; JEB = junctional epidermolysis bullosa; OMIM = Online Mendelian Inheritance in Man database.

Clinical features of EB may be quite variable in newborns. Extracutaneous involvement, due to the presence of structurally defective proteins in tissues other than the skin, occurs especially in patients with recessive forms of EB and adds to the variability in clinical expression. Special attention should be paid to determine if other organ systems are involved to establish the correct clinical diagnosis as well as to prevent potential complications. Sites of extracutaneous involvement most commonly seen in EB are the teeth, gastrointestinal tract, upper respiratory tract, genitourinary tract, eyes, and cardiovascular system (Table 1). Common gastrointestinal manifestations include dysphagia, esophageal stricture or stenosis, pyloric stenosis, and anal stricture. Neonates with a recessive subtype of junctional EB may present with polyhydramnios secondary to pyloric atresia.

Evaluation of a patient with suspected EB should include a mapping of the family pedigree and a skin biopsy. Light microscopy can help determine the level of the cleavage, but the results are often difficult to interpret. Electron microscopy, the gold standard for diagnosis, not only identifies the level of the skin cleavage, but also
the appearance of specific structures that form transmembrane attachment complexes. Immunofluorescent antigen mapping of three known basement membrane antigens may reveal type-specific patterns of binding in the microscopic clefts in EB skin. DNA mutation analysis helps to confirm the clinical and microscopically suspected diagnosis and is the basis for genetic counseling and first-trimester prenatal diagnosis.

Some subtypes of EB are severe and present with life-threatening diseases during the neonatal period. Others are mild and do not manifest symptoms until adolescence. Generally, recessive forms are more severe and at least one recessive subtype of dystrophic EB is associated with low birthweight. Growth restriction has not been reported in the dominant subtypes of the disorder.

Oral mucosal involvement is common among neonates with EB. Oral blistering occurs not only in severe forms of EB such as the recessive pyloric atresia-junctional EB that can be fatal in early infancy, but also in EB simplex, an autosomal dominant relatively mild form of EB. Although oral mucosal involvement does not infer a poor prognosis, it can present care management challenges; oral ulcers may render feeding painful and laborious.

There is no specific cure available for EB (Table 2).

Table 2

<table>
<thead>
<tr>
<th>Management Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minimize trauma to skin</strong></td>
</tr>
<tr>
<td>Handle gently</td>
</tr>
<tr>
<td>When applying instruments or monitors, use wrapping or suturing instead of taping if possible.</td>
</tr>
<tr>
<td><strong>Provide ideal (moist) wound healing environment</strong></td>
</tr>
<tr>
<td>Open and drain tense vesicles larger than a dime with sterile needle or blade, leave roof intact.</td>
</tr>
<tr>
<td>Perform gentle daily desbridement of crust.</td>
</tr>
<tr>
<td>Apply emollients and nonstick primary dressing.</td>
</tr>
<tr>
<td>Protect wound and secure primary dressing with secondary dressing such as gaze wrap.</td>
</tr>
<tr>
<td>Tape dressing to itself</td>
</tr>
<tr>
<td><strong>Prevent sepsis and bacterial superinfection of wounds</strong></td>
</tr>
<tr>
<td>Observe wounds for paresthesia.</td>
</tr>
<tr>
<td>Monitor colonization with weekly surveillance cultures.</td>
</tr>
<tr>
<td>Apply topical antibiotics combined with emollient on open erusions to control colonization.</td>
</tr>
<tr>
<td>Cover gram-positive organisms with intravenous antibiotics if signs or symptoms of sepsis are present.</td>
</tr>
<tr>
<td><strong>Maximize nutrition with minimal trauma</strong></td>
</tr>
<tr>
<td>Recommend breastfeeding if there is mild oral involvement and the infant can feed through pain.</td>
</tr>
<tr>
<td>If not, have mother pump breast milk, and bottle feed with high flow nipple or drip feeds.</td>
</tr>
<tr>
<td>Maximize calories.</td>
</tr>
<tr>
<td><strong>Monitor for extraneous complications</strong></td>
</tr>
<tr>
<td>Eye: Request ophthalmology consultation for redness or photophobia.</td>
</tr>
<tr>
<td>Gastrintestinal: If oral cavity is involved, watch for feeding intolerance.</td>
</tr>
<tr>
<td>Genitourinary: Look for gross hematuria, mental narrowing in boys.</td>
</tr>
<tr>
<td>Polyhydramnios: Look for pyloric stenosis.</td>
</tr>
<tr>
<td>Respiratory: Monitor severity for hoarse cry or stridor as a sign of laryngeal involvement.</td>
</tr>
<tr>
<td><strong>Provide psychosocial support</strong></td>
</tr>
<tr>
<td>Emphasize unpredictability of course even when subtype is known.</td>
</tr>
<tr>
<td>Discuss usual short-term complications in general terms.</td>
</tr>
<tr>
<td>Provide access to peer counseling through Internet sites and local chapters of national patient advocacy groups.</td>
</tr>
</tbody>
</table>

Adapted from Frieden and Howard (2001).

Treatment is directed at preventing skin trauma to avoid formation of new blisters, early management of secondary bacterial infections, support of wound healing, and maintenance of good nutrition. The primary preventive measure in caring for neonates with EB is avoidance of blister formation. Even minimal friction can produce blisters. After blisters have formed, the goal is to promote wound healing by protecting involved skin with nonadherent or petrolatum-impregnated dressings. It is often recommended to drain blisters that are larger than the size of a dime to prevent them from expanding. The blister roof should be left intact. Oozing or bleeding areas should be patted and never rubbed. Artificial skin substitutes can be helpful when applied to areas of skin that will not heal. Analgesia is often needed during dressing changes. Prevention of secondary bacterial infections is vital because sepsis is a leading cause of death in neonates with EB. Topical antibiotics should be applied to open skin surfaces and varied every few months to avoid development of resistance. Prophylactic oral antibiotics are not recommended.
References:


American Board of Pediatrics Content Specification(s):

- Recognize the cutaneous and laboratory manifestations of epidermolysis bullosa
- Understand the inheritance patterns of epidermolysis bullosa
- Know the treatment of epidermolysis bullosa
A mother feels a small neck mass in her 1-month-old infant. The infant's examination reveals a round, skin-colored, mobile, nontender, smooth preauricular swelling in the parotid region. You recommend complete excision to prevent potential complications.

Of the following, the MOST common complication of this neck mass is:

1. squamous cell carcinoma
2. fistula formation
3. hypoglossal nerve palsy
4. localized infection
5. osteomyelitis

You selected 1, the correct answer is 1.

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The child in this vignette has a neck mass that is most consistent with a branchial cleft cyst. Infection is the most common complication of branchial remnants and may develop at any time. This infection is typically localized and can lead to an abscess but does not involve adjacent bones. Squamous cell carcinomas have been reported in rare patients with branchial cleft cysts, but this does not present until adulthood. Cysts are typically isolated and do not lead to fistula formation. Hypoglossal nerve palsy is an unusual complication of branchial cysts that is caused by mechanical compression by the cyst.

Branchial cleft cysts, fistulas, and sinuses are embryonic remnants of the four pairs of branchial arches and their intervening clefts (Table).
In fish and amphibians, these structures are responsible for the formation of gills. Branchial cysts, sinuses, and fistulas consist of a tract with no, one, or two opening(s), respectively. While fistulas and sinuses are thought to arise from incomplete obliteration of branchial clefts and pouches during embryogenesis, branchial cysts are believed to arise from the cystic transformation of lymph nodes.

Although all branchial remnants are congenital, the small external openings of fistulas or sinuses are usually not apparent at birth. The cutaneous openings of these remnants may be evident by adjacent skin tags or cartilage remnants. More commonly, patients with fistulas and sinuses present with spontaneous mucoid drainage during infancy or childhood. Compression along the tract may yield further mucoid material exiting from the opening. A cordlike tract may be palpable by hyperextending the child's neck and tightening the skin.

Cysts developing from branchial structures are usually present along the anterior border of the sternocleidomastoid muscle. Although it was previously thought that left-sided cysts are more common than right-sided lesions, further studies have found that branchial cysts occur equally on either side of the neck. In contrast to branchial sinuses and fistulas, branchial cysts usually appear later in childhood and are more difficult to diagnose. Patients present with one of the following: (1) chronic purulent ear drainage; (2) preauricular swelling in the parotid region; or (3) abscess in the neck. Depending on the size and anatomic extension of the cyst, patients may have dysphagia, dysphonia, dyspnea, or stridor. Cysts may become tender during upper respiratory infections. A branchial cyst can resemble a dermoid or thyroglossal duct cyst, lymphatic nodule, cystic hygroma, or parotid lesion.

Complete excision of the branchial cyst, fistula, or sinus is recommended soon after the diagnosis is made, as long as there is no concurrent inflammation or infection. Inadequate resection is likely to result in recurrence. If the lesion is infected at the time of diagnosis, antibiotics and warm soaks are used to encourage spontaneous drainage of mucoid plugs before definitive excision. If these measures are unsuccessful, a limited incision and drainage procedure may be required to resolve the infection.

Do you want to add anything to your Learning Plan?
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References:


American Board of Pediatrics Content Specification(s):

Recognize the clinical manifestations of branchial cleft cysts
A full-term infant is born with a large, erythematous facial lesion in a beardlike distribution (Figure).

A cleft in the sternum and a supraumbilical raphe are discovered on physical examination.

Of the following, the diagnostic evaluation that RARELY uncovers an abnormality in this syndrome is:

1. echocardiography
2. magnetic resonance imaging of the brain
3. ophthalmology examination
4. renal ultrasonography
5. upper airway endoscopy

You selected 4, the correct answer is 1.

Infants with large, segmental plaquelike hemangiomas on the face, as in the infant in the vignette, may have PHACE syndrome. PHACE syndrome is a neurocutaneous syndrome defined by the presence of a large, segmental hemangioma in association with one or more congenital malformations involving structures of the posterior fossa, arterial and cerebral vasculature, cardiac anatomy, and eye. (Table.)
An 'S' may be added to the end of PHACE(S) because sternal clefting and supraumbilical raphe are commonly present. Generally the kidneys are not involved and few infants manifest the entire constellation of anomalies. Physical examination and imaging studies of the brain, cerebral vasculature, heart, and eye are most relevant to establish the diagnosis of PHACE syndrome. Because the kidneys are usually normal, renal ultrasonography is not likely to detect a structural abnormality.

PHACE syndrome is not rare; 20% of all facial hemangiomas and 2% to 3% of all hemangiomas are a part of the PHACE spectrum. Eighty percent of cases occur in females. Cervicofacial mandibular or "beard" distribution hemangiomas may involve the upper airway. Posterior fossa abnormalities may be associated with developmental delays, motor delays, and pituitary dysfunction. PHACE syndrome is more common than the rare, sporadic Sturge-Weber syndrome, another neurocutaneous syndrome that includes nevus flammeus of the face, unilateral angiomatosis of the meninges, and vascular abnormalities of the choroid of the eye.

Specific more common abnormalities by organ or site found in patients with PHACE syndrome are listed in the Table.

<table>
<thead>
<tr>
<th>Table. PHACE(S) Syndrome</th>
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| **Posterior fossa defects** | • Dandy-Walker complex  
• Cerebellar hypoplasia or atrophy  
• Dysgenesis/agenesis of the vermis |
| **Hemangioma** | • Segmental facial hemangiomas |
| **Arterial Anomalies** | • Aneurysm of the left subclavian artery  
• Atresia of the right carotid artery  
• Calcified cerebral aneurysms |
| **Cardiac Anomalies** | • Coarctation of the aorta  
• Complex aortic arch anomalies  
• Ventricular septal defects  
• Atrial septal defects  
• Tetralogy of Fallot |
| **Eye abnormalities** | • Microphthalmos  
• Retinal vascular abnormalities  
• Persistent fetal retinal vessels  
• Optic nerve atrophy  
• Iris hypoplasia or hypoplasia  
• Exophthalmos  
• Colobomas  
• Excavated optic disc anomalies |
| **Sternal cleft, supraumbilical raphe, or both** | • Ventral developmental defects (sternal clefting or supraumbilical raphe) |
References:


American Board of Pediatrics Content Specification(s):

Know how to diagnose hemangiomas
You are asked by a pediatrician to see a newborn with white skin (Figure 1). As you examine the infant in the mother's room, you see that both parents are black. You plan how you will tell the parents about the various hypopigmentation disorders and associated medical conditions.

Figure 1: An infant with a hypopigmentation disorder (from Kretchmer and Etzwiler [1958])

Of the following, the hypopigmentation disorder MOST associated with abnormal leukocyte function is:

1. albinism
2. Chediak-Higashi syndrome
3. phenylketonuria
4. tuberous sclerosis
5. Waardenburg syndrome

You selected 2, the correct answer is 2.

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Hypopigmentation in the neonate can be a clue to extracutaneous problems. Albinism is associated with eye abnormalities. Phenylketonuria is associated with central nervous system dysfunction. Tuberous sclerosis may present at birth with cardiac rhabdomyomas. Waardenburg syndrome includes hearing loss. The disorder most associated with abnormal leukocyte function is Chediak-Higashi syndrome.
Chediak-Higashi syndrome is an autosomal recessive disorder with an estimated incidence of 1 in 1,000,000 live births. In this disorder, a mutation in the \textit{LYST} gene on chromosome 1q42 results in a defective or absent lysosomal transport protein, which produces large lysosomal granules in myeloid cells (Figure 2).

\textbf{Figure 2: Large lysosomal granules in a leukocyte of a child with Chediak-Higashi syndrome (from Donohue and Bain [1957])}

Melanocytes are unable to release melanin to keratinocytes. Lysosomes are unable to supply enzymes to phagosomes, which result in decreased killing of microbes and an increased susceptibility to infections of the skin and the respiratory tract. Treatment of the infections is the mainstay of therapy. Most patients die in childhood. Successful bone marrow transplantation has been reported in a few cases.

Albinism comprises a group of mainly autosomal recessive disorders affecting the production of melanin. The incidence is 1 in 20,000 live births. A previous classification was based on the absence of tyrosinase ("complete albinism") or its presence ("partial albinism"). Tyrosinase-present albinism is thought to involve other proteins that transport tyrosinase or melanin. Specific genetic markers are now used to identify at least 10 different types of albinism, including a temperature-sensitive type.

Clinical features of complete albinism include white hair and skin, pink or red irides, photophobia, nystagmus, strabismus, and decreased visual acuity. There is a significant risk for cutaneous malignancies. Management is based on photoprotection such as sunscreen and protective clothing. Close follow-up by an ophthalmologist and a dermatologist is indicated.

Phenylketonuria is an autosomal recessive disorder with an incidence of 1 in 10,000 live births. Absence of phenylalanine hydroxylase (or its dysfunction because of an absent cofactor) results in high serum phenylalanine and low tyrosine concentrations. Low tyrosine production results in low or absent melanin production, and gives the infants light hair, blue eyes, and hypopigmented skin. Low concentration of tyrosine, as a precursor to dopamine and norepinephrine, is associated with hyperreflexia, seizures, and mental retardation. Management of phenylketonuria depends on life-long dietary control of phenylalanine intake, monitored with frequent serum phenylalanine measurements.

Tuberous sclerosis is an autosomal dominant disorder with variable penetrance caused by a defect in chromosome 9q34.3 coding for hamartin, or a defect in chromosome 16p13.3 coding for tuberin. Tuberous sclerosis has an estimated incidence of 1 in 10,000 to 1 in 100,000 live births, depending on how stringently it is defined. Case definitions are based on major and minor criteria and may include skin and nervous system abnormalities as well as hamartomas almost anywhere in the body. Newborns may show hypopigmented macules, from one to several centimeters in diameter, with regular or irregular margins. Having four or more macules is highly
suggestive of tuberous sclerosis; having fewer macules may be a variation of normal. Newborns may also show poliosis (a patch of hypopigmented hair). Shagreen patches, adenoma sebaceum, and ungual fibromas are not usually seen until later in childhood.

Noncutaneous manifestations of tuberous sclerosis may include cardiac rhabdomyomas, renal cysts or hamartomas, subependymal nodules or astrocytomas, and lymphangiomatosis. Management of tuberous sclerosis is largely centered on correction or control of any renal or central nervous system dysfunction. Intractable seizures and infantile spasms may require neurosurgical intervention.

Waardenburg syndrome is an autosomal dominant disorder with an incidence of 1 in 15,000 live births. It is seen in 1% to 2% of congenitally deaf children. Several types are described, but the most common are caused by mutations in the \textit{PAX} gene at 2q35 or the \textit{MITF} gene at 3p12.3-14.1. Characteristics of the syndrome may include dystopia canthorum (telecanthus), heterochromic or hypochromic irides, synophrys, poliosis, vitiligo (piebaldism), and a variable sensorineural hearing loss. The areas of local hypopigmentation are caused by defects in melanocyte proliferation and migration. Management focuses on early recognition of the hearing loss.

\textbf{Do you want to add anything to your Learning Plan?}
\textit{(You must be an AAP member or PediaLink® Learning Center Subscriber to use this feature.)}

\textbf{References:}


\textbf{American Board of Pediatrics Content Specification(s):}

Know how to manage hypopigmentation, including albinism, phenylketonuria, Chediak-Higashi syndrome, tuberous sclerosis, partial albinism, and Waardenburg syndrome

Recognize the clinical features of the Waardenburg syndrome
After an uncomplicated pregnancy, a 25-year-old woman delivers her first child at 39 weeks' gestation. The infant's birthweight, length, and head circumference are at the third percentile for gestational age. Palpable violaceous maculopapular lesions and petechiae are noted, particularly on the head, neck, and trunk (Figure).

**Figure**

Photograph courtesy of David A. Clark, NeoPix.

The abdomen is mildly distended with palpable hepatosplenomegaly. Laboratory analysis reveals thrombocytopenia. Intracerebral calcifications are noted on cranial ultrasonography.

Of the following, biopsy of the papular lesions is MOST likely to demonstrate:

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<tr>
<td>1</td>
<td>atypical lymphocytes</td>
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<td>3</td>
<td>intranuclear inclusions</td>
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<td>4</td>
<td>myelogenous infiltrates</td>
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<td>red blood cells</td>
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You selected **3**, the correct answer is **5**.
The infant in the vignette has findings consistent with severe congenital cytomegalovirus infection, including characteristic cutaneous lesions referred to as **blueberry muffin spots** (Figure). During the first 5 months of normal fetal development, extramedullary hematopoiesis occurs in several organs, including dermal mesenchyme. Conditions in the fetus causing anemia or suppression of bone marrow function increase extramedullary hematopoiesis. In the neonate, blueberry muffin lesions represent postnatal reexpression of dermal extramedullary hematopoiesis.

Clinically, blueberry muffin lesions are palpable, firm, nonblanchable round to oval papules, with an infiltrative quality that distinguishes them from petechiae. These violaceous skin lesions occur in a generalized distribution, but tend to concentrate on the head, neck, and trunk. Petechiae often coexist. Postnatally, the lesions may increase in size, and new lesions rarely appear. Typically, the lesions evolve into dark purple and then brown macules, and involute over a 2- to 6-week period.

In the prevaccination era, blueberry muffin lesions were most often attributable to congenital rubella, but currently are most commonly the result of congenital cytomegalovirus infection. The differential diagnosis of dermal erythropoiesis in the newborn includes other intrauterine infections (parvovirus B19 and coxsackievirus B2) and hematologic conditions associated with severe anemia, such as hemolytic disease of the newborn (rhesus and other blood group incompatibility), twin-transfusion syndrome, and hereditary spherocytosis. Fetomaternal and prenatal intracranial hemorrhage also have been reported as causes. Rarely, blueberry muffin lesions occur in otherwise healthy newborns.

Neoplastic infiltrative processes may cause blueberry muffin–like lesions, and include neuroblastoma, rhabdomyosarcoma, and Langerhans cell histiocytosis. These infiltrative lesions tend to be larger, fewer in number, less hemorrhagic, more nodular, and firmer to palpation than lesions of dermal erythropoiesis. **Leukemia cutis** refers to the colorless, or slightly purple blueberry muffin–like lesions that may be seen in up to 50% of infants with congenital monocytic leukemia.

Histopathologic examination of the papular lesions of dermal erythropoiesis (typical blueberry muffin lesion) demonstrates poorly circumscribed collections of nucleated and nonnucleated red blood cells and an occasional myeloid precursor. Atypical lymphocytes, concentrically arranged in a rosette formation, typify the dermal metastatic lesions of neuroblastoma. Collections of proliferated dendritic cells and macrophages (histiocytes) would be found in the cutaneous lesions associated with Langerhans histiocytosis. Intranuclear inclusions and massive enlargement of affected cells (cytomegaly) are characteristic of cytomegalovirus infection, but generally involve epithelial cells. Solid collections of myeloblasts constitute the lesions of leukemia cutis.

**References:**


American Board of Pediatrics Content Specification(s):

Recognize the cutaneous and laboratory manifestations of cytomegalovirus

Understand the clinical manifestations of perinatal infections with herpes 1, herpes 2, cytomegalovirus, Epstein-Barr virus, and varicella-zoster

Understand the clinical manifestations, diagnostic criteria, treatment and complications of perinatal infections with Rubella

Know the etiology and cutaneous manifestations of nonpurpuric skin lesions
A full-term 4.0-kg infant is delivered by a 25-year-old primiparous woman by means of a vacuum-assisted vaginal delivery. Four hours after delivery, the infant is noted to be pale with poor peripheral perfusion. Physical examination reveals the presence of a boggy, fluctuant swelling over the scalp extending from the hairline posteriorly to the orbits anteriorly. The head circumference of the infant has increased by 2 cm from the time of birth.

Of the following, the MOST likely site of hemorrhage in this infant, as shown in Figure 1, is:

![Figure 1]

Rosenberg, 2003, *NeoReviews*

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You selected **1**, the correct answer is **3**.
The infant in this vignette has a subgaleal hemorrhage. The clinical spectrum of traumatic birth injury to the head varies from minor to life-threatening, and includes extracranial hemorrhage, skull fracture, intracranial hemorrhage, and cerebral contusion.

The three major varieties of extracranial hemorrhage are caput succedaneum, cephalhematoma, and subgaleal hemorrhage. These lesions occur in different tissue planes between the skin and the cranial bone (Figure 2).

Figure 2

Rosenberg, 2003, NeoReviews

Caput succedaneum is localized scalp edema caused by local venous congestion from the pressure of the head applied to the dilating cervix. The edema is soft and superficial, crosses suture lines, and resolves during the first few postnatal days.

Cephalhematoma is a subperiosteal collection secondary to rupture of the bridging blood vessels between the skull and the periosteum. It presents as a firm, tense mass delineated by suture lines and may enlarge after birth. Because a small volume can accumulate in the subperiosteal space, its size is limited, and anemia and hypotension are rare complications. Cephalhematoma occurs in 1% to 2% of spontaneous vaginal deliveries, in 6% to 10% of vacuum extractions, and in 4% of forceps-assisted deliveries. Cephalhematoma most commonly occurs over the parietal bones, and is often unilateral.

Subgaleal hemorrhage refers to bleeding beneath the scalp in the subaponeurotic space which extends from the occiput to the eyebrows in the anterior-posterior direction and laterally to the insertion of the temporalis fascia. The hemorrhage results from traction on the scalp that shears the emissary veins between the scalp and intracranial venous sinuses. Underlying linear skull fracture or suture diastasis may also contribute to the hemorrhage. The most common risk factor is a vacuum or forceps extraction. These hemorrhages are characterized by boggy fluid collections beneath the scalp extending anteriorly to the eyes and posteriorly to the insertion of the trapezius muscles. The ears are pushed forward if the subgaleal hemorrhage is large. In contrast to caput succedaneum, this fluid collection increases in volume after birth. The infant's occipitofrontal circumference will increase 1 cm for every 40 mL of blood deposited in the subaponeurotic space. Infants with subgaleal hemorrhage can present early after birth with pallor, tachycardia, tachypnea, mottling, delayed capillary refill, hypotension, and hypotonia. Associated intracranial bleeding also has been reported. Acute blood loss and hypovolemia from subgaleal bleeding is a life-threatening emergency that requires immediate intervention.
Traumatic intracranial hemorrhages include epidural, subdural, subarachnoid, and less commonly, intraventricular, intracerebral, or intracerebellar hemorrhages. Epidural hemorrhage is a blood collection between a calvarial bone and its inner periosteum or between the periosteal membrane and the underlying dura. Linear skull fractures in the parietotemporal region are present in most cases. Irritability, lethargy, and seizures progress to signs of increased intracranial pressure (full fontanelle, hypertension, and bradycardia) and ultimately to unilateral pupil dilatation indicating uncal herniation. Diagnosis is confirmed if computed tomography shows a characteristic convex, lenslike appearance of the epidural blood collection. Hemorrhage over the cerebral convexities is the most common site of subdural bleeding and presents with focal or multifocal seizures and focal cerebral signs. In rare circumstances, the accumulation of blood can be large enough to increase intracranial pressure and lead to uncal herniation. Subarachnoid bleeding, if limited, may be asymptomatic; when the bleeding is more extensive, irritability and seizures alternate with normal interictal periods. Other less common sites of traumatic bleeding are intracerebellar, which presents with signs of brainstem compression, and intraventricular, which usually presents with seizures.

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References:


American Board of Pediatrics Content Specification(s):

Understand the diagnosis, clinical and radiographic features of extracranial hemorrhage, including cephalohematoma and subgaleal hemorrhage

Understand the management and outcomes of extracranial hemorrhage, including cephalohematoma and subgaleal hemorrhage
A male infant, born at 35 weeks’ gestation, presents at 10 weeks of age with a demarcated, erythematous, scaling eruption involving the periorificial region of the face (Figure).

Figure: Picture courtesy of Dean Morrell, MD, The University of North Carolina at Chapel Hill

His diet recently changed from breast milk to standard infant formula. Topical corticosteroids are prescribed. The infant returns the following week with persistence of the facial rash and new lesions involving the hands and anogenital region. Laboratory studies support a diagnosis of acrodermatitis enteropathica.

Of the following, the MOST accurate statement regarding acrodermatitis enteropathica is that:

1. Boys are affected more frequently than are girls
2. Breastfeeding delays the onset of symptoms
3. Serum alkaline phosphatase concentrations are increased
4. The underlying cause is dietary zinc deficiency
5. Treatment beyond infancy is not indicated

You selected 2, the correct answer is 2.
In humans, zinc is a tightly regulated trace element having catalytic, structural, and regulatory functions. Zinc is an essential component of the catalytic site of metalloenzymes, such as carbonic anhydrase, alkaline phosphatase, RNA polymerase, and alcohol dehydrogenase. Also, zinc is a structural component of gene regulatory proteins, facilitating protein folding and playing a key role in the formation and maintenance of tissues, including the skin. Zinc has regulatory properties as well, acting as an ionic signal in cells moving through gated membrane channels, and influencing gene expression by binding to transcription factors.

Cellular zinc homeostasis is regulated by zinc transporters from two gene families, ZnT and Zip. ZnT transporters reduce intracellular zinc and Zip transporters increase intracellular zinc. The primary site of zinc homeostasis is the enterocytes of the duodenum and jejunum, where low dietary zinc results in increased transporter expression and subsequent increased intestinal zinc absorption.

The infant in the vignette has an inherited disorder of zinc deficiency known as acrodermatitis enteropathica (AE). AE results from a defect in the gene, SLC39A4, which encodes for the Zip4 zinc transporter, leading to impaired intestinal absorption of zinc. The estimated worldwide incidence of AE is 1 per 500,000 infants. Boys and girls are equally affected, because the inheritance pattern is autosomal recessive.

Clinically, zinc deficiency dermatitis is characterized by acral and periorificial vesiculobullous, pustular, and eczematous eruptions. Initially the rash is localized around body orifices, symmetrically on the buttocks and the fingers and toes (acro dermatitis). Stomatitis, alopecia, and paronychial lesions may also be seen. Occasionally, diaper dermatitis occurs without facial involvement. Frequently, the lesions are secondarily infected with bacterial or candidal organisms. The infant with AE may be listless, anorectic, and apathetic, or quite irritable. Chronic diarrhea leads to failure to thrive. Untreated, AE results in general disability and death.

Acrodermatitis enteropathica typically presents in infancy. Formula-fed infants develop symptoms within the first 4 to 10 weeks after birth, when stores of zinc acquired during the third trimester of gestation are depleted. In contrast, the onset of symptoms in breastfed infants is delayed until days to weeks after weaning. This delayed onset of symptoms in breastfed infants is attributed to the presence of transport ligands in human milk, which aid in intestinal zinc absorption. Because preterm infants have high zinc requirements and insufficient body stores of zinc, AE may manifest despite breastfeeding.

The diagnosis of AE relies on clinical presentation, consistent laboratory findings, and response to treatment. A serum zinc concentration less than 50 μg/dL (7.6 μmol/L) is typical of AE. Zinc concentrations in erythrocytes and hair may also be measured, but values suggesting deficiency have not been well standardized. Body zinc status is reflected in the concentration of zinc-dependent enzymes. In states of zinc deficiency, low serum alkaline phosphatase concentration is a late and moderately sensitive indicator. Skin biopsy may be helpful, but the histopathologic features of AE are generally indistinguishable from dermatitis associated with nutritional deficiency.

Despite dysfunctional zinc transport at the level of the enterocyte, chronic zinc replacement is the mainstay of treatment for AE. In the presence of high dietary concentrations, adequate amounts of zinc are absorbed paracellularly. Oral zinc sulfate supplementation, starting at dosages of 3 mg/kg per day, leads to dramatic and rapid clinical improvement, but changes in serum zinc concentrations may take longer than days to weeks to normalize. Because zinc requirement changes with age and metabolic needs, serum zinc concentrations should be followed, and the dose of zinc supplementation adjusted accordingly. Lifelong zinc supplementation is indicated.

Dietary or acquired zinc deficiency manifests with dermatitis and symptoms indistinguishable from AE. Infants with increased zinc requirements and/or insufficient dietary concentrations of zinc are at risk. Such transient zinc deficiency most commonly occurs in premature infants who also experience increased urinary and intestinal zinc losses. However, both term and premature breastfed infants are at risk in the presence of impaired mammary zinc secretion.
and low zinc concentrations in maternal milk. Infants with malabsorptive syndromes or cystic fibrosis are also at risk of developing zinc deficiency dermatitis.

References:


American Board of Pediatrics Content Specification(s):

Understand the clinical manifestations and diagnosis of zinc deficiency

Understand the management and prevention of zinc deficiency

Know the cutaneous and laboratory manifestations of acrodermatitis enteropathica

Know the treatment of acrodermatitis enteropathica
The parents of a 2-month-old infant with a segmental hemangioma that is obscuring the eye (Figure 1) are worried about progression of the lesion despite 1 week of systemic corticosteroid treatment.

No other anomalies have been found. In collaboration with the infant’s family and a consulting pediatric dermatologist, you begin another treatment. The treatment is associated with mild wheezing that lasts 2 days. No cyanosis, feeding problems, or other abnormal findings occur and treatment is continued for 9 months.

Of the following, the treatment MOST likely to be associated with transient wheezing in this infant is:

- A. becaplermin
- B. imiquimod
- C. interferon alpha

Figure 1: Hemangioma in 2-month-old infant
Treatment for infantile hemangiomas that are life-threatening or compromise organ function is challenging because options that have been proven efficacious and safe are limited. In cases like the infant in this vignette whose visual development is being compromised by rapid growth of the hemangioma, timely intervention is necessary because progressive impairment of function is the anticipated natural course. About 10% of infantile hemangiomas require treatment.

The infant in this vignette showed a poor response to systemic corticosteroid treatment that was initiated during the proliferative stage of growth at 7 weeks of age. In 30% to 60% of cases, corticosteroids lead to an improvement within the first 2 to 3 weeks of treatment. Propranolol (2 mg/kg per day in three divided doses) was added after a week of corticosteroid treatment, with a significant response occurring within the first days of treatment. Propranolol accelerates the involution of the lesion and facilitates withdrawal of systemic corticosteroids, and it may prevent associated complications such as cushingoid facies, insomnia, irritability, growth failure, gastrointestinal symptoms, hypertension, and hypertrophic cardiomyopathy. A brief period of mild wheezing occurred in the infant in this vignette after starting propranolol; resolution was spontaneous. There was no evidence of hypotension, bradycardia, agitation, excessive sweating, hypoglycemia, or sleep disturbance. Such complications are generally mild, occur in about 30% of cases treated, but usually do not require stoppage of propranolol treatment. At 1 year of age (Figure 2), the hemangioma was reduced to cutaneous telangectasia; no anisometropia, astigmatism, or amblyopia was present.

**Figure 2:** Hemangioma before (A) and after treatment with corticosteroids, followed by propranolol (B-D). A, At age 2 months; B, 1 week after systemic corticosteroids and just before starting propranolol; C, 2 months after starting propranolol; D, 10 months after starting propranolol and after propranolol was stopped.
Propranolol has only recently been reported to be efficacious and safe in a small series of infants with hemangiomas that were life-threatening, at high risk for compromising function or organ development, complicated or associated with painful ulceration, or disfiguring. The mechanism of action of propranolol is unclear but may be related to inhibition of beta-adrenergic receptors with consequent interference of endothelial cell proliferation (by vascular endothelial growth factor and basic fibroblast growth factor) and induction of apoptosis of endothelial cells.

Sans and colleagues described 32 infants who received propranolol to control the growth phase (usually 3 to 6 months, rarely as long as 24 months) of severe hemangiomas. Thirteen of the patients received corticosteroids before propranolol was started. Within 1 to 2 days, all patients showed a change in color of the hemangioma from bright red to purple, softening of the lesions, and improvement in vital signs. By 7 days, cases complicated by ocular obstruction were markedly improved, and by 2 months, painful ulcerations were healed. After the initial rapid improvement phase, the hemangiomas progressively improved in size and color and the impairment or disfigurement decreased during the subsequent months. Mean duration of propranolol treatment was approximately 6 months in 15 cases. No relapse occurred in 10 of the cases. In the five cases that had a relapse after discontinuation of propranolol, four had mild recoloration, three had mild regrowth, and two patients received a second course of propranolol. At the time of the report, 17 patients were in the midst of propranolol treatment. Propranolol appears to be a promising treatment for severe infantile hemangiomas because of an apparent high efficacy rate and low risk of harm.

Becaplermin gel (0.01%), a synthetic form of platelet-derived growth factor, has been applied topically to ulcerated hemangiomas and found to speed healing in small case series. Becaplermin stimulates angiogenesis and theoretically could induce hemangioma growth;
this has not been reported to occur, probably because hemangiomas grow from vasculogenesis (formation of primitive blood vessels from angioblasts) rather than angiogenesis (formation of new vessels from existing blood vessels). Unlike adult diabetic patients treated with becaplermin, malignancy has not been reported in infants with hemangiomas treated with becaplermin. Ulceration in perineal hemangiomas is a treatment challenge. Case reports have described the healing of ulcers and indirect relief of the intense pain associated with such lesions after daily application in 3 to 21 days. Wheezing is not associated with topical becaplermin.

Imiquimod (5%) cream is an immune response modifier and, like becaplermin, has only been reported in case reports and a small, uncontrolled trial in the treatment of infantile hemangiomas. Safety has not been established. Antiangiogenic effects may be associated with activation of toll-like receptor 7 and increased local concentrations of interferon alpha and gamma. In a mouse model of vascular tumors, imiquimod reduced tumor cell proliferation, stimulated tumor apoptosis, increased tissue inhibitor of matrix metalloproteinase 1, and decreased matrix metalloproteinase 9. Similar changes in metalloproteinases have been found during the natural involution stage of infantile hemangiomas. Wheezing has not been reported to be associated with topical imiquimod.

Interferon alpha-2a inhibits endothelial cell migration and proliferation, partly by inhibiting growth factors such as endothelial growth factor and fibroblast growth factor. Subcutaneous interferon alpha-2a is effective at limiting or reversing hemangioma growth in infants, and is usually an option reserved for severe cases unresponsive to all other treatments. Onset of action is slower than with most other treatments. Safety concerns about irreversible spastic diplegia limit its widespread use. Acute complications include flulike symptoms, anemia, neutropenia, and elevated liver enzymes, but not wheezing.

Vincristine induces apoptosis of tumor and endothelial cells. Because of the risk of spastic diplegia with interferon alpha-2a, vincristine has been a second option in steroid-unresponsive infantile hemangiomas that are life-threatening, cause abnormal development or organ function, or are disfiguring. Intravenous dosing of 3 million units/m² per day has been recommended, with effects being noticeable weeks to months after initiation. Complications include peripheral neuropathy, constipation, jaw pain, leukopenia, and anemia, not bronchospasm.

**References:**


**American Board of Pediatrics Content Specification(s):**

13_Skin: Know how to diagnose and manage capillary and cavernous hemangiomas
October

In the past year, you have seen four infants with infantile hemangiomas (Figure). You are discussing infantile hemangiomas with the medical students.

Figure: Infantile hemangiomas. (From Sans and associates [2009].)

Of the following, the MOST accurate statement regarding infantile hemangiomas is that they are:

- A. a source of hyperthyroidism
- B. associated with thrombocytopenia
- C. differentiated by presence of a glucose transporter
- D. located most often on the trunk and extremities
E. multiple, diffuse and familial in occurrence

Correct

The Figure represents four examples of infantile hemangiomas, the most common vascular tumor of infancy. Infantile hemangiomas are found in about 10% of infants by 1 year of age, with girls being affected more than boys in a 2:1 to 5:1 ratio. The incidence in preterm infants is about 25%.

Infantile hemangiomas are benign vascular tumors composed of proliferating endothelial cells. The clinical course is characteristic with early proliferation and growth (6-10 months) followed by involution (6 months to 9 years). Most infantile hemangiomas are clinically insignificant but occasionally disfigure, impede function and organ development, ulcerate, bleed, cause pain, become infected, or cause high-output cardiac failure. Thrombocytopenia because of platelet sequestration (Kasabach-Merritt phenomenon) does not complicate infantile hemangiomas. Vascular tumors such as Kaposiform hemangioendotheliomas and tufted angiomas, however, are associated with the Kasabach-Merritt phenomenon.

Infants who develop hemangiomas are more frequently associated with placental abnormalities during gestation than infants without hemangiomas. Hemangiomas may be superficial (60% of cases), combined (25% of cases), or deep (15% of cases), with 80% affecting the head and neck. Shapes of hemangiomas are also described as tumorlike, focal and plaque-like, and segmental. Most hemangiomas are solitary, localized, and occur sporadically; familial and syndrome-associated cases are unusual. Multiple cutaneous hemangiomas (hemangiomatosis) are infrequent and associated with chorangioma of the placenta during pregnancy.

The pathophysiology of infantile hemangiomas continues to be elucidated. During the proliferative stage, plump endothelial cells initially are in disarray but in time form lobules of red blood cell–containing vascular spaces and channels characterized by thick multilaminated basement membranes. Evidence points to an intrinsic abnormality in endothelial cells of hemangiomas. Hemangioma endothelial cells most resemble those found in placental tissue and the similarity has prompted the hypothesis that the source of hemangioma endothelial cells is via embolization of placental endothelial cells. Although prominent in the literature, the placental endothelial cell embolization hypothesis is yet to be proven.

Whether occurring de novo or because of an inherited defect, it is likely that hemangioma endothelial cell abnormalities lead to dysregulated proliferative capacity or responses to angiogenic factors. During involution, apoptosis of endothelial cells occurs, and basement membranes are replaced by adipocytes and fibrous tissue. The proliferation-involution life cycle of hemangiomas follows the transition between endothelial cell proliferation and apoptosis during the first years after birth. Mast cells are present in hemangiomas and increase in number during involution. Mast cells may promote regression by changing the balance of angiogenic factors. Macrophages, fibroblasts, pericytes, and dendritic cells in hemangiomas also may influence the development and resolution of hemangiomas. Differentiation of hemangiomas from other vascular tumors is evident by the presence of the glucose transporter GLUT-1 in hemangiomas and absence in other vascular tumors.

Complications associated with hemangiomas lead to treatment in 10% to 20% of cases. Cellulitis and superficial infection of hemangiomas may be seen, although infrequently. The irregular structure of large hemangiomas predisposes the infant to local bacterial overgrowth. Hemangiomas, because they enlarge over time, may have a mass effect that invades locally and impairs function. When located around the mouth, eye, or nose or adjacent to extremities, hemangiomas may impair oral feeding, vision, breathing, or physical movement. Airway obstruction because of laryngeal hemangioma is particularly problematic in infants whose hemangiomas have a beardlike distribution. Excruciating pain often accompanies ulceration of hemangiomas. In the perianal area, hemangiomas that ulcerate often scar. Diffuse neonatal hemangiomatosis and congenital anomalies are infrequently found with hemangiomas. Hypothyroidism, caused by high activity of type 3 iodothyroinine
deiodinase (degrades thyroxine to reverse triiodothyronine in large hemangiomas, may go unrecognized and contribute to developmental disabilities. After the involution stage, excessive fatty and skin tissue may require surgical excision. Psychosocial problems for the child and parents may complicate the presence of hemangiomas or their sequelae.

**References:**


**American Board of Pediatrics Content Specification(s):**

13_Skin: Know how to diagnose and manage capillary and cavernous hemangiomas
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ASSESSMENT PROGRESS: Total Questions: 10  Questions Answered: 4  Correct Answers: 2

Question 4

You are called to the newborn nursery by a pediatric colleague to see a crying 1-day-old girl with epiphora. Your colleague tells you that the child was born at 42 weeks through thick meconium, but had no respiratory distress. Erythromycin ophthalmic ointment was administered after birth. During your examination of the child, you note excessive tearing from the right eye, clear conjunctivae, and a blinking rate of 20 per minute. The child's long fingernails are consistent with a postdates gestational age. Fluorescein staining of the right eye shows a lesion (Figure). No foreign body is found on eversion of either eyelid.

Figure: Corneal abrasion (arrow) revealed by fluorescein staining and Wood lamp illumination. The dye stains the damaged cornea. (American Academy of Pediatrics 2009 PREP Self-Assessment, question 211; courtesy of Wake Forest University Eye Center.)

Of the following, MOST appropriate treatment is:

- A. oral acyclovir
- B. oral analgesic
- C. tight patching of the eye
- D. topical anesthetic drops
- E. topical steroid drops

Incorrect:
The combination of epiphora, clear conjunctivae, an increased blinking rate, and a lesion on the cornea suggests a corneal abrasion, most likely caused by the child's long fingernails. Of the choices, the most appropriate treatment for a simple corneal abrasion is an oral analgesic. In addition, the child's fingernails should be filed to prevent further abrasions.

Oral acyclovir is not useful for treatment of simple corneal abrasion. Herpes keratitis shows a dendritic ulcer on fluorescein staining (see http://archive.student.bmj.com/issues/02/12/education/452.php), and is best treated with parenteral acyclovir and topical antiviral drugs. Tight patching of the eye does not hasten the healing process and is no longer recommended for simple corneal abrasions. Topical anesthetic drops may help during the eye examination, but may also slow recovery and cloak continued symptoms. Topical steroid drops may interfere with wound healing.

Epiphora, or excess tearing, can be caused by obstruction of lacrimal drainage, glaucoma, or corneal irritation. Infection may cause both corneal irritation and lacrimal duct obstruction.

The rate of eye blinking of a normal newborn is 2 to 4 per minute. The adult rate is 10 to 15 per minute but may go as low as 4 per minute when reading or when afflicted with Parkinson disease. Irritation or pain will increase the blinking rate, as in the vignette.

References:


McNaught A. The painful red eye. studentBMJ 2002;10:441-484

Related articles from NeoReviews.org


American Board of Pediatrics Content Specification(s):

17_EENT_mouth_neck: Know the causes and management of excess tearing
Question 3

A pediatrician e-mails you a digital photograph of a 1-day-old male infant. The infant, born after a normal pregnancy and vertex vaginal birth, has edema localized to the left foot and leg (Figure 1).

The infant’s mother reports that she also was born with swelling of her right foot and leg. Furthermore, this focal swelling has persisted throughout the mother’s adult life and become slightly more noticeable (Figure 2).
She has had several episodes of cellulitis in her right leg during the last several years. The mother, who is of normal stature, has an otherwise normal physical examination. Although the pediatrician reports that the physical examination findings of the infant’s heart, chest, thorax, and abdomen are normal, he questions whether an additional physical finding is associated with the infant’s condition.

Of the following, the MOST likely additional physical finding noted by the pediatrician is a (an):

- A. cleft palate
- B. cryptorchidism
- C. distichiasis
- D. hydrocele
- E. webbed neck

Incorrect: Correct Answer: D

The infant in the vignette most likely also has a hydrocele. Isolated peripheral limb edema, as found in the infant and mother in the vignette, is limited in most individuals by the balance between the hemodynamic forces along the capillary wall and the intact function of the lymphatic system. Capillary hydrostatic pressure favors movement out of the capillary and into the interstitium, and oncotic pressure inside the capillary favors retention of fluid within the vessel. Under normal conditions, a small amount of net fluid movement into the interstitium is seen. The lymphatic system returns this excess interstitial fluid to the venous system. In common edematous states caused by an increased venous pressure, hypoalbuminemia, or enhanced capillary permeability, the movement of fluid out of the capillary is increased. Although lymphatic flow can accommodate some excess interstitial fluid, it may not be able to remove all of it, resulting in edema. Patients with lymphedema, such as the neonate in the vignette and his mother, exhibit either impaired lymphatic transport because of lymphatic obliteration (secondary lymphedema) or lymphatic malformation (primary lymphedema). As a result, fluid normally
filtered from the capillaries cannot be returned to the circulation and accumulates in the interstitium.

Primary, or hereditary, lymphedema can occur as an autosomal dominant condition. Milroy disease is an autosomal dominant condition in which lymphedema is the only clinically apparent abnormality. Lymphedema also may occur as one manifestation of several complex genetic syndromes with autosomal dominant or recessive patterns of inheritance (Table).

**Table: Mendelian Disorders Affecting Lymphatics**

<table>
<thead>
<tr>
<th>Autosomal Dominant Disorders</th>
<th>Locus</th>
<th>Gene</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milroy disease</td>
<td>5q34-q35</td>
<td>VEGFR3</td>
<td>Congenital lymphedema of the legs</td>
</tr>
<tr>
<td>Lymphedema-distichiasis</td>
<td>16q24.3</td>
<td>FOXC2</td>
<td>Peripubertal onset</td>
</tr>
<tr>
<td>Lymphedema and yellow nails</td>
<td>—</td>
<td>FOXC2</td>
<td>Shares features with lymphedema distichiasis</td>
</tr>
<tr>
<td>Lymphedema, microcephaly,</td>
<td>—</td>
<td>—</td>
<td>Microcephaly with normal intelligence, congenital lymphedema, progressive visual impairment</td>
</tr>
<tr>
<td>and chorioretinopathy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intestinal lymphangiectasia</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Noonan syndrome</td>
<td>12q24.1</td>
<td>PTPN11</td>
<td>Lymphedema, pterygium colli, congenital heart defects</td>
</tr>
<tr>
<td>Cholestasis-lymphedema</td>
<td>15q</td>
<td>—</td>
<td>Recurrent cholestasis, lymphatic hypoplasia</td>
</tr>
<tr>
<td>syndrome (Aagenaes syndrome)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hennekam lymphangiectasia–</td>
<td>—</td>
<td>—</td>
<td>Protein-losing intestinal lymphangiectasia, abnormal facies, mental retardation</td>
</tr>
<tr>
<td>lymphedema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hereditary lymphedema</td>
<td>—</td>
<td>—</td>
<td>Not well defined</td>
</tr>
</tbody>
</table>

* Adapted from Ferrell (2002).

The infant and mother in the vignette have Milroy disease, a rare disorder characterized by hypoplasia or aplasia of the lymphatic vessels. The defect in most families with Milroy disease involves the gene located at 5q35.3, which encodes for the vascular endothelial growth factor receptor-3 (VEGFR-3). VEGFR-3 is expressed in the lymphatic endothelium and has an important role in lymphatic development. In humans, missense mutations of the VEGFR-3 prevent normal lymphatic growth.

In families with Milroy disease, lymphedema begins at an early age; in 96% of the cases, lymphedema is present at birth. Infants may have small upslanting, dysplastic nails and deep interphalangeal toe creases from intrauterine edema. Milroy disease is not associated with other major congenital anomalies or intellectual disability. At least 37% of males with Milroy disease have hydroceles. Milroy disease may affect one or both limbs, and progresses from a mild painless swelling to a large swollen extremity later in life. As the edema progresses, the skin becomes hyperkeratotic, the underlying tissue becomes fibrotic, and the risks for cellulitis and lymphatitis increase.

The onset of lymphedema is most commonly at or around puberty in lymphedema-distichiasis, an autosomal dominant syndrome. Individuals with the disorder have distichiasis, an extra row of eyelashes that arises abnormally from the meibomian glands. Lymphedema-distichiasis is associated with other congenital anomalies that may include congenital heart defects, pterygium, ptosis, cleft lip, or cleft palate. Lymphedema-distichiasis is caused by a mutation in the FOXC2 gene on chromosome 16q24.3. The mother’s physical examination did not reveal distichiasis. Because most patients with the FOXC2 mutation develop lymphedema around puberty, the additional physical finding noted by the pediatrician in the newborn in the vignette is not likely to be a cleft palate or distichiasis.

Lymphedema with ptosis and yellow nail syndrome are two rare autosomal dominant...
conditions that also have FOXC2 mutations. Some experts suggest that these rare entities are variants of the lymphedema distichiasis syndrome.

Patients with Noonan syndrome may have a webbed neck, facial abnormalities, cryptorchidism (60%-77%), congenital heart defects such as pulmonary stenosis (50%-60%), and a shield chest with a pectus excavatum or pectus carinatum. Noonan syndrome is inherited in an autosomal dominant fashion, but 60% of cases are sporadic. Mutations in PTPN11, a gene encoding the nonreceptor protein tyrosine phosphate SHP-2, are responsible for some cases. Lymphedema is a variable component of Noonan syndrome (20% of cases) and can be diagnosed any time from the perinatal period through adulthood. At least one author has suggested that edema from dysplastic lymphatic vessels may play a causative role in the Noonan phenotype by disrupting cell migration or organ placement during development. Peripheral lymphedema, which may present at birth, usually resolves with time, but can recur throughout childhood. Because the infant’s thorax examination findings are normal, he has no findings to suggest pulmonary stenosis, and his mother has no findings suggestive of Noonan syndrome, it is unlikely the infant would have Noonan syndrome.

References:


American Board of Pediatrics Content Specification(s):

05_Genetics_Dysmorphism: Differentiate between a malformation, a deformation, and a disruption

05_Genetics_Dysmorphism: Know the components of a complete family history for genetic disorders

05_Genetics_Dysmorphism: Recognize the clinical features and know how to diagnose and manage congenital anomalies of the lower extremities, such as metatarsus adductus, talipes equinovarus, syndactyly, polydactyly, limb reduction
An infant has a progressively enlarging, soft mass just to the right of the nasal bridge extending into the medial aspect of the orbit. Noted shortly after birth, at that time it was diagnosed to be a capillary hemangioma. No intracranial brain anomalies or vascular malformations were noted. Because the lesion was small, no treatment was begun. Progressive enlargement led to the initiation of oral corticosteroid treatment at age 3 months, with no slowing of the lesion's growth during the following month. Now at 4 months' age, the lesion is beginning to encroach upon the eye (Figure 1).

**Figure 1**: Infant with infantile hemangioma (Reprinted with permission from AAP News. March 2010.)

Of the following, the treatment MOST effective for reversing the lesion's further growth is:

- A. higher dose of corticosteroid
- B. intravenous vincristine
- C. oral propranolol
- D. subcutaneous interferon
- E. topical timolol

Infantile hemangiomata (IH) occur in about 5% to 10% of otherwise healthy infants. Lesions are more commonly noted among white infants than darker pigmented children, and are associated with preterm birth (15% incidence of IH), advanced maternal age, multiple gestation, and female sex. Most are not associated with other syndromes. Although changes in vascular signaling in affected areas begins as early as 8 to 10 weeks gestation, most lesions are not clinically evident until about 4 weeks after birth (longer among premature infants). Their natural history is one of increasing growth velocity (for about 6 months), after which reduction and cessation in growth velocity are followed by transient stabilization and subsequent gradual involution. The entire process may take up to 10 years. Among infants having an enlarging orbital lesion in spite of systemic corticosteroid treatment, of the options...
presented, oral propranolol offers the greatest likelihood of safely inhibiting growth and initiating involution.

Because of their eventual spontaneous resolution, many infants having IH are treated expectantly, especially if the lesions are not likely to be subjected to trauma or affect important organ functions. In approximately 10% of patients, the size, position, rate of growth, local ulceration, or psychosocial effects indicate a need for treatment. As used in the infant in the vignette, oral corticosteroids have been the standard initial systemic treatment for rapidly growing IH. Although oral corticosteroid treatment is effective in stopping the growth of IH, the lesion is noted to shrink in only one third of cases. For superficial lesions, the use of a topical gel, timolol maleate, a nonselective beta-blocker, has been reported to be successful. This topical alternative has been applied to superficial, accessible lesions, and thus would not be the next best treatment option for the infant in the vignette. Topical timolol has been successfully used among patients with visual obstruction because of IH lesions affecting the eyelid.

For cases in which progressive IH growth persists despite oral corticosteroid treatment, recent studies show oral propranolol to be effective in stopping growth and decreasing tumor mass. Side effects such as bradycardia, hypoglycemia, and asthma exacerbation are infrequent, but can occur. Thus, for the infant in the vignette, oral propranolol offers a potentially effective treatment to avert visual complications from orbital expansion of the lesion. This is an off-label use of the drug, and as such, its use should be carefully considered with monitoring of both therapeutic efficacy and side effects.

What makes propranolol the best treatment for this infant among the choices listed? The relationship between propranolol administration and rapid onset of resolution of IH was first suspected by a group of French cardiologists, who were using propranolol to treat infants with cardiac disorders. They noted a prompt change in IH lesions, with softening and lightening, often within 24 hours of starting propranolol. A subsequent study by the same group demonstrated a similar rapid response among all 9 patients evaluated in a noncontrolled study. Subsequent investigations have confirmed dramatic responsiveness. Infants included in the propranolol case series usually had IH lesions associated with a high risk for visual, hemodynamic or respiratory compromise or ulceration.

Propranolol’s mechanism of action on IH is under investigation but appears related to the combined effects of vasoconstriction, decrease in expression of vascular endothelial growth and basic fibroblast growth factors and apoptosis of capillary endothelial cells.

Dermatologists experienced with propranolol often begin dosing at 2 to 3 mg/kg per day (three doses per day, no closer than 6 hours apart). Although some case studies to date have demonstrated few side effects, propranolol is reported to produce bradycardia, low blood pressure, bronchospasm, or hypoglycemia in some instances. Monitoring for hypotension, bradycardia, and hypoglycemia is recommended following initiation of treatment or dosage changes. More detailed cardiovascular monitoring is performed in some centers. Families are counseled to watch carefully for decreased responsiveness, the initial symptom in the reported cases of propranolol-associated hypoglycemia. When propranolol is discontinued, gradual weaning is recommended to avert tachycardia. For patients with a history of bronchospasm, or for those who have intracraniaw or vascular syndromes or conditions that could predispose to stroke during a hypotensive episode, such as the PHACE syndrome (posterior fossa lesions, hemangiomas, arteriovenous malformations, cardiac lesions, eye abnormalities), beta-blocker treatment usually is not recommended. Propranolol is contraindicated in children with bradycardia or heart block.

Because of the uncertainties in drug administration and dosing, incidence of side effects, duration of treatment, and criteria for discontinuation, consultation with dermatologists experienced in treating IH lesions is helpful. Studies are ongoing to confirm effectiveness and to determine optimal treatment schedules. The effectiveness of early use of oral propranolol for superficial IH lesions is currently being evaluated in a randomized, controlled trial (http://www.clinicaltrials.gov; study NCT00744185).

For the infant in the vignette, propranolol was begun at 5 months of age and changes in lesion size and color were noted within 48 hours. The lesion had resolved by 10 months of age (Figure 2).

Infants with progressive IH growth treated with oral corticosteroids may have drug-associated side effects because of adrenal-axis suppression, growth impairment—especially central nervous system and longitudinal growth—immunosuppression, weight gain, and gastrointestinal complications. In addition, oral corticosteroids are relatively ineffective in reducing tumor volume, which is the cause of the concern in the infant in the vignette. Higher doses of oral corticosteroids would likely potentiate risks without reducing tumor size.

Intravenous vincristine has been demonstrated to reduce IH lesion growth, but its need for intravenous administration and its toxic profile mitigate against its use.

Treatment with subcutaneous interferon, which had been enthusiastically embraced to treat IH in the past, has been associated with a risk of neurotoxicity resulting in spastic diplegia (up to 20% of cases), and hence is not recommended as a preferred second-line treatment in cases such as presented in the vignette.

Additional readings:

References


Mancini AJ. Propranolol for infantile hemangioma: new use for an old drug. AAP News. 2010;March:14


American Board of Pediatrics Content Specification(s)

Skin Disorders: Know how to diagnose and manage capillary and cavernous hemangiomas
A full-term male infant who had clinical hypoxic-ischemic encephalopathy shortly after birth and had undergone a course of whole-body cooling ending on day 4, develops red and violaceous subcutaneous nodules on the upper back area and buttocks and indurated plaques on the posterior aspect of the arms on the seventh day after birth. He has a red and inflamed, soft, fluctuant central abscess surrounded by similar indurated plaques on the lower back. Biopsy of a lesion reveals lobular panniculitis with adipose cell necrosis and dense inflammatory infiltrates involving lymphocytes, histiocytes, lipophages, and giant cells in granuloma formation.

Of the following, the electrolyte abnormality MOST likely associated with the skin lesion in this child is:

- A. hypercalcemia
- B. hyperkalemia
- C. hypermagnesemia
- D. hypernatremia
- E. hyperuricemia

The neonate in the vignette has subcutaneous fat necrosis of the newborn (SCFN), a transient panniculitis typically presenting within the first 6 weeks after birth in term and post-term infants. Infants having SCFN often have a history of birth asphyxia, meconium aspiration, cyanosis,
seizures, and/or hypothermia. The natural history of the condition is resolution without scarring in most cases. The most common and serious complication of SCFN is late-onset hypercalcemia. The other electrolyte abnormalities have no association with SCFN.

Typically SCFN presents in the first 4 weeks after birth and resolves spontaneously over weeks to 6 months. Lesions present as firm, mobile, circumscribed nodules and plaques overlying bony prominences on the trunk, buttocks, extremities, and cheeks. The overlying skin may be flesh-colored, red, or violaceous. Lesions heal over weeks to months, with minimal scarring. The development of fluctuant and draining nodules has been described. In some cases, liquefaction may be so severe that serial aspiration is required to minimize pain and skin breakdown.

Major differential diagnoses of SCFN include sclerema neonatorum, bacterial cellulitis, erysipelas, abscess, hematoma and other causes of subcutaneous nodules, including dermoid cysts; benign tumors such as hemangiomas and infantile myofibromatosis; and malignant tumors such as rhabdomyosarcoma, infantile fibrosarcoma, neuroblastoma, and congenital leukemia.

Histopathologic changes diagnostic of SCFN consist of:

- necrosis of fat
- a granulomatous cellular infiltrate composed of lymphocytes, histiocytes, multinucleated giant cells, and fibroblasts
- radially arranged clefts of crystalline triglyceride within fat cells and multinucleated giant cells

Calcium deposits are commonly found in areas of fat necrosis.

A number of risk factors, including gestational diabetes, preeclampsia, maternal cocaine use, birth asphyxia, meconium aspiration, and neonatal hypothermia, have been associated with SCFN. Birth asphyxia is overwhelmingly the most commonly identified predisposing factor. The shunting of blood away from subcutaneous tissue creates an environment of hypoxia and hypothermia, which is believed to lead to a cycle of granulomatous inflammation and necrosis of adipose tissue. Furthermore, neonatal adipose tissue is unique in that it is composed of a higher concentration of saturated fatty acids (palmitic and stearic acids) that have a higher melting point (64°C), making them more likely to crystallize under cold stress.

Several cases of SCFN related to induced hypothermia have been reported in the literature. In most of these cases, the skin changes manifested after cooling had been discontinued, occurred in areas in contact with the surface cooling blanket, and were transient. It has been proposed that parents and caregivers of infants undergoing therapeutic hypothermia should be made aware of this side effect, but because of its transient nature, this should not deter them from consenting to hypothermia treatment in asphyxiated infants. In addition, newborns who undergo therapeutic cooling should have frequent dermatologic assessments and should be turned regularly to avoid prolonged direct pressure against the cooling interface if surface cooling methods are used to induce hypothermia.

While most cases of SCFN spontaneously resolve, complications such as pain, hypoglycemia, thrombocytopenia, hypertriglyceridemia, and hypercalcemia have been reported. Thrombocytopenia, hypoglycemia, and hypertriglyceridemia are usually transient and resolve spontaneously or with minimal treatment.

Hypercalcemia, the most serious potential complication of SCFN, carries a risk of intellectual impairment, calcification of soft tissues, seizures, cardiac arrest, renal failure, and death. Hypercalcemia may not manifest until 1 to 6 months after the skin lesions resolve. Clinically, the most common feature is failure to thrive (90% of cases), followed by fever,
vomiting, feeding difficulties, irritability, and listlessness.

In neonates with SCFN, hypercalcemia is the result of unregulated, increased extrarenal production of 1,25-dihydroxyvitamin D₃ by the granulomatous cells of fat necrosis, leading to increased intestinal absorption of calcium. Treatment options include conservative management, including use of low calcium and vitamin D formula, promoting calciuresis through fluids, and use of furosemide or anti-inflammatory low-dose corticosteroids. The use of pamidronate also has been shown to be safe and to normalize calcium levels rapidly in refractory cases. Because hypercalcemia often develops after the patients are discharged from the hospital and after resolution of the lesions, monitoring of serial calcium concentration is indicated.

**Suggested Readings**


**American Board of Pediatrics Content Specification(s)**

Skin Disorders: Know the complications and management of various neonatal skin injuries, including IV infiltrates and chemical and thermal burns

Asphyxia and Resuscitation: Recognize the neonatal systemic complications and vascular redistribution of blood flow caused by perinatal hypoxia or asphyxia

Endocrine/Metabolic/Thermal: Know the etiology and clinical manifestations of neonatal hypercalcemia

Endocrine/Metabolic/Thermal: Know the laboratory features and approach to therapy of
neonatal hypercalcemia

Asphyxia and Resuscitation: Know the clinical features, diagnosis, and management of perinatal hypoxic ischemic encephalopathy
A full-term male infant is admitted with a vesiculopustular rash initially characterized by vesicles containing bright yellow to creamy white fluid with underlying erythema. Crusting and weeping erosions are also noted (Figures 1 through 4).

Figures 1 - 3: Vesicles and pustules with yellow crusting and eschars on the face, scalp, and trunk of the infant in the vignette
Figure 4: Erythema toxicum–like lesion on the trunk of the infant in the vignette
Lesions are diffusely located but concentrated on the face, scalp, and trunk; palms and soles are also affected. Physical features include a flat facies and occiput, excess nuchal skin, epicanthal folds, brachydactyly, bilateral transverse palmar creases, wide space between first and second toes, a systolic heart murmur, and hypotonia. The infant is alert and responsive, but requires nasal cannula oxygen for nasal flaring and low oxygen saturation.

White blood cell count is 65,000/μL (65×10^9/L). The peripheral smear shows 55% blasts; neutrophil and lymphocyte counts are normal. The platelet count is 21×10^3/μL (21×10^9/L) and hemoglobin concentration is 15 g/dL (150 g/L*). Serum transaminases are normal, Tzanck smear is negative, and culture specimens do not yield any pathogens after 72 hours of incubation. Skin biopsy of a lesion from an extremity shows an infiltrate of immature myelocytes, promyelocytes, and blastlike cells located in intradermal blisters and the dermis; neutrophils, eosinophils, lymphocytes, and plasma cells are also present.

Of the following, the disorder MOST likely to be associated with the infant’s skin manifestations is:

- A. bullous impetigo
- B. congenital syphilis
- C. epidermolysis bullosa
- D. staphylococcal scalded skin syndrome
- E. transient myeloproliferative disorder
Vesicular, pustular, and bullous lesions can be an obvious visual sign of a number of infectious, systemic, and benign medical conditions in neonates. Vesicular and pustular skin disorders such as erythema toxicum, neonatal pustular melanosis, miliaria crystallina and rubra, and neonatal acne are particularly common, whereas more severe disorders such as *Staphylococcus aureus* pyoderma and congenital candidiasis are less frequent but may cause serious illness. Uncommon causes of vesicles and pustules in neonates include congenital candidiasis, herpes simplex infection, scabies, acropustulosis of infancy and incontinentia pigmenti. A rare condition that is associated with vesicles and pustules is the transient myeloproliferative disorder found in neonates with trisomy 21 or infants who are mosaic for trisomy 21, as in the infant in the vignette.

The dermatologic findings of a vesiculopustular rash with papules, erythema, and crusting and weeping erosions may accompany the transient myeloproliferative disorder of Down syndrome. These lesions may closely resemble the rashes of herpes simplex infection, erythema toxicum, or impetigo (Figures 1 through 4). Although located primarily on the scalp, face, trunk, and extremities, the palms and soles also can be involved. The rash resolves over weeks without scarring. If corticosteroids and chemotherapeutic medications are administered, the skin lesions may fade more quickly. Skin biopsy characteristically reveals immature myeloid precursors such as promyelocytes and myelocytes and blastlike cells located within intradermal vesicles and the dermis.

*Staphylococcus aureus* pyoderma refers to superficial staphylococcal infections such as crusted impetigo, bullous impetigo, and pustular folliculitis. Vesicles and pustules often appear days to weeks after birth in neck folds, the diaper area, and axillae. This distribution differs from the vesiculopustular lesions associated with transient myeloproliferative disorder, herpes simplex infection, and erythema toxicum. Fluid within the vesicles is initially clear or yellow but with time becomes purulent or turbid. Crusted impetigo also presents without vesicles or pustules. Infants with staphylococcal pyodermas frequently appear well.

Staphylococcal infections of the skin also can present as bullous lesions, either bullous impetigo or staphylococcal scalded skin syndrome (SSSS). These bullous lesions are caused by exotoxin-producing *S. aureus*, phage type 1, 2, or 3. Impetigo-associated bullae often rupture, leaving moist superficial erosions or thin crusty areas with a collarette of scale. SSSS is an acute, life-threatening disorder. Superficial bullae, diffuse erythema, dermal tenderness, widespread skin fragility (skin separation from the epidermis is easily provoked by rubbing the skin [Nikolsky sign]), and erosions characterize the lesions in SSSS. Onset is usually between 3 and 7 days or more after birth, beginning in a perioral distribution that rapidly progresses to involve all skin surfaces. The bullae rupture in 1 to 2 days leaving areas of denuded skin over mechanical stress sites such as the shoulders, buttocks, body folds, hands, and feet. Impetigo lesions localized to the umbilicus or abscesses at different sites may accompany SSSS. The infant in the vignette did not have bullous lesions.

Congenital syphilis may present with blistering and ulcerations of the skin but this only occurs in 3% of cases. Bullae, not vesicles or pustules as in the infant in the vignette, are often located on the palms, soles, knees, and abdomen. Furthermore, these bullae are often superimposed on dusky, hemorrhagic, or erythematous skin. Bullous lesions on the hands and feet that present at birth also may be found with congenital candidiasis, infantile acropustulosis, and epidermolysis bullosa. Additional testing may be required to make this differentiation.

Epidermolysis bullosa is a group of inherited blistering *mechanobullous* diseases characterized by defects in the protein structure of the skin responsible for adherence to the underlying tissues. Vesicles and pustules do not characterize epidermolysis bullosa. Mechanical or frictional stresses cause bullae formation. Molecular defects, inheritance patterns, and the pathologic location of blistering are used to classify these disorders.
Presentations of the different subtypes of epidermolysis bullosa vary in morphology, time, extent of skin involvement, and extradermal abnormalities. Severe subtypes that present during the neonatal period may be lethal. Bullae may be located anywhere including the hands and feet, diaper area, back, mouth, gums, gastrointestinal tract, larynx, extremities, and trachea. Like SSSS, blisters frequently develop at sites of friction. Bullae may rupture and leave open erosions. Bullae may also be tense or hemorrhagic if located deep within the skin. With time, a foul smelling and purulent crust develops as the lesions become secondarily infected. Scarring may occur. Nails may be absent, dystrophic, or shed.

*Corrected from (15 g/L) to (150 g/L) on 7/13/11.

**Suggested Readings**


**American Board of Pediatrics Content Specification(s)**

- Skin Disorders: Know the inheritance patterns, cutaneous and laboratory manifestations, management, and outcome of epidermolysis bullosa
- Skin Disorders: Know the etiology and differential diagnosis of bullous skin lesions
- Skin Disorders: Know the management of bullous skin lesions in the newborn infant
- Skin Disorders: Know the cutaneous manifestations of congenital syphilis
- Genetics/Dysmorphism: Be aware of the maternal factors, incidence, and clinical manifestations of Down syndrome
- Infectious Diseases: Know the clinical manifestations and diagnostic features of perinatal infections with Treponema pallidum
- Infectious Diseases: Know the clinical manifestations and diagnostic features of perinatal infections with Treponema pallidum
Figure 2: Diagram of the three sensory trigeminal areas that can be affected in individuals with Sturge-Weber syndrome. The dermatomes are highlighted in yellow (V1), white (V2), and green (V3). (Adapted from Enjoras [1985].)
Question: 5

Physical examination of a full-term infant who presents with a facial lesion shows that the infant has port-wine stains involving both sides of the face (Figure 1). A unilateral leptomeningeal angiomma is identified on magnetic resonance imaging. You then meet with the family to discuss potential outcomes for this infant.

Figure 1: Neonatal skin (Reprinted with permission from Trevino JJ, Bakos MA, Janik MP. Neonatal skin. In: AAP Textbook of Pediatric Care. Chapter 85:Figure 0472.) Available at: http://www.pediatriccareonline.org. Accessed January 4, 2010.

Of the following, the MOST likely clinical outcome for this infant is:

- A. cognitive deficits
- B. glaucoma
- C. headaches
- D. hemiparesis
- E. seizures

**Incorrect**
Correct Answer: E

The infant in this vignette most likely has Sturge-Weber syndrome (SWS), also known as encephalotrigeminal angiomatosis. Sturge-Weber syndrome occurs sporadically in 1 in 40,000 to 50,000 live births. This neurocutaneous disorder is characterized by angiomatous malformations of the face, eye, and central nervous system. The syndrome is classified into three types based on the extent of involvement.
Type I is the most common type and manifests as a facial vascular malformation, commonly known as a port-wine stain. In addition, patients have an ipsilateral intracranial leptomeningeal vascular malformation, with or without ocular abnormalities.

Type II is characterized by a facial port-wine stain and possible ipsilateral glaucoma, but with no intracranial abnormalities.

Type III is characterized by leptomeningeal angiomatosis without skin or ocular abnormalities.

Sturge-Weber syndrome is most likely caused by the persistence of embryonic veins surrounding the cephalic portion of the neural tube and under the ectoderm in the region that will form facial skin. Failure of the normal regression of this vascular plexus by the ninth week of gestation results in residual vascular tissue and angiomata of the leptomeninges, face, and ipsilateral eye. The secondary effects of this residual vascular plexus on the surrounding brain tissue include hypoxia, ischemia, venous occlusion, thrombosis, infarction, and vasomotor abnormalities.

Leptomeningeal angiomias in patients with SWS are usually unilateral and most commonly involve the parietal and occipital lobes. The resulting neurologic manifestations vary and depend on the location of the cerebral angiomias and their secondary effects. Seizures are the most common clinical manifestation observed in affected individuals, occurring in 75% to 93%, and are the most likely outcome of the infant in this vignette. Seizures typically develop by the age of 3 years and involve the side of the body that is contralateral to the port-wine stain. Because seizures may exacerbate brain injury in patients with SWS, aggressive epilepsy management is important to minimize long-term effects. If seizures are refractory to medical therapy, surgical lobectomy or hemispherectomy may also be indicated.

Developmental delay, learning disabilities, and cognitive deficits occur in 50% to 75% of patients with SWS. The degree of neurologic impairment correlates with the severity of brain involvement. These outcomes are more likely to occur if the leptomeningeal angiomias are bilateral.

Vascular headaches occur in 30% to 45% of affected individuals with SWS. This symptom develops because the angioma predisposes patients to neuronal hyperexcitability, leading to changes in cortical perfusion and oxygenation. Similar to individuals who develop migraines, patients with SWS have trigeminal afferent stimulation and release of vasoactive peptides, resulting in vascular dilation.

Transient stroklike episodes are a unique feature of SWS, with the most common manifestation being transient episodes of hemiparesis or visual field defects that can last hours to several days. Hemiparesis may occur in 25% to 60% of affected patients and affects the side of the body that is contralateral to the cortical abnormality. These episodes are thought to result from recurrent thromboses, which are attributable to venous stasis of the malformation. Thus, in addition to anticonvulsants, low-dose aspirin is often prescribed at the time of diagnosis, in an attempt to prevent the progression of impaired cerebral blood flow and minimize future deficits.

Glaucoma is the most common ophthalmologic complication of SWS, occurring in 30% to 70% of patients, and associated with secondary visual loss. If the facial port-wine stains involve the forehead, eye and maxillary regions, there is a 45% chance of glaucoma. If the forehead and eye are not involved or if the forehead and eye are involved without maxillary lesions, glaucoma is rare. While 60% of cases will occur during infancy, the remaining 40% occur during childhood to early adulthood. During infancy, the mechanism of glaucoma is related to increased resistance to outflow of aqueous fluid, resulting in elevated intraocular pressure. In contrast, patients with late-onset glaucoma usually develop increased intraocular pressure because of elevated episcleral venous pressure caused by shunts within the episcleral hemangioma.
A facial port-wine stain is typically flat, pink or red, and blanches with pressure. The malformation consists of dermal capillaries and small venules, both with decreased perivascular innervations. Port-wine stains grow proportionately with the child and persist throughout life. Only 8% of patients with this facial malformation will have SWS. Individuals with SWS most often have a port-wine stain located in the trigeminal I sensory distribution (ie, ophthalmic), but the lesion may be more widespread and extend to the second (V2, maxillary) and third (V3, mandibular) divisions of the trigeminal distribution of the face, occasionally involving the neck and trunk (Figure 2). If the port-wine stain involves the V1 distribution, the risk of brain and eye involvement is as high as 35%. Up to 20% of affected individuals can have bilateral involvement. The infant described in this vignette has bilateral V1 and right-sided V2 facial port-wine stains (Figure 1). No association has been found between the presence or severity of the skin lesions and neurologic symptoms. Indeed, 5% to 15% of individuals with SWS will have leptomeningeal vascular abnormalities without cutaneous involvement (ie, type III).

**Suggested Readings**


**American Board of Pediatrics Content Specification(s)**

Neurology: Know the clinical features, diagnosis, management and outcome of neuromuscular disorders including neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, etc.

Skin Disorders: Know how to diagnose and manage port wine stain and know the association with Sturge-Weber syndrome
Question: 4

A male infant born to a mother with limited prenatal care is noted to have an umbilical cord abnormality (Figure 1). The infant was delivered vaginally after an uneventful labor. He voided in the delivery room. Abdominal ultrasonography revealed no abdominal masses and two normal kidneys; findings on voiding cystourethrography were unremarkable.

Figure 1: Umbilical cord lesion originating from the side of the umbilical cord. Lesion is filled with a clear yellow fluid.

Of the following, the umbilical cord mass MOST likely contains:

- [x] A. liquefied Wharton jelly
- [ ] B. omphalomesenteric remnants
- [ ] C. pancreatic tissue
Cystic masses of the umbilical cord, similar to that of the neonate in the vignette, are often detected during prenatal ultrasonography. True cysts are lined with epithelium and originate from embryonic remnants such as the omphalomesenteric duct and urachus. Umbilical cord pseudocysts, such as that in the vignette, are more common than true cysts; do not have an epithelial lining; and do not communicate with abdominal structures. Prenatal identification is useful because umbilical cord pseudocysts have been associated with fetal trisomy and other congenital anomalies. The cause of umbilical pseudocysts and their association with chromosomal abnormalities is not completely understood. Increased vascular pressure in the umbilical-placental circulation could increase hydrostatic umbilical cord pressure which is transferred into Wharton jelly, cause localized edema and form pseudocysts. Others have suggested that focal degeneration of Wharton jelly from an unidentified local pathologic process could be responsible for pseudocyst formation.

During the fourth week of embryogenesis, the embryonic disc begins to fold into a cylindrical C-shaped structure. The opening of the yolk sac, which contains the umbilical vessels, the urachus, and the omphalomesenteric duct, begins to narrow (Figure 2). The omphalomesenteric duct is connected to the developing gut at one end and the yolk sac at the other end. The allantois, a diverticulum of the caudal hindgut, develops into the urachus, which connects the genitourinary tract to the umbilicus. With normal development, the omphalomesenteric duct and urachus involute and leave no remnants.

Failure of the omphalomesenteric duct to involute can result in a wide range of omphalomesenteric remnants (Figure 3) because of the varying degrees of involution and location of duct patency.

- A persistently patent omphalomesenteric duct results in a direct connection of the umbilicus to the terminal ileum. Intestinal drainage can occur from a “stoma” in the umbilical stump after cord separation.
- An umbilical cord polyp occurs if there is a remnant of tissue without intestinal connection at the umbilical end of the involuted omphalomesenteric duct.
- Meckel diverticulum occurs when there is a remnant of tissue without umbilical connection at the ileal end of the involuted omphalomesenteric duct.
- An omphalomesenteric duct cyst forms if both the umbilical and ileal ends of the omphalomesenteric duct remain patent.
- A fibrous cord remnant of the omphalomesenteric duct occurs between the umbilicus and the ileum if the involution process is incomplete and results in fibrosis rather than complete dissolution of the duct.

The cystic lesion in the vignette contained clear fluid, not intestinal secretions or stool, and did not appear to be a polyp. Abdominal ultrasonography failed to reveal cystic lesions or other masses that would suggest that the lesion was a remnant of the omphalomesenteric duct.
A solid mass of pancreatic or hepatic tissue can be found in the umbilicus. These rare ectopic tissues can arise from the pluripotent cells of the omphalomesenteric duct, or from mechanical entrapment when the umbilical ring closes. The lesion in the vignette was pseudocystic, not solid, and thus would not be likely to contain pancreatic tissue.

Urachal remnants account for about a half of all umbilical anomalies that require surgical attention. With normal involution, the urachus becomes a fibrous cord between the umbilicus and the bladder. If normal involution is disrupted a number of anomalies may occur along the preperitoneal midline (Figure 4).

- A persistently patent urachus results in free communication between the bladder and the umbilicus. In such cases the umbilicus will be persistently wet or draining.
- A solid polyp occurs at the umbilicus without connection to the bladder when the urachus incompletely involutes at the umbilical end of the urachus.
- A bladder diverticulum occurs without connection to the umbilicus when the urachus incompletely involutes at the bladder end of the urachus.
- A middle duct urachal cyst occurs when the umbilical and bladder ends of the urachus close and the middle of the duct remains patent.

In a series of 45 urachal anomalies, 15 presented with an umbilical cyst or mass, 10 with periumbilical pain, and 19 with periumbilical discharge. One case presented with dysuria. Of the 45 cases, a urachal sinus was diagnosed in 22, cysts in 16, and a patent urachus in 7.

The location of urachal anomalies allows for ultrasonographic evaluation; voiding cystourethrography will assist in diagnosing urachal sinuses, bladder diverticuli, and vesicoureteral reflux. Because abdominal ultrasonography and voiding cystourethrography failed to show that the umbilical lesion of the neonate in the vignette was contiguous with urachal structures, it could not contain urachal remnants or urine.

Suggested Readings


Vane DW, West KW, Grosfeld JL. Vitelline duct anomalies: experience with 217 childhood


**American Board of Pediatrics Content Specification(s)**

Skin Disorders: Know how to evaluate and manage disorders of the umbilical cord, including granulomas, persistent omphalomesenteric duct remnant, and patent urachus

Gastroenterology: Realize the association of major congenital anomalies involving the GI tract and abdominal wall with those involving other organs

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Figure 2: Embryology of the umbilical cord structures.

Five-week embryo

Gastrointestinal tract

Cloaca (bladder)

Umbilical vein

Umbilical arteries

Allantois

Umbilical cord

Omphalomesenteric duct

September

ASSESSMENT PROGRESS:  Total Questions: 10  Questions Answered: 10  Correct Answers: 9

Question: 4

A male infant born to a mother with limited prenatal care is noted to have an umbilical cord abnormality (Figure 1). The infant was delivered vaginally after an uneventful labor. He
**Figure 3:** Abnormalities caused by a persistence of omphalomesenteric duct remnants. 

- **A,** A fibrous cord remnant of the omphalomesenteric duct is seen between the umbilicus and the ileum because of an incomplete dissolution of the duct. 
- **B,** A patent omphalomesenteric duct can be seen that results in a direct connection of the umbilicus to the terminal ileum. 
- **C,** An umbilical cord polyp is noted. A polyp can occur if there is a remnant of omphalomesenteric duct tissue without intestinal connection at the umbilical end of the involuted duct.
**Figure 4:** Abnormalities caused by a persistence of urachal remnants. **A,** The persistently patent urachus that is shown will result in a fistula that freely communicates between the bladder and the umbilicus. **B,** A urachal sinus is illustrated. The proximal aspect of the urachus attached to the bladder has involuted but the distal aspect remains patent to form a sinus tract to the umbilicus. **C,** An urachal cyst is noted. Urachal cysts occur when the umbilical and bladder ends of the urachus close and the middle of the urachus remains patent.
Question: 4

A male infant born to a mother with limited prenatal care is noted to have an umbilical cord abnormality (Figure 1). The infant was delivered vaginally after an uneventful labor. He voided in the delivery room. Abdominal ultrasonography revealed no abdominal masses and two normal kidneys; findings on voiding cystourethrography were unremarkable.

**Figure 1: Umbilical cord lesion originating from the side of the umbilical cord. Lesion is filled with a clear yellow fluid.**
**Question: 5**

You are consulted for an infant with lesions on the upper alveolar ridge (Figure 1). Other than the lesions in the mouth, his physical examination findings are normal. He is breastfeeding without difficulty.
Of the following, the MOST likely diagnosis in this infant is:

- [✓] A. Bohn nodules
- [ ] B. dental lamina cysts
- [ ] C. epulis
- [ ] D. Fordyce spots
- [ ] E. ranula

**Correct**

Bohn nodules are keratin cysts derived from remnants of dental lamina at embryonic lines of tissue fusion. Such lesions are usually 1 to 2 mm in size, though larger cysts also occur (Figure 1). The nodules are smooth and yellow to gray-white in color and isolated, scattered, or clustered. They are located on the buccal and lingual bases of the mandibular and maxillary alveolar ridges. Such cysts are located on the maxillary ridge most frequently and, rarely, on both maxillary and mandibular alveolar ridges. On the hard palate, such lesions are called Epstein pearls. Bohn nodules are often found in Caucasian infants, are asymptomatic, and do not interfere with oral feeding. Some authors report that 22% of neonates have Bohn nodules and about 75% have Epstein pearls. Spontaneous resolution within a few weeks to months of birth is the usual course. Of note, milia are also microkeratocysts.

Dental lamina cysts, or eruption cysts, develop on a maxillary or mandibular alveolar ridge over the site of an erupting tooth (Figure 2). They are circumscribed, sometimes hemorrhagic, cysts. Dental lamina cysts usually overlie eruption of permanent, or
deciduous, teeth but can develop over natal teeth too. Although variable in size, cysts are commonly about 6 mm in diameter. Color may be fleshlike or bluish red to black if hemorrhagic. Such cysts resolve spontaneously.

A congenital epulis is usually a single soft nodule that forms over the gingival margin of the anterior maxillary ridge or incisor-canine location (Figure 2). Congenital epulis is often pedunculated and variable in size. Multiple lesions are sometimes present. Large lesions may interfere with oral feeding and respiration. Histologically, the tissue contains granular cells that are tightly packed with a prominent fibrovascular network. Treatment, if necessary, is with excision.

Fordyce spots, or granules, are hyperplastic sebaceous glands usually found on the upper and lower lips but also on the buccal mucosa, tongue, gingiva, and palate (Figure 2). Such spots are macular or papular and white to yellow in color. Fordyce spots vary in size from 1 to 3 mm and may be found in clusters that appear as plaques; Fordyce spots resolve spontaneously and are asymptomatic.

Congenital ranula is a translucent, firm papule or nodule commonly arising from the anterior floor of the mouth just lateral to the lingual frenulum (Figure 2). It is rare. The ranula forms because of an obstruction or atresia of the duct from a sublingual or submandibular gland. The color is that of the overlying mucosa but sometimes may be bluish. Differentiation from mucous retention cysts requires biopsy and a histopathologic examination, which shows absence of epithelial lining of the lesion consistent with a pseudocyst. Mucous retention cysts are lined by epithelium. Ranulas may rupture spontaneously. Marsupialization of obstructed ducts is recommended to avoid development of sialadenitis.

**Suggested Readings**


**American Board of Pediatrics Content Specification(s)**

Gastroenterology: Recognize the developmental anomalies of the mouth and pharynx.
ASSESSMENT PROGRESS:  Total Questions: 15  Questions Answered: 10  Correct Answers: 9

Question: 8

A term infant is admitted with abnormal findings involving the skin (Figures 1 and 2). The prenatal and perinatal history is unremarkable. No one is the family has had similar findings.

Figure 1: Verrucouslike lesions on the left arm of the infant in the vignette. (Courtesy of Melissa Piepkorn, MD.)

Figure 2: Verrucouslike lesions on the left leg of the infant in the vignette. (Courtesy of Melissa Piepkorn, MD.)
Of the following, the skin lesions MOST likely represent a(n):

- [ ] A. condyloma acuminata
- [x] B. epidermal nevus
- [ ] C. incontinentia pigmenti
- [ ] D. molluscum contagiosum
- [ ] E. smooth muscle hamartoma

**Correct**

Warty papules that are distributed in linear and swirled patterns along the lines of Blaschko represent a linear verrucous epidermal nevus. Epidermal nevi are hamartomas found in about 1 in 1,000 people and include distinct entities: linear verrucous epidermal nevus (or epidermal nevus unless otherwise described), inflammatory linear verrucous epidermal nevus, nevus sebaceous, and nevus comedonicus. Other epidermal lesions include syringocystadenoma papilliferum, linear porokeratosis, and porokeratotic eccrine and ostial dermal duct tumor. Epidermal lesions are often isolated findings but may be part of the Proteus syndrome (hamartomas from various tissue lines, asymmetric bone growth, hemihypertrophy, macrodactyly) or CHILD syndrome (congenital hemidysplasia, ichthyosiform nevus, limb defects). The “epidermal nevus syndrome” may involve various organ systems including the brain, skeleton, eye, heart, and genitourinary tract; precocious puberty and vitamin-D resistant rickets also
may occur.

Linear verrucous epidermal nevi can present in newborns and young infants and may extend over various times. Extension subsides after adolescence. The distribution of warty papules can be limited to clusters or may be more widespread involving an extremity, half the body, and/or the trunk and scalp. Lesions exposed to amniotic fluid can appear macerated. A genetic basis for epidermal nevi has been proposed. Treatment is limited to excision of focal lesions or administration of oral retinoids and 5-fluorouracil; such treatments are not curative and recurrence is common.

Condyloma acuminata are anogenital warts caused by the human papilloma virus. Human papilloma viral warts rarely present at birth; usual presentation is during late infancy through the first 2 years after birth. The incubation period for human papilloma virus is 1 to 20 months, thus the later presentation in most cases. Transmission may be via direct nonsexual contact with vaginal secretions or other fomites at birth and thereafter, respectively. Although about 30% to 50% of newborns born to mothers with genital human papilloma virus infections have virus in their pharyngeal mucosa, the duration of colonization is brief and rarely leads to clinical disease. In older patients, direct sexual contact is a common source of spread. Presentation at birth or during the early neonatal period implies that transplacental or ascending infection is possible. Human papilloma warts in neonates usually involve the anogenital region or larynx. Stridor may be the presenting sign. Spontaneous remission is anticipated. The cure rate is about 25% to 50% with various treatments (such as liquid nitrogen, podophyllin, interferon, electrodesiccation, laser treatment, and excision). Malignant transformation most frequently has been associated with human papilloma virus subtypes 16, 18, 30, 31, and 33.

Incontinentia pigmenti is a multisystem disorder with skin manifestations presenting at birth and the first weeks of age. The skin lesions, like epidermal nevi, follow the lines of Blaschko and present in patterns such as curvilinear streaks or splashes. The lesions may present in one or more of the following four classic stages:

- Inflammatory vesicles and bullae containing eosinophils are often found at birth or in the first weeks of age
- Papules, pustules, warts, lichenoid lesions are found 2 to 6 weeks after birth and resolve within weeks to months
- Hyperpigmented macules in whorls and linear distribution intensify over time
- Hypopigmented macules and loss of hair and sweat glands replace hyperpigmented lesions

Extracutaneous manifestations of incontinentia pigmenti include eosinophilia; alopecia; abnormalities of dentition, eyes, central nervous system, skeleton, nails, immune system; developmental disorders, and malignancies. The disorder is X-linked dominant and lethal in hemizygous males. Management is personalized depending on associated extracutaneous manifestations.

Molluscum contagiosum is a viral infection that typically manifests in the skin as small skin-colored or pink papules that evolve to dome-shaped, pearly or white, 1- to 5-mm papules with central umbilication. It rarely presents in neonates. Acquisition is by contact with infected lesions or fomites or autoinoculation from scratching. The incubation period is 2 weeks to 6 months and generally resolves without treatment within weeks to a year. Lesions that involve the conjunctiva, are disfiguring, or are bleeding or spreading rapidly are candidates for treatment. Treatments such as curettage and chemical agents such as podophyllin are inconsistently effective.

Congenital smooth muscle hamartoma is a benign accumulation of arrector pili muscle in the reticular dermis. The skin lesion is plaquelike with overgrowth of hair within the lesion. Congenital smooth muscle hamartoma usually is found on the lumbosacral trunk.
and less frequently on the limbs. It presents at birth or shortly thereafter and occurs in about 1 in 2,600 live births; males are slightly more affected than females. There is no malignant potential and treatment is unnecessary.

**Suggested Readings**


**American Board of Pediatrics Content Specification(s)**

Skin Disorders: Know the diagnostic approach and genetic basis of heritable disorders

Skin Disorders: Know the differential diagnosis and syndromes associated with hyperpigmented lesions, including cafe au lait spots, giant hairy nevus, incontinentia pigmenti, and pigmented nevi

Skin Disorders: Know the diagnoses associated with abnormalities of hair and nails

Skin Disorders: Know the etiology and differential diagnosis of bullous skin lesions

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Question: 6

A 3,080-g female infant is born at term after an uncomplicated pregnancy. Physical examination reveals an erythematous ulceration located between the mandible and sternal notch. A nipplelike protrusion is noted at the cranial end of the lesion, and a nondischarging sinus is noted at the caudal end of the lesion (Figure 1).

**Figure 1: Anterior neck anomaly**

Of the following, the MOST likely diagnosis in this neonate is:

- [ ] A. branchial cleft anomaly
- [ ] B. dermoid cyst
- [X] C. midline cervical cyst
The neonate in the vignette presents with a congenital cervical anomaly. The midline, vertical cutaneous ulceration with a nipplelike protrusion of skin cranially and a nondischarging sinus caudally is characteristic of a midline cervical cleft (Figure 2).

Midline cervical clefts comprise 2% of all congenital cervical anomalies, and usually occur sporadically. The developmental mechanism is thought to be a mesodermal fusion abnormality involving the first (mandibular) or second (hyoid) branchial arches. Second-arch defects result in isolated clefts that are limited to the neck. First-arch defects may involve clefts of the lower lip, tongue, or mandible.

The central feature of the midline cervical cleft is the midline vertical opening along the ventral neck. At birth, the cleft may be weeping, but toughens and dries with time. A skin protuberance is present at the cranial end and the insertion may be divided with attachment to each side of the mandible, resulting in a bifid appearance. The caudally located sinus ends in a blind pouch, and the caudal direction of the tract differentiates the lesion from thyroglossal disorders, which contain cranially directed tracts. A subcutaneous fibrous cord originating from the deep layer of the skin protuberance and ending in the subcutaneous tissue of the chin may cause webbing of the neck with extension (pterygium colli medianum) or a torticolislike contracture of the neck.

Defects associated with the midline cervical cleft include hypoplastic or absent hyoid, cleft sternum, midline abdominal raphe, midline hemangioma, and congenital cardiac lesions. Bronchogenic cysts and thyroglossal duct abnormalities may occur in association. Surgical excision with closure by multiple Z-plasties within the first year reduces neck contractures and growth deformities of the mandible and sternum.

Branchial cleft anomalies include cysts, sinuses, and fistulae, and result from incomplete obliteration of embryologic branchial clefts and pouches. Branchial cleft anomalies are located between the external auditory canal and the anterior border of the sternocleidomastoid muscle. Branchial anomalies derived from the second branchial arch are most common (95% of cases), and are found on the lateral aspect of the neck, along the sternocleidomastoid muscle. Branchial cysts do not move with swallowing or tongue protrusion. Branchial sinuses and fistulae are remnants of the branchial cleft depressions and are commonly located along the lateral lower third of the neck. Associated findings often include a skin tag with a small amount of cartilage. Branchial cleft anomalies are excised to prevent infection.

Dermoid cysts are congenital subcutaneous lesions that result from entrapment of epithelial elements along embryonic lines of fusion. Cervical dermoids present as painless, superficial nodules in the anterior neck that are noncompressible, nonpulsatile, and bluish or skin-colored. Because the nodule may overlay the hyoid bone and move with swallowing or tongue protrusion, cervical dermoids may be confused with thyroglossal duct cysts. Accumulation of sebum over time causes the dermoid to increase in size, and diagnosis often is made before age 3 years. Infection is rare, but dermoid cysts can rupture, resulting in granulomatous inflammation. Surgical excision is indicated for lesions that are symptomatic, enlarging, or ruptured.
Ranulas are midline cervical mucocysts resulting from obstructed, imperforate, or atretic sublingual or submandibular salivary gland ducts. A ranula presents as a bluish cystic swelling in the floor of the mouth, lateral to the lingual frenulum, and rarely may grow deep into the fascial planes of the neck. Large ranulas may displace the tongue and impair sucking and swallowing. Treatment options include marsupialization or surgical resection of the cyst.

Thyroglossal duct cysts account for approximately 70% of congenital neck masses and occur in up to 7% of individuals, though typically are asymptomatic. During gestation, the thyroid gland forms from a diverticulum located between the anterior and posterior muscle complexes of the tongue, and with growth of the embryo, this diverticulum is caudally displaced into the neck and anteriorly to the hyoid bone. The elongating diverticulum forms the thyroglossal duct, which is obliterated by 5 to 8 weeks of gestation. Failure of obliteration results in a thyroglossal duct cyst. The cyst most commonly presents as a painless cystic neck mass located in the midline near the hyoid bone, but can be present anywhere from the base of the tongue to the suprasternal notch. Characteristically, the mass moves with swallowing or protrusion of the tongue. Large lesions may present with stridor, apnea, or respiratory distress. Surgical excision prevents infection of the cyst, but should be performed only after ectopic thyroid tissue has been excluded.

**Suggested Readings**


Dela Cruz RH, Barton M, Tully J. Index of suspicion in the nursery. *NeoReviews.* 2009;10:e89-e92. Accessed March 15, 2011 at: [http://neoreviews.aappublications.org/cgi/content/full/10/2/e89](http://neoreviews.aappublications.org/cgi/content/full/10/2/e89)


**American Board of Pediatrics Content Specification(s)**

Eyes, Ears, Nose, Mouth, Throat, and Neck: Know the clinical manifestations of branchial cleft cysts

Eyes, Ears, Nose, Mouth, Throat, and Neck: Know the clinical manifestations and approaches to therapy of neck masses in the newborn infant

Eyes, Ears, Nose, Mouth, Throat, and Neck: Know the normal development of the nose, mouth, throat and neck
Figure 2: Midline cervical cleft. Nipplelike protrusion located cranially (blue arrow) and sinus located caudally (black arrow).

Question: 6

A 3,080-g female infant is born at term after an uncomplicated pregnancy. Physical examination reveals an erythematous ulceration located between the mandible and sternal notch. A nipplelike protrusion is noted at the cranial end of the lesion, and a nondischarging sinus is noted at the caudal end of the lesion (Figure 1).

Figure 1: Anterior neck anomaly