RESIDENT ROUNDS: PART II

A Review of Neonatal and Infantile Rashes

Kehinde Ogunmakin MD, Bryan Carroll MD, and Daneeque Woolfolk MD
Texas Tech University Health Sciences Center, Lubbock, TX

ABSTRACT

Patients under two years old comprise a small fraction of the population of patients seen in general dermatology clinics. Newborns and infants have immature skin barriers and immune systems, and as a result may be afflicted with different cutaneous diseases than adults. Additionally, common conditions may present differently in this population and may not be as easily recognized. This may make evaluation and diagnosis challenging for dermatologists. We provide a comprehensive review of rashes seen in neonatal and infantile patients to aid with proper diagnosis and treatment of this population. This review may also serve as a useful reference for board preparation.

Papulopustular Eruptions						
	Presentation	Pathogenesis	Work up	Histopathology	Treatment	Comments
Erythema toxicum neonatorum	2 – 5 days after birth; asymptomatic erythematous macules, papules, pustules and wheals surrounded by blotchy erythema that start on the face and spread to the trunk, proximal upper extremities and buttocks	Unknown; may be due to fragility and hypersensitivity of neonatal skin	May be diagnosed clinically; pustular smear with Giemsa reveals eosinophils	Subcorneal eosinophilic vesicles centered upon a follicle; perivascular eosinophils with mild papillary edema	None required; self-limited, resolves within 14 days	Affects full term neonates; spares palms/soles
Transient neonatal pustular melanosis	Birth; non-erythematous pustules on the forehead, chin, neck, palms and soles of darker pigmented neonates; pustules rupture and leave a collarette of scale and hyperpigmentation	Unknown	May be diagnosed clinically; pustular smear with Giemsa reveals neutrophils +/- eosinophils	Subcorneal neutrophilic +/- eosinophilic microabscesses; superficial perivascular lymphocytes, neutrophils >> and eosinophils; older lesions may only display basal hypermelanosis	None required; vesicles rupture after 1-2 days but hyperpigmentation may last for months	Affects full-term neonates; more common in skin of color
Eosinophilic pustular folliculitis	Occurs before 1 year of age; M>F; pruritic indurated erythematous plaques with folliculocentric pustules most commonly on the scalp and eyebrows, occasionally on the trunk and extremities that wax and wane	Unknown	Pustular smear with Giemsa reveals eosinophils; CBC w/ diff may reveal leukocytosis and eosinophilia; skin biopsy	Intrafollicular and perifollicular mixed infiltrate with numerous eosinophils and follicular spongiosis; subcorneal eosinophilic pustules sometimes; perivascular and interstitial lymphocytes; rarely flame figures	None required; self-limited, resolves in 3 months to 5 years; anti-histamines and topical steroids for symptomatic relief	Frequently crusted and impetiginized
Acropustulosis of Infancy	3 – 6 months; pruritic pustular and vesicular papules on the hands and feet, occasionally on the trunk and scalp, that recur in crops	Unknown	Mineral oil preparation to rule out scabies; pustular smear with Giemsa reveals neutrophils +/- eosinophils	Subcorneal neutrophilic >> and eosinophilic pustules; perivascular neutrophils and lymphocytes	Self-limited, resolves by age 3; anti-histamines and topical steroids for symptomatic relief; dapsone for severe cases	Recurs in crops every 3-4 weeks, decreases in severity with each episode; may be associated with scabies
Pustular psoriasis	First weeks of life; pustules on an erythematous base, most commonly on the palms or soles, but may affect any site or may be generalized	Autoinflammatory T-cell mediated condition of unknown etiology; altered expression or function of interleukin (IL)-1 family proteins may play a role[1]	Skin biopsy; pustular smear with Giemsa reveals neutrophils	Subcorneal neutrophilic microabscesses, confluent parakeratosis, psoriasiform epidermis with dilated capillaries in the suprapapillary plates	Acitretin, methotrexate, cyclosporine, PUVA, NBUVB, dapsone; often resistant to therapy	Commonly associated with HLA-Cw6
Neonatal cephalic pustulosis (Neonatal Acne)	First month of life; erythematous papules and pustules on the cheeks, nasal bridge and chin, may also affect neck and upper trunk	Inflammatory response to *Malassezia* spp; active sebaceous glands and high sebum excretion rate in neonates	May be diagnosed clinically; pustular smear with Giemsa reveals neutrophils	Mixed perifollicular infiltrate of neutrophils, lymphocytes, plasma cells and histiocytes	None required; resolves within 3 months; topical imidazoles	Comedones are rare

Infantile acne	3 – 12 months; mostly commonly presents as comedones, but may have cystic and suppurative nodules on the face, occasionally upper trunk	Increased androgen production	May be diagnosed clinically; pustular smear with Giemsa reveals neutrophils	Follicular plugging; mixed perifollicular infiltrate of neutrophils, lymphocytes, plasma cell and histiocytes	Topical retinoids and benzoyl peroxide are first-line; oral antibiotics and isotretinoin if severe and recalcitrant	May result in pitted scarring
Langerhans Cell Histiocytosis	Hashimoto-Pritzker: Birth; red-brown papules, nodules, and pustules in a generalized distribution; usually without mucosal or extracutaneous involvement Letterer-Siwe: 0-2 years; red-brown purpuric nodules, pustules, and vesicles on the scalp, trunk, and intertriginous areas; mucosal and extracutaneous (bone, bone marrow, lymph nodes, spleen, liver, and lungs) involvement is frequently present	Clonal neoplastic disorder; may be associated with BRAF V600E mutation[2]	Biopsy with immunostaining (CD1a, S100, +/- CD207); +/- electron microscopy; CBC w/ diff; coagulation studies, complete skeletal radiograph survey and CXR; +/- bone marrow biopsy	Lichenoid and perivascular infiltrate of reniform lymphocytes with epidermotropism; polymorphous infiltrate of lymphocytes, eosinophils, neutrophils or plasma cells; ERBCs, +S100, +CD1a, + CD207; Birbeck granules seen w/ electron microscopy	Hashimoto-Pritzker is self-limited; Letterer-Siwe is treated with topical steroids, nitrogen mustard, phototherapy, curettage or radiation, chemotherapy (thalidomide, vinblastine or etoposide; multidrug chemotherapy has shown a greater response rate with fewer recurrences)	The other variants of LCH (Hand-Schüller-Christian disease and eosinophilic granuloma) affect children 2-6 years old, and 7-12 years old respectively
Early Congenital Syphilis	Birth – 2 years; erythematous papules and pustules worse on the palms and soles; may have purpuric macules and papules from extramedullary hematopoiesis; perianal and perioral verrucous lesions (condyloma lata)	Maternal *Trepenoma pallidum* infection transmitted transplacentally	Screen for TORCH infections; darkfield microscopy; CBC/CMP, serology; xray	Epidermis may be normal, psoriasiform, or hyperkeratotic with neutrophilic pustules; rich lymphoplasmocytic and histiocytic infiltrate	IV Aqueous crystalline penicillin G or IM Procaine penicillin G	Neonates may be asymptomatic at birth or present with other features such as snuffles, pneumonia, and bone lesions
Candidiasis	Congenital candidiasis: Birth; widespread erythematous papules, pustules and scaling on the face, trunk, and extremities; involves palms and soles. Neonatal candidiasis: After the first week of life; erythematous patches with satellite papules and pustules in the diaper area, intertriginous areas and face; oral thrush	Infection with *Candida albicans*; infection occurs in- utero in congenital cases and during delivery or postnatally in neonatal cases	KOH; fungal culture; serology	Stratum corneum with parakeratosis, neutrophils, pseudohyphae and budding yeast; perivascular lymphocytes and neutrophils; PAS/GMS may better reveal the organisms	Topical imidazoles	Frequently associated with nail dystrophy
Scabies	Following exposure; intensely pruritic erythematous papules, pustules and vesicles on hands, axilla, groin and face	Infestation with *Sarcoptes scabiei var hominis*	Mineral oil preparation; dermoscopic evaluation of burrows may reveal mites, "delta sign"	Subcorneal zone with eggs, mites or scybala; spongiosis or epidermal hyperplasia sometimes; perivascular or moderately diffuse dermal lymphocytes and eosinophils	Permethrin 5% topical cream; tx household members; wash linens with hot water	Lindane contraindicated due to neurotoxicity

Vesicular Disorders						
	Presentation	Pathogenesis	Work up	Histopathology	Treatment	Comments
EBS	Birth – early infancy; non-inflammatory blisters on areas with increased trauma like the elbows, knees, and distal extremities; Dowling-Meara presents with widespread herpetiform vesicles and development of a diffuse PPK; Koebner variant is characterized by generalized bullae	Autosomal dominant mutation of keratin 5 & 14	Skin biopsy for light and electron microscopy or immunomapping; DNA analysis	Basal and suprabasal keratinocytes display cytolytic degeneration; dyskeratosis is a feature of Dowling-Meara; blister may appear subepidermal on light microscopy; electron microscopy or immunomapping may be needed to visualize the suprabasilar location of the blister[3,4]; clumped tonofilaments are seen with electron microscopy in Dowling-Meara	Prevention of mechanical trauma; wound care with non-stick dressings; bleach baths to prevent secondary impetiginization	Autosomal recessive plectin mutation associated with muscular dystrophy and pyloric atresia

Junctional EB	Birth; Herlitz variant characterized by generalized bullae and exuberant granulation tissue periorificially and on the scalp; non-Herlitz variant characterized by bullae on the extremities that heal with atrophic scarring	Autosomal recessive mutation of laminin 5 (332) and BPAG2 (collagen XVII)	Skin biopsy for light and electron microscopy or immunomapping; DNA analysis	Light microscopy appears to reveal a subepidermal blister, but with immunomapping or electron microscopy can visualize the basement membrane on the dermal side of the split; PAS may be useful to visualize the basement membrane[3,4]	Prevention of mechanical trauma; wound care with non-stick dressings; bleach baths to prevent secondary impetiginization	Autosomal recessive mutation of α6β4 integrin associated with pyloric atresia
Dystrophic EB	Birth – early infancy; bullae that may be localized or widespread and heals with atrophic scarring; dystrophic or absent nails	Autosomal recessive or dominant mutation of collagen VII	Skin biopsy for light and electron microscopy or immunomapping; DNA analysis	True subepidermal blister with the basement membrane on the roof of the blister, may be better visualized with PAS; can use electron microscopy or immunomapping to distinguish between the variants of EB as all may appear to be subepidermal blisters on light microscopy	Prevention of mechanical trauma; wound care with non-stick dressings; bleach baths to prevent secondary impetiginization	Recessive mutation (Hallopeau-Siemens) associated with mitten deformity and increased risk of SCC
Epidermolytic Hyperkeratosis (Bullous Congenital Ichthyosiform Erythroderma)	Birth; erythroderma with widespread bullae, erosions and denuded skin; may have secondary sepsis and electrolyte imbalance; blistering and erythema improve with time, and in late infancy and adulthood, develop severe hyperkeratosis over extensor surfaces	Autosomal dominant mutation of keratin 1 & 10	Skin biopsy; sepsis work-up (blood/ urine culture, tissue culture); CBC, CMP	Epidermis with epidermolysis and hyperkeratosis	Fluid and electrolyte management in the NICU; broad spectrum IV abx until cultures are negative; systemic retinoids, emollients, and bleach baths (in late infancy and adulthood)	Patients with epidermal nevi with incidental epidermolytic hyperkeratosis noted on histology are at risk of having children with full-blown EHK
Incontinentia pigmenti (Bloch-Sulzberger Syndrome)	Vesicular stage may occur in utero or at birth; healthy appearing neonates with vesicles in a blaschkoid arrangement most commonly on the extremities but may be generalized	X-linked dominant mutation of NF-κβ portion of NEMO gene	Skin biopsy; Tzanck smear to rule out HSV; CBC w/ diff may reveal eosinophilia	Eosinophilic microabscesses with spongiosis and dyskeratotic keratinocytes	Referral to an ophthalmologist; referral to a dentist at age 1, referral to a neurologist; resources for support groups (www.ipif.org)	Patients develop peg/conical teeth, dystrophic nails, scarring alopecia; mental retardation and seizures are common
Miliaria crystallina	1 – 2 weeks of age; non-erythematous fragile blisters on the forehead, neck, trunk, and occluded areas	Obstruction of eccrine ducts in the stratum corneum	May be diagnosed clinically; Tzanck smear to rule out HSV	Non-inflammatory corneal vesicles; may note keratinaceous obstruction of the eccrine ducts in the stratum corneum	Cooling; resolves within 1-2 days	History of fever or overheating may be reported
Sucking blisters	Birth; solitary non-inflammatory flaccid bullae at site of sucking -- most commonly the wrist and hand, occasionally on the foot	Sucking of the affected site in utero	May be diagnosed clinically	Not generally biopsied	Self-limited; resolves in days to weeks	Patients are healthy
Bullous impetigo	Few days to weeks old; vesicles and bullae with mild surrounding erythema on the face, trunk, buttocks, perineum and axilla	Infection with *Staph. aureus* group 2 type 71; results from production of exfoliative toxins (ETA/ETB) which cleave desmoglein 1	Gram stain, bacterial culture; +/- skin biopsy	Subcorneal blister with acantholytic keratinocytes and very little inflammation, sparse neutrophils; rare bacterial cocci in the stratum corneum; neutrophilic infiltrate may be noted in upper dermis	Uncomplicated infections should be treated with mupirocin or retapumulin ointment; complicated infections should be treated w/ IV ceftriaxone or IV ampicillin/sulbactam	Rare reports of SSSS developing from bullous impetigo in infants and adults with immunosuppression or renal disease
Bullous mastocytosis	Birth to months; yellow-brown papules or nodules with hyperpigmentation and superimposed blisters; may be localized or diffuse	Activating c-kit mutations seen in 40% of children and a majority of adult patients	Skin biopsy; Giemsa/ toluidine blue/ Leder stain, CD117 immunostaining; serum tryptase and urine histamine levels	Infiltrate of mast cells in the dermis, hyperpigmentation of the epidermal basal layer; eosinophils commonly seen in the dermis	Topical and oral corticosteroids, oral H2RA, cromolyn, oral PUVA, avoidance of potent mast cell stimuli (alcohol, aspirin, NSAIDs, narcotics, anesthetics); in severe cases: cladribine, IFN-α-2b, imatinib	May present with irritability, diarrhea, flushing, and abdominal pain
Syphilitic pemphigus	0 – 2 years; flaccid blisters and erosions on the palms and soles	Maternal *Trepenoma pallidum* infection transmitted transplacentally	Skin biopsy, darkfield microscopy, serology	(see above -- congenital syphilis)	IV aqueous crystalline penicillin G or IM procaine penicillin G	Occurs in patients with early congenital syphilis
HSV	Congenital HSV: Birth; vesicles, pustules and erosions diffusely Neonatal HSV: Day 5 to 2 weeks; vesicles, pustules and erosions on the torso and scalp; may have mucosal involvement; patients are irritable and lethargic; both forms may rarely present with blueberry muffin lesions	Infection with HSV1/2; infection occurs in utero in congenital cases and during delivery or postnatally in neonatal cases	Tzanck smear, DFA; viral culture; sepsis work-up (CBC, CMP, blood cultures); screen for TORCH infections if presents with blueberry muffin lesions	Multinucleated giant cells; chromatin margination and steel gray nuclei; acantholysis and intraepidermal vesicles ; lymphocytic dermal infiltrate with occasional vasculitis	Oral or IV acyclovir	Patients may be septic with multi-organ failure; microcephaly and chorioretinitis are seen in congenital herpes

Varicella	Neonatal varicella: Birth to 2 weeks; generalized distribution of vesicles on an erythematous base, "dew drop on a rose petal" Congenital varicella: Birth; presents with scarring and erosions on any location, but most commonly on the extremities	Neonatal varicella occurs w/ primary maternal infection 7 days before to 2 days after delivery; congenital varicella occurs w/ maternal infection in the first or early second trimester	Tzanck smear, DFA, viral culture, skin biopsy	Findings same as HSV	Varicella-zoster immunoglobulin (VZIG); oral or IV acyclovir	Extracutaneous findings include neurologic and eye abnormalities, chorioretinitis, limb hypoplasia, and pneumonia
Scabies	(see above)					

Petechial And Purpuric Eruptions						
	Presentation	Pathogenesis	Work up	Histopathology	Treatment	Comments
CMV	Birth; "blueberry muffin" lesions: dark blue to red non-blanchable papules in a generalized distribution; may see jaundice, hepatosplenomegaly, thrombocytopenia, chorioretinintis, seizures and intracranial calcifications; vast majority of infections show no signs or symptoms at birth	Transplacental transmission of CMV virus, a ubiquitous virus; risk of transmission to the fetus is much higher in primary infection of the mother compared to reactivation; congenital CMV is most often asymptomatic; true "blueberry muffin" lesions represent extramedullary hematopoiesis;	Screen for TORCH infections, CBC/CMP, serology; can culture CMV in human fibroblasts (gold standard); faster more commonly used methods include CMV-specific serology or PCR; ophtho exam to diagnosis CMV retinitis; CT scan of head may show intracranial calcification	Extramedullary hematopoiesis- variable amounts of myeloid cells, erythroid cells and megakaryocytes in the dermis and subcutis; CMV specific findings include enlarged endothelial cells with purplish crystalline intranuclear inclusion bodies surrounded by a clear halo ("owl's eye")	First line is ganciclovir or valgancivlovir. Second line is foscarnet or cidofovir	Leading infectious cause of deafness and mental retardation; acyclovir is not an effective treatment option; CMV is #1 cause of extramedullary hematopoiesis
Rubella (German measles)	Birth; occasionally see "blueberry muffin" lesions; more numerous birth defects than CMV, including cataract, deafness, heart defects (PDA and VSD), microcephaly and developmental delay	Transplacental transmission of rubella virus; occurs when a non-immune pregnant woman contracts the virus; birth defects more likely if infection occurs < 16 weeks gestation; "blueberry muffin" lesions represent extramedullary hematopoiesis	Screen for TORCH infections, CBC/CMP, serology; anti-rubella IgM or 4x increase in specific IgG antibodies in mother; PCR testing of nasal wash, throat swab or urine	Extramedullary hematopoiesis- variable amounts of myeloid cells, erythroid cells and megakaryocytes in the dermis and subcutis	Prevention with MMR vaccine; for non-immune pregnant women exposed to rubella can give IMIG/IVIG but this is not reliably effective; supportive care for neonate infected with rubella; can correct cardiac defects and cataract surgically	Deafness in 50% patients; most severe when transmitted during first trimester of pregnancy
Toxoplasmosis	Typically asymptomatic at birth; might see hemorrhagic or necrotic papules which favor the trunk; classic triad of chorioretinitis, hydrocephalus and intracranial calcifications; may see deafness, seizures, and microcephaly	Transplacental transmission of the protozoan *Toxoplasma gondii; T. gondii* acquired by pregnant mother through cat feces, uncooked meat, unpasteurized goat milk and unwashed fruits/vegetables; not true blueberry muffin lesions because it lacks extramedullary hematopoiesis	Screen for TORCH infections, CBC/CMP, serology; IgM and IgG toxoplasma titers in mother; CT scan may show intracranial calcification; optho exam for chorioretinitis	Purpuric lesions are due to extravasated RBCs; can see trophozoites or cysts containing numerous small bradyzoites in macrophages or free in the dermis in 50% of cases; immunostains and PAS may be positive	First line is sulfadiazine + pyrimethamine and folic acid Second line is clindamycin	70 – 90% of infected neonates are asymptomatic at birth, but 10 – 30% develop visual loss from chorioretinitis and >20% develop neurologic abnormalities
Early Congenital Syphilis	(see above – congenital syphilis)					
HSV	(see above – HSV)					
Parvovirus B19, coxsackie virus, Rh incompatibility, maternal-fetal ABO blood group incompatibility, spherocytosis, twin transfusion syndrome[5]	Birth to first few days; these are other assorted causes of true "blueberry muffin" lesions	Depending on etiology	Screen for TORCH infections; CBC/CMP, serology; skin biopsy	Extramedullary hematopoiesis (see above -- CMV)	Supportive therapy; phototherapy, IVIG, and exchange therapy may be indicated for hyperbilirubinemia	--
Letterer Siwe (LCH)	Usually < 1 yr old (almost always < 2 yrs); small papules, pustules and vesicles of the scalp, trunk and flexural areas of neck, axilla and perineum; can see a seborrheic dermatitis-like presentation with multiple petechiae/purpura; rare reports of LCH presenting with diffuse "blueberry muffin" lesions	Skin lesions are due to infiltrating neoplastic Langerhans cells; "blueberry muffin" lesions in this entity reflect collections of neoplastic cells, not extramedullary hematopoiesis; petechiae and purpura are due to extravasated RBCs	Skin biopsy, CBC/CMP, urinalysis, coagulation studies, complete skeletal radiograph survey and CXR; consider bone marrow biopsy, PFTs, lung biopsy, small bowel series, liver biopsy, dental films and CT/MRI of the brain	Lichenoid infiltrate of Langerhans cells which have reniform nuclei; epidermotropism is common; polymorphous infiltrate of lymphocytes, eosinophils, neutrophils or plasma cells; LCH cells are +S100, +CD1a, + CD207; Birbeck granules seen w/ electron microscopy	For skin-limited disease, topical corticosteroids, phototherapy or nitrogen mustard; treat bone lesions w/ NSAIDS, intralesional corticosteroids, curettage or radiation; multiorgan disease require thalidomide, vinblastine or etoposide; multidrug chemotherapy has shown a greater response rate with less recurrences	Five-year survival rate with treatment is 50%

Purpura fulminans	Hours to days after birth; non-inflammatory retiform purpura and large scale cutaneous necrosis	Homozygous deficiency or dysfunction of protein C or S; proteins C and S are vitamin K-dependent antithrombotic proteins; a deficiency or dysfunction of these antithrombotic factors leads to intravascular coagulation	Skin biopsy; protein C and S assays for level and function; blood coagulation study studies are consistent with DIC; a thorough evaluation for sepsis should be performed to rule out an infectious cause of DIC (CBC/CMP, blood/urine/CSF cultures)	Early biopsies show occlusion of dermal vessels by microthrombi; more advanced lesions show hemorrhage and dermal necrosis	Heparin followed by lifelong coumadin; if protein C deficient, give protein C concentrate followed by lifelong coumadin; protein S is not available commercially	Infants often born with thrombosis of cerebral and retinal vessels which may result in blindness
Acute hemorrhagic edema of infancy	4 – 24 months; well-appearing child with circular, annular, or targetoid purpuric plaques commonly affecting the face and extremities; characteristic tender non-pitting edema of the face, ears, extremities and scrotum	Unknown etiology; infections, drug exposure or immunization is associated in many cases	May be clinically diagnosed; can screen for infectious associations; +/- skin biopsy	Leukocytoclastic vasculitis of capillaries and postcapillary venules; DIF shows perivascular IgA in ⅓ of cases	Supportive care, antihistamines; antibiotics if associated with an underlying infection; no benefit from systemic corticosteroids	Infectious prodrome in 2/3 of cases (80% URI, 12% diarrhea, 6% UTI); affected individuals are healthy-appearing
Neuroblastoma	More than ⅓ of patients are < 1 yr old; bluish papules and nodules distributed diffusely resemble the "blueberry muffin" baby; characteristic blanch response on palpation leaves a surrounding rim of erythema[6]; may see periorbital ecchymoses, "raccoon eyes"	Metastasis of neuroblastoma cells to the skin; most common primary site is the adrenal gland	Screen for TORCH infections, CBC/CMP, serology; skin biopsy; CT or MRI scan to locate the primary tumor; increased serum and urine catecholamines	Infiltrative small dark blue cells in the dermis and/or subcutis form Homer Wright rosettes with characteristic central fibrillary material	Surgery, chemotherapy and radiation	Most common malignant tumor in neonates
Rhabdomyosarcoma	May present with "blueberry muffin" lesions; however, cutaneous involvement is rare; can also present as a persistent lump/swelling of various body sites or bulging of the eye	Rhabdomyosarcoma is a malignant mesenchymal tumor with skeletal muscle differentiation that comprises the majority of soft tissue sarcomas in infants; bluish nodules represent metastasis of rhabdomyosarcoma cells to the skin	Screen for TORCH infections; CT or MRI scan to locate the primary tumor; CBC with peripheral smear can occasionally detect metastatic cells; FOXO1 translocation portends a poorer prognosis	Small to medium-sized darkly staining cells with round nuclei and scant cytoplasm; an alveolar pattern is most commonly seen in the setting of cutaneous involvement; positive staining for vimentin, desmin, and muscle actin	Multi-agent chemotherapy with vincristine, dactinomycin and cyclophosphamide (VAC); radiation therapy for most with surgical resection for some	Primary sites of skin metastases include the extremities, head, neck, orbit, trunk and urogenital region
Leukemia cutis	Congenital or later; can present with blue nodules commonly on the trunk or generalized; may see blue-green nodules referred to as chloromas; commonly see pallor, lethargy, hepatosplenomegaly, fever and CNS involvement	Infiltration of the skin with malignant leukocytes; blue-green color of chloroma is due to myeloperoxidase granules in the malignant leukocytes; AML is most common cause of leukemia cutis	Skin biopsy; CBC with peripheral smear and cytogenetic studies; abdominal US and/or CT/MRI scans to assess extent of involvement	Nodular or diffuse infiltrate of atypical myeloid cells most commonly involving the subcutis; +Grenz zone; numerous mitotic figures; can see "single-filing" between collagen bundles; staining is positive for lysozyme, myeloperoxidase, CD68, CD74, CD43 and CD45	Cytarabine combined with an anthracycline is a common therapy for AML; can consider allogenic stem cell transplantation	Leukemia cutis may precede the appearance of leukemia; most common cutaneous metastasis in neonates

Diaper Dermatitis						
	Presentation	Pathogenesis	Work up	Histopathology	Treatment	Comments
Irritant contact dermatitis	Glazed erythema +/- scale; favors convex surface and spares folds; can develop pseudoverrucous papules and punched-out erosions	Protracted contact with urine and feces as well as friction are the primary factors leading to ICD of the diaper area	May be diagnosed clinically	Spongiosis with variable presence of neutrophils and ballooning degeneration of keratinocytes with necrosis	Frequent changing of diapers; barrier protection with vaseline or zinc paste; mild topical steroids; imadazole creams to treat secondary candida	Rash spares the folds
Candidiasis	Intense erythema with erosions, peripheral scale and satellite pustules; favors folds and genitalia; may also see thrush	Warm moist environment promotes the growth of yeast; +/- recent antibiotic use; most commonly due to *Candida albicans*	KOH preparation shows pseudohyphae and yeast; close observation and cultures in premature neonates if concern for systemic involvement	Stratum corneum with parakeratosis, neutrophils, pseudohyphae and budding yeast; perivascular lymphocytes and neutrophils; PAS/GMS may better reveal the organisms	Imidazole creams typically sufficient; parental antifungals if concern for systemic involvement	Rash favors folds; scrotal involvement common
Seborrheic dermatitis	1 week – several months old; well-circumscribed erythematous moist or scaly plaques favoring the folds of the diaper area; usually see scalp (cradle cap) and other flexural site involvement; no pruritus; characteristic yellow greasy scale not typically seen in diaper or flexural areas	Increased sebum production in the neonatal period with overgrowth of *Malassezia furfur* and immune system activation	May be diagnosed clinically	Variable spongiosis and acanthosis with perifollicular parakeratosis; can see yeast forms in the stratum corneum	Bathing with mild shampoo to remove scale + emollients; ketoconazole cream or shampoo for more severe or persistent cases; low potency topical corticosteroids can be used	Look for involvement of scalp and other intertriginous regions

Atopic dermatitis	> 2 months; erythematous scaly pruritic papules and plaques at the diaper margins; classic eczema sites also involved, including the cheeks and neck; marked pruritus leads to excoriations and lichenification; irritability and poor feeding	Multifactorial; filaggrin mutation leading to barrier compromise is strongest known genetic factor; *Staphylococcus aureus* colonization is prominent and can lead to exacerbations through toll-like receptor 2 (TLR-2)	May be diagnosed clinically	Prominent spongiosis with perivascular lymphocytes and exocytosis; eosinophils in acute lesions; less spongiosis and reduced inflammatory infiltrate with increased acanthosis in chronic lesions	Emollients, topical corticosteroids, topical calcineurin inhibitors, therapy to decrease bacterial colonization (bleach baths, etc); for more severe disease can use phototherapy, systemic corticosteroids, cyclosporine, azathioprine, mycophenolate mofetil or MTX	Relative sparing of the diaper area, favors skin at diaper margins
Psoriasis	Well-demarcated pink shiny plaques of skin folds, convex surfaces, and genitalia; may see typical psoriasis lesions including nail changes; erythrodermic variant somewhat common in neonates	Multifactorial; + family history is common; HLA-Cw6 most important susceptibility gene; may have a preceding URI infection, most commonly *Strep. pyogenes;* increased epidermal turnover rate leading to thickening of the skin and development of scale	May be diagnosed clinically; consider bacterial culture to rule out perianal Strep if prominent perianal involvement; +/- skin biopsy	Hyperkeratosis with confluent parakeratosis; regular acanthosis with hypogranulosis; neutrophils in the stratum corneum (Munro's microabcesses) and spinous layer (spongiform pustules of Kogoj); dilated capillaries in dermal papillae	Often difficult to treat; mild topical steroids are first line; can use topical vit D analogues and topical calcineurin inhibitors; for widespread involvement can consider phototherapy, cyclosporine, retinoids and MTX	Rash involves the folds
Allergic contact dermatitis	Eczematous plaques which typically spare the inguinal folds (however may affect folds if ACD to topicals or baby wipes); "holster" distribution affecting the hips and outer buttocks if ACD to rubber components of diapers	Delayed-type hypersensitivity to rubber additives in diapers, baby wipes or other topical preparations; consider if not responding to typical therapies	Patch testing	Spongiosis with perivascular lymphocytes and eosinophils; exocytosis of inflammatory cells into the epidermis; less spongiosis and development of irregular acanthosis in chronic lesions	Recalcitrant to initial therapy; removal of the offending agent and mild topical steroids	Rarely occurs secondary to food allergies
Langerhans cell histiocytosis	(see above)					
Acrodermatitis enteropathica	Develops within 1 – 2 weeks of weaning from breast milk or at 4 – 10 weeks of age if bottle-fed; eroded erythematous plaques with scale-crust affecting periorificial (mouth, nose, eyes, genitalia) and acral sites; also see diarrhea, alopecia and irritability	Autosomal recessive form caused by mutation in the SLC39A4 gene which encodes a transmembrane zinc uptake protein; acquired zinc deficiency can occur with prematurity, maternal milk deficient in zinc (maternal alcoholism, anorexia nervosa, veganism) or inborn errors of metabolism	Low serum zinc and alkaline phosphatase (zinc is essential for this enzyme)	Verrucous epidermis with pallor of the malpighian layer (basal + spinous layer); extensive necrosis of individual keratinocytes; mild perivascular lymphocytic infiltrate; chronic lesions may demonstrate psoriasiform hyperplasia	Zinc replacement with zinc sulfate or zinc gluconate; rash improves rapidly within 1 – 2 days	Breast milk zinc is more bioavailable than zinc from formulas so true hereditary AE typically does not appear in infants actively breast-feeding
Other "nutritional dermatoses"	Identical presentation to acrodermatitis enteropathica but does not respond to zinc replacement therapy	Essential fatty acid deficiency, biotin deficiency, organic acidurias (propionic acidemia, methylmalonic acidemia, maple syrup urine disease, citrullinemia) or cystic fibrosis	Serological evaluation for vitamin and nutrient deficiencies; sweat chloride test	Parakeratosis with irregular acanthosis and superficial epidermal pallor; mild superficial perivascular lymphocytic infiltrate; chronic lesions may demonstrate psoriasiform hyperplasia	Treatment variable depending on cause of nutritional dermatosis	--
Perianal Streptococcus	Boys < 4 yrs old; bright red erythema extending a few centimeters around the anal verge; can be pruritic or painful; may see painful defecation, blood-streaked stools or anal leakage; no systemic symptoms	Infection with group A β-hemolytic *Streptococcus*; may be preceded by pharyngitis; reports of staphylococcus species becoming more prevalent in this disease presentation	Culture from skin scraping grows group A *Strep* or less commonly *Staph* species	Rarely biopsied; may see diffuse infiltration of the dermis and SC with lymphocytes and neutrophils similar to classic cellulitis	Oral penicillin or 1st/2nd generation cephalosporin; if penicillin-allergic can use a macrolide	Rash may involve skin folds
Granuloma gluteal infantum	Red-brown to violaceous firm ovaloid nodules on the groin, buttocks, and occasionally, upper thighs and lower abdomen	Multifactorial; may be secondary to irritation from urine and feces, maceration, candidal infections	May be diagnosed clinically; KOH may reveal pseudohyphae and yeast if satellite lesions exist	Parakeratosis overlying an acanthotic epidermis; mixed perivascular dermal infiltrate[7]	Minimize irritation: frequent diaper changes, use of barrier paste such as zinc oxide; topical imidazoles to treat candidal infections; is self-limited and resolves in weeks to months	Spares the skin folds; may occur following use of fluorinated corticosteroids
Jacquet's erosive dermatitis	Punched out eroded papules and nodules on the buttocks, perianal skin, and groin	Multifactorial; may be secondary to irritation from urine and feces, maceration, candidal infections	May be diagnosed clinically; KOH may reveal pseudohyphae and yeast if satellite lesions exist	Eroded acanthotic epidermis with parakeratosis and spongiosis; mixed perivascular dermal infiltrate[8]	Minimize irritation: frequent diaper changes, use of barrier paste such as zinc oxide; topical imidazoles to treat candidal infections	Erosions may be painful

Perianal pseudoverrucous papules and nodules	2-8mm erythematous shiny flat-topped papules and nodules in a perianal, genital, and suprapubic distribution	Chronic irritation from feces and urine	May be diagnosed clinically; extensive history is needed as lesions may occasionally resemble condyloma accuminata	Parakeratosis overlying a markedly acanthotic epidermis with pale keratinocytes; mixed perivascular dermal infiltrate[9]	Minimize irritation: frequent diaper changes, use of barrier paste such as zinc oxide; topical imidazoles to treat candidal infections	Child abuse sometimes suspected as lesions may clinically resemble condyloma accuminata[6]
Granular parakeratosis	Two patterns of involvement reported; bilateral linear plaques of the inguinal folds or erythematous geometric plaques underlying pressures points from the diaper[10]; thick flaky scale is characteristic	Rarely reported disease with unknown etiology; diaper wearing, friction, moisture and occlusion seem to play a role; there is retention of keratohyalin granules within the stratum corneum which may be due to a defect in processing profillagrin to fillagrin	Skin biopsy	Thickened stratum corneum containing basophilic keratohyalin granules within areas of parakeratosis	Unclear whether treatment is effective; typically resolves within 1 month to a year	Rarely occurs in infants; more commonly reported in axillae of women
Dermatophytosis	Erythematous sharply-demarcated scaly plaques with an advancing raised inflammatory border and central clearing	Invasion of stratum corneum by dermatophytes; *Trichophyton rubrum*, *Epidermophyton floccosum* and *Trichophyton verrucosum* have been reported[11]	KOH preparation shows branching septate hyphae without budding yeast; consider fungal culture	Neutrophils may be present in the stratum corneum; compact orthokeratosis may be a clue if present; "sandwich sign;" orthokeratosis or parakeratosis alternated in layers with basket-weave stratum corneum; hyphae in the stratum corneum may be seen on H&E; hyphal staining with GMS or PAS	Topical therapy with azoles or allylamines	Rare; few cases reported
Scabies	(see above)					
Congenital syphilis	(see above)					

REFERENCES

1. Popadic S, Nikolic M. Pustular psoriasis in childhood and adolescence: A 20-year sing-center experience. *Pediatr Dermatol.* 2014 Sep-Oct;31(5):575-9.
2. Bolognia JL, Jorizzo JL, Schaffer JV. *Dermatology.* 3r ed. Vol. 1. Edinburg: Elsevier Saunders, 2012. Print.
3. Barnhill RL, Crowson AN, Magro CM, Piepkorn MW. Dermatopathology. 3rd ed. New York: McGraw Hill, 2010. Print.
4. Rapini R. Practical Dermatopathology. 2nd ed. Edinburg: Elsevier Saunders, 2012. Print.
5. Baselga E, Drolet BA, Esterly NB. Purpura in infants and children. *J Am Acad Dermatol.* 1997 Nov;37(1):673-705.
6. Vandana M, Balachandran C, Lonikar V. Blueberry muffin baby: A pictoral differential diagnosis. *Dermatol Online J.* 2008 Feb;14(2):8.
7. Al-Faraidy NA, Al-Natour SH. A forgotten complication of diaper dermatitis: Granuloma gluteale infantum. *J Family Community Med.* 2010 May – Aug; 17(2): 107 – 109.
8. Van L, Harting M, Rosen T. Jacquet erosive diaper dermatitis: a complication of adult urinary incontinence. *Cutis.* 2008 Jul;82(1):72-4.
9. Dandale A, Dhurat R, Ghate S. Perianal pseudoverrucous papules and nodules. *Indian J Sex Transm Dis.* 2013. Jan-Jun; 34(1): 44 – 46.
10. Chang MW, Kaufmann JM, Orlow SJ, Cohen DE, Mobini N, Kamino H. Infantile granular parakeratosis: Recognition of two clinical patterns. *J Am Acad Dermatol.* 2004 May; 50(5 Suppl):S93-6.
11. Baudraz-Rosselet F, Ruffieux P, Mancarella A, Monod M, Frenk E. Diaper dermatitis due to trichophyton verrucosum. *Pediatr Dermatol.* 1993 Dec;10(4):368-9.

DISCLOSURES

None of the authors have a conflict of interest.

AUTHOR CORRESPONDENCE

Kehinde Ogunmakin MD
E-mail:..... kenne.ogunmakin@ttuhsc.edu