When the Skin Falls Apart……
Neonatal Blistering Disorders

Steven Teich, M.D.
Neonatal Blistering Disorders

- Suction blisters
- Staphylococcal scalded skin syndrome
- Aplasia cutis congenita
- Congenital herpes simplex virus infection
- Bullous congenital ichthyosiform erythroderma
- Epidermolysis bullosa
Suction Blisters
Suction Blisters

- Presumed to be induced by vigorous sucking on the affected part in utero
- Seen in up to 0.5% of normal newborns at birth
- 0.5- to 2-cm oval bullae or erosions on the dorsal aspect of the fingers, thumbs, wrists, lips, or radial aspect of the forearms
- Spontaneous resolution without sequelae
Staphylococcal Scalded Skin Syndrome (SSSSS)
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- Blistering skin disorder caused by the epidermolytic toxin-producing *S. aureus*
- Occurs at 2-30 days of life
- Abrupt onset of erythema followed by blistering and exfoliation
Staphylococcal Scalded Skin Syndrome (SSSS)

- SSSS generally begins with localized infection of the conjunctivae, nares, peri-oral region, perineum, or umbilicus
- Fever, malaise, lethargy, and poor feeding subsequently develop, and the generalized eruption begins
- The rash is characterized by erythema that progresses to large, superficial fragile blisters that rupture easily, leaving behind denuded, erythematous, and tender skin
Staphylococcal Scalded Skin Syndrome (SSSS)

- Eruption most marked in flexural creases but may involve entire skin
- With extensive denudation neonate may have decreased thermoregulatory ability, extensive fluid losses, and electrolyte imbalance, and are at serious risk for secondary infection and sepsis
- With appropriate management the skin heals without scarring given the superficial plane of the cleavage
Staphylococcal Scalded Skin Syndrome (SSSS) Epidemiology

- SSSS preferentially affects neonates and children—two theories:
  - Lack of protection from antitoxin antibodies
  - Decreased renal excretion of the toxin

- Outbreaks of SSSS reported in NICU’s and well-baby nurseries
  - Asymptomatic or clinically infected health care providers act as carriers of epidemic strain of *S. aureus*
  - Prompt recognition with institution of strict infection control strategies vital to control nosocomial spread
Staphylococcal Scalded Skin Syndrome (SSSS) Treatment

- Treatment of SSSS directed at eradication of toxin-producing staphylococci to terminate toxin production
- A penicillinase-resistant penicillin, first- or second-generation cephalosporin, or clindamycin are appropriate initial choices, with modification based on sensitivity testing
- In patients with MRSA infection, parenteral vancomycin or other agents (based on local resistance patterns) would be indicated
Aplasia Cutis Congenita (ACC)
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- Congenital defect of skin characterized by localized absence of dermis, and at times, subcutaneous tissue
- ACC generally occurs on the scalp but it may also involve the skin of the face, trunk, and extremities
Aplasia Cutis Congenita (ACC) - Epidemiology

- Most cases appear to be sporadic but a variety of potential associations have been proposed:
  - teratogens
  - limb abnormalities
  - epidermal nevi
  - underlying embryologic malformations
  - epidermolysis bullosa
  - malformation syndromes
  - infections
Aplasia Cutis Congenita (ACC) - Presentation

- ACC classically presents as solitary or multiple, sharply demarcated, weeping or granulating, oval to circular, stellate defects ranging from 1 to 3 cm in diameter.
- The most common location for ACC is the scalp, and in those cases 80% occur in close proximity to the hair whirl.
- Scalp lesions:
  - 70% isolated
  - 20% double
  - 8% three or more defects
Aplasia Cutis Congenital (ACC)

- Face lesions are uncommon.
- Treatment generally unnecessary, however, large scalp lesions (i.e., greater than 4 cm) may require surgery with grafting.
- At birth the skin defect may vary from an ulceration with a granulating base to a superficial erosion or well formed scar.
Aplasia Cutis Congenita (ACC) - Etiology

• Etiology of ACC remains unknown
• Although most cases sporadic, familial case reports suggest autosomal dominance with reduced penetration
• Recognition of ACC and differentiation from forceps or other birth injury will help prevent medico-legal complications
Aplasia Cutis Congenita (ACC) - Treatment

- In patients with localized sporadic lesions, aside from cutaneous scarring the prognosis is excellent.
- With conservative therapy to prevent further tissue damage and secondary infection, most small defects of the scalp heal well during first few weeks to months of life.
- With aging the scars become relatively inconspicuous and plastic surgery is only required for large and obvious scars.
Congenital Herpes Simplex Virus Infection
Neonatal Herpes

• Neonatal herpes simplex virus (HSV) may range from mild, self-limited illness to one with devastating neurologic consequences or even death

• Affects 1500 to 2000 infants per year in the United States

• Up to 70% of neonatal HSV infections caused by type 2 ("genital") HSV

• Disease acquired by ascending in utero infection or by spread during delivery through infected birth canal

• Risk of neonatal HSV in infant born by vaginal delivery to mother with primary genital infection is 40-50%
Neonatal Herpes - Clinical Presentation

- Clinical presentation divided into three patterns:
  - Skin, eyes, and mouth (SEM) disease
  - Central nervous system disease
  - Disseminated disease
- Most infants with neonatal HSV become sick within first 4 weeks, and 2/3 in first week of life
- SEM disease appears to be least severe and has most favorable prognosis
- Most infants present with SEM disease but 60-70% progress to more diffuse involvement
Neonatal Herpes - Presenting Features

- Skin lesions, fever, respiratory distress, and CNS dysfunction - seizures, lethargy, poor feeding, irritability, and hypotonia
- Skin eruption varies from erythematous macules to individual or grouped vesicles
- Skin lesions usually occur on the scalp and face but in breech deliveries have a predilection for presenting part
- Fetal scalp monitoring is a risk factor for HSV with quick entry for virus into lacerated scalp
Neonatal Herpes

• Disseminated form may affect several organs including liver, adrenal glands, lungs, and CNS
• Mortality of disseminated form 60%
• Diagnosis of HSV infection can be made by:
  o scrapings from skin lesions-operator dependent with low sensitivity and specificity
  o direct fluorescent antibody study of skin lesion scrapings- high sensitivity (80-90%)
  o Viral cultures from skin, eyes mouth, CSF, rectum, or blood- gold standard
Neonatal Herpes - Outcomes

• Outcome of neonatal HSV infection quite variable

• Prospective outcomes study by Collaborative Antiviral Study Group demonstrated that risk factors for mortality include:
  - CNS and disseminated disease
  - Decreased LOC at start of therapy
  - Prematurity

• In those with disseminated disease, pneumonitis and DIC were important risk factors

• Mortality greatest in infants with encephalitis, disseminated infection, seizures, or infection with HSV-2 (versus HSV-1)
Neonatal Herpes - Education

• Education vitally important in prevention of HSV (and therefore neonatal HSV) during pregnancy
• Acquisition of infection near the time of labor associated with neonatal HSV and perinatal morbidity whereas acquisition of infection with seroconversion before labor does not affect outcome of pregnancy
• Overall, 70% of infants with neonatal HSV born to mothers with no signs or symptoms of genital infection at the time of delivery
• Cesarean delivery should be offered to all women with active HSV lesions at the time of labor
• Fetal electrodes should be avoided with known history of maternal HSV
Neonatal Herpes
Management of Suspected Cases

- Newborns with vesicular lesions or suspected HSV should be isolated (contact precautions), evaluated for systemic infection, and treated with empiric antiviral therapy.
- Ophthalmologic evaluation and prophylactic topical ophthalmic preparations should be initiated.
- Supportive measures: management of seizures, respiratory distress, hemorrhage, and metabolic derangements.
- Women with active HSV infection may handle and feed their infants with careful hand-washing and disposable surgical mask or covering lesions until they have crusted over.
- Breast feeding by mother with recurrent HSV infection may be acceptable since no unequivocal evidence that HSV transmitted by breast milk.
Neonatal Herpes - Medical Therapy

- Acyclovir is treatment of choice in the treatment of neonatal HSV due to safety profile
- Dose range of 15-30 mg/kg/day for affected infants
- Survival rate for patients with disseminated HSV treated with high-dose acyclovir (60 mg/kg/day) significantly higher, with borderline decrease in morbidity
- Toxicity limited to transient neutropenia during therapy so important to monitor neutrophil counts
- Current treatment recommendations are 14 days for SEM disease and 21 days for CNS and disseminated disease
Bullous Congenital Ichthyosiform Erythroderma (BCIE)
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- BCIE is distinctive, dominantly inherited form of ichthyosis characterized by verruciform scales that are predominantly in flexural areas
- Affects 1 in 300,000 individuals, 50% of patients have new mutations
Bullous Congenital Ichthyosiform Erythroderma (BCIE)

- Skin red and tender at birth
- Superficial bullae appear within first weeks of life and often within few hours of delivery
- May initially be confused with epidermolysis bullosa
- Hyperkeratosis often appears from the third month on but subtle thickening over the elbows and knees may be detectable during first month of life
- Blisters occur in crops and may vary from 0.5 cm to several centimeters in diameter
- When ruptured they discharge clear fluid and leave raw denuded areas
- Secondary bacterial infection, especially with *Staph aureus* commonly occurs
Epidermolysis Bullosa (EB)
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- Epidermolysis bullosa refers to a heterogeneous group of inherited disorders characterized by extreme fragility of the skin.
- Patients have recurrent blisters throughout life, sometimes brought on by trauma as light as finger pressure.
- When blisters break they leave nonhealing wounds that are prone to infection and scarring.
- In most patients, chronic blood loss from denuded areas results in anemia and hypoalbuminemia.
- Neonates born with large denuded areas are susceptible to dehydration and secondary infections.
Epidermolysis Bullosa (EB)

- Depending on specific type, EB has range of severity
- In mild cases, patients have occasional blisters that are merely a nuisance
- In other types, extensive blistering not only occurs on the skin but can also involve any mucosal surface including the mouth, GI tract, trachea, and bladder
Epidermolysis Bullosa (EB)

- Onset is usually in the neonatal period
- Patients may have blisters at birth caused by passage through the birth canal
- In some cases, patients appear normal at birth but develop blisters within a few days, wherever the skin is subject to trauma or friction
- Examples include sites where adhesive tape is applied to the skin, parts of the body by which the infant is lifted or handled, and sites under BP cuffs or tourniquets
- A positive family history helps to establish the diagnosis but will be negative in patients with dominant types of EB caused by a new mutation and in patients with recessive dystrophic EB who are offspring of unaffected parents carrying the gene
Classification of EB subtypes is based on the microscopic anatomy of the basement membrane zone - the area sandwiched between the epidermis and the dermis.

Depending on precise level at which blistering occurs three main types of EB are recognized.
# Epidermolysis Bullosa - Subtypes

<table>
<thead>
<tr>
<th>EB Subtype</th>
<th>Level of Split</th>
<th>Inheritance Patterns</th>
<th>Number of Subtypes</th>
<th>Scarring</th>
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</thead>
<tbody>
<tr>
<td>EB Simplex</td>
<td>Basal Cells</td>
<td>Autosomal Dominant</td>
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<td>No</td>
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<tr>
<td>Junctional EB</td>
<td>Lamina lucida between dermis and epidermis</td>
<td>Autosomal recessive</td>
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<td>Yes</td>
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<tr>
<td>Recessive dystrophic EB</td>
<td>Dermis below lamina densa</td>
<td>Autosomal recessive</td>
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<td>Yes</td>
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<tr>
<td>Dominant Dystrophic EB</td>
<td>Dermis below lamina densa</td>
<td>Autosomal dominant</td>
<td>2</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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**Diagram:**
- Basal Cell
- Lamina Lucida
- Lamina Densa
- Dermis
- Hemidesmosome
- Bullous Pemphigoid Antigen
- Laminin
- Type IV Collagen
- Anchoring Fibril

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**Nationwide Children’s Hospital**
Epidermolysis Bullosa - Newborn Care

- If fetus likely to have EB, Cesarean section should be considered over vaginal delivery
- May be large denuded areas due to *in utero* damage
- Neonate should be protected from trauma by careful handling
- Fluid and electrolyte balance along with good nutrition must be maintained
- Reverse isolation should be utilized until infant stable to minimize risk of infection and sepsis
- Narcotics and analgesics are not advised but may be necessary for dressing changes
- Normothermia must be maintained, especially during dressing changes
Epidermolysis Bullosa - Newborn Care
Epidermolysis Bullosa - Newborn Care

- Clothing should be soft and nonirritating
- Socks and mittens should be used to prevent hands and feet from rubbing together or scratching face
- Plastic or rubber should not come in contact with baby’s skin
- Sponge baths/ Pat dry, never rub
- Bottle or breast feed ASAP
- Blisters of oral cavity may interfere with feeding
- Nasogastric tube should be used as last resort due to possible esophageal blistering
- Parents and other family members must be actively involved in the baby’s care
<table>
<thead>
<tr>
<th>Organ System</th>
<th>Potential Complications</th>
</tr>
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<tbody>
<tr>
<td>Gastrointestinal</td>
<td>- Esophageal strictures of upper and lower thirds</td>
</tr>
<tr>
<td></td>
<td>- Hemorrhoids</td>
</tr>
<tr>
<td></td>
<td>- Anal erosions and stenosis</td>
</tr>
<tr>
<td>Ocular</td>
<td>- Corneal erosions with scarring</td>
</tr>
<tr>
<td></td>
<td>- Lacrimal duct obstruction</td>
</tr>
<tr>
<td>Oral/Dental</td>
<td>- Teeth poorly formed with hypoplastic enamel</td>
</tr>
<tr>
<td></td>
<td>- Microstomia</td>
</tr>
<tr>
<td>Hands and Feet</td>
<td>- Pseudosyndactyly</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>- Urethral meatal stenosis</td>
</tr>
</tbody>
</table>
### Neonatal Blistering Disorders – Differential Diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Onset</th>
<th>Clinical Features</th>
</tr>
</thead>
</table>
| Suction Blisters                               | At birth               | -One or few blisters on thumb, radial aspect of forearm, presumably due to sucking in utero  
|                                                |                        | -Spontaneous resolution                                                           |
| Staphylococcal Scalded Skin Syndrome           | 2-30 days              | -Abrupt onset of erythema followed by blistering and exfoliation                   
|                                                |                        | -Responds to antibiotics                                                           |
| Aplasia Cutis Congenita                        | At birth               | -Focal absence of hair on scalp                                                   
|                                                |                        | -Similar cutaneous defects may be present elsewhere                                
|                                                |                        | -Limb abnormalities                                                                
|                                                |                        | -Some cases associated with EB                                                    |
| Congenital Herpes Simplex Virus Infection      | First 20 days (mean 6 days) | -Blisters and bullae                                                               
|                                                |                        | -Large denuded areas                                                               
|                                                |                        | -Positive viral cultures                                                           
|                                                |                        | -Fever, poor feeding, hypothermia, lethargy                                         |
| Bullous Congenital Ichthyosiform Erythroderma  | At birth               | -Red, scaly skin                                                                  
|                                                |                        | -Secondary bacterial infection                                                     
|                                                |                        | -Thick, grayish brown scales after age 3 months                                     |
| Epidermolysis Bullosa                          | Usually at birth       | -Blisters at sites of trauma                                                       |