Pediatric Bullous Disease

Lehigh Valley Health Network/PCOM

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Overview

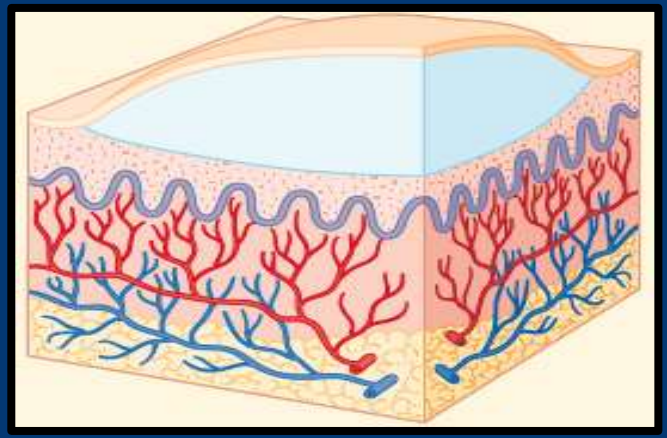
- Briefly review the various categories of pediatric bullous dermatoses
- Discuss some of the most common, board relevant and life threatening pediatric bullous diseases
  - Clinical features
  - Pathogenesis
  - Histopathology and immunofluorescence findings
- Updates on new studies and treatment options

Pediatric Bullous Disease

- Infectious
  - Staphylococcal scalded skin syndrome
    - Bullous impetigo
  - Bullous tinea, eczema herpeticum
  - Blistering distal dactylitis
  - Bullous scabies
  - Varicella virus, herpes simplex virus
- Infectious or medication induced
  - Stevens Johnson Syndrome & Toxic epidermal necrolysis
- Hereditary
  - Epidermolysis Bullosa (EB)
    - Subtypes (simplex, junctional, dystrophic)
  - Kindler syndrome
  - Bullous CIE- Epidermolytic Hyperkeratosis
  - Incontinentia Pigmenti
- Autoimmune
  - Linear IgA bullous dermatosis of childhood
  - Dermatitis herpetiformis
  - Bullous systemic lupus erythematosus
  - Epidermolysis bullosa acquisita
  - Bullous pemphigoid (BP)
  - Pemphigus (folicaeous, vulgaris, drug induced PNP, IgA)
  - Herpes gestionis
- Miscellaneous
  - Contact dermatitis
  - Phytodermatitis
  - Phytophotodermatitis
  - Bullous Erythema Multiforme
  - Bullous Fixed drug
  - Bullous Mastocytosis
  - Porphyrias

Pediatric Bullous Disease

- Blisters- Fluid filled lesions on skin or mucous membranes
  - Vesicles <1cm (Hurwitz)
  - Bullae ≥1cm



Paller et al. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence*, 2011.

- Nikolsky sign
  - Spread of blister with lateral pressure
- Asboe-Hansen sign
  - Spread of blister with perpendicular pressure

Infectious Bullous Disease

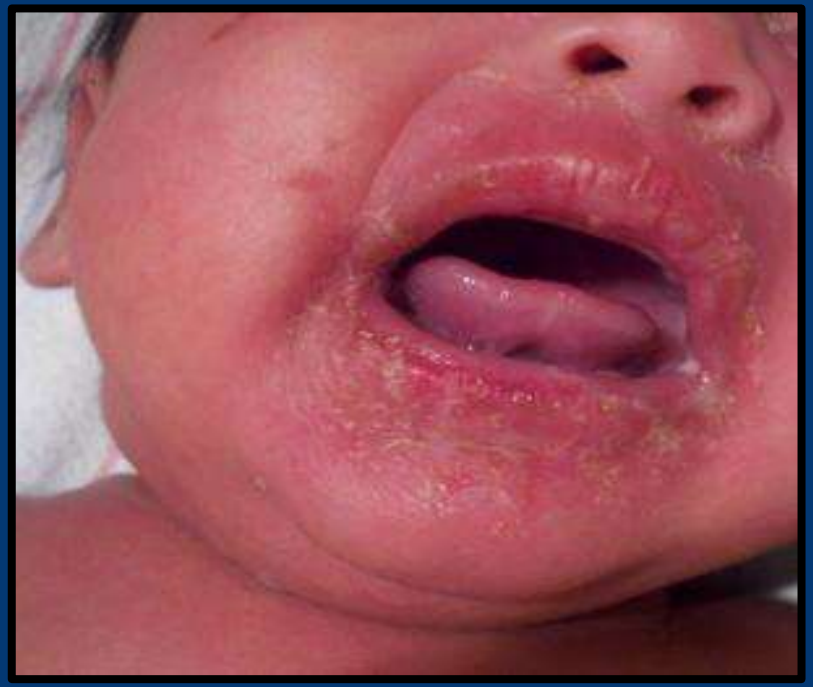
- Staphylococcal Scalded Skin Syndrome (SSSS)
  - Bullous impetigo
- Bullous tinea, eczema herpeticum
- Blistering distal dactylitis
- Bullous scabies
- Varicella virus, herpes simplex virus

Staphylococcal Scalded Skin Syndrome (SSSS)

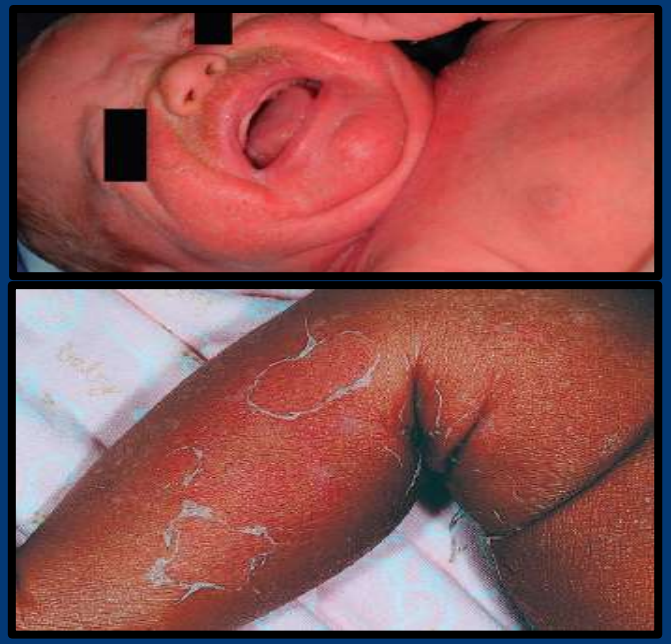
Clinical Presentation

- Neonates and young children
  - Irritability, fever, malaise, poor feeding
  - Due to infection of conjunctivae, nares, perioral region or perineum
  - Generalized erythema then fragile sterile blisters of flexures
    - Positive Nikolsky sign
  - Perioral radial fissuring is common
    - No mucous membrane involvement

SSSS



http://pediatrics.ucsf.edu/blog/unknowns-part-2#.VcZGCbqdLzI



Paller et al. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence*, 2011.

SSSS

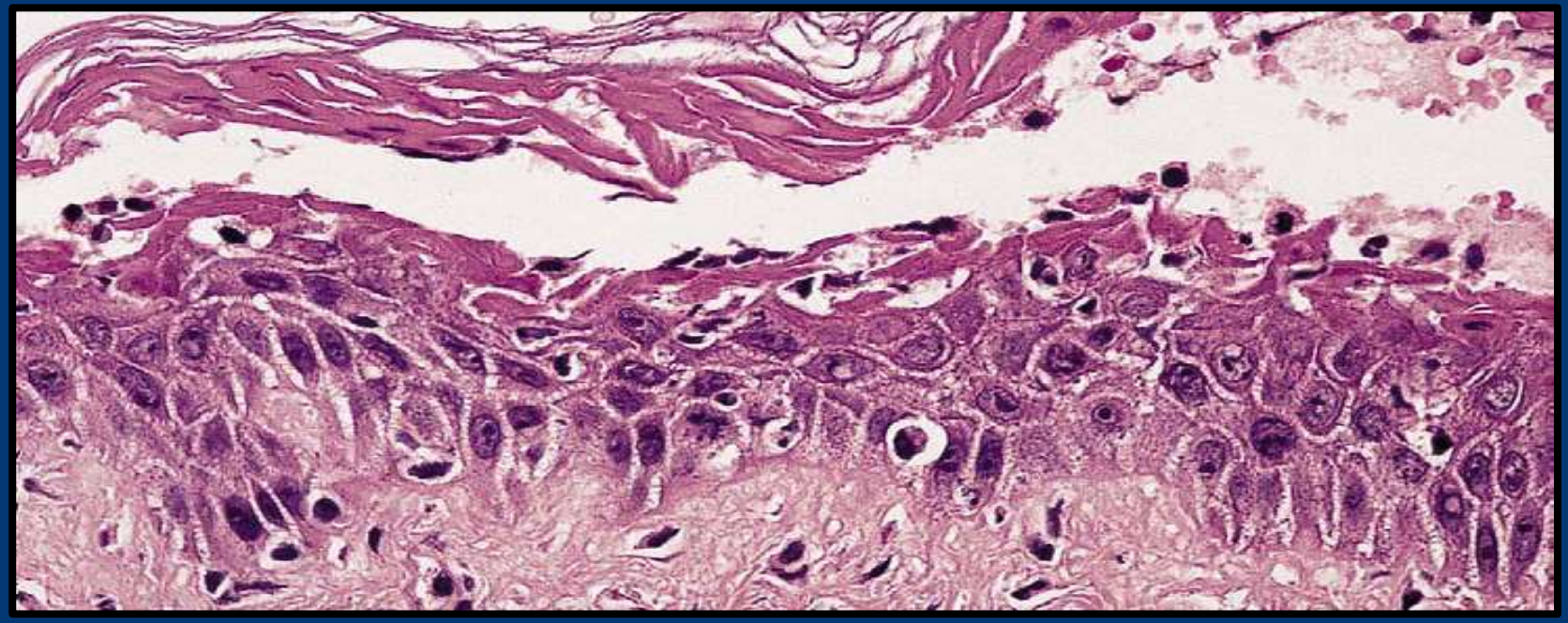
Pathogenesis

- Toxin mediated disease produced by *S. aureus* type 71 of phage group II
  - Exfoliative toxins ETA and ETB
  - Targets desmoglein 1 in superficial epidermis (stratum granulosum)
    - Bullous impetigo localized form
  - Poor renal clearance and low titers of antibodies

Diagnosis

- Bacterial culture from pustule or site of colonization (nares, nasopharynx, perineum)
  - Blisters are typically sterile

SSSS Histopathology



Weedon D. *Skin Pathology 3rd ed*. Elsevier, 2010.

SSSS Treatment

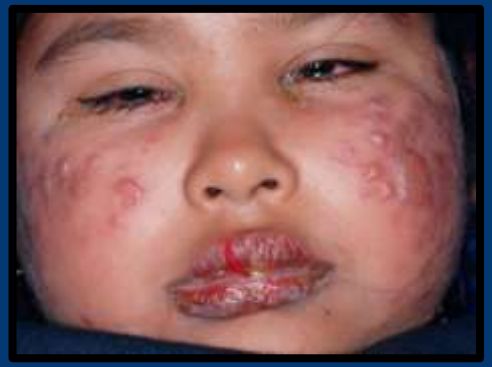
- Eradicate toxin producing bacteria
  - Anti-staphylococcal antibiotics
    - SSSS requires systemic therapy
      - Penicillinase resistant penicillin, 1st or 2nd generation cephalosporins, clindamycin, vancomycin
    - Bullous impetigo may be treated topically or systemically
- Studies suggested fresh frozen plasma or IVIG to neutralize exfoliative toxin

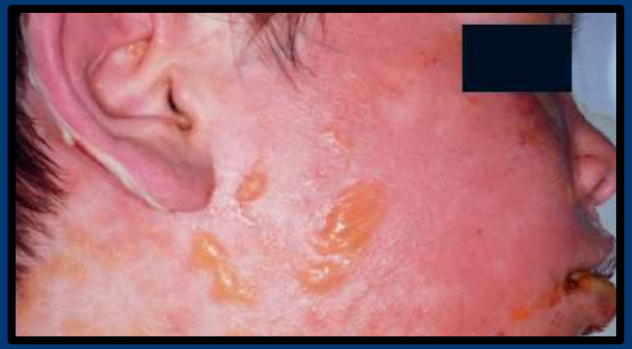
Stevens Johnson Syndrome (SJS) & Toxic Epidermal Necrolysis (TEN)

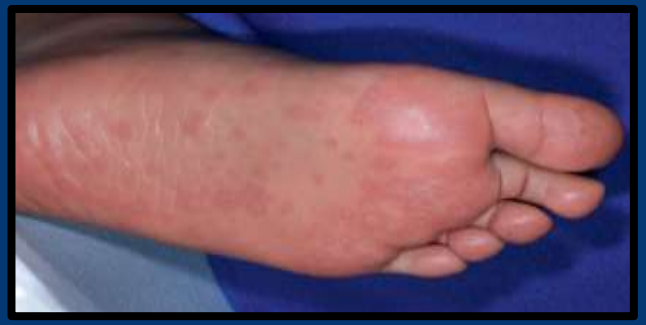
Clinical presentation

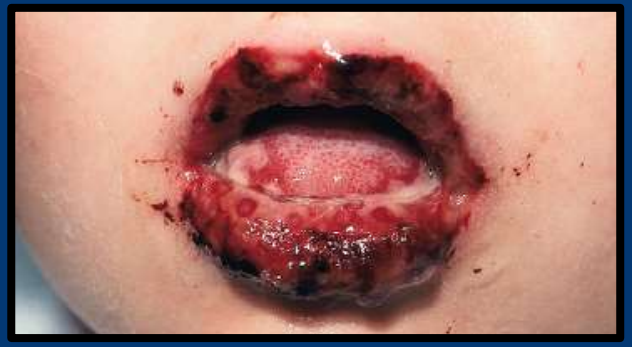
- Life threatening
  - Older children and adults
- Prodromal period 1-14 days
  - High fever, malaise, poor feeding, arthralgias, cough
  - Mucosal symptoms may precede skin findings by 1-2 days
- Painful erythematous or purpuric macules, develop dusky color and bullae become confluent
- Full thickness epidermal detachment
  - Positive Nikolsky and Asboe-Hansen signs
- Visceral involvement and lab abnormalities

SJS/TEN



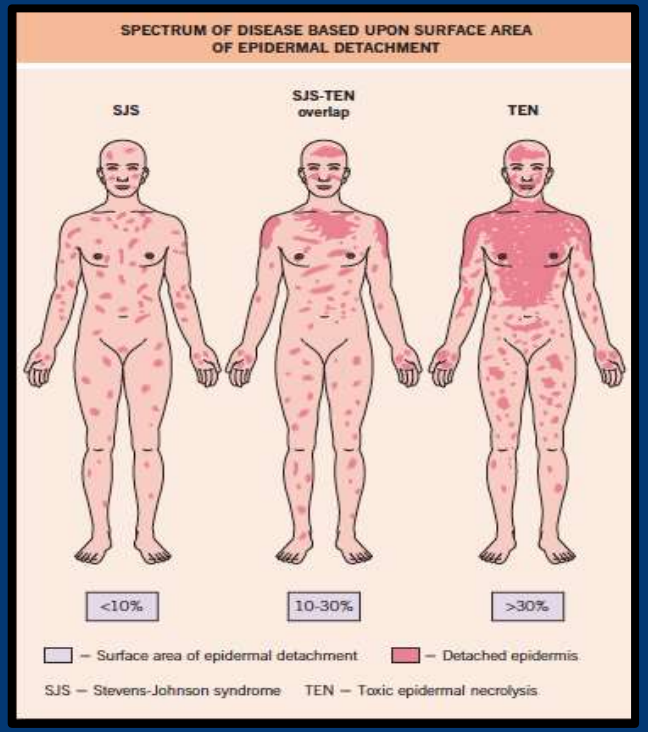






Paller et al. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence*, 2011.

SJS/TEN

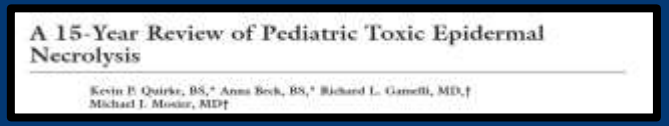


Bolognia J, et al. *Dermatology 3rd ed*. Saunders Elsevier. 2012.

SCORTEN

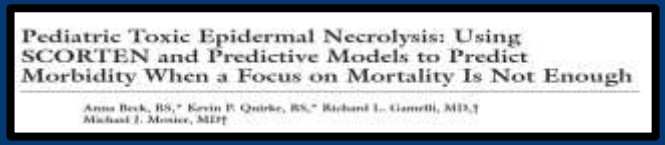
SCORTEN	
Prognostic factors	**Points**
Age >40 years	1
Heart rate >120 bpm	1
Cancer or hematologic malignancy	1
BSA involved on day 1 above 10%	1
Serum urea level (>10 mmol/l)	1
Serum bicarbonate level (<20 mmol/l)	1
Serum glucose level (>14 mmol/l)	1
SCORTEN	**Mortality rate (%)**
0–1	3.2
2	12.1
3	35.8
4	58.3
≥5	90

Bolognia J, et al. *Dermatology 3rd ed*. Saunders Elsevier. 2012.


A 15-Year Review of Pediatric Toxic Epidermal Necrolysis

Kevin P. Quirke, BS,* Anna Beck, BS,* Richard L. Gamelli, MD,† Michael J. Mosier, MD†

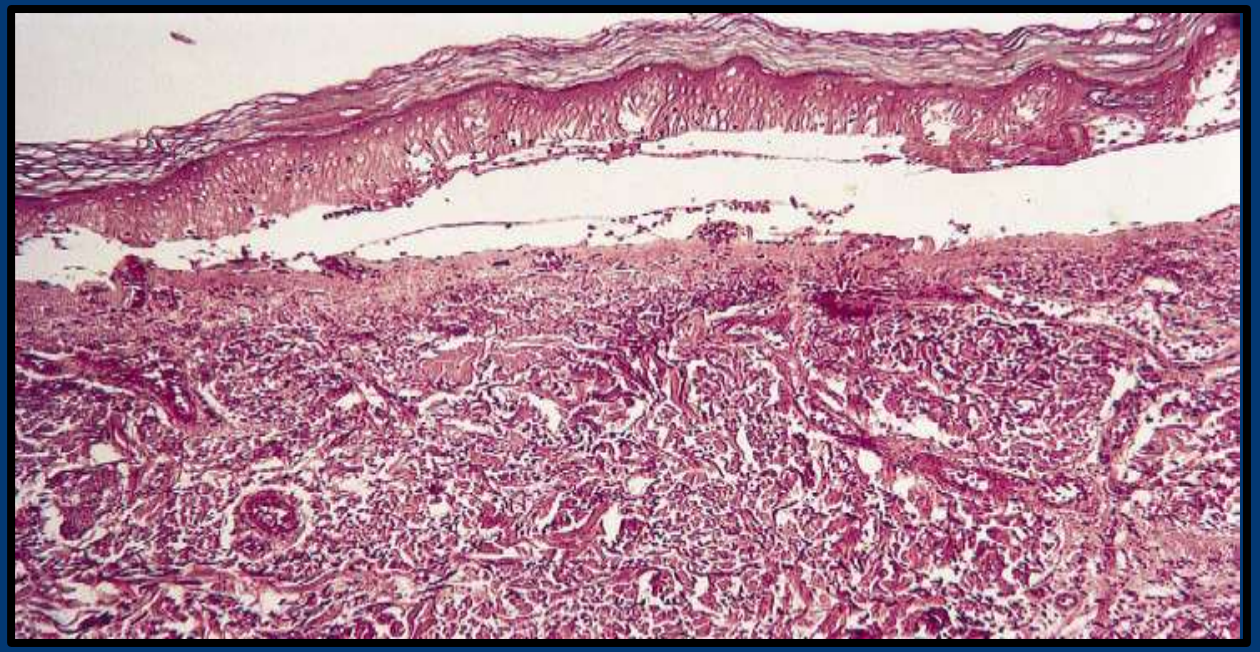
- Lower chance of mortality
- 70% experience morbidity with long term sequelae


Pediatric Toxic Epidermal Necrolysis: Using SCORTEN and Predictive Models to Predict Morbidity When a Focus on Mortality Is Not Enough

Anna Beck, BS,* Kevin P. Quirke, BS,* Richard L. Gamelli, MD,† Michael J. Mosier, MD†

- SCORTEN better predicts morbidity in pediatric patients
  - Days on mechanical ventilation
  - Infectious complications

SJS/TEN histopathology



Weedon D. *Skin Pathology 3rd ed.* Elsevier, 2010.

SJS/TEN

- Pathogenesis
  - SJS-*Mycoplasma pneumoniae* infection and medications
  - TEN- medications (antibiotics & anticonvulsants in children)
  - Fas-Fas ligand mediated keratinocyte apoptosis
- Treatment
  - Discontinue medications, treat underlying infection, supportive care, wound care and prevention of infection
    - IVIG
    - Systemic corticosteroids
    - Anti-TNF alpha
    - Cyclophosphamide
    - Cyclosporine
- Retrospective study by Ahluwalia et al demonstrated corticosteroids as monotherapy or with IVIG result in shorter length of stay and fewer febrile days in mycoplasma-associated SJS

Hereditary Bullous Diseases

- Epidermolysis Bullosa
  - Simplex
  - Junctional
  - Dystrophic
- Kindler syndrome
- Congenital Ichthyosiform Erythroderma
  - Bullous and non-bullous
- Incontinentia Pigmenti

Epidermolysis Bullosa (EB)

Group of >30 inherited blistering disorders

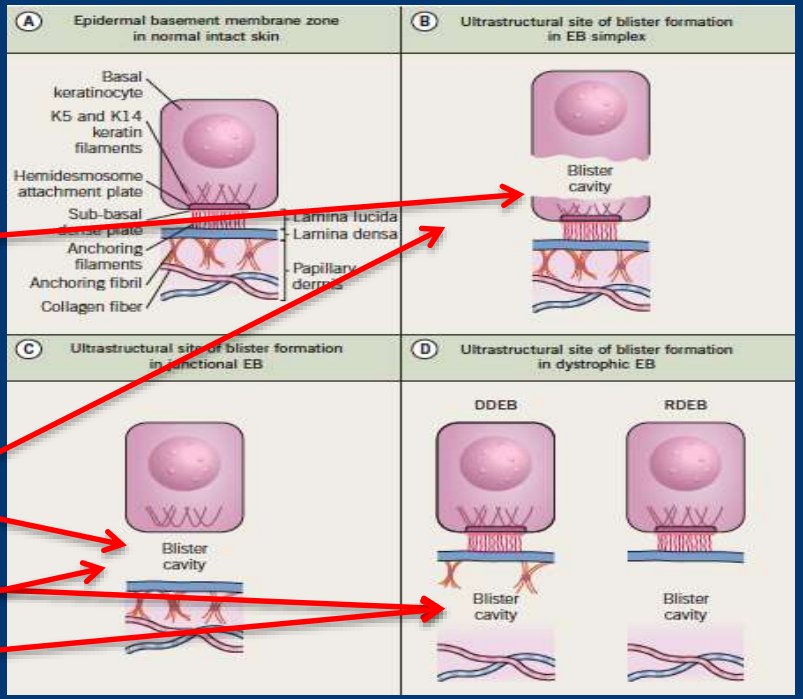
- Blisters and scarring from minor trauma due to skin fragility from inherited structural defects
- EB Simplex

  Split: Epidermal Basal Layer
- Junctional EB

  Split: Basement Membrane

  (Lamina Lucida)
- Dystrophic EB

  Split: Dermal (Sublamina Densa)
- Kindler syndrome

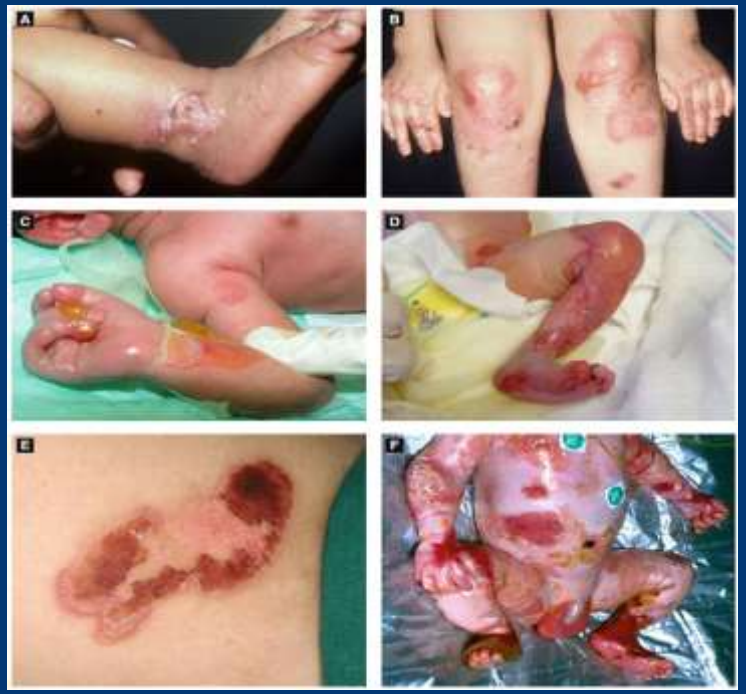


Bolognia J. et al. *Dermatology essentials 1st ed.* Saunders Elsevier. 2014. Print.

Epidermolysis Bullosa

A: EBS-localized (Weber–Cockayne)

B: Dominant DEB (Cockayne–Touraine)



C: Recessive DEB-severe generalized

D: Recessive DEB-severe generalized

E: EBS Dowling-Meara

F: EBS Dowling-Meara

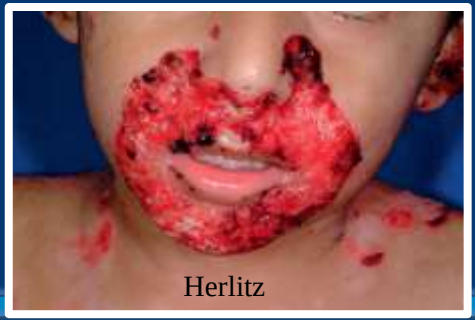
http://www.skin-disease-care.com/815bullous_diseases.php

EB Simplex

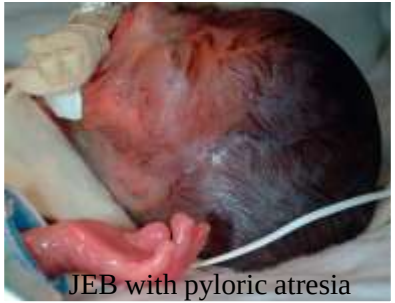
Subtype	Inheritance	Defective Protein	Clinical
EBS-Dowling-Meara (herpetiformis)	AD	K5/K14	Onset at birth, mucosal membrane involvement, nail dystrophy, scarring, early death
EBS-localized (Weber-Cockayne)	AD	K5/K14	Onset childhood, palmoplantar bullae/erosions, heals without scarring
EBS-other generalized (Koebner)	AD	K5/K14	Generalized bullae at birth, PPL, nail dystrophy, heals without scarring
EBS Muscular Dystrophy	AR	Plectin	Widespread bullae at birth, muscular dystrophy, scarring, early death
EBS Mottled Pigmentation			Resembles localized and generalized EBS, reticulated hyperpigmentation over trunk

Junctional EB

Subtype	Inheritance	Defective Protein	Clinical
Herlitz	AR	Laminin 332 (5)	Nonhealing exuberant granulation tissue, enamel defects, mucosal involvement, early death
Non-Herlitz	AR	Laminin 332 (5) or BPAG2 (Type XVII collagen)	Heals with atrophic scars, widespread bullae at birth, scarring alopecia
JEB with Pyloric Atresia	AR	Alpha 6 beta 4 integrin	Severe congenital blistering, pyloric atresia, hydronephrosis, mucosal erosions, aplasia cutis congenita, malformed ears


Herlitz


Non-Herlitz


JEB with pyloric atresia

Paller et al. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence*, 2011.

Dystrophic EB

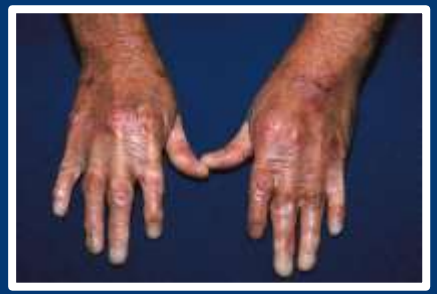
Subtype	Inheritance	Defective Protein	Clinical
Recessive DEB-severe generalized (Hallopeau-Siemens)	AR	Type VII collagen	Severe widespread bulla at birth, heals with atrophic scarring, "mitten deformity", mucosal scarring, esophageal involvement, high risk of SCCs
Recessive DEB, other	AR	Type VII collagen	Less severe than the HS variant, skin changes localized to acral bone prominences
Dominant DEB (Cockayne-Touraine)	AD	Type VII collagen	Bullae mainly over extremities, heals with scarring, nail dystrophy
Pasini Variant (DDEB-P)	AD	Type VII collagen	Similar to Cockayne subtype + white perifollicular papules

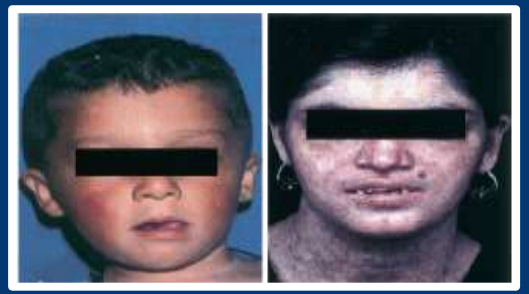
Epidermolysis bullosa acquisita (EBA) – autoimmune T-cell mediated and neutrophilic blistering disease Type VII collagen with linear IgG +/- C3 in sublamina densa (U-serrated pattern)

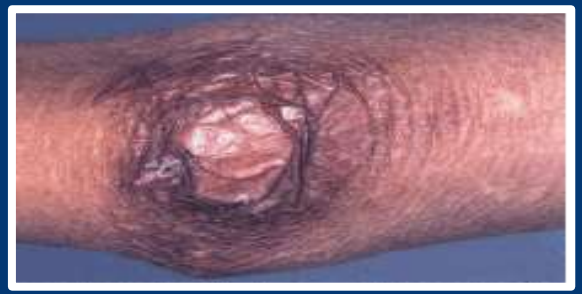
- Subtypes: inflammatory, non-inflammatory & cicatricial pemphigoid

Kindler Syndrome

Name	Inheritance	Defective Protein	Clinical
Kindler Syndrome	AR	Kindlin-1 (mediates anchoring between anchoring fibrils and ECM) due to mutation in KIND1 (FERMT1)	Acral blistering during infancy +/- digital webbing, PPK, photosensitivity, progressive poikiloderma “cigarette paper”atrophy, gingivitis, colitis, stenoses, ectropion







Paller et al. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence*, 2011.

Ashton G, Mclean I, South A, et at. Recurrent mutations in Kindlin-1, a novel keratinocyte focal contact protein, in the autosomal recessive skin fragility and photosensitivity disorder, Kindler syndrome. *J Invest Dermatol*. 2004;122:78-83.

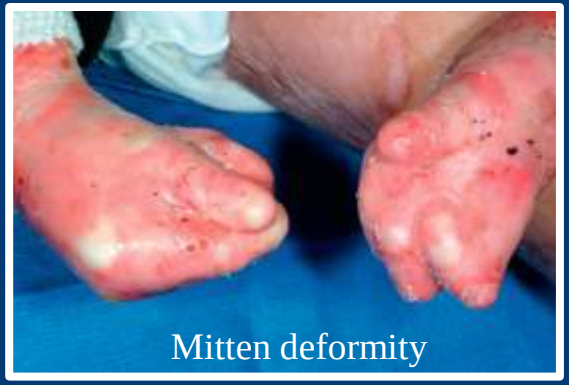
EB

Diagnosis

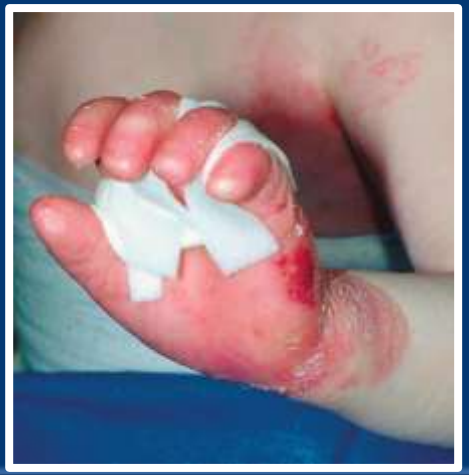
- Genetic analysis
- Transmission electron microscopy
- Immunofluorescence antigen mapping (IFM)

Treatment

- Avoidance of mechanical trauma
- Preventing infections
- Non-adherent dressings
  - Prevent "mitten deformity" (pseudosyndactyly) in DEB
  - Petrolatum-impregnated gauze, soft silicone dressings
- Biopsy non-healing ulcers to exclude SCC
- Multidisciplinary approach



Mitten deformity



Paller et al. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence*, 2011.

New Therapies Dystrophic EB

- Gene therapy
  - Viral vector used to insert functional collagen into skin
- Cell-based therapy
  - Intradermal injections of allogenic fibroblasts used to generate new collagen
- Protein therapy
  - Recombinant collagen produced in vitro is injected into blistering skin
- Bone marrow derived stem cell transplantation
  - Donor cells localize to skin and Type VII collagen deposition at DEJ

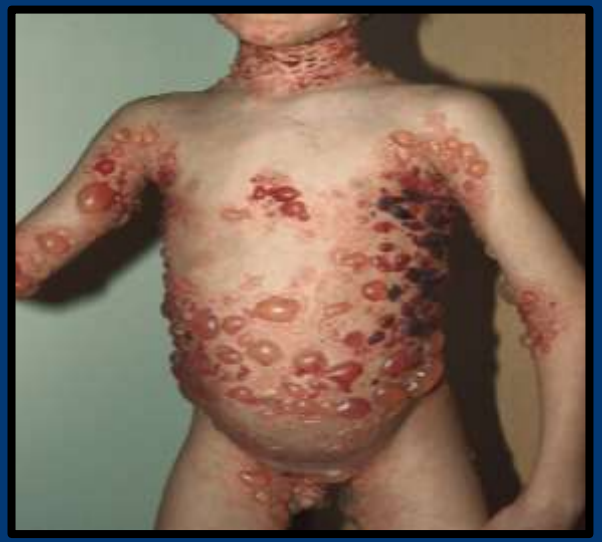
Autoimmune Bullous Diseases

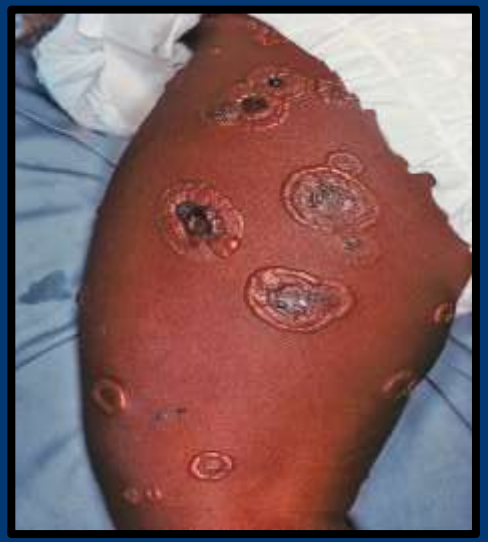
- Linear IgA bullous dermatosis
- Dermatitis herpetiformis
- Bullous systemic lupus erythematosus
- Epidermolysis Bullosa Acquisita
- Bullous pemphigoid
- Pemphigus (foliaceous, vulgaris, PNP, drug-induced)

Linear IgA Bullous Dermatosis (LABD)

Chronic bullous disease of childhood

- Clinical Presentation
  - Tense, clear or hemorrhagic bullae
    - lower trunk, thighs & groin
  - Annular or rosette-like lesions with sausage-shaped blisters
  - Annular erythema with blisters
    - "Crown of jewels"





Paller et al. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence*, 2011.

LABD Pathogenesis

- Immune-mediated subepidermal blistering disease in both adults and children
  - Idiopathic, autoimmune disorders, malignancy
  - Medications- vancomycin, amoxicillin-clavulanate, TMP-SMX
- Linear IgA deposits in two distinct patterns:
  - Classic
    - IgA antibodies to 97-kDa and/or 120 kD fragment of BP180
    - Split in the lamina lucida
  - Recently described

Type VII Collagen Is the Major Autoantigen for Sublamina Densa–Type Linear IgA Bullous Dermatosis

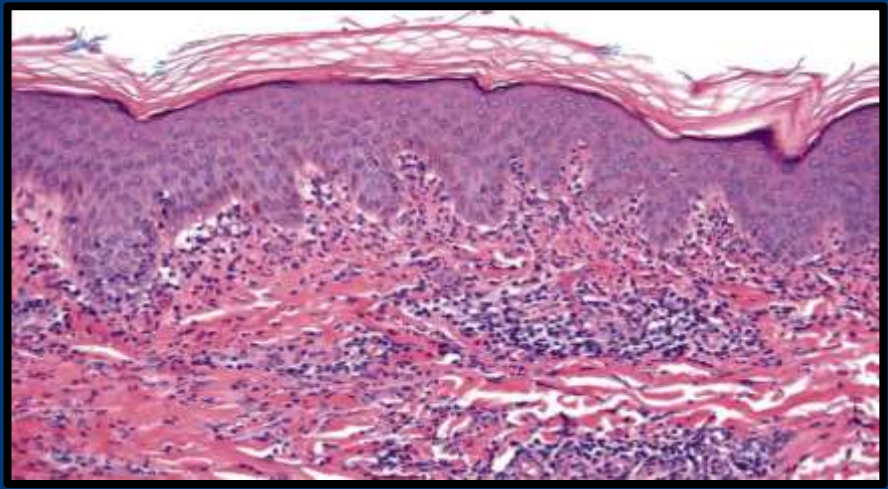
Journal of Investigative Dermatology (2015) **135,** 626–629; doi:10.1038/jid.2014.381; published online 23 October 2014

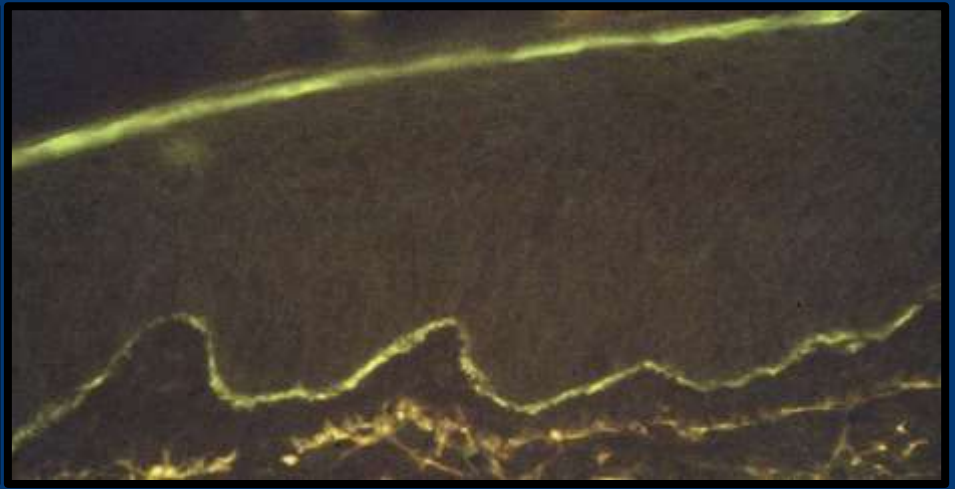
LABD Histopathology and DIF

H&E: Subepidermal bullae with edema of adjacent dermal papillae and dermal infiltrate of neutrophils, eosinophils, mononuclear cells

DIF: linear IgA along DEJ

IIF: Epidermal side of salt split skin





Weedon D. *Skin Pathology 3rd ed.* Elsevier, 2010. Print

LABD Treatment

- Spontaneous remission often occurs within months-years
  - typically by puberty
- Dapsone
  - Clinical improvement 48-72 hours
- Oral corticosteroids
- Antibiotics: dicloxacillin, erythromycin, tetracycline (age >9), trimethoprim/sulfamethoxazole
- Refractory: mycophenolate mofetil, azathioprine, IVIG

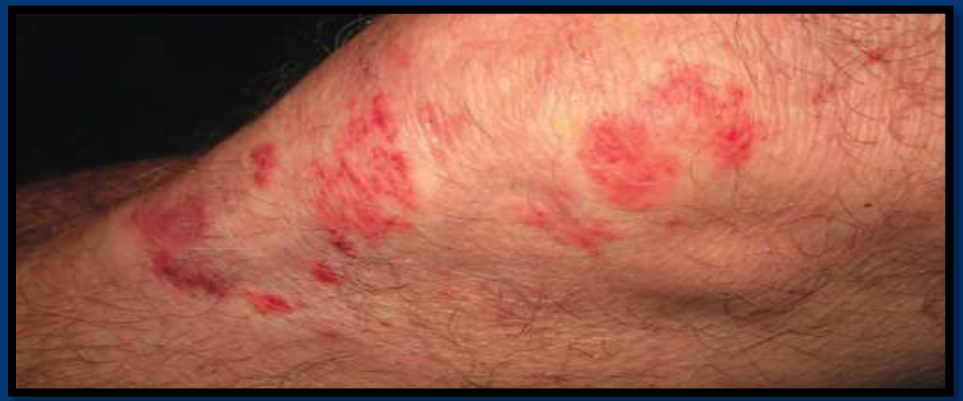
Dermatitis Herpetiformis (DH)

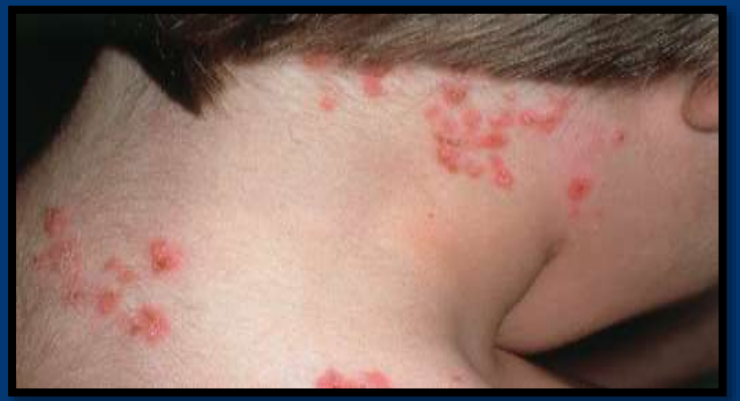
- DH is the specific cutaneous manifestation of celiac disease
  - Sensitivity to gluten found in wheat, barley, and rye
    - Gliaden soluble fraction
    - >90% of patients with DH have evidence of gluten sensitive enteropathy
    - 20% have intestinal symptoms of celiac disease
- Genetic association with HLA-DQ2 and DQ8

Dermatitis Herpetiformis (DH)

- Symmetric grouped vesicles or herpetiform polymorphic lesions
  - Extensor surfaces
  - Knees, elbows, sacral region, shoulders, buttocks, neck, face & scalp
- Intensely pruritic
  - Associated diseases
    - Hashimoto's thyroiditis
    - Insulin dependent diabetes
    - Enteropathy associated T-cell lymphoma
- IgA autoantibodies to tissue transglutaminase (endomysial)
  - Form complexes in the papillary dermis with epidermal transglutaminase-3

DH Clinical Features

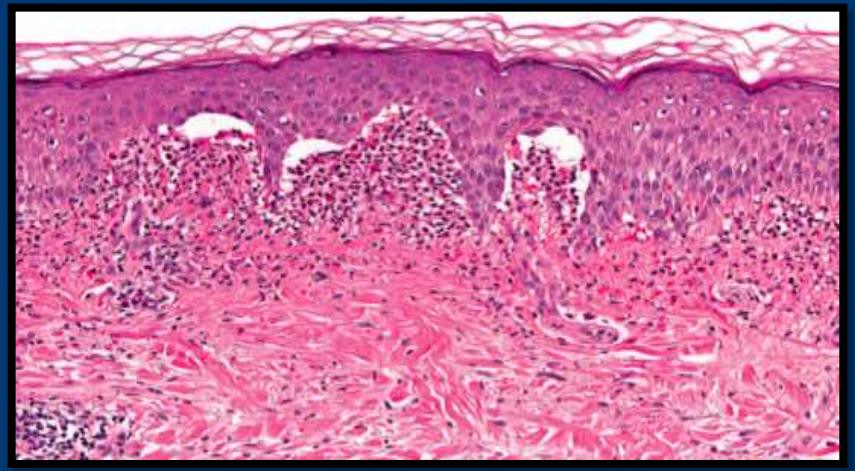




Hall, C, Zone, J. "Dermatitis Herpetiformis and Linear IgA Bullous Dermatosis" *Dermatology*. Ed. Bolognia, J. Elsevier. 2012. 491-496.

DH Histopathology and DIF

H&E: subepidermal vesicles and blisters with accumulation of neutrophils at the papillary tips



Hall, C, Zone, J. "Dermatitis Herpetiformis and Linear IgA Bullous Dermatosis" *Dermatology*. Ed. Bologonia, J. Elsevier. 2012. 491-496.

DIF: Granular or fibrillar IgA at the tips of the dermal papillae, along BMZ

Bolotin D, Petronic-Rosic V. *Dermatitis herpetiformis. Part II. Diagnosis, management, and prognosis.* J Am Acad Dermatol. 2011 Jun;64(6):1027-33.

DH Treatment

- Gluten free diet
- Dapsone
  - sulfasalazine, sulfapyridine, sulfamethoxypyridazine
- Superpotent topical corticosteroids
- Systemic corticosteroids or antihistamines for pruritis

- Case reports:
  - topical dapsone, cyclosporin A, azathioprine, colchicine, heparin, tetracyclines, nicotinamide, mycophenolate mofetil, and rituximab

DH Potential New Therapies

- Prevention
  - Late introduction of gluten to infants with first degree relatives with celiac disease
- Enzyme therapy
  - Supplemental bacterial-derived peptidases may promote digestion of gluten proteins
    - ALV003, is currently in clinical trials and has shown promising safety and efficacy data.
  - Pretreatment of foods with peptidases to decrease gluten content

DH Potential New Therapies

- Immunomodulatory strategies
  - Selective inhibition of TTG in the small intestine to counter the immunotoxic response to dietary gluten
- Correction of the intestinal barrier defect
  - An investigational agent, larazotide acetate, a zonulin inhibitor, decreases intestinal permeability abnormalities and exposure to dietary gluten

Bullous Systemic Lupus Erythematosus (BSLE)

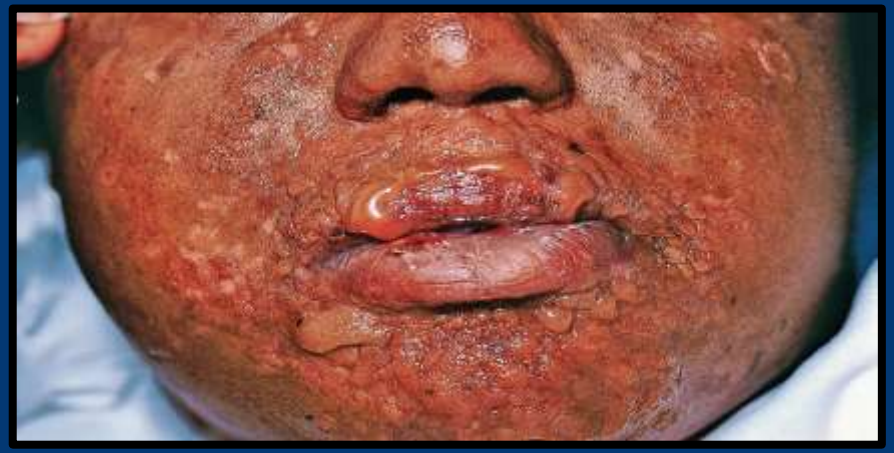
Clinical presentation

- Recurrent blistering disease
- Pruritic vesicles and tense bullae in patients with SLE
- Sun exposed sites
- 30% have mucosal lesions
- Young African American women & adolescents

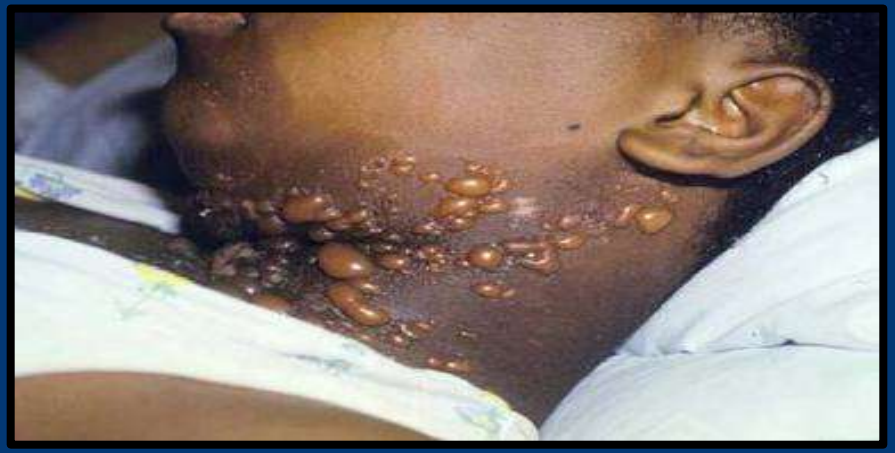
Pathogenesis:

- Circulating antibodies to **type VII collagen** (same as EBA)
  - HLA-DR2 positive

Bullous SLE



Paller et al. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence*, 2011.



Camacho I. Bullous systemic lupus erythematosus. *Medscape emedicine*. http://emedicine.medscape.com/article/1065402-overview

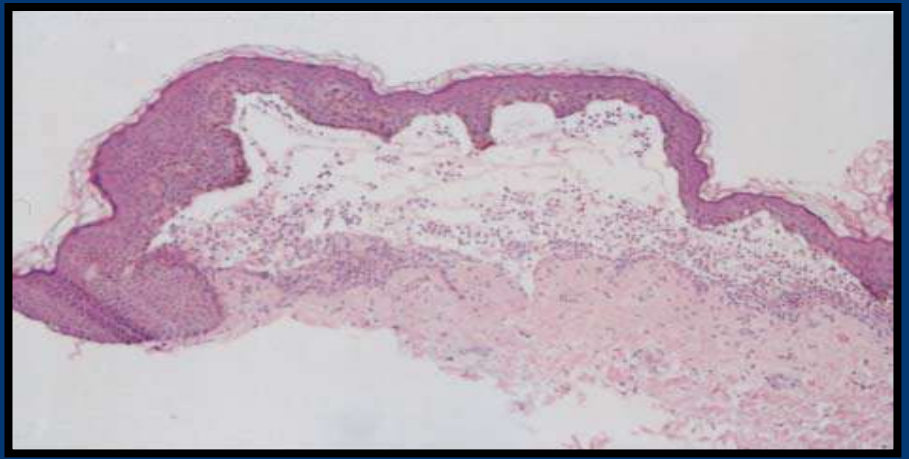
Bullous SLE Histopathology

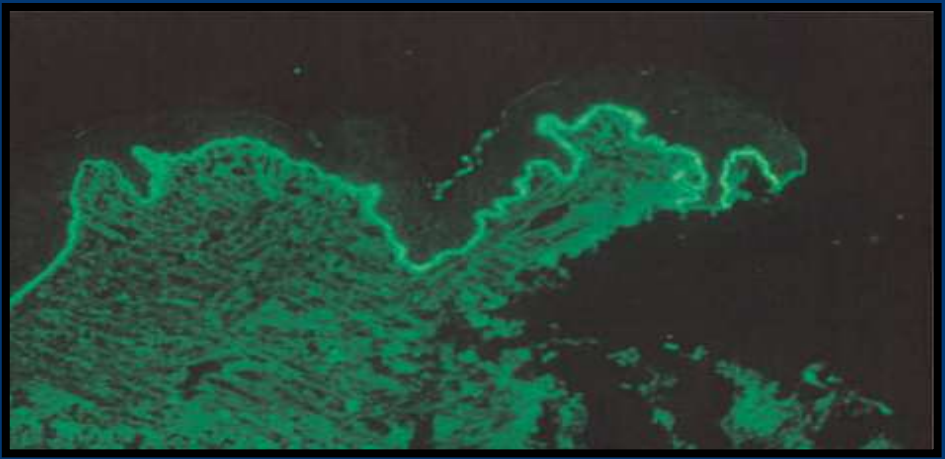
H&E: Subepidermal blister with neutrophil predominant inflammation

DIF : "full house" continuous granular pattern at BMZ of IgG, IgM, IgA, C1q and/or C3

- U-serrated pattern

IIF: Dermal side of salt split skin





Harris-Stith et al. Bullous Eruption. Cutis. 2003.

BSLE Treatment Update

- Review article by Duan et al in the Journal of Immunology Research 2015 on the treatment of BSLE:
  - Dapsone resulted in dramatic response
    - Methotrexate
    - Prednisolone
    - Colchicine
    - Azathioprine
    - Cyclophosphamide
    - Mycophenolate mofetil
    - Rituximab
- Prognosis:
  - Determined largely by visceral manifestations of SLE
  - Good response to dapsone correlates with better prognosis

Summary

- Many diseases present with blisters and bullae in the pediatric population
- Diagnosis is made based on thorough clinical history, physical exam, biopsy, immunofluorescence findings and/or serology
- Studies to further delineate pathogenesis and treatment options to improve patient outcomes

References

1. Antiga E, Caproni M. The diagnosis and treatment of dermatitis herpetiformis. Clin *Cosmet Investig Dermatol*. 2015;8:257-265.
2. Ashton G, Mclean I, South A, et at. Recurrent mutations in Kindlin-1, a novel keratinocyte focal contact protein, in the autosomal recessive skin fragility and photosensitivity disorder, Kindler syndrome. *J Invest Dermatol*. 2004;122:78-83.
3. Barzegar M, Asani-Kani Z, Mozafari N. et al. Using immunofluorescence (antigen) mapping in the diagnosis and classification of epidermolysis bullosa: a first report from Iran. *Int J Dermatol*. 2015;IJD12804.Epub.
4. Beck A, Quirke K, Gamelli R, et al. Pediatric toxic epidermal necrolysis: Using SCORETEN and predictive models to predict morbiidity when a focus on mortality is not enouhg. *J of Burn Care & Research.* 2015;36(1):167-177.
5. Berk DR, Jazayeri L, Marinkovich MP, et al. Diagnosing epidermolysis bullosa type and subtype in infancy using immunofluorescence microscopy: the Stanford experience. *Pediatric Dermatol.*2013;30(2):226-233.
6. Bolognia JL, Jorizzo JL, Scaffer JV, et al. *Dermatology. 3rd ed*. Saunders 2012
7. Bolotin D, Petronic-Rosic V. Dermatitis herpetiformis. Part II. Diagnosis, management, and prognosis. *J Am Acad Dermatol*. 2011;64(6):1027-33.
8. Bolotin D, Petronic-Rosic V. Dermatitis herpetiformis. Part I. Epidemiology, pathogenesis, and clinical presentation. *J Am Acad Dermatol*. 2011;64(6):1017-24.
9. Chen S, Mattei P, Fischer M, et al. “Linear IgA Bullous Dermatosis” from interesting case series. Dept of Dermatology and Dermatopathology and Department of Plastic and Reconstructive Surgery, Johns Hopkins School of Medicine, Baltimore, MD.

References

10. Chmel N, Danescu S, Gruler A. A Deep-intronic FERMT1 mutation causes Kindler Syndrome: An explanation for genetically unsolved cases. *J of Invest Dermatol*. 2015; online.
11. Duan L, Chen L, Zhong S, et al. Treatment of bullous systemic lupus erythematosus. *J of Immunol Res.* 2015; 6 pages. http:dx.doi.or/10.1155/2015/167064. Web.
12. Handler MZ, Schwartz RA. Staphylococcal scalded skin syndrome: diagnosis and management in children and adults. *J of the European Acad of Dermatol and Venereology. 2014;28:1418-1423.*
13. Fasano A, Novel therapeutic/integrative approaches for celiac disease and dermatitis herpetiformis. *Clin Dev Immunol*. 2012;2012:959-61.
14. Heras M, Navedo DL. Linear IgA Bullous Dermatosis of Childhood: Good Response to Antibiotic Treatment. *Clin Exp Dermatol.* 2013;39(3): (395-97).Web,
15. Intong LR, Murrell DF. Inherited epidermolysis bullosa: New diagnostic criteria and classification. *Clin Dermtol* 2012;30: 70-77.
16. Kanwar AJ, Sandu K, Handa S. Chronic bullous dermatosis of childhood in north India. *Pediatr Dermatol*, 2004; 21:(610-612).
17. Lugwig R. Clinical presentation, pathogenesis, diagnosis and treatment of epidermolysis bullosa acquisita. *ISRN Dermatology.*2013;Article ID 812029. 25 pages.
18. Lyngs K, Bygum A. Linear IgA Bullous Dermatosis: A Retrospective Study of 23 Patients in Denmark. *Acta Dermato-Venereologica*, 2015;95(466-71). Web.

References

19. Murauer EM, Gache Y, Gratz IK, et al. Functional correction of type VII collagen expression in dystrophic epidermolysis bullosa. *J Invest Dermatol* 2011; 131: 74-82.
20. Moleiro S, Santos V. Atypical Response to Treatment in Linear IgA Bullous Dermatosis of Childhood: Revision of Literature. *Dermatology Online Journal* 5th ser. 2011;17(6):Web. 16 Aug. 2015.
21. Paek S, Steinberg S, Katz S. Remission in dermatitis herpetiformis: a cohort study. *Arch Dermatol*. 2011;147:301-301.
22. Paller AS, Mancini AJ. Bullous Disorders of Childhood. *Hurwitz Clinical Pediatric Dermatology a Textbook of Skin Disorders of Childhood and Adolescence.* London: Elsevier Health Sciences. 2011. Print.
23. Patsatsi A. Chronic Bullous Disease or Linear IgA Dermatosis of Childhood –Revisited. *J Genet Syndr Gene Ther.* 2013;4(6). Web. 16 Aug. 2015.
24. Quirke K, Beck A, Gamelli R, et al. A 15-year review of pediatric toxic epidermal necrolysis. *J of Burn Care & Research.* 2015;36(1):130-136.
25. Tsuchisaka A, Koji O, Norito I, et al. Type VII Collagen Is the Major Autoantigen for Sublamina Densa–Type Linear IgA Bullous Dermatosis. *J Investig Dermatol Journal of Investigative Dermatology,* 2014;135(2): 626-29. Web.
26. Uitto J. Epidermolysis bullosa: Prospects for cell-based therapies. *J Invest Dermatol* 2008; 128:2140-2142.
27. Vargas TJS, Fialho M, Santos LT, et al. Linear IgA dermatosis associated with ulcerative colitis: complete and sustained remission after total colectomy. *Anais Brasileiros de Dermatologia*. 2013; 88(4): 600-603. Retrieved August 16, 2015, from http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0365-05962013000400600&lng=en&tlng=en. 10.1590/abd1806-4841.20131949.
28. Weedon D. *Weedon's Skin Pathology. 3rd ed.* Elsevier. 2010. Print

Thank you!

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