RASH IN INFECTIOUS DISEASES OF CHILDREN

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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 streptoccus
• 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

- Blacklegged Tick (*Ixodes scapularis*)
  - adult female
  - adult male
  - nymph
  - larva

- Lone Star Tick (*Amblyomma americanum*)

- Dog Tick (*Dermacentor variabilis*)

» 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

“In different stages of healing”

“Dewdrop on a rose petal”
Varicella

- Varicella zoster virus infection
- 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
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SMALLPOX: PROGRESS OF LESIONS,
DAYS 1 THROUGH 7 OF RASH

Measles

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

Erythematous palatal lesions seen on day 1 of rash

Forchheimer Spots

Fine, pink-red maculopapular rash

Morbilliform, but less red

Posterior auricular or occipital LAD
Rubella (German measles)

- Many cases are subclinical
- Mild disease with rash, LAD, and slight fever
- Polyarthralgia and arthritis common in adolescents
Congenital Rubella Syndrome

Maternal rubella during pregnancy can result in miscarriage, fetal death, or congenital anomalies.

- Cataracts
- "Blueberry muffin rash" from dermal erythropoesis
- Microcephaly
- Also: 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

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

- “Classical”: Fever $\geq$ 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 ($\geq$ 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, protozoan, 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