Visual Diagnosis: ID the Disease Workshop
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Case 1
9 day old female infant presents to dermatology clinic for evaluation of vascular stains and possible Sturge Weber syndrome
On exam, noted to have several vesicles on the left chest, back, and neck which began 1-2 days prior to clinic visit
Dad reports there is a cat at home and he is concerned about flea bites
No fever, malaise, feeding issues or systemic symptoms
No affected family members
PMH: uncomplicated pregnancy; no maternal infections

The most likely diagnosis in this infant is:
A) Bullous impetigo of the newborn
B) Self-healing histiocytosis
C) Incontinentia pigmenti
D) Herpes Simplex Virus
E) Scabies infestation

Work-Up
Concern for neonatal HSV led to following work-up:
- Viral culture from skin lesion
- PCR for HSV 1 & 2 from skin lesion
- Bacterial culture from skin lesion

Admitted to hospital for evaluation for possible disseminated or CNS HSV infection and empiric antiviral therapy.
Hospital Management

- Viral culture from skin lesion: Positive HSV
- Viral cultures from eye: positive HSV (neg. anus, nose)
- PCR for HSV 1 & 2: positive for HSV 1
- PCR Plasma: 3800 copies of HSV 1
- CSF HSV PCR negative (WBC 4, gluc 36, prot 77)
- ALT elevated (60)
- Bacterial culture from skin lesion negative

*Treated with Acyclovir 20 mg/kg q 8 hrs for 21 days

**Discharged home suppressive acyclovir therapy for 6 months

Diagnosis of Neonatal HSV

- Swab specimen of eye, NP, mouth, anus, & lesions
  - Culture and/or PCR
- PCR of CSF
- PCR of whole blood
- ALT
### Treatment Neonatal HSV

- Acyclovir 20 mg/kg/dose q 8 hours
  - Skin Eye Mucous Membrane (SEM) - 14 days
  - Disseminated or CNS - 21 days
- Repeat LP at the end of therapy to ensure clearance and continue if not clear
- Suppression for 6 months following infection

### Bullous Impetigo

- Most common in neonates, infants, young children
- Nearly always caused by *Staphylococcus aureus*
  - Usually phage group 2 (approx. 80%)
  - Represent localized form of Staphylococcal scalded skin syndrome
- Presents with flaccid bullae which rupture quickly leaving erosions often with overlying crust and/or eschar
  - Blister in epidermal granular layer
  - May occur singly or in clusters
  - May develop generalized lesions following varicella – bullous varicella

### Work-up & Management in the Neonate:

- **Febrile neonate**
  - Admission, blood culture, culture of lesion, IV oxacillin
- **Afebrile neonate**
  - Typically admission, as above
  - Consider outpatient Rx if well & only 1-2 localized lesions
- **Febrile infant (>28 days)**
  - Admission, as above
- **Afebrile infant (>28 days)**
  - Culture of lesion, oral anti-staphylococcal antibiotics
Transient Neonatal Vesiculopustular Eruptions

- Erythema toxicum neonatorum
- Transient neonatal pustular melanosis
- Miliaria rubra
- Neonatal acne (benign cephalic pustulosis)

Erythema Toxicum

- More common in African-American infants
- 1st stage: Scattered, subcorneal pustules
  - Usually do not see this stage; rupture quickly
- 2nd stage: Superficial erosion/collarette of scale
- 3rd stage: Hyperpigmented macules
  - May persist for several months
- Wright stain: Many neutrophils, no bacteria

Transient Neonatal Pustular Melanosis
Miliaria Rubra

Neonatal Acne
(Benign Cephalic Pustulosis)

Scabies

- Infestation caused by *Sarcoptes scabiei* ssp. *Hominis*
- Usually associated with generalized pruritus in older children/adults
  - Can present as irritability, insomnia, poor feeding in infants
- Characteristic features in infants:
  - Pustules & vesicles on palms/soles, dorsal foot
  - Facial & scalp involvement more common
  - Nodules on back, axillae, inguinal folds
- Pathognomonic skin features: the burrow
  - Hands, flexural wrists, lateral feet
  - Present in all ages

Scabies

- Mite unable to survive more than few days without the human host
  - Lifespan of mite: up to 30 days

- Mite burrows into the stratum corneum laying up to 3 eggs per day
  - Larvae hatch in 3-4 days; mature into adult mites in 10-14 days

- Treatment:
  - 5% permethrin cream x 8-12 hours (infants > 6-8 weeks age)
  - Reapplication in 1 week
  - Treatment of all household members
  - Launder clothing/bedding in hot water
  - Symptomatic care: antihistamines, emollients, topical steroids
Incontinentia Pigmenti (IP)

- X-linked dominant disorder
- Mutations in NEMO gene
- 97% female patients
- Affects eyes, teeth, CNS
- May affect hair & nails
- Eosinophilia in infancy

IP Cutaneous Stages:

1st: Inflammatory vesicles
2nd: Verrucous lesions
3rd: Whirled / Blaschkoid hyperpigmentation
4th: Streaks of hypopigmentation + atrophy

Langerhans Cell Histiocytosis
Case #2

13 month old female with fever and new onset of a vesicular skin eruption.

Patient developed erythematous macules on her neck, scalp and trunk that subsequently become more raised and vesicular in nature over the last week. She continued to get new lesions while old ones became crusted.

Her skin eruption was preceded by low grade fever and 3 weeks of nasal congestion, loose stools and slight decrease in oral intake.

Family denies any skin contact exposures. Her immunizations are up to date.

Clinical Exam

- Vitals: 36.9 C, HR 156, RR 20
- General: Alert, NAD
- HEENT: Clear
- Chest: Equal breath sounds bilaterally with good air movement
- CVS: RRR, no murmurs, CR<1s
- Abdomen: Soft, non-tender, no HSM
- Skin: Crusted erythematous papules with excoriations and scattered vesicles on the scalp, neck, and trunk. Scattered erythematous macules and small papules on the extremities
Which diagnosis best fits the clinical presentation?

A. Bullous impetigo  
B. Eczema coxsackium  
C. Varicella infection  
D. Eczema herpeticum  
E. Sweet’s syndrome

Varicella Diagnosis

- Primarily clinical
  - Dewdrop on a rose petal
  - Lesions in different stages

Varicella Diagnosis

- PCR of lesions
- Slow to grow in cell culture

Varicella Treatment

- Supportive care
- Oral acyclovir/valacyclovir - not recommended routinely
- Consider for healthy children at increased risk of moderate/severe disease:
  - Unvaccinated >12 yrs
  - Chronic cutaneous or pulmonary disorders
  - Long term ASA therapy
  - Short / intermittent oral or aerosolized steroids

Varicella Exposure

- Consider acyclovir for secondary contacts
- Vaccinate if unimmunized
- VariZIG (IVIG) if indicated

Varicella Zoster
Bullous Impetigo

- Common, contagious, superficial skin infection
- *Staphylococcus aureus*
- Results from production of exfoliative toxin (ETA, ETB)
  - Binds to desmosomal protein
  - Desmoglein 1 in the granular layer of the epidermis

Bullous Impetigo

- Common in infants & children
- Start as small vesicles that enlarge up to 5cm
- Flaccid bullae that rupture, leave a collarette of scale with minimal surrounding erythema
- Face, diaper area and extremities
- Resolve without scarring

Bullous Impetigo

- Work up
  - Culture exudate/crust or lesion fluid
- Treatment
  - Clean area
  - Limited infection: topical medications
    - Mupirocin 2% or retapamulin 1%
  - Multiple lesions: enteral antibiotic
    - First generation cephalosporin, clindamycin
  - Complicated: IV antibiotics
    - β-lactamase-resistant penicillin, cefazolin

Enterovirus

- Hand, Foot & Mouth- CVA16 & EV71
  - Oral erosions
  - Oval vesicles on hands, feet, and buttocks
- Atypical presentation- CVA6
  - More wide-spread, severe and varied presentations
- Peak outbreaks in fall & summer months
Enterovirus

- **Clinical manifestations**
  - Commonly involve skin & mucous membrane
  - Severe disease can involve CNS
  - Aseptic meningitis, acute focal paralysis, brainstem encephalitis

- **Diagnosis**
  - Clinical, viral culture, PCR

- **Supportive care**

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Classic Hand, Foot & Mouth Disease

- Self-limited febrile illness
- Oral ulcerations within 1-2 days of fever onset
  - Tongue, palate, buccal mucosa
- Skin eruption palms, soles, groin
  - Macules, papules, vesicles
  - Can be painful

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Atypical Hand, Foot & Mouth

- Vesiculobullous & erosive eruption
  - Widespread, perioral, acral, buttock
  - Bullae <1 year

- Eczema Coxsackium
  - Vesicles & erosions in areas of eczema

- Acral eruption
  - Acrofacial papulovesicles with sparing of the trunk

- Petechial & purpuric rash
  - >5 years of age
  - Acral

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Eczema Coxsackium


**Vesiculobullous & Erosive Eruption**

**Petechial & Purpuric Rash**

**Delayed Cutaneous Findings**

**Eczema Herpeticum**

**Eczema Herpeticum**

- Associated findings include:
  - Viremia
  - Fever
  - Lymphadenopathy
  - Meningitis
- Predilection for the face & chronic areas of dermatitis
- Widespread punched out erosions

**Eczema Herpeticum**

- Herpes simplex virus in patients with atopic dermatitis or other skin diseases
- Acute onset of clustered vesicles or punched out erosions
- 3% atopic dermatitis patients
  - Tend to have more severe AD
  - Earlier onset of disease
  - Increase risk of food allergies and asthma
  - Tend to have recurrent Staphylococcus aureus infections

- Special considerations:
  - Keratoconjunctivitis
  - Dehydration
- Treatment:
  - Antivirals +/- antibiotics
  - Supportive care (skin, hydration)
  - Ophthalmologic evaluation
Other Herpes Infections
- Cutaneous herpes can occur on any body surface
- Clustered vesicles or erosions on erythematous base
- Can have secondary bacterial infection

Diagnosis and Rx of Pediatric HSV
- Viral culture or PCR of blister or erosion
- CSF PCR if concern for encephalitis
- Acyclovir (PO)
  - Orolabial: 20 mg/kg/dose q 6-8 hours
  - Genital: 400 mg PO TID for 10 days
- Valacyclovir (PO)
  - Genital: 1 gram BID for 10 days

Neutrophilic Dermatoses
- Rare in children
- Vesiculopustular eruption
- Dense infiltrate of inflammatory cells (neutrophils)
- Autoinflammatory conditions associated with systemic diseases

Sweet’s Syndrome
- Acute febrile neutrophilic dermatosis
- Painful papules, nodules, plaques, bullae
- Fever & leukocytosis
- Steroid responsive

Sweet’s Syndrome
- Diagnosis: Skin Biopsy
  - Dense infiltrate of inflammatory cells (neutrophils)
- Associated with underlying disease:
  - Infections
  - Immunodeficiency
  - Inflammatory conditions
  - Malignancy
  - Medications
- Can be idiopathic

Case 3
8 year old presents with one week history of sore throat, cough and red eyes. Seen by PCP 3 days prior to presentation and started on amoxicillin.

2 days prior to presentation, he developed recurrent fever and blisters/lesions on the lips and oral mucous membranes causing difficulty eating. There were several scattered papules and blisters on the face, trunk and extremities.

PMH negative for chronic diseases. No prior hospital stays or surgeries. No other medication exposure aside from occasional antipyretics.

FH: Negative for affected family members.
Case 3

The most likely diagnosis is:

A. Kawasaki Disease
B. Hand Foot Mouth Disease
C. Staphylococcal scalded skin syndrome
D. Stevens Johnson Syndrome
E. Mycoplasma related rash & mucositis

Mycoplasma - Induced Skin Disease

- Nanta M. Front Microbiol 2016
- Vujic et al. JEDADV 2015
- Olson et al. Pediatrics 2015
- Varghese et al. BMJ Case Rep 2014
- Wanat et al. Cutis 2014
- Campagna et al. Pediatr Dermatol 2013
- Kunimi et al. Allergol Int. 2011

Mycoplasma-Induced Rash & Mucositis (MIRM)

- Comprehensive literature search
  - 95 articles; 202 cases
  - Mean age 11.9 years; Males 66% patients
- Cutaneous involvement:
  - Absent (34%), Sparse (47%), Moderate (19%)
- Mucosal involvement:
  - Oral (94%), Ocular (82%), Urogenital (63%)
- Complications:
  - Mucosal damage (10%), scarring (5.6%), recurrence (8%), mortality (3%)

Diagnosis of *Mycoplasma pneumoniae*

- NP specimen for PCR
- Serology
- Cold agglutinins not routinely recommended
Treatment of *Mycoplasma pneumoniae*

- Azithromycin x 5 days
- Doxycycline or levofloxacin x 7-14 days
- No indication for prolonged therapy, even with cutaneous sequelae

Stevens Johnson Syndrome (SJS) / Toxic Epidermal Necrolysis (TEN) vs. Erythema Multiforme

- Nosology previously confusing
- SJS & TEN now considered variants within a spectrum of adverse drug reactions
- Erythema multiforme considered a distinct disorder with different clinical features & precipitating factors

SJS & TEN

- Typically occurs 4-28 days after initiation of drug
- Prodromal symptoms: fever, malaise, myalgias, headache, sore throat
- Mucosal lesions may precede skin eruption
  - Usually ≥ 2 mucous membranes involved (esp. eyes, lips)
  - Ophthalmologic emergency – can result in to permanent visual impairment
- Eruption often begins on face, upper trunk, & proximal extremities
  - Dusky, dark red, purpuric macules with necrotic center (atypical targets); occasionally with typical target lesions

Stevens Johnson Syndrome & TEN

- < 10% BSA involved = SJS
- 10-30% BSA involved = SJS/TEN overlap
- > 30% BSA involved = TEN
Causes of SJS / TEN

- Usually drug-induced:
  - Sulfa antibiotics
  - Aromatic anticonvulsants
  - Lamotrigine
  - Penicillins/cephalosporins
  - Minocycline/tetracycline/doxycycline
  - Allopurinol
- Other: *Mycoplasma pneumoniae*
Staphylococcal Scalded Skin Syndrome

- Disease of young children – majority < 5 y/o
- Rare in adults – renal failure, malignancy, immunosuppression, chronic alcohol abuse, HIV infection
- Toxin-producing \textit{S. aureus} detected, typically MSSA

Clinical features:
- Fever
- Irritability
- Skin tenderness
- Scarlatiniform erythema with flexural accentuation
- Sterile blisters & erosions develop within 24-48 hours
- Intraoral lesions do not occur (absence of granular layer)
- Sepsis rare in children, more common in adults

Skin cultures positive for \textit{S. aureus} from perinasal, axillary, & perianal skin

References:
Treatment of Staphylococcal Scalded Skin Syndrome

- Oxacillin or cefazolin is preferred
  - Consider addition of clindamycin
  - Typically 10 days

- May need admission for hydration due to increased insensible losses

- Oral therapy once improved

Drug Reaction with Eosinophilia & Systemic Symptoms (DRESS)

- Evolving Nomenclature:
  - Drug-induced pseudolymphoma syndrome (1959)
  - Anticonvulsant hypersensitivity syndrome (1960's)
  - Drug-induced hypersensitivity syndrome (DIHS)
  - Hyper sensitivity syndrome (HSS)
  - Drug reaction with eosinophilia & systemic symptoms (DRESS)
  - Boquet et al 1996
DRESS: Clinical Evolution

- Usually begins 2-6 weeks after drug introduced
- Fever, rash, lymphadenopathy, pharyngitis
  - Fever usually precedes cutaneous eruption
  - High spiking temperature, usually 38 - 40°C
- Symptoms may persist beyond discontinuation of offending medication

DRESS Systemic Manifestations

- Hepatic
- Hematologic (atypical lymphocytosis, eosinophilia)
- Renal
- Pulmonary
- Musculoskeletal
- Gastrointestinal
- Cardiac
- Neurologic
- Endocrine

DRESS with Stevens Johnson Syndrome

Kawasaki Disease (KD)
## Diagnosis of KD
- Fever >101°F for 5 days & 4/5 clinical criteria:
  - Conjunctival injection w/o exudate (limbic sparing)
  - Erythematous mouth/pharynx, red, cracked lips, strawberry tongue
  - Polymorphous generalized erythematosus rash; can be morbilliform maculopapular, scarlatiniform or resemble EM
  - Peripheral extremity induration of hands/feet w/ erythema of palms and soles and periungual desquamation later
  - Acute non-suppurative, usually unilateral cervical lymphadenopathy of 1.5 cm

## KD Treatment
- IVIG 2 grams/kg
- ASA 80-100 mg/kg divided q 6 hours
- Echocardiogram
- ~10% need retreatment after 36 hours

## Case # 4
A 4 year old male presents with 6 days of fever and 5 days of rash.

Mom says that the rash started on his wrists and ankles and then spread to the palms and soles and the rest of his body.

The rash started as a light red color and has now become darker.

## Clinical Exam
Vitals: 39°C, HR 130, RR 24, BP 85/50, 02 sat 93%

On exam, he is an ill appearing child with a non-exudative conjunctivitis and mixed petechial/purpuric rash covering his body with concentration on the palms and soles.

He has no murmur, lungs are clear, and abdominal exam is benign. He has mild extremity swelling.

## History
He is a fully immunized child and has no history of recurrent infections.

The family history is non-revealing.

They have one dog in the home, and he attends a pre-school.

They have not had any recent international travel, but the family returned from a week long camping trip in Arkansas 5 days ago.
Of the following, the diagnosis that BEST fits this clinical picture is:

A. Henoch-Schönlein purpura
B. Meningococcemia
C. Rocky Mountain spotted fever
D. Enterovirus

RMSF Epidemiology

- 60% of disease burden from 5 states
- Mortality is <1% since 2001
- Cases occur year-round; but peak in May through September
- Older adults at highest risk

Clinical Features

- Initial: non-specific fever, nausea, vomiting, abdominal pain, altered mental status
- Day 2-4: rash development (pink macules) in 90% of children
- Day 5-6: progression to petechial rash
- Arthralgia, some eyelid and dorsal extremity swelling

Diagnosis and Treatment

**Diagnosis:**
- High index of suspicion
- May be tick exposed w/o bite history
- Hematologic and metabolic derangement
- Serology

**Treatment:**
- Decision to treat is based on clinical diagnosis; not laboratory results
- Do not delay treatment
- Doxycycline 2 mg/kg/dose BID for 7-10 days (ALL ages)

Ehrlichiosis

- Difficult to distinguish clinically from RMSF
- Lab derangement is more common; rash less common
- Risk factor: tick exposed
- Treatment is doxycycline
Ehrlichiosis

- Similar geographic area to RMSF
- Mortality ~1-2%
- Same seasonality
- Similar age distribution
- Fewer cases reported compared to RMSF

Meningococcemia

Clinical Presentation
- Fever, myalgia, altered mental status, prostration
- Rapidly progressive disease with rash evolution over hours from macular to petechial-purpuric

Diagnosis & Treatment
- High index of suspicion
- Blood and CSF culture; culture of lesion; PCR
- Shock management
- 3rd gen cephalosporin
- Sequelae in up to 20%

Pneumococcal Sepsis

- Risk factor for fulminant disease: asplenia
- Immunization prior to splenectomy w/ PCV13 & PPSV23
- Diagnosed through blood cx
- Treated with ampicillin, 3rd generation cephalosporin

Henoch-Schönlein Purpura

- Systemic small vessel vasculitis
  - Most common cause of vasculitis in children
- Primarily in children (3-15yrs)
- Clinical features:
  - Joint pain/arthritis
  - Abdominal pain
  - Glomerulonephritis

- Palpable purpura in dependent areas (legs & buttock)
- Crops and fade within 5 days
- Edema of hands, feet, face, scrotum
Henoch-Schönlein Purpura

- Possible triggers
  - Group A streptococcal infection
  - Other viral & bacterial infections
  - Vaccination

- Fall, winter & spring

Henoch-Schönlein Purpura

- 80% systemic involvement
  - Glomerulonephritis 40-50%
  - Gastrointestinal
  - Joint involvement
  - CNS & Pulmonary involvement

Henoch-Schönlein Purpura

- Histopathologic exam
  - IgA + direct immunofluorescence

- Laboratory work up
  - R/o other vasculitides
  - Identify complications

- Cutaneous findings < 2 months
  - 1/3 have recurrences

- Supportive care for most

Henoch-Schönlein Purpura

- 80% systemic involvement
  - Glomerulonephritis 40-50%
  - Gastrointestinal
  - Joint involvement
  - CNS & Pulmonary involvement

Other Leukocytoclastic Vasculitides

- Hypersensitivity Vasculitis
  - Rare in children
  - Tends to occur in crops in dependent areas
  - Often caused by medication or infection
  - Evaluate for systemic involvement

Other Leukocytoclastic Vasculitides

- Acute Hemorrhagic Edema of Infancy
  - Infants and young children
  - Limited to the skin
  - Non-ill appearing
  - May be triggered by a viral illness

Questions?