RASH IN INFECTIOUS DISEASES OF CHILDREN

Andrew Bonwit, M.D.
Infectious Diseases
Department of Pediatrics
OBJECTIVES

- Develop skills in observing and describing rashes
- Recognize associations between rashes and serious diseases
- Recognize rashes associated with benign conditions
- Learn associations between rashes and contagious disease
Descriptions

• Rash
• Exanthem
• Vesicle
• Bulla
• Macule
• Papule

• Petechiae
• Purpura
• Erythroderma
• Erythema
• Enanthem
• Eruption
Period of infectivity in relation to presence of rash

- **VZV** incubates 10 – 21 days (to 28 d if VZIG is given)
  - Contagious from 24 - 48° before rash to crusting of all lesions
- **Fifth disease** (parvovirus B19 infection): clinical illness & contagiousness *pre*-rash
  - Rash follows appearance of IgG; no longer contagious when rash appears
- **Measles** incubates 7 – 10 days
  - Contagious from 7 – 10 days post exposure, or 1 – 2 d pre-Sx, 3 – 5 d pre-rash; to 4th day after onset of rash
Associated changes in integument

• Enanthems
  • Measles, varicella, group A streptococcus

• Mucosal hyperemia
  • Toxin-mediated bacterial infections

• Conjunctivitis/conjunctival injection
  • Measles, adenovirus, Kawasaki disease, SJS, toxin-mediated bacterial disease
Pathophysiology of rash: epidermal disruption

• Vesicles: epidermal, clear fluid, ≤ 5 mm
  • Varicella
  • HSV
  • Contact dermatitis

• Bullae: epidermal, serous/seropurulent, > 5 mm
  • Bullous impetigo
  • Neonatal HSV
  • Bullous pemphigoid
  • Burns
  • Contact dermatitis
  • Stevens Johnson syndrome, Toxic Epidermal Necrolysis
Bacterial causes of rash

• *S. pyogenes* (GAS): scarlet fever, rheumatic fever, erythema marginatum
• *S. aureus*: SSS/Ritter’s syndrome, TSS
• Endocarditis: Osler nodes, Janeway lesions, splinter hemorrhages
• *N. meningitidis*: purpura
• *B. burgdorferi*: erythema migrans
• *T. pallidum*: 2° syphilis
• *Leptospira* spp.
Scarlet Fever

- Flushed face with perioral pallor
- Blanching, sandpaper rash
- Pastia lines (linear petechiae along creases)
- White strawberry tongue (days 1-2)
- Red strawberry tongue
- Desquamation as acute phase resolves
Scarlet Fever

• Group A streptococcus infxn
• Usually associated with GAS pharyngitis
• Rarely with skin infections
• Fever, sore throat, headache, abdominal pain
• Rash develops within 24 hours of symptoms
Scarlet Fever

• Tx of choice: penicillin
  • Most β-lactams effective
• Contagious until 24 hours of Abx
  • Droplet precautions
• Important to treat for full 10 days to prevent Rheumatic Fever
Streptococcal Pathogenesis

- Streptococcal Pyrogenic Exotoxins
  - Associated with scarlet fever, strep toxic-shock-like syndrome
  - SPE-A, SPE-B, SPE-C
    - bind to MHC II receptors
- **M protein** (antiphagocytic) → Entry of GAS into deep tissues
- Monocytes → cytokines → clinical illness
- Peptidoglycans & lipoteichoic acid → production of TNF-alpha, IL-1B
- SPE-B: bradykinin release
• Rebecca Lancefield, 1895 – 1981. Devised classification scheme for the streptococci
Staphylococcal scalded skin syndrome (Ritter’s disease)

- Staphylococcal exfoliatins
- Desquamation
  - Nikolsky’s sign
- May have edema at areas of erythema
- Localized infection +/- bacteremia
- Anti-staphylococcal antibiotic
Mixed Streptococcal & Staphylococcal Skin Infection Complicating Varicella
A Case...

- 8 year old boy
- Acute onset of fever, prostration
- Progresses to shock
- Rash...
Meningococcemia

- *Neisseria meningitidis*
- Gram-negative diplococcus
  - Genus named for Albert Neisser, 1855 – 1916; Anton Weichselbaum isolated the pathogen from CSF in 1887
- Serotypes A, B, C, Y, W-135 serotypes most associated with human disease
- Commonly causes asymptomatic colonization, increase in bactericidal antibody titers w/in 2 weeks
- Susceptibility greatest in 1st year of life
  - Predisposing factors: crowding, poverty, cigarette smoke (active or passive), prior viral respiratory infxn, winter/dry season, move to new community, impaired phagocytosis
Rickettsial causes of rash

• *Rickettsia rickettsii*: Rocky Mountain Spotted Fever
• *Ehrlicia chaffeensis*: Human monocytic ehrlichiosis (HME)
• *Anaplasma phagocytophilum*: Human granulocytic anaplasmosis (HGA) [formerly HGE]
• *E. ewingii* infection
• 2 year old girl admitted with fever and rash
• Crying, cranky, appears to “hurt everywhere”
• 3rd day of illness, faint rash at wrists, ankles, which blanched on pressure
• Family went on picnic in forest preserve about 10 days ago
Rocky Mountain Spotted Fever

- *Rickettsia rickettsii*
- *Dermacentor* tick vectors (*D variabilis, D andersonii*)
- Infection of vascular endothelium →
  - thrombocytopenia, leukopenia, hyponatremia, hypoalbuminemia
  - May progress to multisystem organ failure, shock, death
- Rash goes wrists & ankles → hands, feet → progress up limbs to central & generalized petechial rash
- Treatment of choice = Doxycycline
  - Treatment benefits greatly outweigh risk of dental staining
  - Alternative: Chloramphenicol; may be clinically inferior
  - Treatment duration: usually 5 – 7 days, and at least 3 d beyond clear clinical improvement
Dermacentor variabilis
(American Dog Tick)
Diagnosis?

• Erythema migrans (EM)
• Which is diagnostic of...
Lyme disease

- *Borrelia burgdorferi* spirochete
- Ixodid tick vectors (*Ixodes scapularis, I pacificus*)
- Early (single EM), early disseminated, late stages
- Doxycycline for early/early disseminated, > 8 yo
- Amoxicillin for < 8 yrs old
- Ceftriaxone or penicillin for late disease
*Ixodes scapularis* (hard-bodied Deer Tick)—”Questing” Behavior

Source: University of Florida Institute of Food and Agricultural Sciences, www.creatures.ifas.ufl.edu/urban/medical/deer_tick.htm
Size comparisons of ticks

- Source: CDC
*Ixodes* ticks, unengorged and engorged

Distribution of Reported Cases of Lyme Disease, U.S.A., 2005

Source: www.cdc.gov/mmwr/preview/mmwrhtml/mm5623a1/htm?s_cid=mm5623a1_e
Viral causes of rash

- Rubeola (Measles)
- Rubella (German Measles)
- Enteroviruses
- Parvovirus B19
- HHV – 6

- HSV
- Adenoviruses
- HBV (Gianotti-Crosti)
- HIV (acute retroviral syndrome)
Varicella

Vesicles on an erythematous base

“Dewdrop on a rose petal”

In different stages of healing
Varicella

- Varicella zoster virus infxn
- Incubation: 10-21 days
- Contagious from 1-2 days before onset of rash until all lesions crusted
- Itchy, vesicular rash, fever, rhinorrhea, cough
- Trunk/face/scalp → extremities (not usually distal)
- New lesions, in crops, for 3 – 7 days
- Negative-pressure room; contact precautions; airborne precautions (N95 for nonimmune)
Complications of varicella

Necrotizing fasciitis

Hemorrhagic varicella

Also:
Pneumonia
Acute cerebellar ataxia
Encephalitis
Herpes zoster

• Virus establishes latency in dorsal root ganglia during primary infection

• Grouped vesicular lesions in dermatomal distribution

• Rash may be preceded by pain
Smallpox: a brief, historical (we hope!) digression

• Bioterrorism threat (we hope not)
• We view to compare with chickenpox
SMALLPOX: PROGRESS OF LESIONS—DAYS 1 THROUGH 4

SMALLPOX: PROGRESS OF LESIONS—DAYS 1 THROUGH 4

SMALLPOX: PROGRESS OF LESIONS, DAYS 1 THROUGH 7 OF RASH

Measles

- Blotchy, erythematous, maculopapular
- Starts at hairline & postauricular; spreads cephalocaudally
- Conjunctivitis with watery discharge
- Koplik Spots: bluish white w/red halo on buccal mucosa; precedes exanthem
- Involves palms and soles
Measles (Rubeola)

• 8-12 day incubation period
• Cough (hacking, “brassy”), fever, coryza, conjunctivitis (nonpurulent)
• Koplik spots at 2 – 3 days
• Maculopapular rash, becomes confluent, starts @ forehead, occiput/behind ears
  • “Morbilliform” rash means “resembling measles”
• Contagious from 1-2 days before onset of symptoms until 4 days after rash appears
• Historically, late winter – early spring
Measles diagnosis

• Primarily clinical
• Reportable disease
• CBC: leukopenia & lymphopenia
• Serologies preferred for confirmation of Dx
  • complement fixation, hemagglutination, EIA
  • Ab rise 1 – 3 days post onset of rash
  • Ab peaks 2 – 4 weeks later
• Serology preferred
  • Ag tests of respiratory cells, PCR tests also available
Measles complications

• Mostly, respiratory and CNS
• 1,000,000 deaths per year in developing world
• Lower respiratory tract complications
  • Pneumonia (broncho-, lobar, interstitial)
  • Laryngotracheobronchitis
  • Extension of measles down the tract, or bacterial superinfection
    • 1% - 6% of cases
    • Up to 60% of the attributable mortality
• Otitis media
• ↓ platelets, hepatitis, appendicitis, GN, myo-/pericarditis
Measles complications-CNS

• Encephalitis in 0.01% – 0.1% of cases
  • Fever, headache, lethargy 2 – 6 d post rash onset
  • Usually self limited, but 15% of encephalitis cases rapidly progressive, fatal
  • Moderate pleocytosis, protein elevation
  • About one-quarter of survivors w/long-term neuro deficits
    • Seizures, devel delay, hearing loss, paralysis

• SSPE (subacute sclerosing panencephalitis)
  • Rare (1 per 100,000 measles cases)
  • Progressive, ultimately fatal
  • Burst-suppression on EEG
Measles vaccination issues

• Current vaccine about 95% protective
• First vaccine: 1963 – 1968
  • killed or live-attenuated; only partial immunity
• 99% drop in measles cases, then...
• ↑ incidence in 1980s
  • 1497 cases in 1983 → 6282 cases in 1986
• Problems: ↓ rate in childhood vaccinations, and primary vaccine failures
Measles vaccination issues

• Vaccine-era in U.S.
  • peak in 1990 with \( \approx 28,000 \) cases
  • record low in 2004 with 37 cases

• Of \( \approx 17,000 \) cases, 1985 – 1988:
  • 26% nonpreventable
    • infants < 16 mo; persons born before 1957; previously physician dx’d; medical contraindications
  • 42% in vaccinated persons
  • 32% in unvaccinated persons w/o vaccine contraindications
Measles vaccine

• Effective as post-exposure prophylaxis w/in 72 hours in susceptible person
  • For exposed infant 6 – 12 m.o., monovalent preferred, MMR acceptable

• If vaccinating infant 6 – 12 months of age, must reimmunize @ 12 – 15 months of age and then boost as usual

• Passive immunization, IG 0.25 mL/kg IM within 6 days (0.5 mL/kg for immunocompromised)
Rubella

- Fine, pink-red maculopapular rash
- Morbilliform, but less red

Erythematous palatal lesions seen on day 1 of rash
*Forchheimer Spots*

- Posterior auricular or occipital LAD
Rubella (German measles)

- Many cases are subclinical
- Mild disease with rash, LAD, and slight fever
- Polyarthritis and arthritis common in adolescents
Maternal rubella during pregnancy can result in miscarriage, fetal death, or congenital anomalies:

- **Cataracts**
- **“Blueberry muffin rash” from dermal erythropoiesis**
- **Microcephaly**
- **Deafness**
- **Congenital heart disease**
- **Thrombocytopenia**
Rubella

- Treatment is supportive care
- Vaccinate with MMR vaccine at 12 months and 5 years
Roseola

Discrete, rose colored macules

Prominent scalp involvement

May appear generalized or start centrally and spread outward

Usually appears abruptly after 3 days of fever and irritability
Roseola

• Caused by HHV-6 (and HHV-7?)
  • *Roseolovirus* genus, beta herpesviruses
• High fever x 3-7 days
• Rash appears within 24 hours of defervescence
• 10-15% have febrile seizures
• Treatment is supportive care
Hand-Foot-and-Mouth Disease

Shallow, yellow ulcers surrounded by red halos
On labial or buccal mucosa, palate, or tongue

Thick-walled gray vesicles on erythematous base
On hands, feet, and buttocks
Hand-Foot-and-Mouth Disease

- Coxsackievirus A16 & Enterovirus 71
  - Coxsackie B, rare cause
- Herpangina when only oral involvement
- Oral lesions usually precede skin lesions
- Typically in summer and fall
Hand-Foot-and-Mouth Disease

• Typically lasts 2-7 days
• Complications are rare
  • Enterovirus 71—sporadic cause of encephalitis
• Treatment is supportive care
Herpetic Gingivostomatitis

- 90% primary HSV infections are subclinical
- Most common form of primary infection
- Fever, irritability, mouth pain, LAD
- Acyclovir is selectively useful in severe cases

Diffuseness of lesions & severity of inflammation & gingivitis distinguish from herpangina

Discrete mucosal ulcerations and diffuse gingival erythema

Yellow-white ulcerations with red halo

Yellowish-white debris on tongue

Thick-walled vesicles on erythematous base on peri-oral skin
Ocular Herpes

• Primary herpetic infection of eye
• Keratoconjunctivitis
• Can cause permanent visual impairment
• Urgent ophthalmology evaluation
  • Topical (ophthalmic) Trifluridine or Idoxuridine gtt
  • +/- topical steroids
5 day old infant admitted with these skin lesions

• Had fetal scalp electrode during delivery
Neonatal HSV infections

• Skin-eye-mucous membrane; 7 – 14 d
• Disseminated; 5 – 10 d
  • Multisystem involvement, including CNS
  • Shock, hepatomegaly, jaundice, bleeding, resp distress
  • Acyclovir 60 mg/kg/d IV div q 8 hr
• CNS; 14 – 21 d
  • Retrograde axonal spread to temporal lobes
Mother trimmed infant’s nails using her teeth...

• And this is how it looked when she came to you...
Herpetic Whitlow

- Primary herpetic infection of the skin
- Direct inoculation of traumatized skin
- Fever, localized pain, regional LAD
Recurrent Herpes Labialis

• Following primary infection, HSV latency in cutaneous nerve ganglia
• Reactivation: fever, sunlight, local trauma, menses, stress
• Vesicles small, thin-walled compared to primary lesions
• Oral Tx marginally useful
• Prophylaxis (acyclovir) for frequent recurrence
• Topical Tx not useful
Eczema herpeticum

- Primary HSV infection in patient with atopic dermatitis
- High fever, irritability
- Can result in severe fluid losses and death
- Management of fluids & electrolytes, parenteral acyclovir
Erythema infectiosum

Warm, erythematous, circumscribed patches over cheeks

Erythematous, lacy, reticular rash develops 2-3 days later

Starts on trunk and spreads to arms and legs
Erythema infectiosum

• “Fifth Disease”
• Caused by infection with Parvovirus B19
• Fever, malaise, myalgias precede rash by 7-10 days
• Arthralgia and arthritis in 10% children
• Most contagious before the onset of rash
Erythema infectiosum

• Causes aplastic crisis in pts with hemolytic anemia

• Primary infection in pregnancy can cause fetal hydrops, IUGR, and fetal death
  • Virus replicates in late erythroid progenitor cells

• Treatment is supportive care
The Historical Six Exanthems of Childhood

• 1\textsuperscript{st} – Measles—rubeola
• 2\textsuperscript{nd} – Scarlet Fever—\textit{S. pyogenes}
• 3\textsuperscript{rd} – Rubella, German measles—\textit{Rubivirus}
• 4\textsuperscript{th} – Dukes’ Disease—echovirus, enterovirus, coxsackie
• 5\textsuperscript{th} – Fifth Disease—parvovirus B19
• 6\textsuperscript{th} – Exanthema subitum ("sudden"), roseola infantum—human herpesvirus 6
Kawasaki Disease

• “Classical”: Fever > 5 days, with at least 4 of:
  • Bilateral, non-exudative, bulbar conjunctivitis (suffusion)
  • Erythematous mouth/pharynx, strawberry tongue, red/cracked lips
  • Polymorphous, genlzd, erythematous rash, morbilliform, maculopapular, scarlatinaform
  • Hand/foot changes: redness, edema, periungual desquamation
  • Acute nonsuppurative cervical LAD (≥ 1.5 cm)

• No alternative dx explains the findings

• IVIG 2 grams/kg (↓ incidence of CAA to about 2%)

Others?

• Erythema multiforme, major & minor
  • Large differential dx including viral, bacterial, mycoplasma, protozooan, fungal; drugs; food sensitivity

• Kawasaki disease

• Drug eruptions
Stevens-Johnson Syndrome

• Erythema multiforme with bullous lesions of mouth, oropharynx
• Skin lesions may become bullous
• Supportive fluid & electrolyte therapy
Kawasaki Disease

- Mainly in children 1 – 8 yrs of age
  - 80% of cases, ≤ 5 yrs of age
- Etiology unknown; cytokine release (superantigen-mediated?)
- Generalized vasculitis
- Consequent coronary artery aneurysms in ≈20% of untreated
Allergic Urticaria on Back
www.answers.com/topic/urticaria
Allergic Urticaria on Foot
www.answers.com/topic/urticaria
Allergic Urticaria on Arm

www.answers.com/topic/urticaria