Pediatric Dermatology Urgencies and Emergencies

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Disclosures

- Clinical trials participation with institutional support from:
  - Abbvie Inc (atopic dermatitis)
  - Arcutis (atopic dermatitis)
  - Palvella Therapeutics (pachyonychia congenita, lymphatic malformations)
  - Amgen (psoriasis)
  - Leo Pharmaceuticals (atopic dermatitis)
- Paid consulting or advisory board participation:
  - Arcutis (atopic dermatitis)
  - Palvella Therapeutics (pachyonychia congenita, lymphatic malformations)
  - Sanofi/Regeneron (atopic dermatitis)
  - Incyte Corporation (atopic dermatitis)
- Off-label use of medications

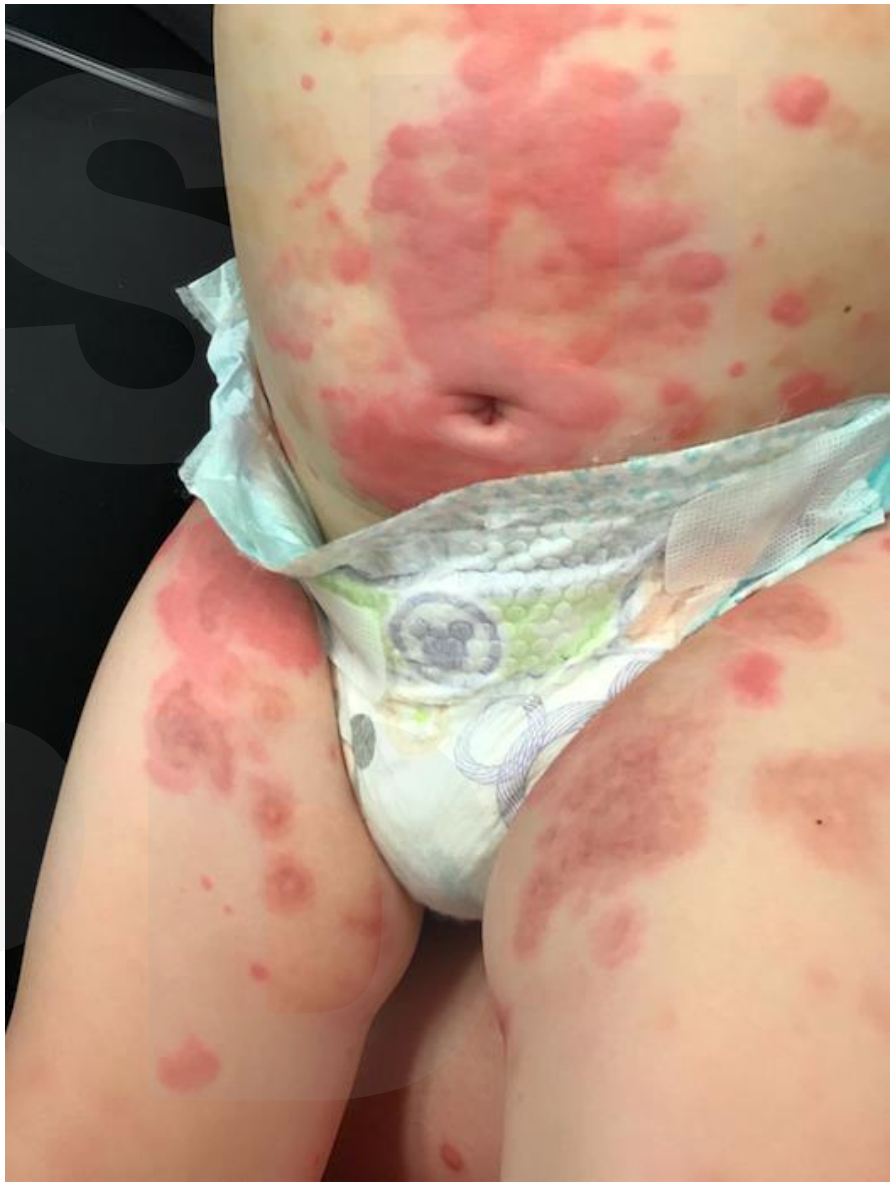
Objectives

1. Increase awareness of urgent pediatric dermatology conditions
2. Discuss work-up and treatment recommendations for urgent dermatologic conditions
3. Review hemangioma referral guidelines

Case 1

- 18-month-old male
- 2 days rash and fever, Tmax 101.4
- Day 8/10 Amoxicillin for AOM
- Fussy, non-toxic, well-hydrated
- Widespread edematous pink papules and plaques with ecchymotic patches
- No mucosal involvement

Dermatologic emergency?



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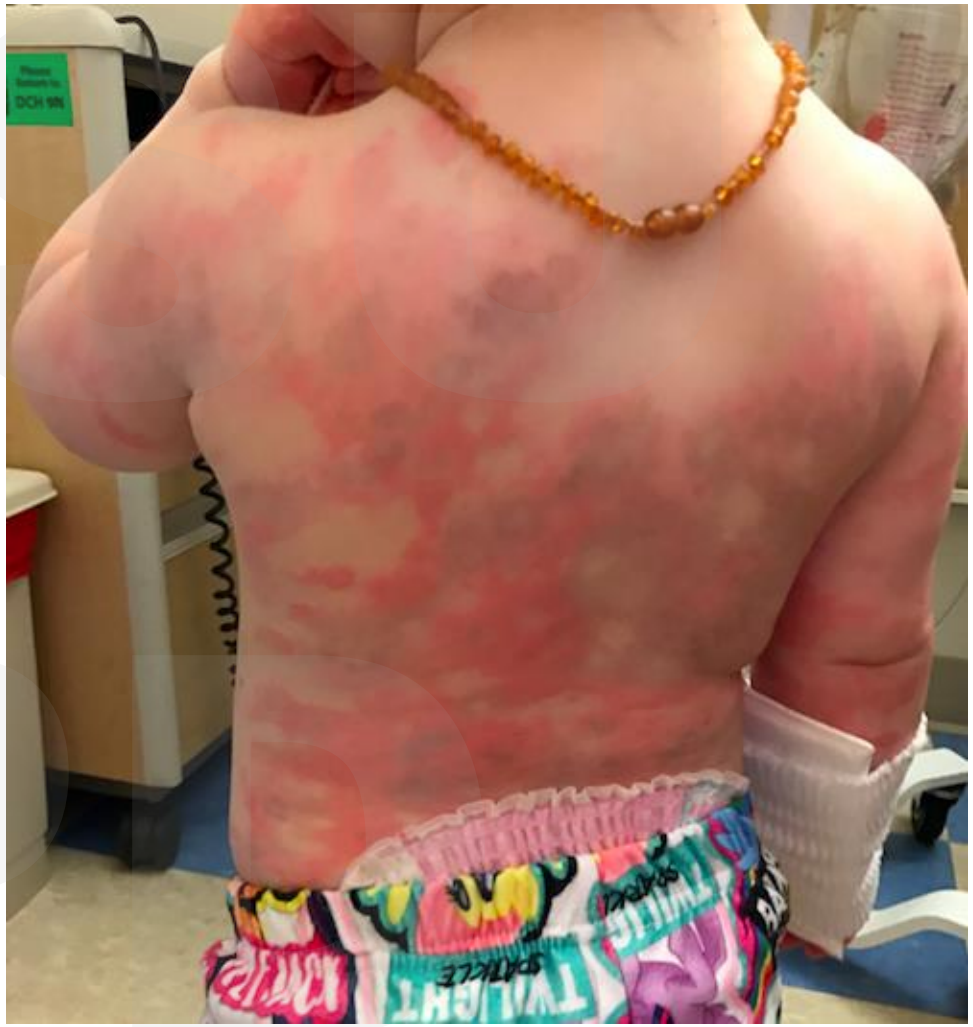
Urticaria Multiforme

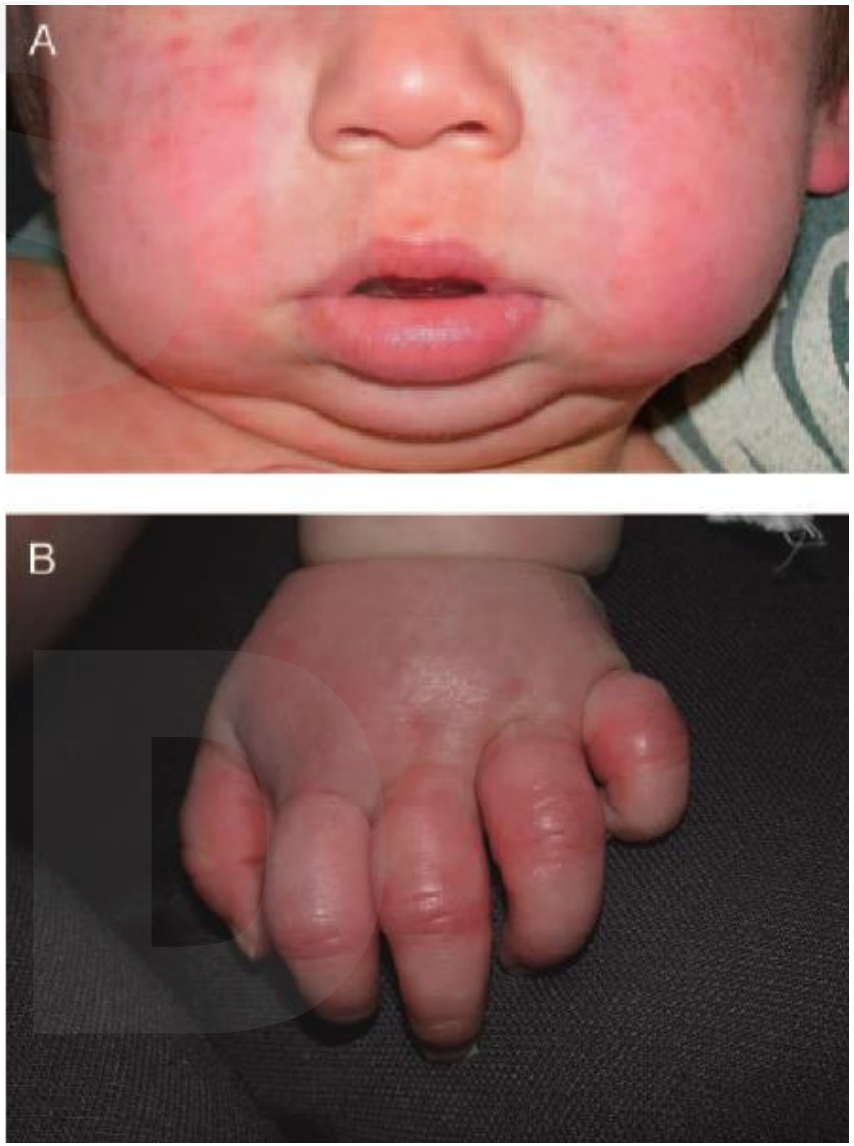
- Acute urticarial hypersensitivity syndrome
  - Response to infection
- More common in children 4 months to 4 years of age
- Self-limited, resolves in 8-10 days
- Often mistaken for EM or serum-sickness-like reaction



Shah, et al. Pediatrics. 2007.

Urticaria Multiforme

- Acute onset, blanchable annular, arcuate and polycyclic erythematous wheals
  - Dusky, ecchymotic center
- Can have associated angioedema of the face, hands, feet
- Dermatographism
- Fever 1-3 days +/- symptoms of other illness
- Non-toxic appearing

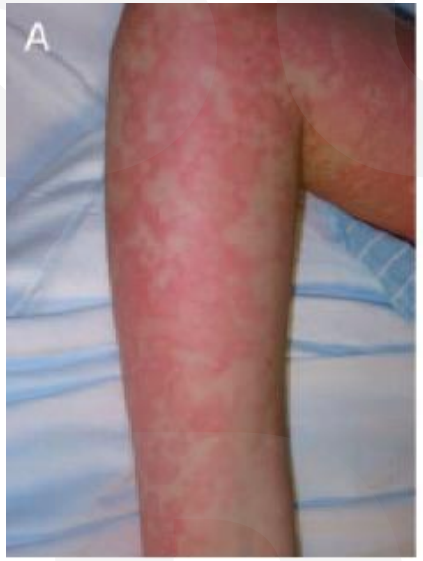


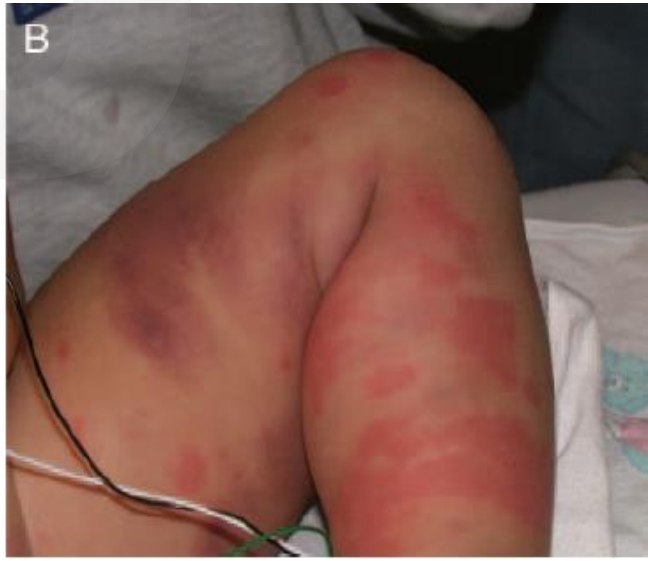
Shah, et al. Pediatrics. 2007.

Urticaria Multiforme

TABLE 1 Diagnostic Criteria for Urticaria Multiforme

- Typical annular and polycyclic morphology and configuration to urticarial lesions
  - Transient, ecchymotic skin changes may be present
  - Absence of true target lesions and/or skin necrosis or blistering
  - Absence of mucous membrane involvement with blisters or erosions
- Duration of individual lesions of <24 h
- Dermatographism
- Angioedema but not arthralgias or arthritis
  - Angioedema typically involves the hands and/or feet but may also involve the periocular or oral mucosa; children with significant edema of the feet may find walking difficult, which should not be confused with arthritis or arthralgias
- Favorable response to antihistamines
  - May require combination therapy with a long-acting antihistamine such as cetirizine in conjunction with a short-acting agent such as diphenhydramine or cetirizine in conjunction with ranitidine
- Modest but not-significant elevations in acute-phase reactants may be present
  - White blood cell count, erythrocyte sedimentation rate, or C-reactive protein level may be mildly elevated but does not demonstrate the elevations typically seen in patients with rheumatologic disorders, serious systemic infections, or Kawasaki disease





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Urticaria Multiforme

TABLE 4 Distinguishing Features of Urticaria Multiforme, Erythema Multiforme, and Serum-Sickness–Like Reactions

Feature	Urticaria Multiforme	Erythema Multiforme	Serum-sickness–Like Reactions
Appearance of individual lesions	Annular and polycyclic wheals with central clearing or ecchymotic centers	Classis target lesion with annular lesions with purpuric or dusky, violaceous center (may blister), middle ring of pallor and edema, outer ring of erythema or blisters	Polycyclic urticarial wheals with central clearing; may appear purpuric
Location	Trunk, extremities, face	Involvement of palms, soles common	Trunk, extremities, face, lateral borders of hands and feet
Duration of individual lesions	<24 h	Days to weeks	Days to weeks
Fixed lesions	No	Yes	Yes
Total duration of rash	2–12 d	2–3 wk	1–6 wk
Mucous membrane involvement	Oral edema common, no erosions or blisters	May see oral erosions or blisters of lips, buccal mucosa, and tongue; rarely involves conjunctivae, nasal, or urogenital mucosa; usually involving only a single site	Oral edema common, no erosions or blisters
Facial or acral edema	Common	Rare	Common
Dermatographism	Yes	No	No
Fever	Occasionally, low-grade	Occasionally, low-grade	Prominent, high-grade
Associated symptoms	Pruritus	Mild pruritis or burning	Myalgias, arthralgias, lymphadenopathy
Common triggers	Antibiotics, immunizations, viral illness	Herpes simplex virus, other viral illness	Antibiotics
Treatment	Discontinue any new or unnecessary antibiotics or medications; combinations of H1 and H2 antihistamines may be helpful; systemic steroids can be helpful in more recalcitrant cases	Supportive care; early institution of systemic steroids can sometimes be helpful	Discontinue any new antibiotics or medications; H1 and H2 antihistamines; supportive care; consider systemic corticosteroids

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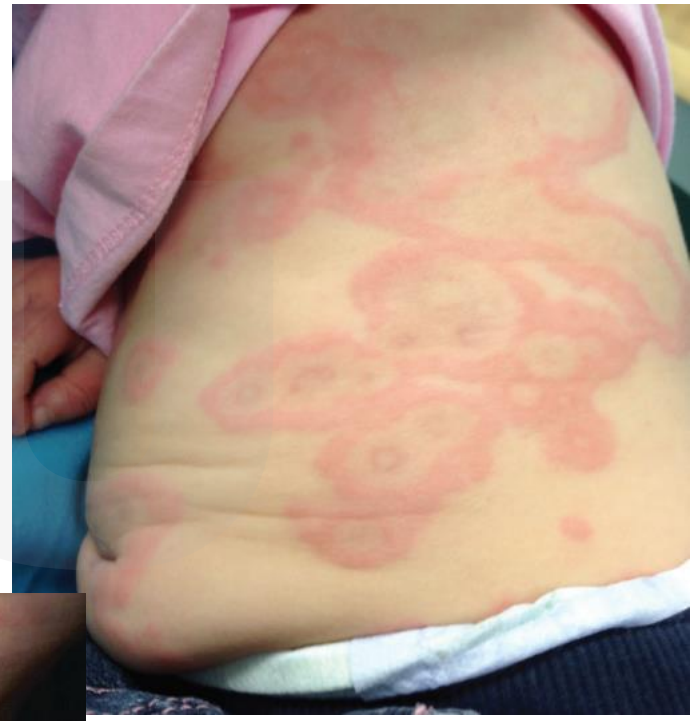
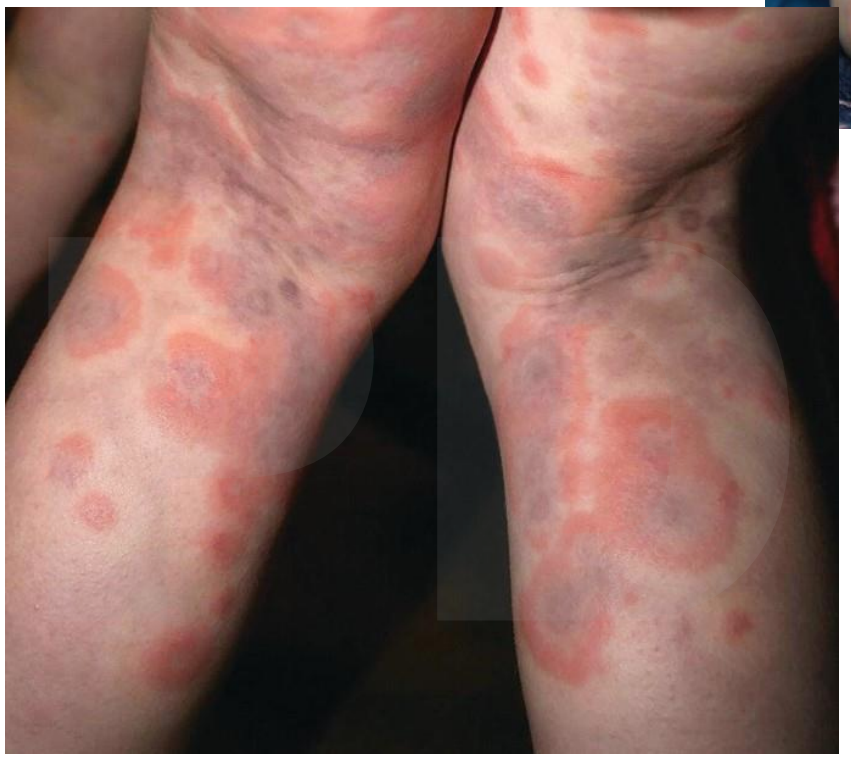
Urticaria Multiforme

- Treatment:
  - Discontinue antibiotics if relevant/possible
  - Scheduled antihistamines
  - Supportive care

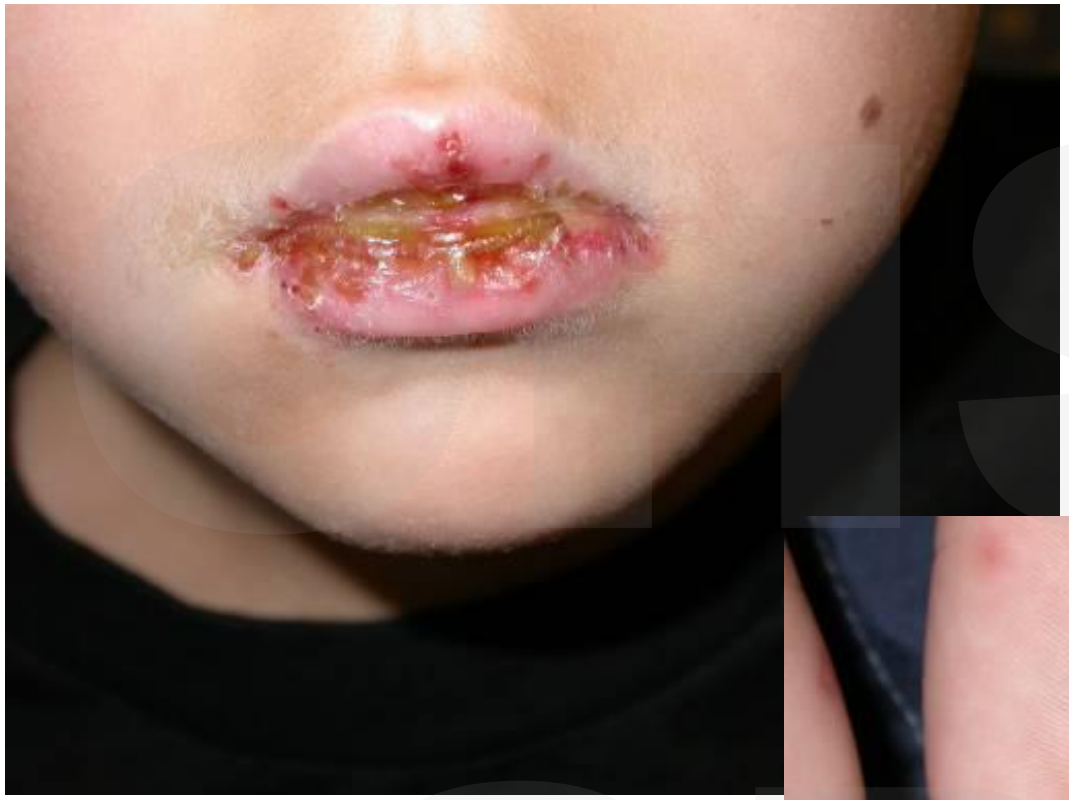




Shah, et al. Pediatrics. 2007.

Case 2

- CC: 8 YO male with a rash on the palms x 1 day
- He has crusting of his lips and reports a recent cold sore outbreak
- T 100.2



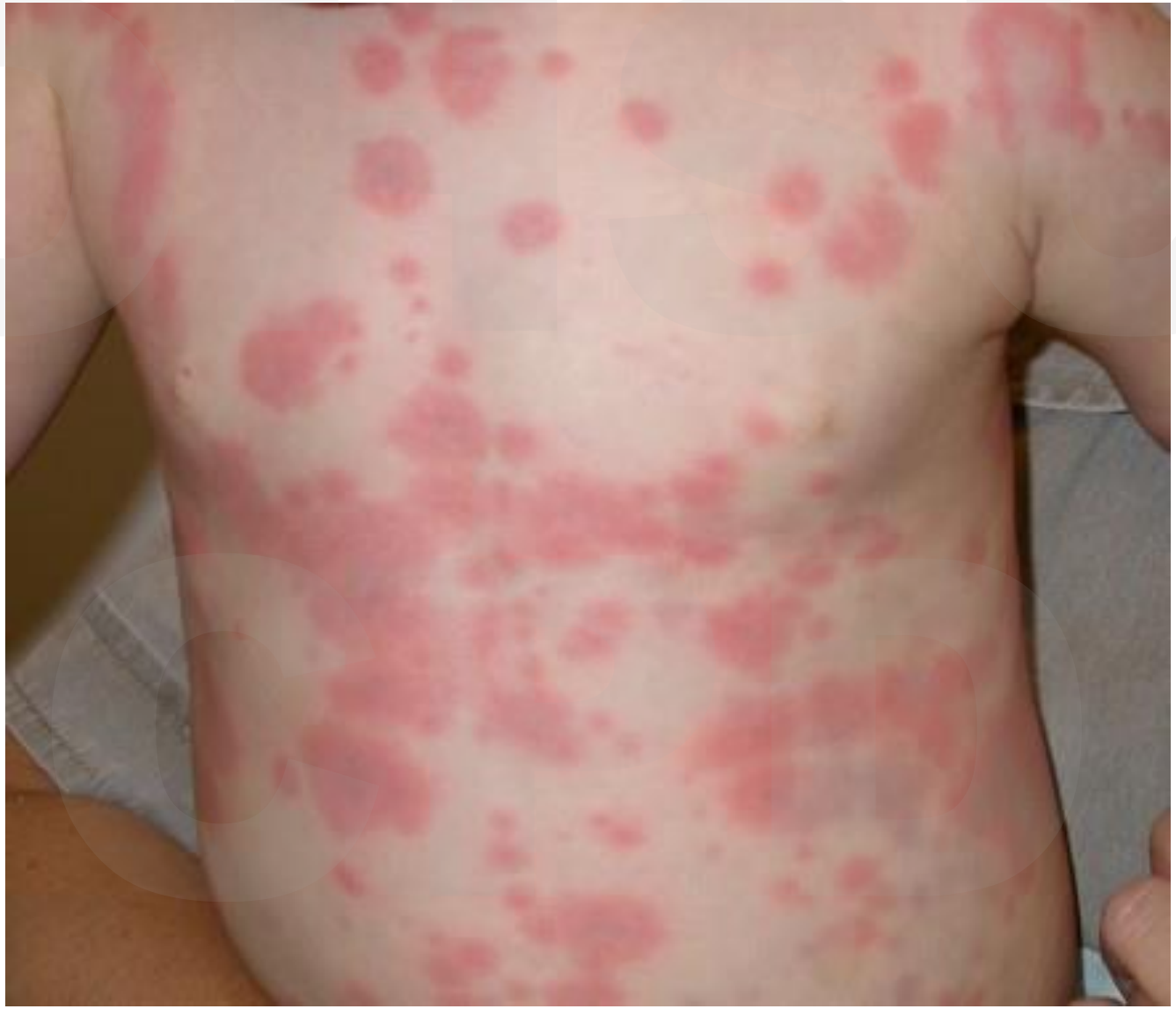
Erythema Multiforme

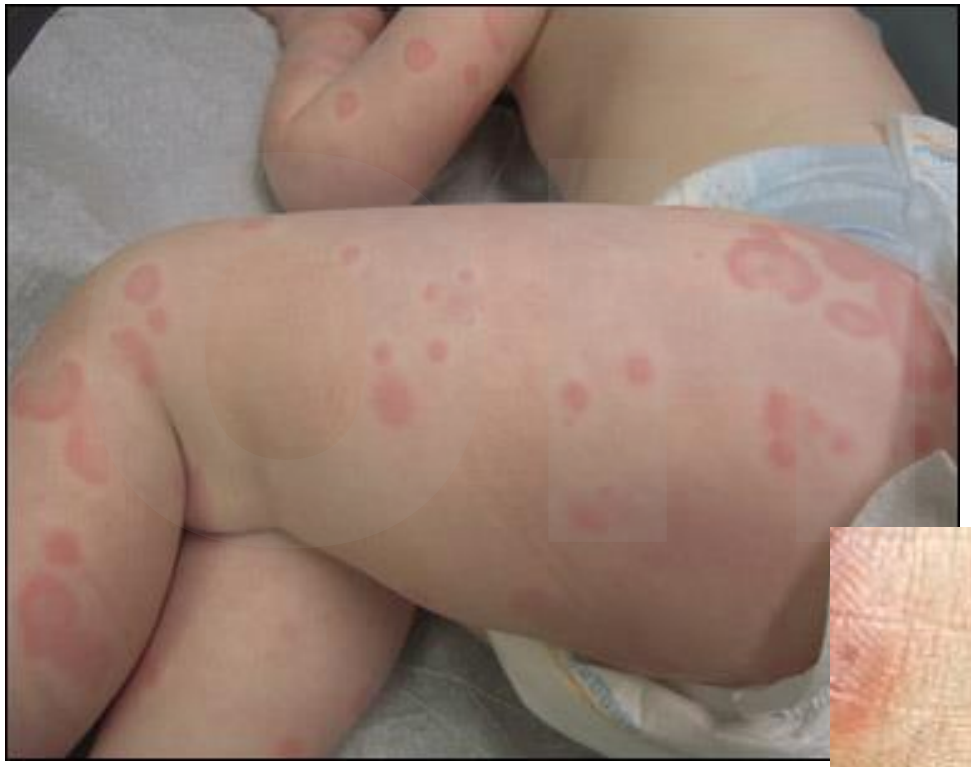
- Self-limited, mucocutaneous reaction
- Most cases in children follow HSV1 infection outbreaks, usually by 3-14 days
- Hallmark is target lesion with papule, vesicle, or bulla centrally
- Symmetric, can be diffuse, predilection for hands and feet
- Most lesions asymptomatic
- Individual lesions are fixed for 7+ days
- Oral lesions are present in 25-50% children
- Persists x 2-4 weeks
- Does *not* progress to Stevens-Johnson syndrome

Erythema Multiforme: Treatment

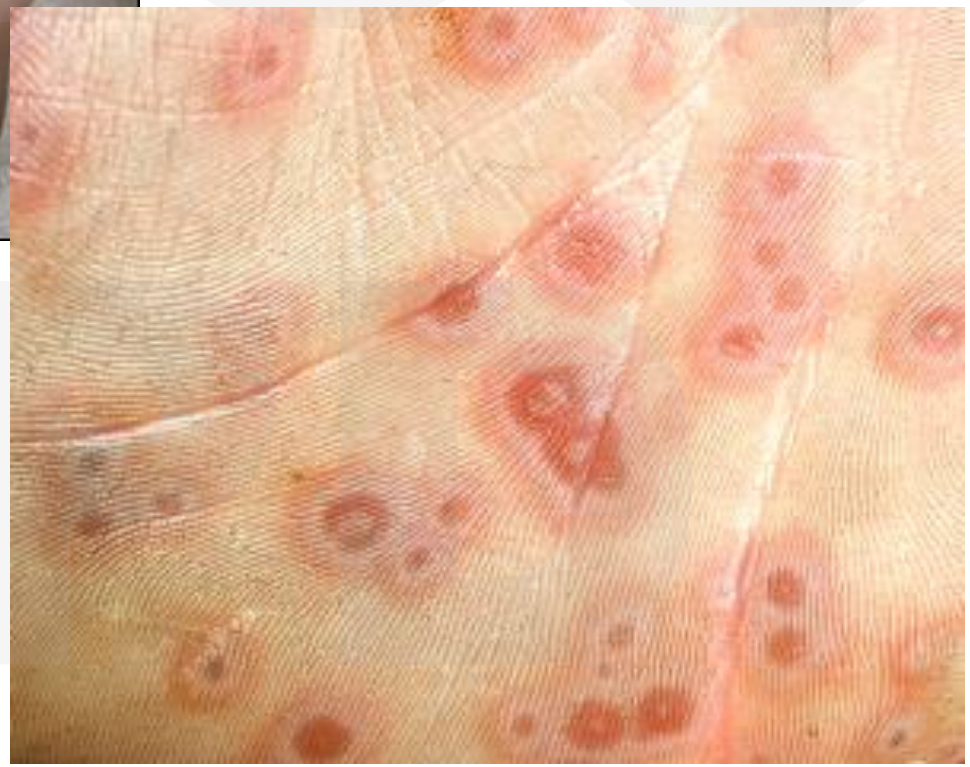
- Antivirals if infection is ongoing
- Symptomatic treatment
  - Antihistamines, topical steroids, analgesics to relieve itch and discomfort
- Recurrence common
  - Prophylactic acyclovir or valacyclovir

Erythema Multiforme?

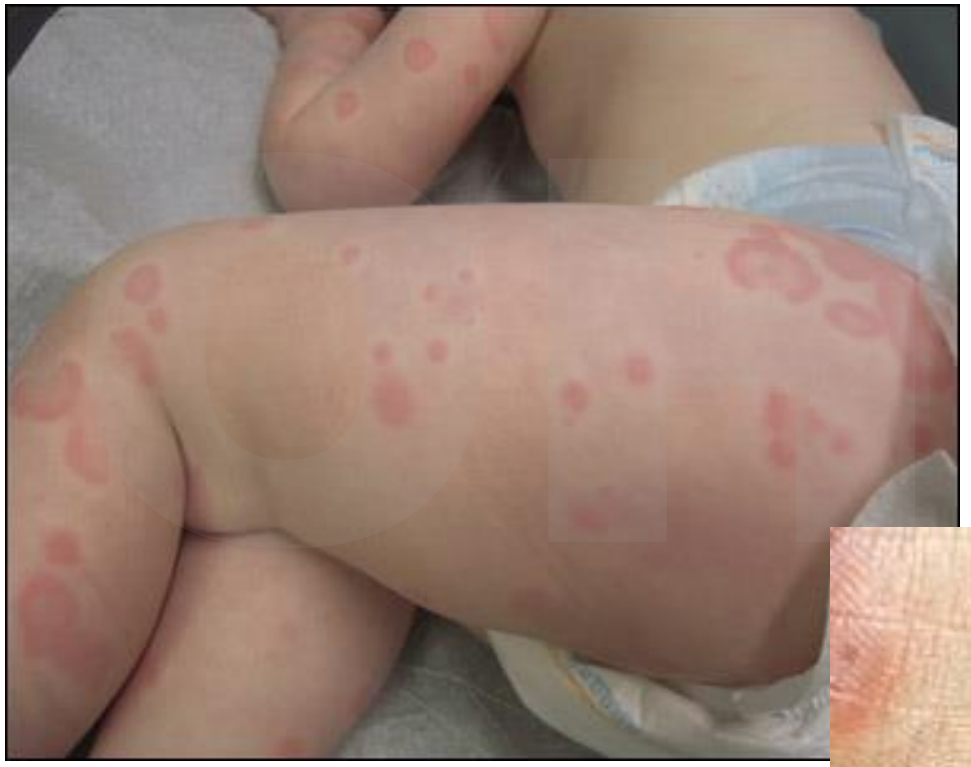




Atypical target lesions



Target lesions



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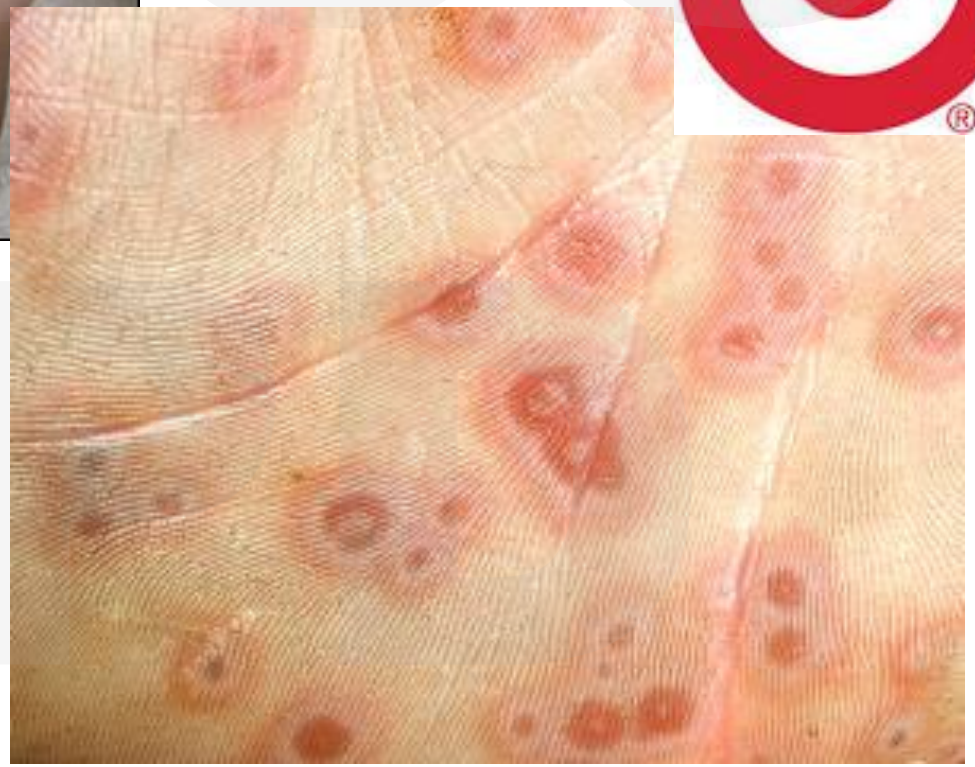
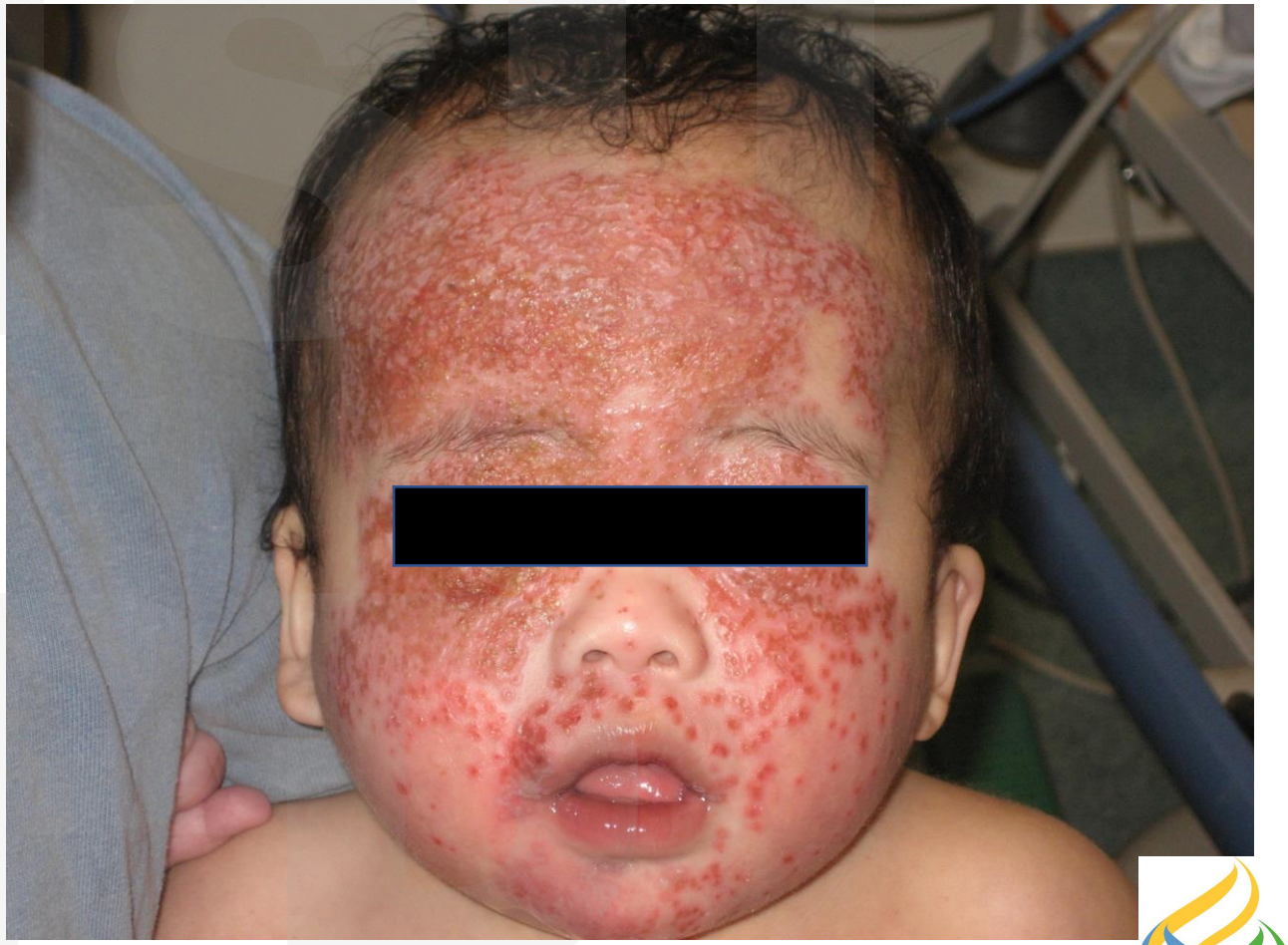


Target lesions

Case 3

- 9-month-old male
- 2 days of fever (Tmax 102.5), worsening rash x 3 days
- Known history of atopic dermatitis
- Fussy, drooling
- Extensive crusted erosions on face, arms, hands, feet



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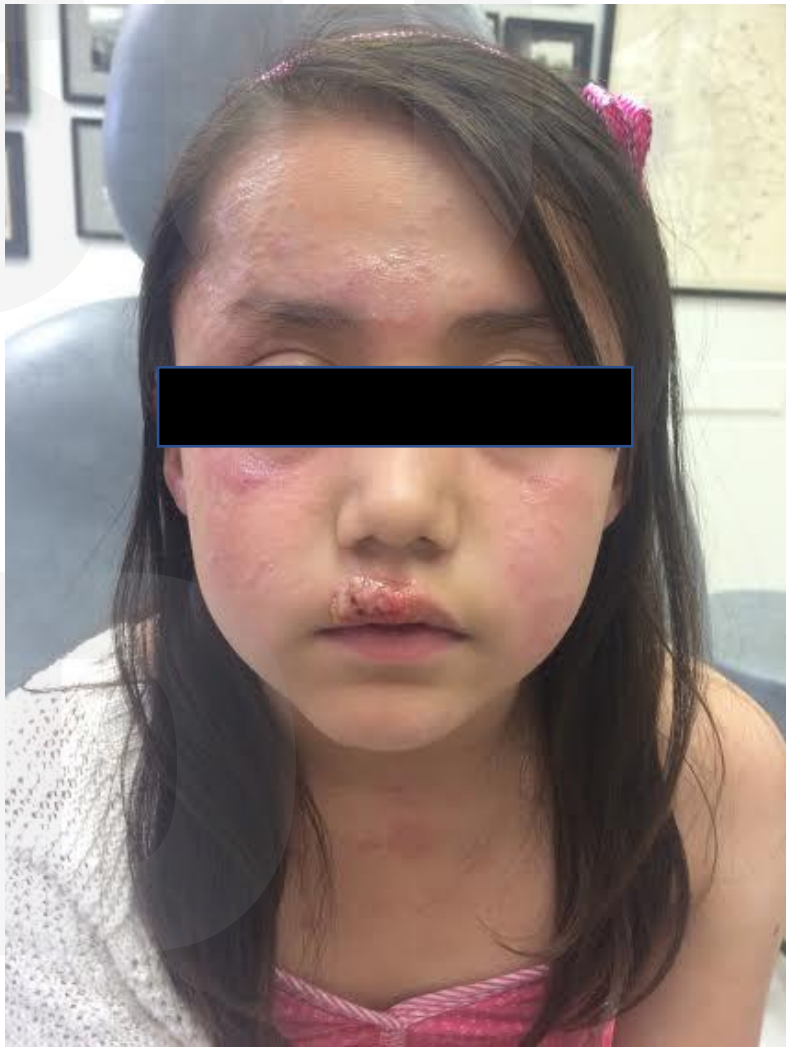
Eczema Herpeticum

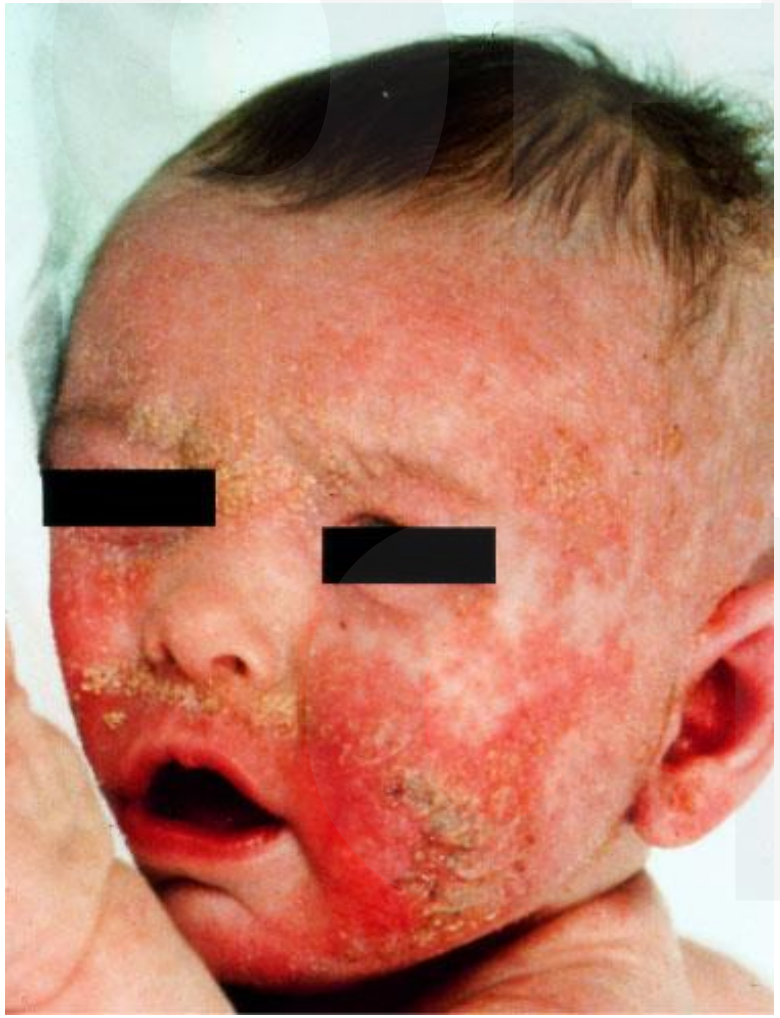
- Rapid spread of HSV in individuals with atopic dermatitis
  - Also seen with varicella, coxsackie virus (eczema coxsackium)
  - Small, round umbillicated vesicles and punched out erosions
- Severity varies, but can be associated with high fever, widespread skin involvement (especially with primary HSV infection), risk for death
- New lesions may appear for 7-10 days
- Secondary bacterial infection common

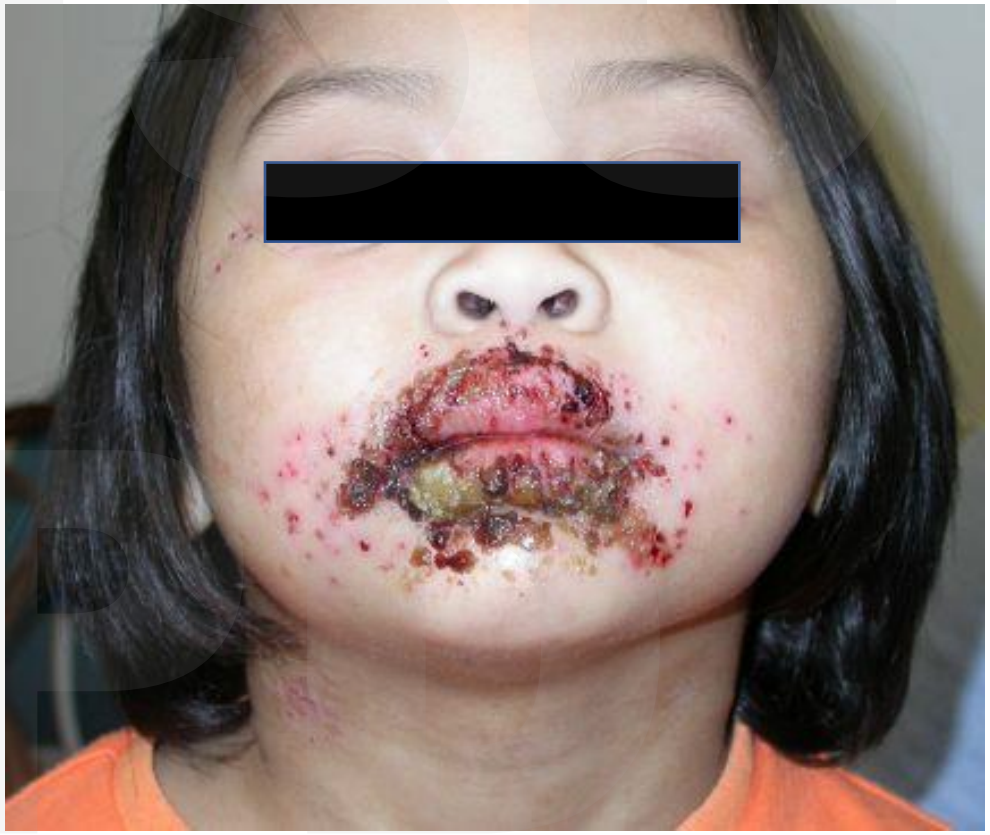
Eczema Herpeticum: Work-up and treatment

- Ophthalmology consultation if near eye
- Admission for observation, management of fluid and electrolyte status
- HSV PCR or viral culture, bacterial culture
- Systemic acyclovir for 7-10 days
- Antibiotics for secondary bacterial infection
- Treat the underlying atopic dermatitis!
  - Bland emollients
  - Topical steroids

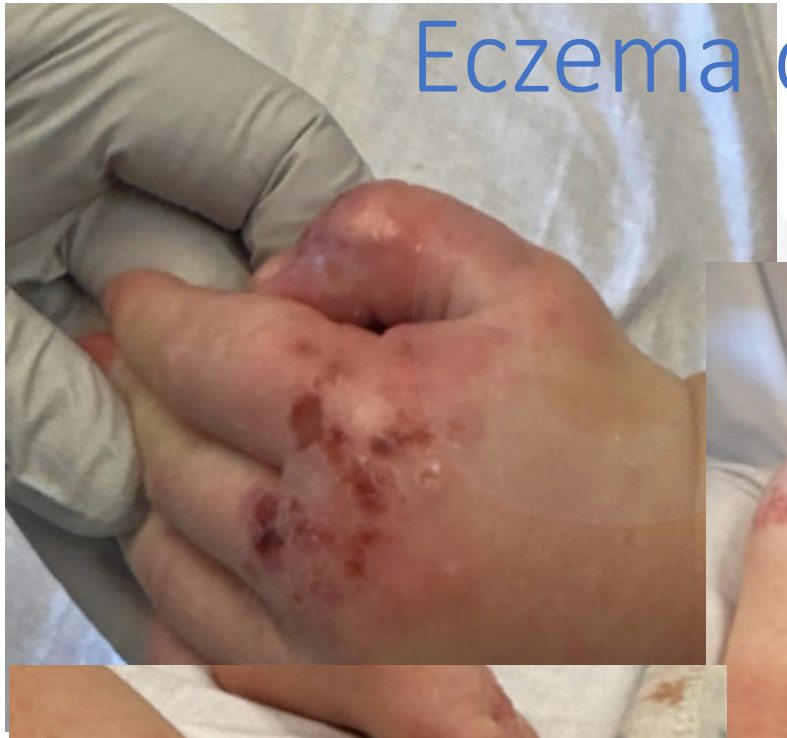


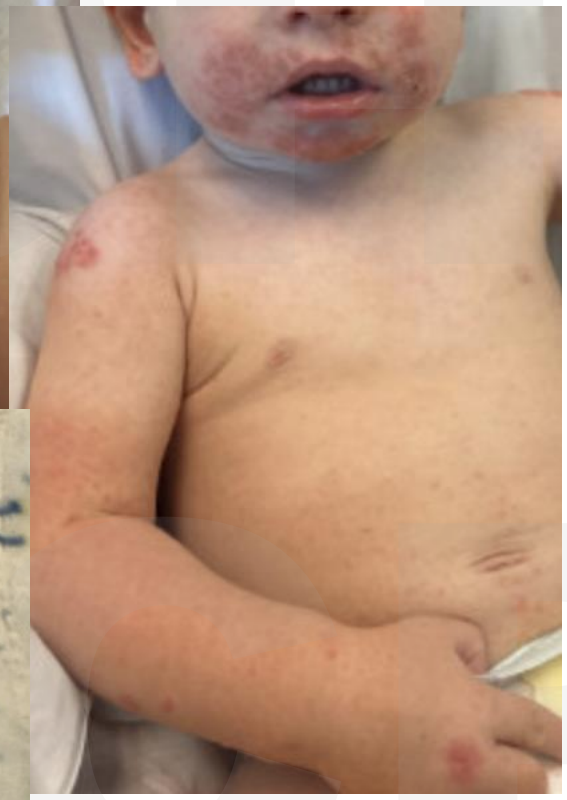
Impetigo vs. eczema herpeticum

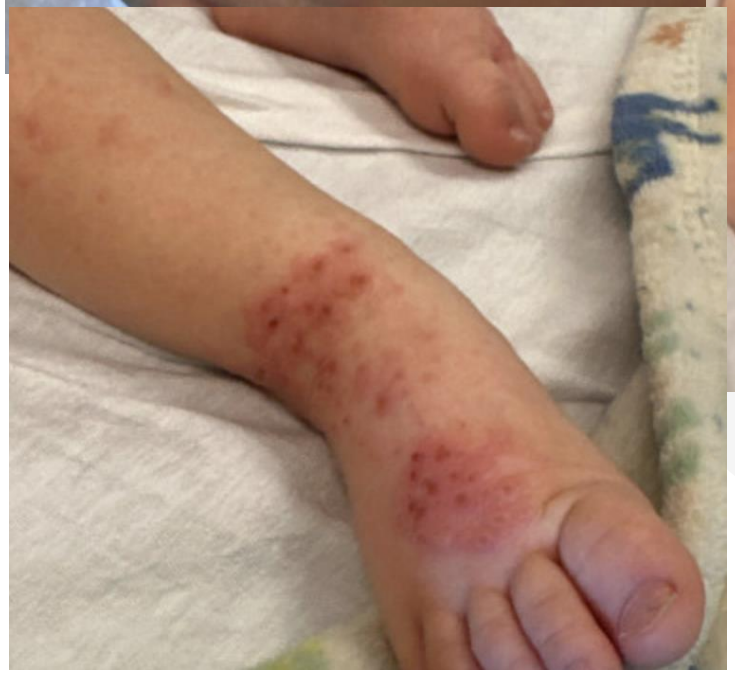


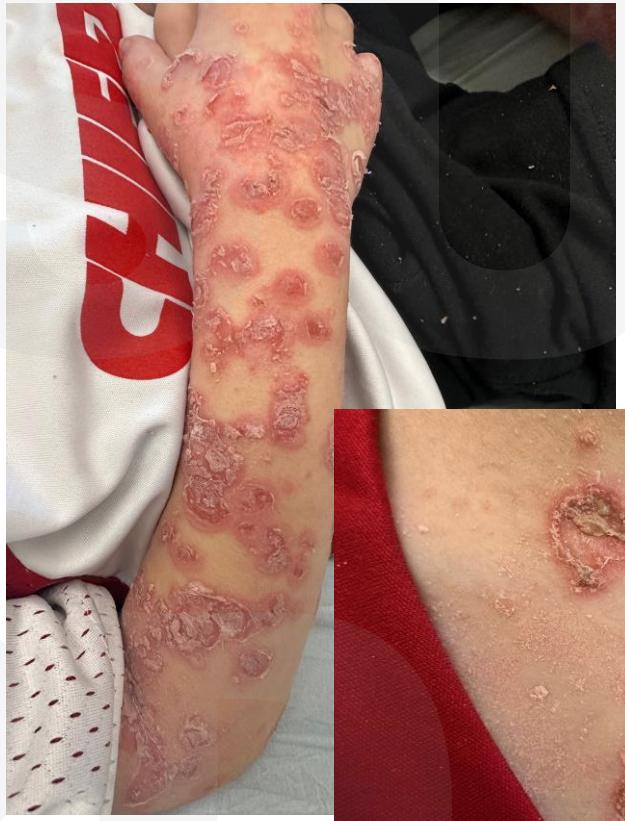


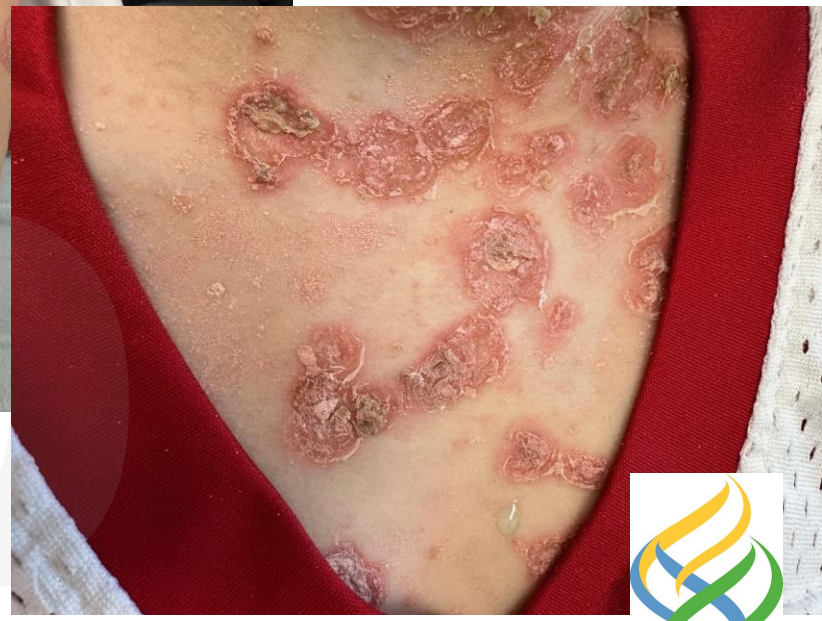
Eczema coxsackium; bullous impetigo





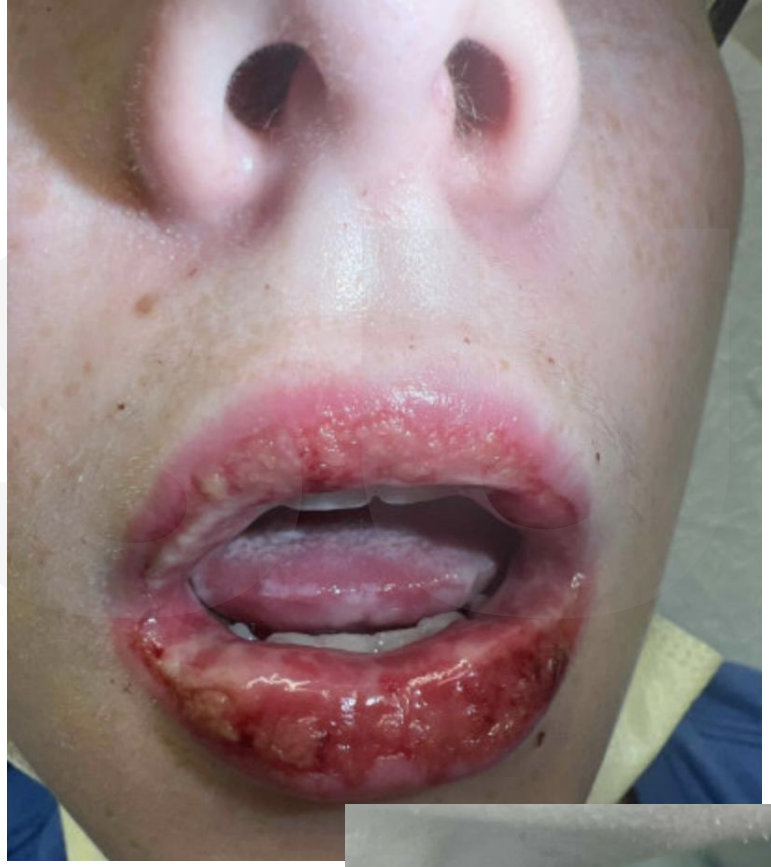


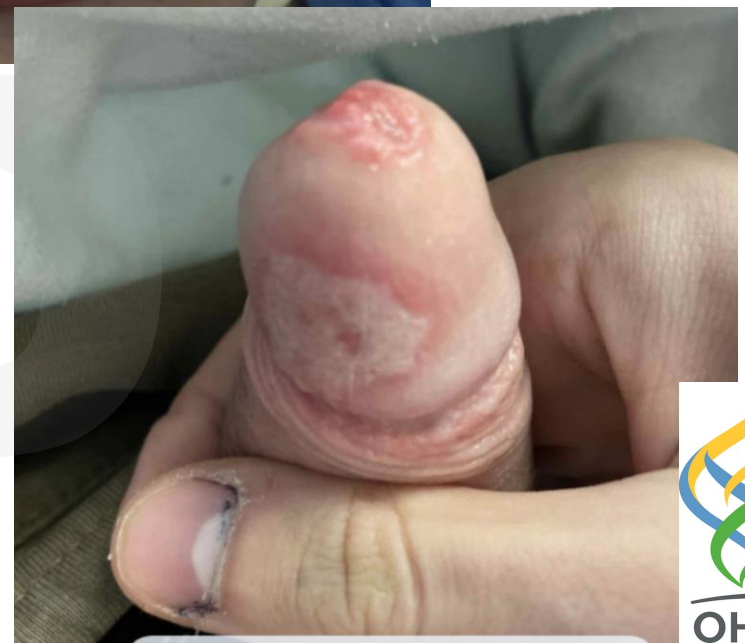




Case 4

- 15 YO Male, vaccinations UTD
- History VUR and double ureter, not on antibiotics
- Sore throat, fever (101F), poor PO intake, dysuria, oral and genital lesions
- Scant skin lesions (<5% BSA)
- HSV PCR neg
- Treated with Valacyclovir x 7 days
- Other med exposures: oxycodone, ibuprofen, acetaminophen





Reactive Infectious Mucositis (RIME)

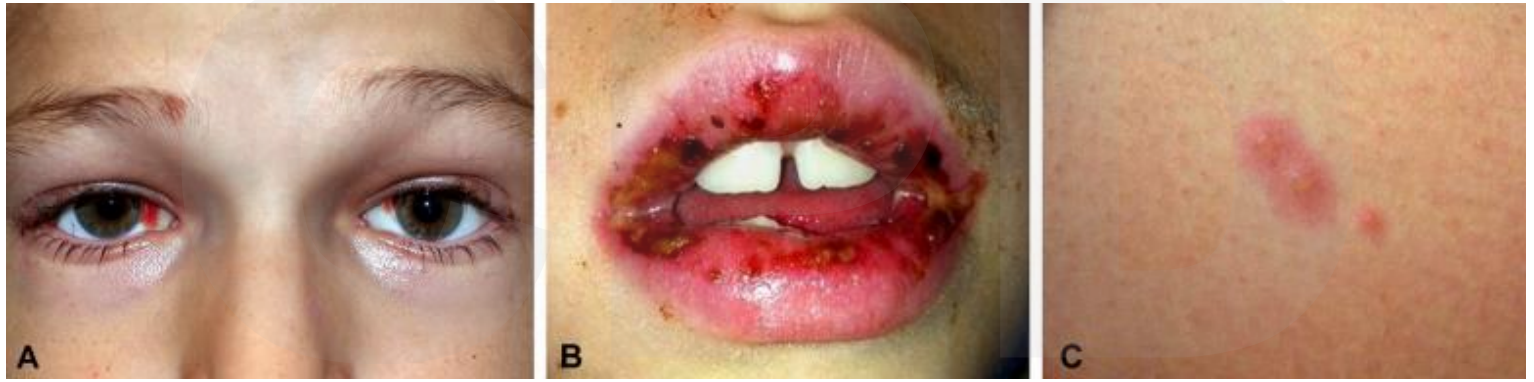
- Formerly “Mycoplasma-Induced Rash and Mucositis” (MIRM)
- Young, mean age 11.9
- 66% male
- Prodromal sx: cough, malaise, fever, preceding by ~1 week
- Skin: acral or extremity distribution most common (46%), generalized (31%), and truncal (23%)
- Oral lesions (94%): isolated erosions, ulcers, vesiculobullous lesions, significant denudation
- Ocular involvement (82%)
- Urogenital lesions (36%)

Canavan, et al. J Am Acad Dermatol. 2015.

Reactive Infectious Mucositis (RIME)

- Eruptions are diverse
  - Mucositis alone
  - Prominent mucositis with sparse cutaneous involvement (most common)
  - Mucositis with moderate skin involvement (least common)
- Characterized as vesiculobullous, targetoid, atypical targets, or macules

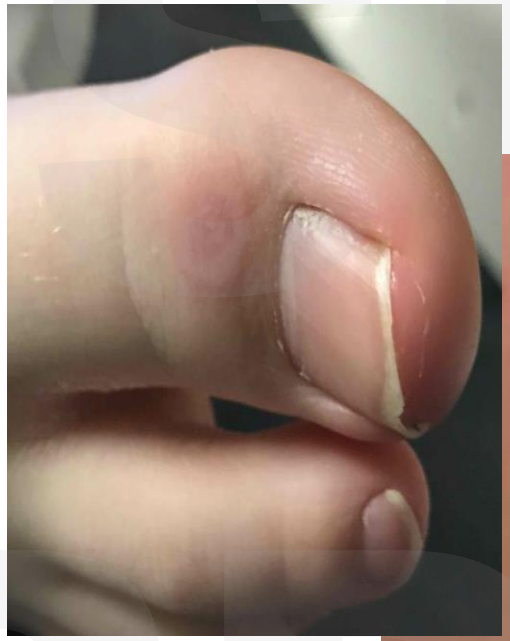
- *M. pneumoniae* is a common cause ("MIRM")

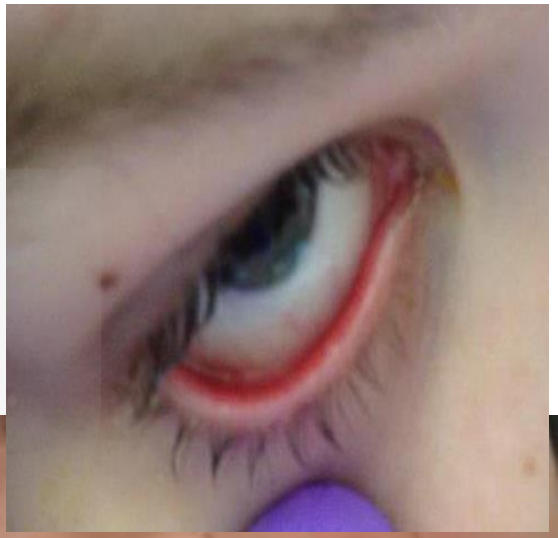


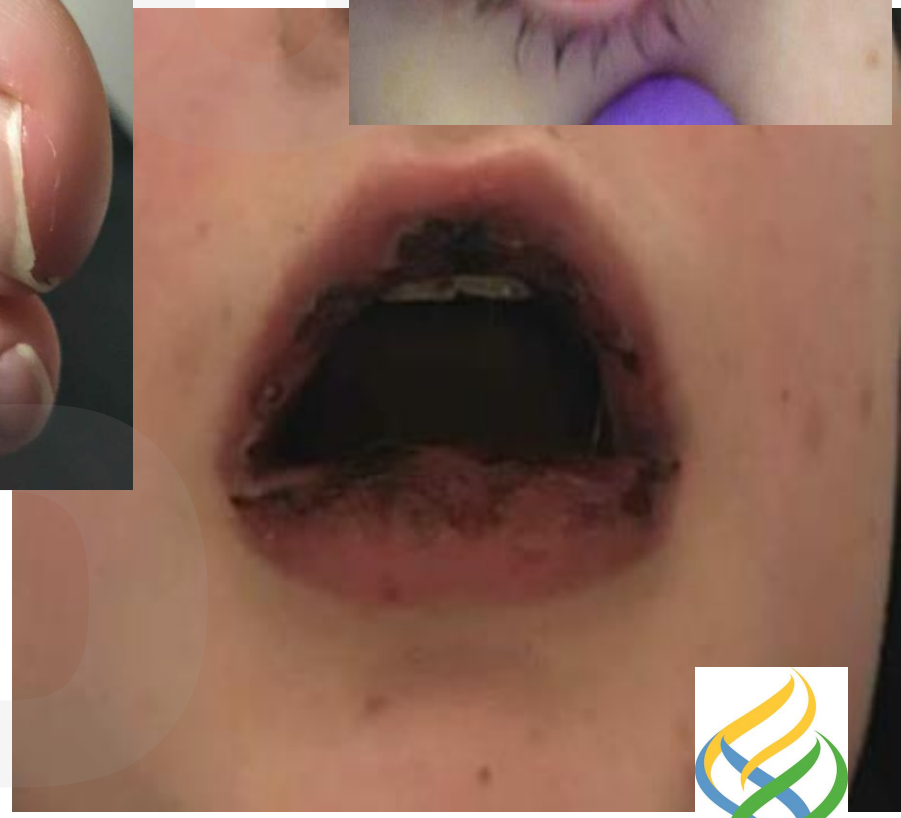
Canavan, et al. J Am Acad Dermatol. 2015.
Ramien. Clinical and Experimental Derm. 2021

Reactive Infectious Mucositis (RIME)

- Pathophysiology
  - Unclear
  - Immune complex deposition and complement activation?
  - Molecular mimicry?
  - Genetic susceptibility suggested
- Work-up
  - *Mycoplasma* PCR or culture
  - HSV PCR
  - Respiratory virus panel







Canavan, et al. J Am Acad Dermatol. 2015.

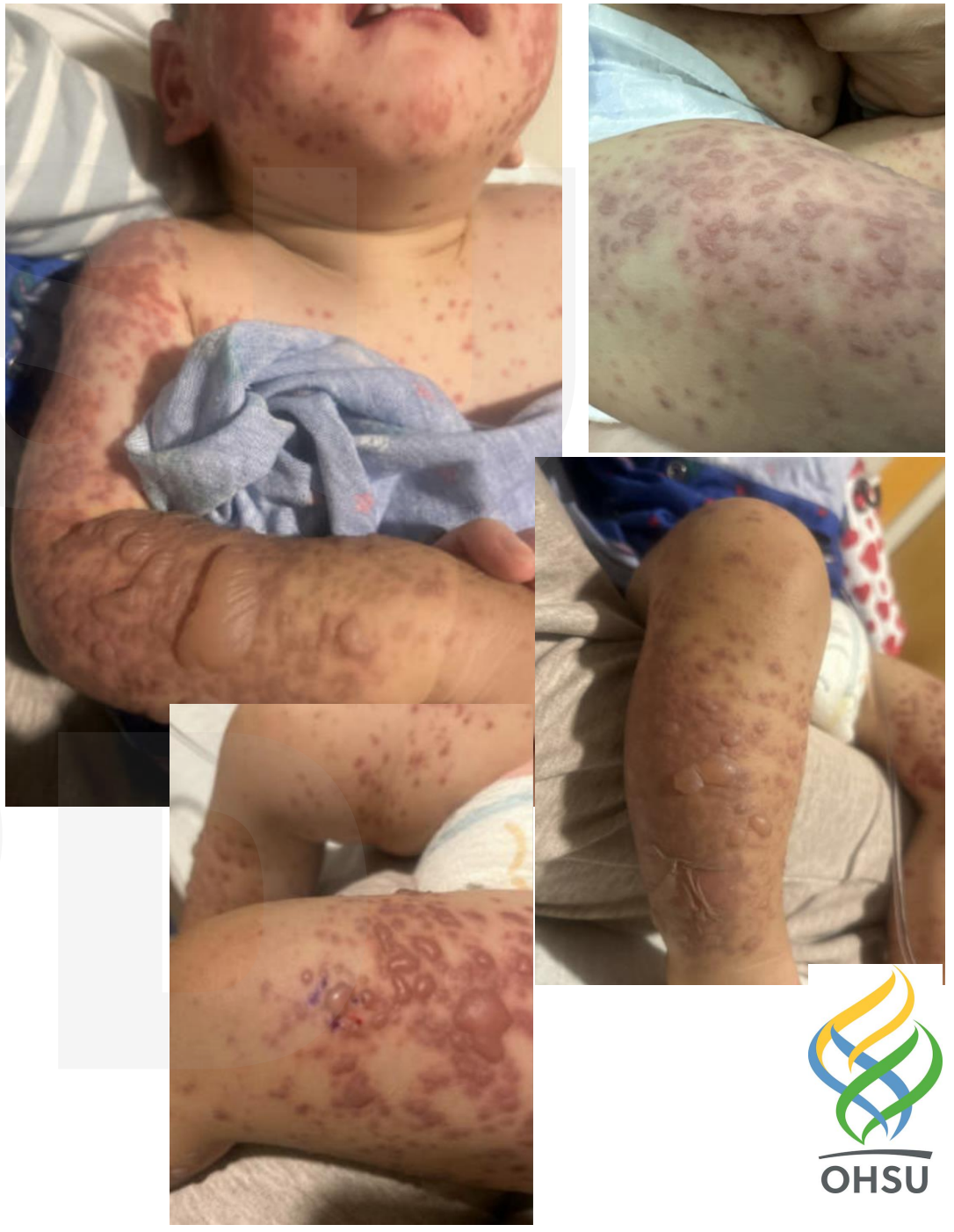
Reactive Infectious Mucositis (RIME)

- Treatment
  - No evidence-based guidelines
  - Systemic immunosuppression (steroids)
  - Antibiotics (macrolides or doxycycline)
- Supportive care
  - Analgesics, fluids, nutrition
  - Consultations: ophthalmology, urology
- Outcome
  - Full recovery 81%
  - Post-inflammatory pigmentation changes 6%
  - Mucosal complications 10%
  - Recurrence 8%

Canavan, et al. J Am Acad Dermatol. 2015.
Vujic, et al. JEADV. 2015.

Case 5

- 13-month healthy male
- Hand, foot and mouth 3 weeks prior
- 4 days fever (103 F), diarrhea, and rash, diagnosed with RIME
- Transferred from OSH for worsening skin blistering
- Medications include acetaminophen prior to onset, azithromycin at OSH

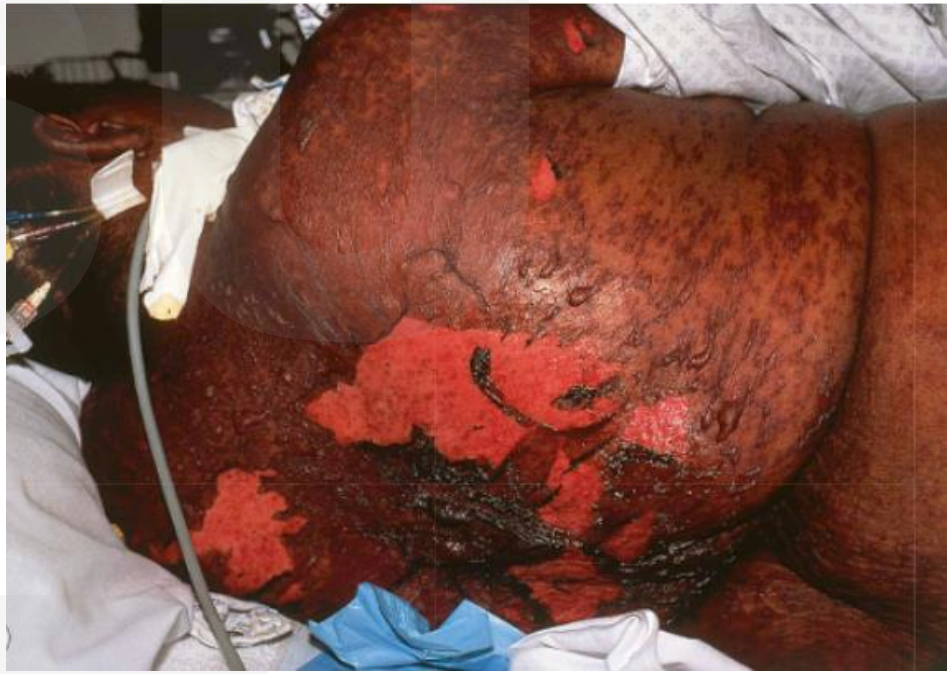


Case 5

- Exam:
  - Fussy, tachycardic, tachypneic
  - Extensive red-brown macules and patches
  - Overlying vesicles and large flaccid bullae
  - Lips with crusting and vesicles
  - Urethral meatus, glans penis and scrotum with erythema, crusting, superficial erosions
- Labs:
  - HSV, enterovirus PCR neg
  - Respiratory viral panel negative
  - Na 130, K 4.6, Cl 94, Co2 18 (gap 18) BUN 8, total protein 5.1, albumin 2.6, alk phos 826, ALT 264, AST 210, WBC 5.6, Hb 14.1, plt 239

Stevens Johnson Syndrome/Toxic Epidermal Necrolysis

- Almost all cases due to medication
- 1-3 weeks after starting medication (can be later)
- Immune-mediated, life-threatening inflammatory blistering
- Two mucosal surfaces + cutaneous blistering
- SJS = < 10% BSA detachment
- TEN = > 30% BSA detachment
- Erythematous, dusky red or purpuric macules coalescing → gray hue → necrotic epidermis detaches = blisters (flaccid) and denudation



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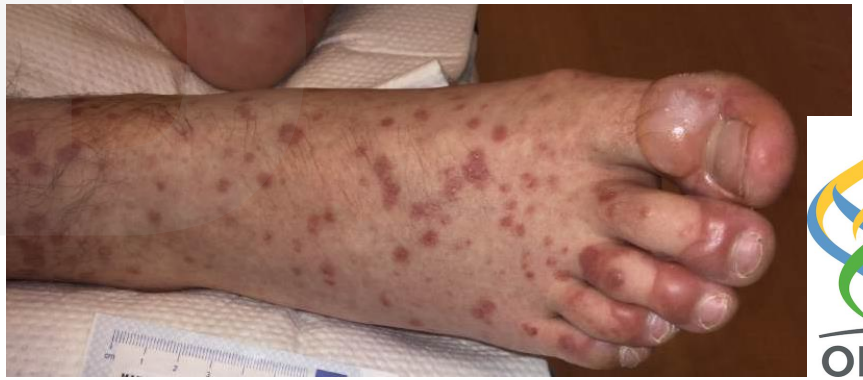
Stevens Johnson Syndrome/Toxic Epidermal Necrolysis

- Skin and mucosal pain
- Erythema and erosions of buccal, ocular, genitourinary, and anal mucosae
- Respiratory and GI epithelium can be involved
- Systemic: fever, lymphadenopathy, hepatitis and cytopenias
- Mortality up to 35% adults and children
- As BSA increases, risk of electrolyte loss “Score of Toxic Epidermal Necrosis” (SCORTEN) created 2000 to predict outcome (adults)
- ~17-50% SJS/TEN patients are children

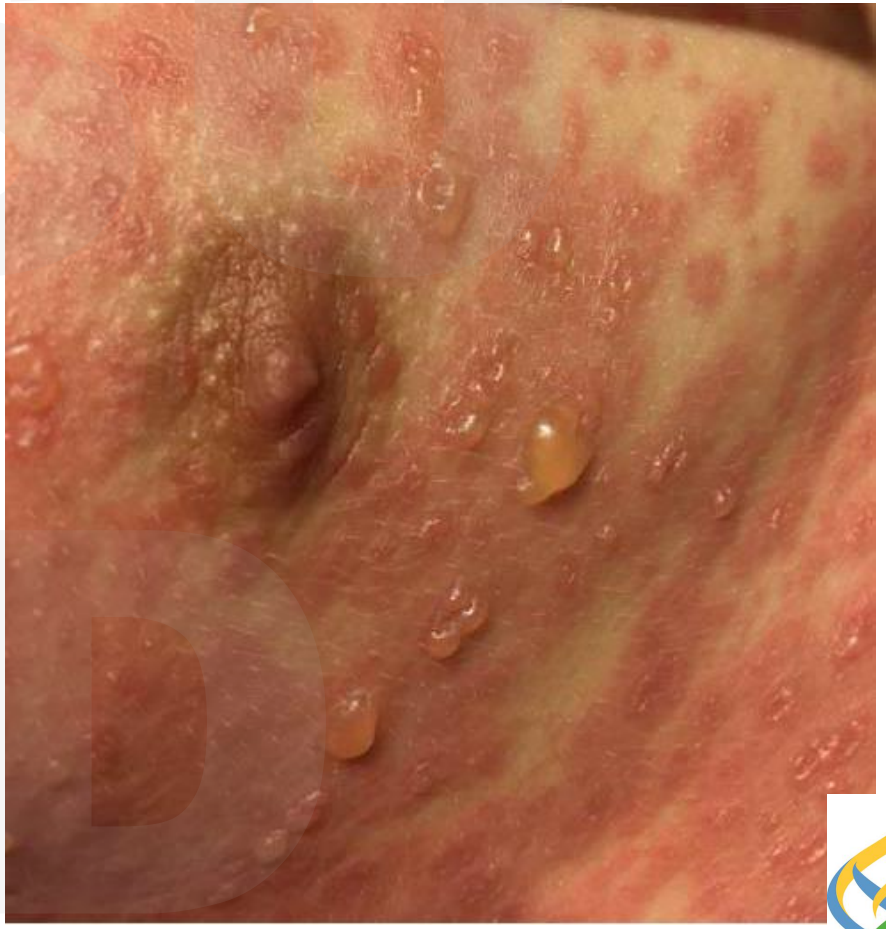
- Known risk factors for mortality:
  - History of malignancy and/or stem cell transplant
  - Body surface area
  - Abnormal labs



Stevens Johnson Syndrome/Toxic Epidermal Necrolysis

Treatment:

- Discontinue medication ASAP and avoid forever
- No gold standard
- Decision between supportive care and immunosuppression challenging
  - Supportive care (usually ICU or burn center)
    - Wound care, fluids, nutrition, infection control, consultants
  - Immunsuppression
    - IVIG +/- steroids, cyclosporine, infliximab, etanercept, JAK-I



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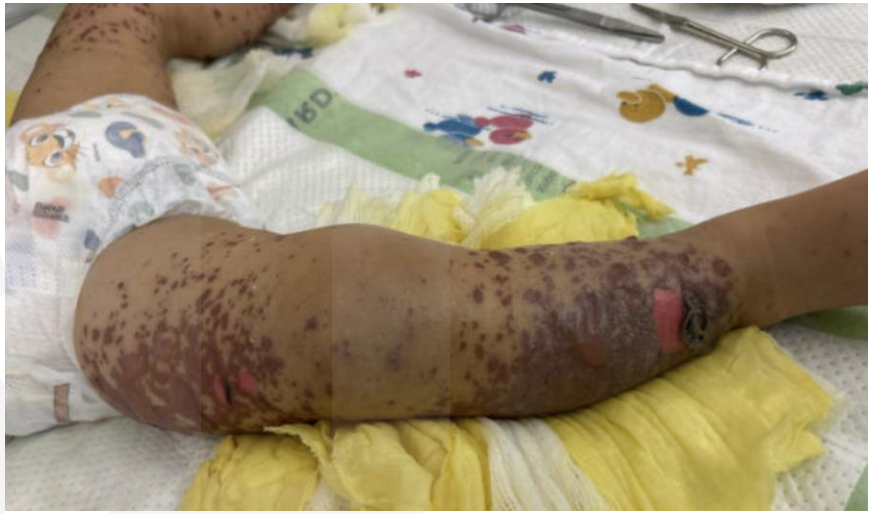
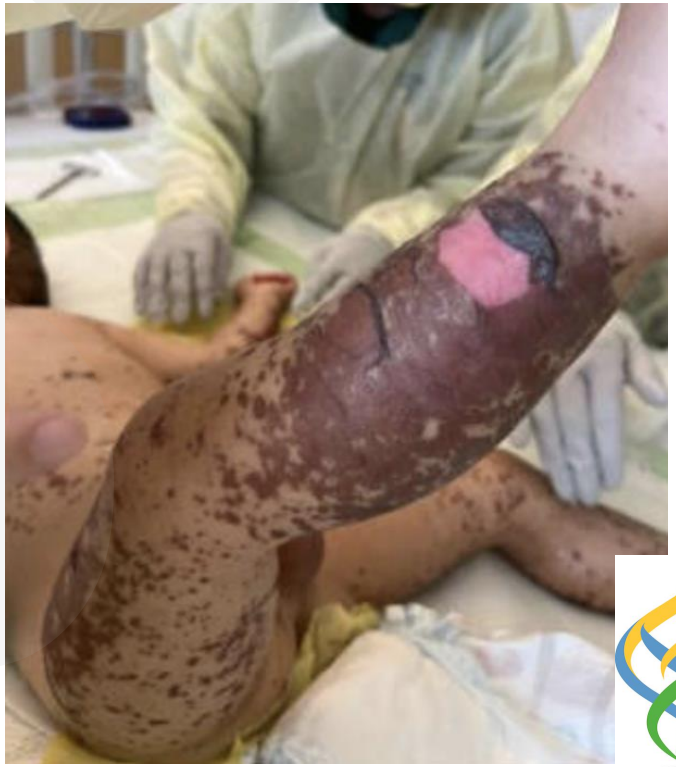
Case 5

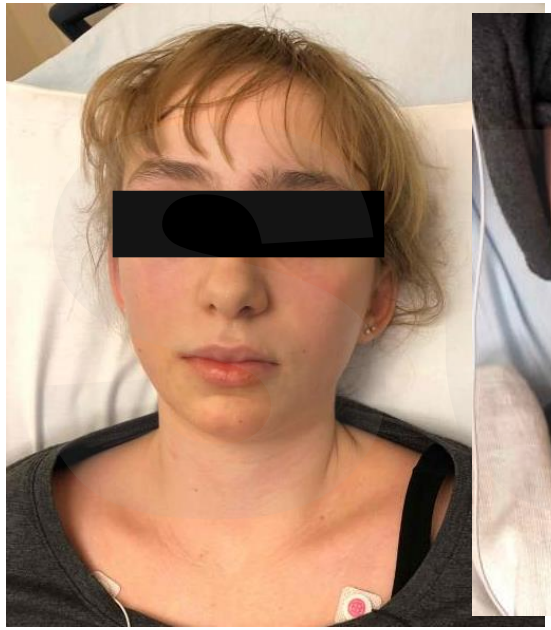
- Transferred to PICU
- Received single dose of etanercept 0.8 mg/kg
- Skin stabilized
- 1 week later, developed bloody diarrhea
- Gastrointestinal SJS/TEN, hospitalized 36 days

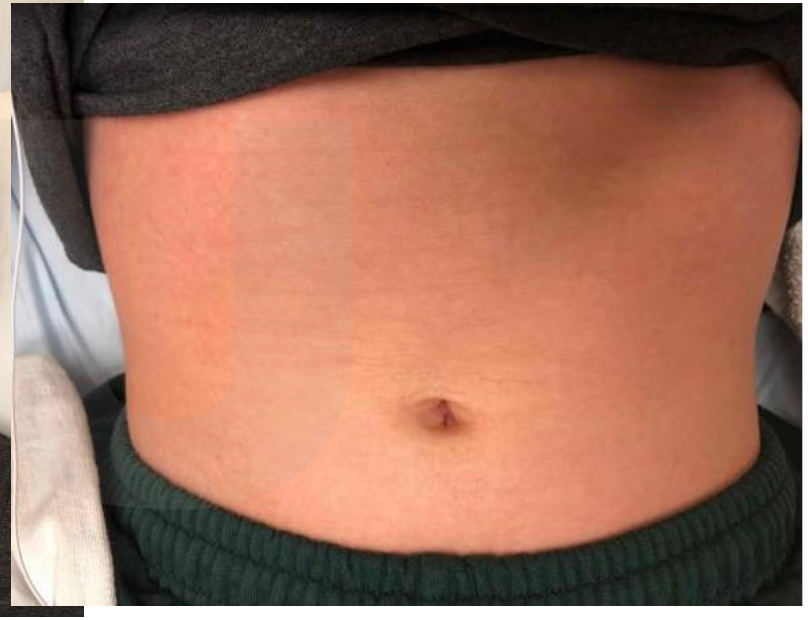


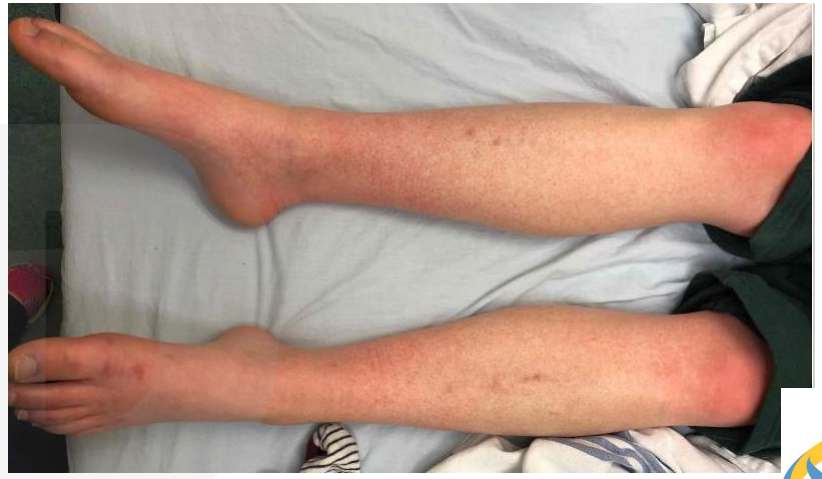


Case 6

- Previously healthy 15-year-old female
- Started isoniazid 4 weeks prior for latent TB after routine PPD +
- Rash, facial edema, fever (39 C), lymphadenopathy, arthralgias, and abdominal pain
- Admitted to the ICU in fulminant hepatic failure

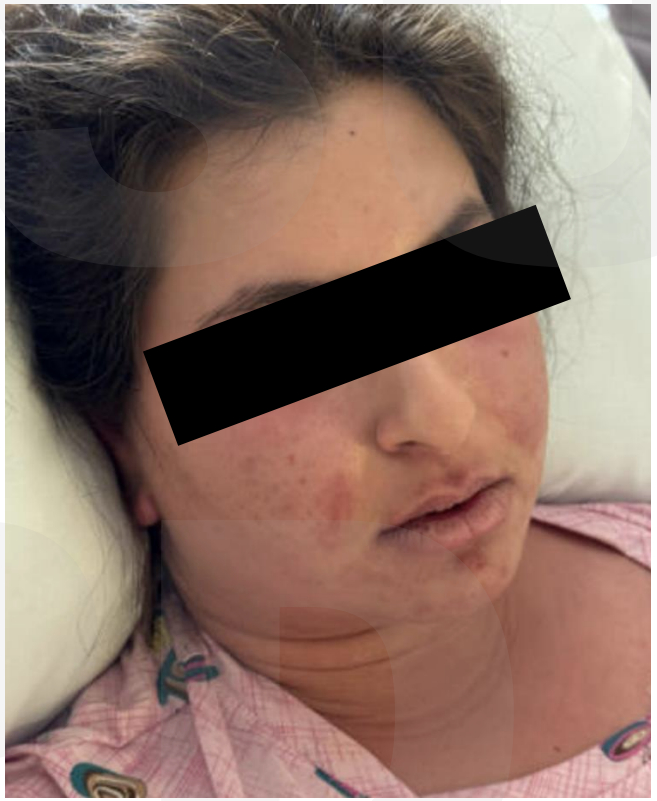


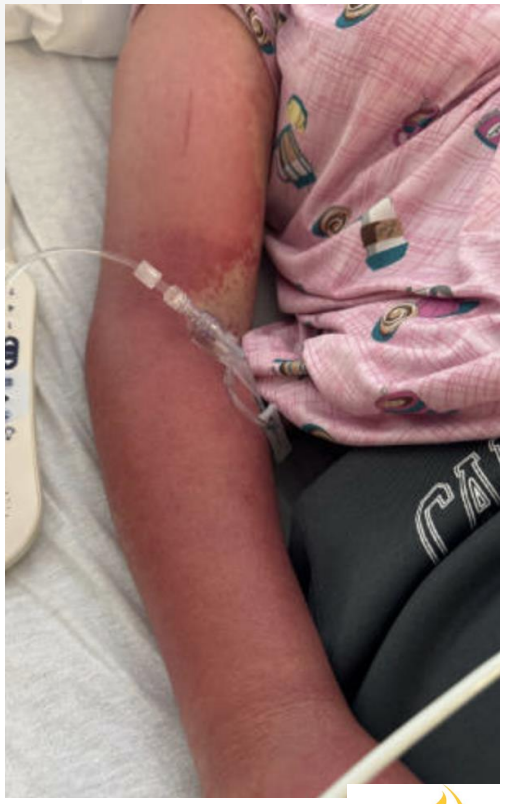




Drug Induced Hypersensitivity Syndrome

- Formerly called Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)
- Adverse drug reaction
  - Antiepileptics, allopurinol, sulfonamides, antibiotics
  - Onset 2-6 weeks following drug
- Rare, can be life threatening
- Features:
  - Multi-organ involvement
  - Lymphocyte activation
    - Lymph node enlargement, lymphocytosis (atypical)
  - Eosinophilia





Kardaun, et al. BJD. 2013.

Table 1 Scoring System for Classifying DRESS Cases as Definite, Probable, Possible, or No Case, from Kardaun et al[11]

Score	−1	0	1	2
Fever ≥38.5°C	No/U	Yes		
Enlarged lymph nodes		No/U	Yes	
Eosinophilia		No/U		
Eosinophils			0.7-1.499 × 10^9 L^{-1}	≥1.5 × 10^9 L^{-1}
Eosinophils, if leukocytes <4.0 × 10^9 L^{-1}			10%-19.9%	≥20%
Atypical lymphocytes		No/U	Yes	
Skin involvement				
Skin rash extent (% body surface area)		No/U	>50%	
Skin rash suggesting DRESS	No	U	Yes	
Biopsy suggesting DRESS	No	Yes/U		
Organ involvement*				
Liver		No/U	Yes	
Kidney		No/U	Yes	
Muscle/heart		No/U	Yes	
Pancreas		No/U	Yes	
Other organ		No/U	Yes	
Resolution ≥15 days	No/U	Yes		
Evaluation of other potential causes				
Antinuclear antibody				
Blood culture				
Serology for HAV/HBV/HCV				
Chlamydia/mycoplasma				
If none positive and ≥3 of above negative			Yes	

DRESS = Drug Reaction with Eosinophilia and Systemic Symptom; U = unknown/unclassifiable; HAV = hepatitis A virus; HBV = hepatitis B virus; HCV = hepatitis C virus.

*After exclusion of other explanations: 1, one organ; 2, two or more organs. Final score < 2, no case; final score 2-3; possible case; final score 4-5, probable case; final score > 5, definite case.

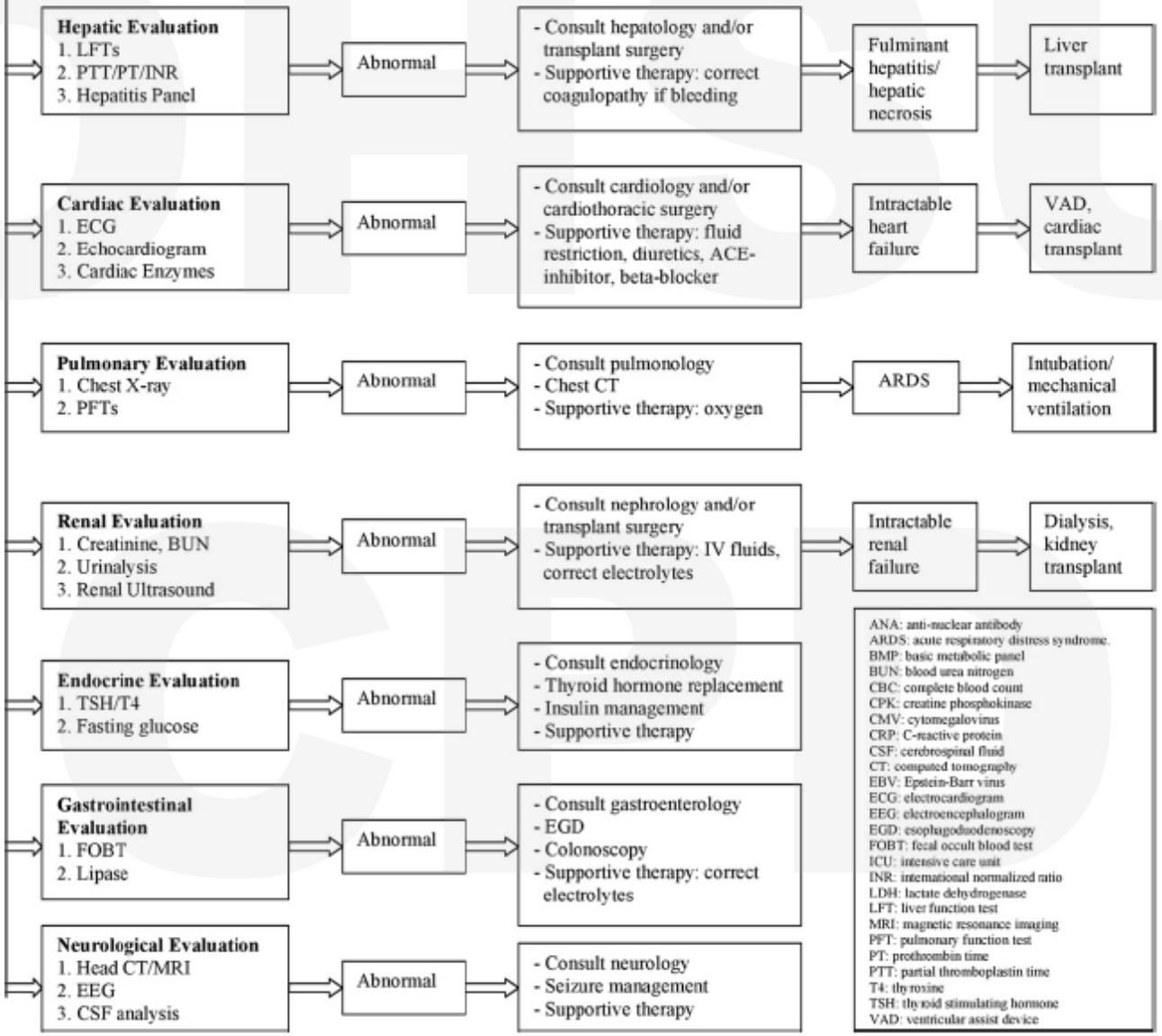
Cacoub, et al. Am J Med. 2011

Drug Induced Hypersensitivity Syndrome

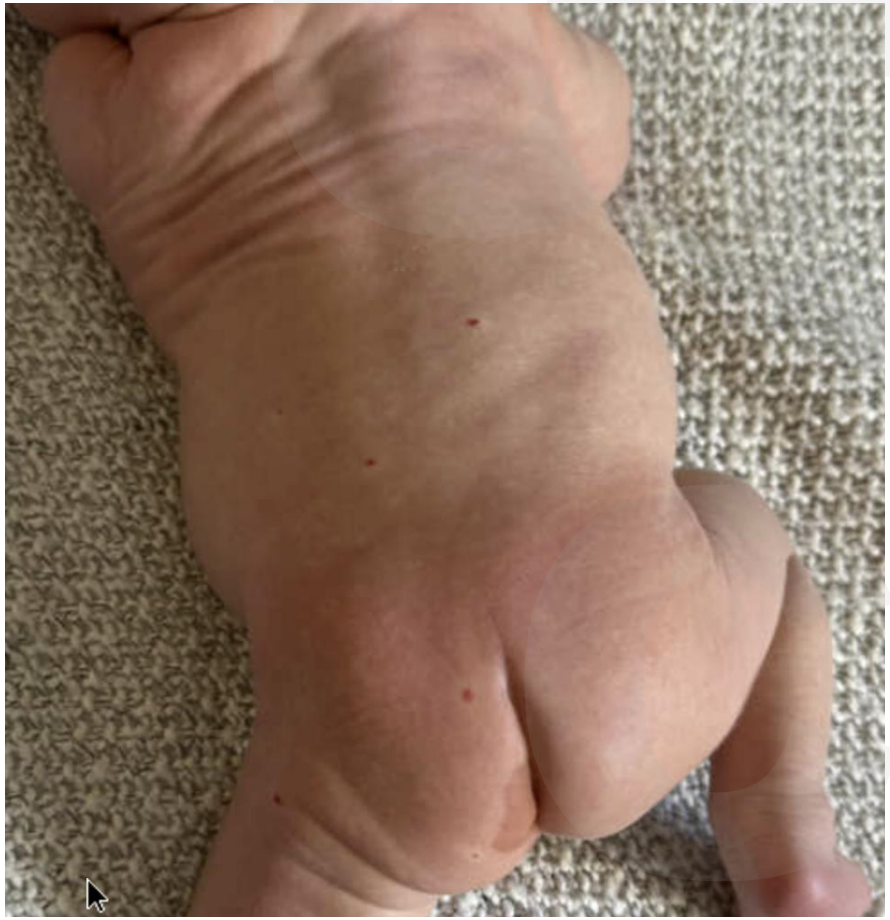
- Management:
  - Immediate withdrawal of offending drug
  - Lab work-up: CBC, CMP, CPK, LDH, ferritin, TSH PCR for HHV6 and7, CMV, EBV, others depending on risks factors and presenting sx
  - Supportive care
  - Start prednisone 1 mg/kg/day, topical steroids
- Most complete recovery
- Estimated mortality: 10%, hepatic necrosis is most common cause of death, in kids seems lower at 3-5%
- Children recover more quickly and completely
- Poor prognostic indicators:
  - AEC >6000, thrombocytopenia, pancytopenia, hx renal insufficiency, multi-organ involvement, multiple underlying diseases
- Poor outcomes:
  - Tachycardia, leukocytosis, tachypnea, coagulopathy, GI bleeding, SIRS

Acute Management and Treatment

- Immediate withdrawal of causative drug.
- Admit to ICU or burn unit: fluid replacement, correction of electrolyte abnormalities, warming the environmental temperature, providing high caloric intake, treatment of superinfections/bacteremia, and skin care with appropriate dressings.
- Order labs: CBC, LFT, BMP, 24 hour urine protein and urinary eosinophil count, CPK, LDH, ferritin, triglycerides, calcium, PTH, TSH, blood glucose, PT and PTT, lipase, protein electrophoresis, CRP, quantitative PCR for HHV-6, 7, EBV and CMV, blood culture, ANA.
- Start high-dose systemic corticosteroids at ≥ 1 mg/kg/day. Consider other immunosuppressant medications. Topical corticosteroids for symptomatic relief.



Case 7



- 4 week old
- Full term
- Several scattered vascular papules on scalp, trunk and extremities
- Otherwise healthy

Infantile Hemangiomas

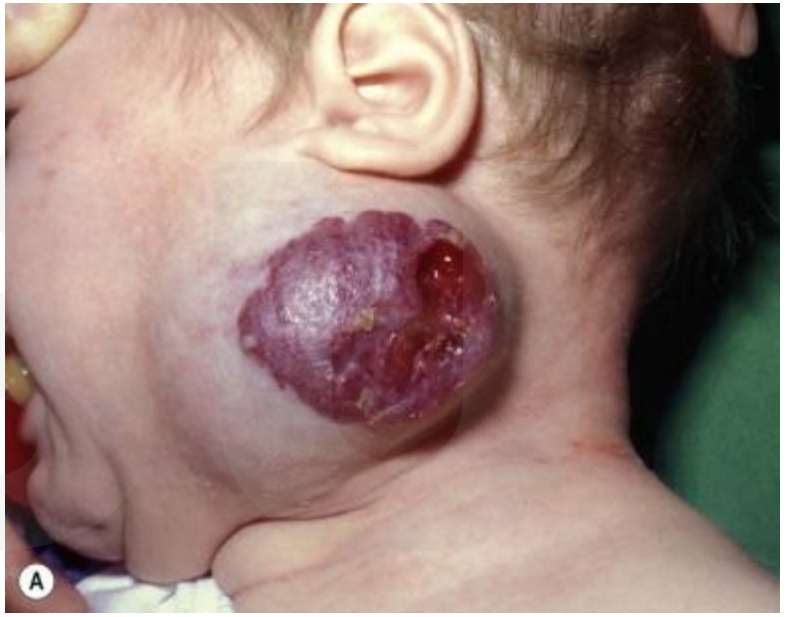
- Most common vascular tumor in infancy
  - Affect 3-5% children
- Increased incidence:
  - Caucasians
  - Females
  - Premature infants
  - Multiple gestation
- Majority sporadic, some with family history
- Characteristic growth pattern

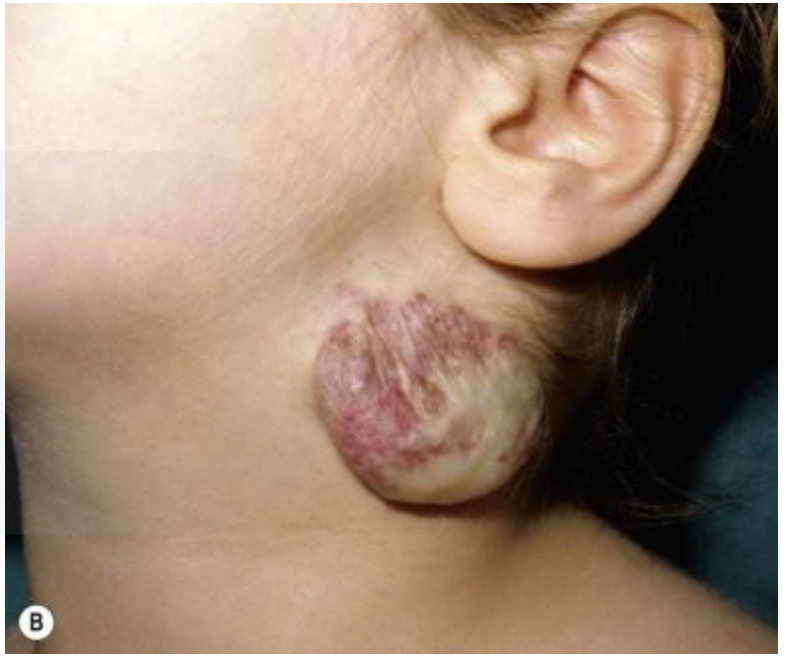
Infantile Hemangiomas

- May have faint pink patch/telangiectasias at birth
- Rapid proliferation starts in first weeks of life, maximizes between 5-8 weeks of age
- 80% of growth occurs within *3 months*
- Most hemangiomas fully formed by 5 months of age
  (Large and deep hemangiomas grow longer)
- Mean age of presentation to a dermatologist is too late
- Interventions are substantially less effective after 3 months of age
- Ideal referral age = 4 weeks

Infantile Hemangiomas

- IH involute at rate of 10% per year
  - 30% involuted at 3 years
  - 50% involuted at 5 years
- Some with normal-appearing skin
- Many with
  - Residual telangiectasia
  - Fibrofatty tissue
  - Scarring
  - Atrophy





AAP Referral Recommendations

CLINICAL PRACTICE GUIDELINE Guidance for the Clinician in Rendering Pediatric Care

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Clinical Practice Guideline for the Management of Infantile Hemangiomas

Daniel P. Krowchuk, MD, FAAP,[a] Ilona J. Frieden, MD, FAAP,[b] Anthony J. Mancini, MD, FAAP,[c] David H. Darrow, MD, DDS, FAAP,[d] Francine Blei, MD, MBA, FAAP,[e] Arin K. Greene, MD, FAAP,[f] Aparna Annam, DO, FAAP,[g] Cynthia N. Baker, MD, FAAP,[h] Peter C. Frommelt, MD, FAAP,[i] Amy Hodak, CPMSM,[j] Brian M. Pate, MD, FHM, FAAP,[k] Janice L. Pelletier, MD, FAAP,[l] Deborah Sandrock, MD, FAAP,[m] Stuart T. Weinberg, MD, FAAP,[n] Mary Anne Whelan, MD, PhD, FAAP,[o] SUBCOMMITTEE ON THE MANAGEMENT OF INFANTILE HEMANGIOMAS

OHSU

Infantile Hemangiomas

› Pediatr Dermatol. 2021 Sep;38(5):1393-1395. doi: 10.1111/pde.14783. Epub 2021 Aug 31.

Measuring the impact of clinical practice guidelines on infantile hemangioma referrals

Michael T Barton [1], Emile Latour [2], Alison Small [1], Sabra Leitenberger [1], Tracy Funk [1]

Affiliations + expand

PMID: 34467544 DOI: 10.1111/pde.14783

- Retrospective review
- Enrolled ~500 infants
- Referral time for high-risk lesions decreased from 11.9 weeks to 9.5 weeks of age

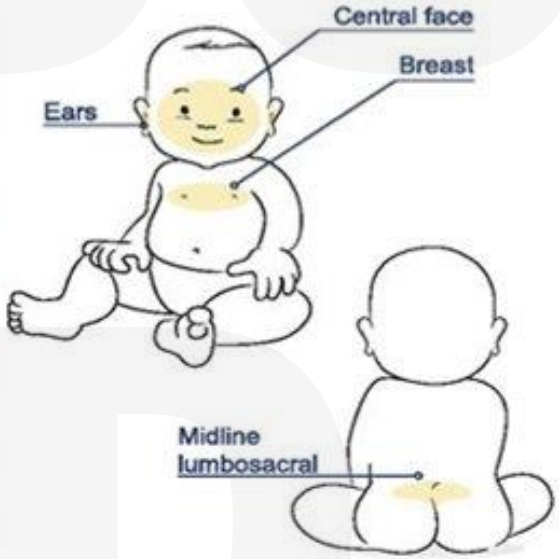
IH Referral Score

IHReS

Infant's name .....
Age .....
Hemangioma onset __/__/__
Expert center .....

To answer the 6 questions below, tick **"Yes"** or **"No."**

Complications or potential risk of complications (ulceration, visual compromise, feeding difficulties, stridor)	○ Yes ○ No
Central face and/or **ears**	○ Yes ○ No
Breast (in girls)	○ Yes ○ No
Midline lombosacral	○ Yes ○ No
Size ≥4 cm (focal or segmental)	○ Yes ○ No
Number of hemangiomas ≥5	○ Yes ○ No



If at least 1 of the previous situations is ticked "Yes," please refer the patient to an expert center.

If you ticked "No" to all questions, please fill in the table on the next page.

Note: In the case of multiple IHs, the score should be done for each IH.

IH Referral Score

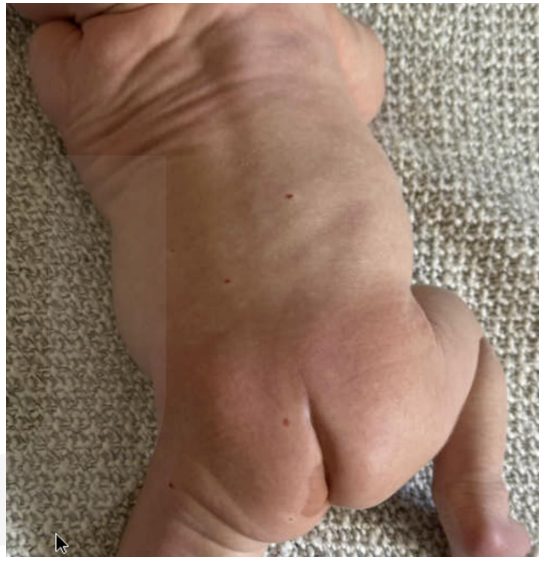
The total score is the sum of the scores from each parameter below.

Parameters	Items			Score Please consider only the highest score for each parameter
Location of hemangioma	Other facial areas than those mentioned previously	○ Yes ○ No	If yes: 3 points *(if no: 0 point)*	○ 3 ○ 2 ○ 0
	Neck, diaper area, scalp	○ Yes ○ No	If yes: 2 points *(if no: 0 point)*	
Size of the biggest hemangioma	≥1 cm on other facial area than those mentioned previously	○ Yes ○ No	If yes: 3 points *(if no: 0 point)*	○ 3 ○ 2 ○ 0
	2 to 4 cm on other body area than those mentioned previously	○ Yes ○ No	If yes: 2 points *(if no: 0 point)*	
Current child age and growth of hemangioma	The infant is <2 months	○ Yes ○ No	If yes: 3 points *(if no: 0 point)*	○ 3 ○ 2 ○ 0
	The infant is ≥2 and ≤4 months, with an evident growth within the last 2 weeks	○ Yes ○ No	If yes: 2 points *(if no: 0 point)*	
			Total	

Score ≥4: please refer the patient to an expert center.
Score <4: the patient is not to be referred and should be monitored. The score will be done at every visit.

The final decision to refer the patient to an expert centre is up to the physiciab and the parents.

Return to Case 7



- Presented to dermatology 9/18, 4 weeks of age
- US 9/19:

Liver:
* Length: 4.8 cm.
* Parenchyma: At least 5 separate lesions are noted within the liver parenchyma with central hypoechoic regions and peripheral echogenic halos. These lesions are all vascular and some of them demonstrate portal venous shunting for example between the middle hepatic vein and the left portal vein. The lesions vary in size between approximately 1 cm in diameter and 1.4 cm. They involve both the right and left lobes.
* Intrahepatic bile ducts: Normal
* Common bile duct diameter: 1 mm.
* Main portal vein: Patent with normal direction of flow

Gallbladder: Normal

IVC (limited evaluation): Normal

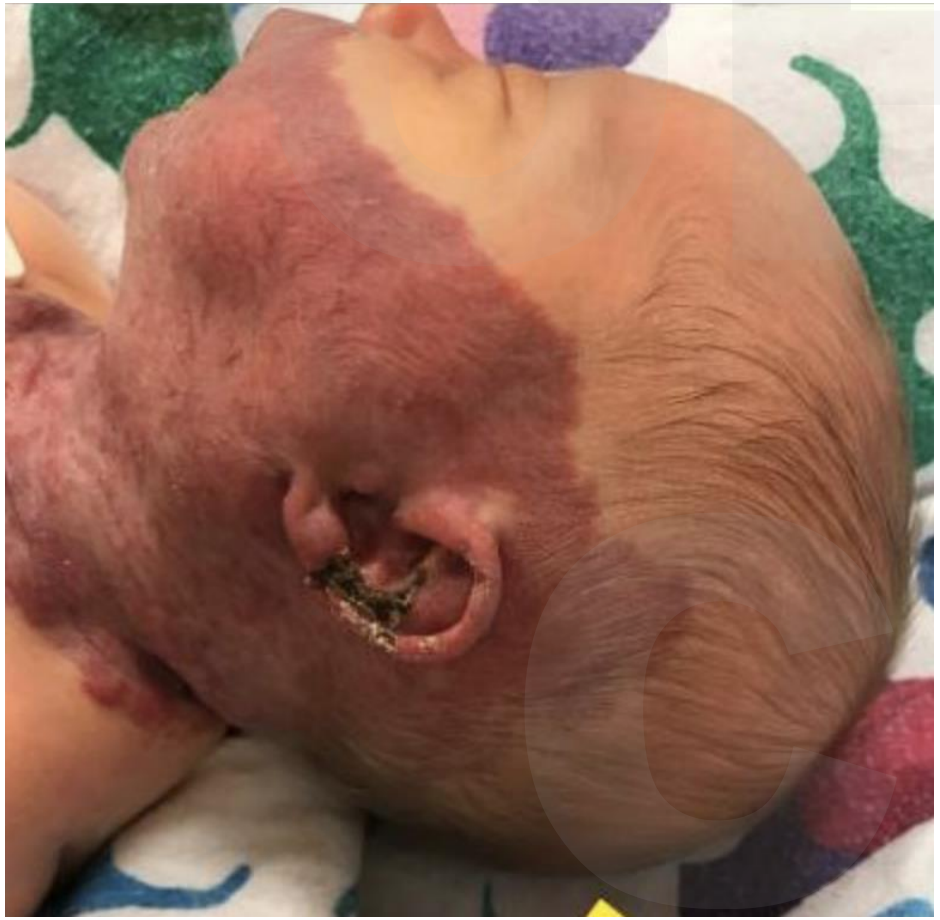
Right kidney (limited evaluation): Normal

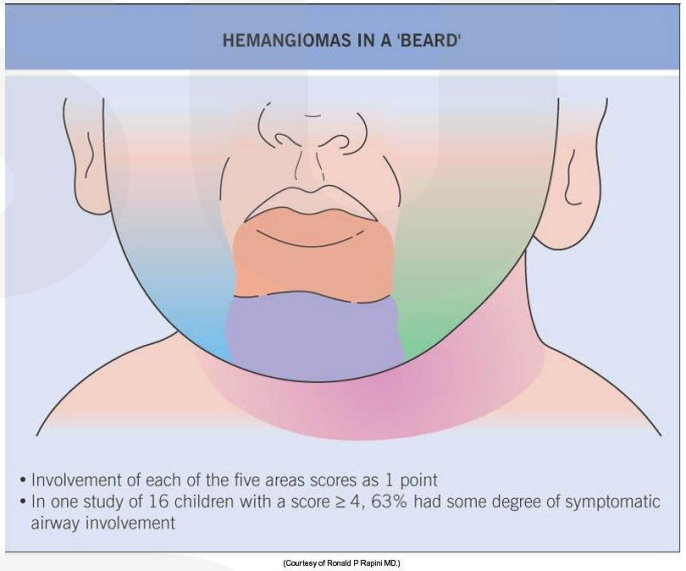
Pancreas :Not visualized

IMPRESSION:

Multiple hepatic hemangiomas (at least 5), at least one of which demonstrates likely portal venous shunting.

Other Infantile hemangioma urgencies





- Segmental IH, beard distribution
  - Risk of airway involvement
  - Croup-like cough, hoarseness, stridor

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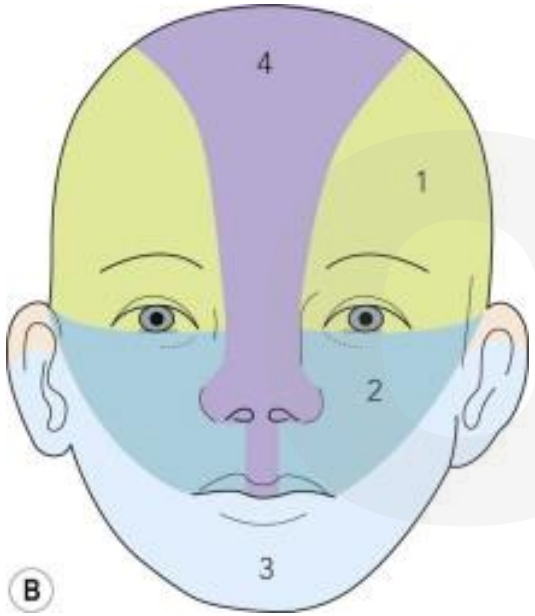
PHACE Syndrome



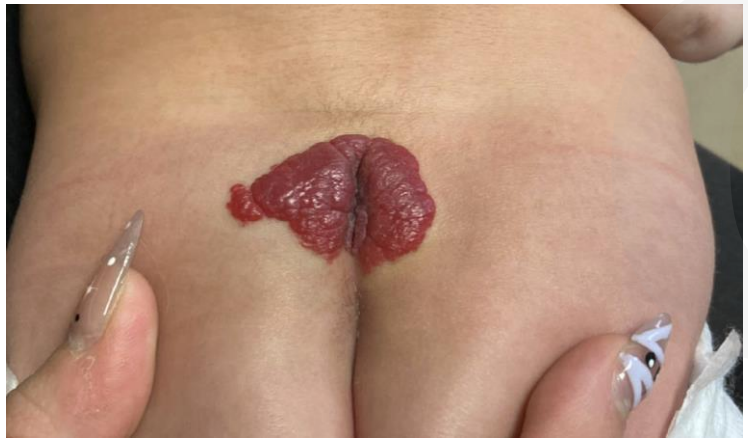
- Segment one = highest risk of PHACE

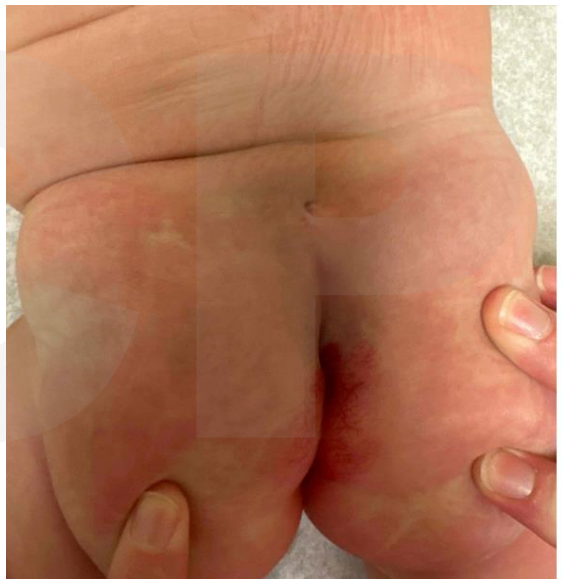
- Posterior fossa malformations
- Hemangiomas
- Arterial anomalies
- Cardiac abnormalities/coarctation of the aorta
- Eye abnormalities

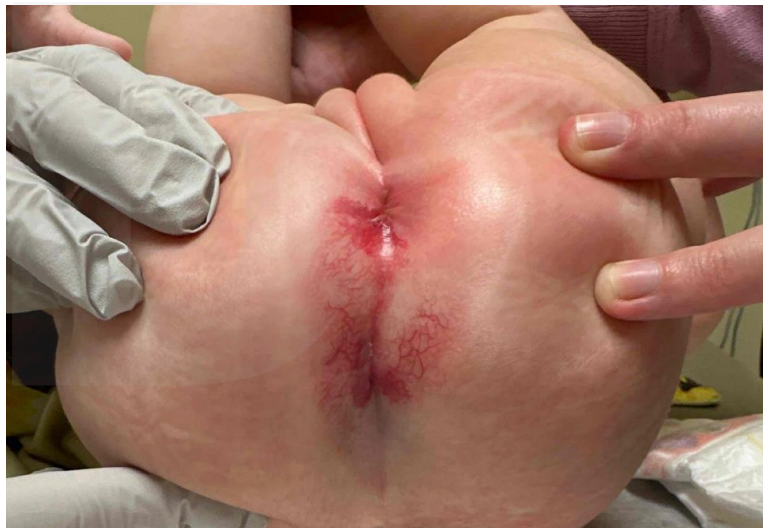
- Refer to pediatric dermatology
  - ECHO
  - Brain and neck MRI/MRA
  - Ophthalmology examination

Lumbosacral hemangioma

- Lumbosacral hemangiomas, early US spine (by 12 weeks)
- Tethered cord or other spinal dysraphism
  - Not thoracic or cervical spine







Hemangioma urgencies and referrals

- If you are not sure, please refer!
- Multiple hemangiomas (5 or greater), early US liver (~4 weeks)
- Lumbosacral hemangiomas, early US spine (by 12 weeks)
- Beard distribution, segmental hemangiomas of head and neck and diaper area

Summary

1. Increased concern for rash +:
   - Mucosal involvement (oral, ocular, genital)
   - Blistering
   - Fever
   - Medication exposure
2. Drug-induced reactive mucositis has a more severe course and worse prognosis
3. Refer high-risk infantile hemangiomas early

Questions?