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
- Exantheme
- Vesicle
- Bulla
- Macule
- Papule
- Petechiae
- Purpura
- Erythodermia
- Erythema
- Enanthem
- Eruption

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 – Exantheme subitum (“sudden”), roseola infantum—human herpesvirus 6

Period of infectivity in relation to presence of rash

- VZV incubates 10 – 21 days (to 28 d if VZIG is given)
  - Contagious from 24 - 48h before rash to crusting of all lesions
- Fifth disease (parovirus 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

- Enantheams
  - 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

Viral causes of rash
- Rubeola (Measles)
- Rubella (German Measles)
- Enteroviruses
- Parvovirus B19
- HHV – 6
- HSV
- Adenoviruses
- HBV (Gianotti-Crosti)
- HIV (acute retroviral syndrome)

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.*

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

Others?
- Erythema multiforme, major & minor
  - Large differential dx including viral, bacterial, mycoplasma, protozoan, fungal; drugs; food sensitivity
- Kawasaki disease
- Drug eruptions

Varicella
- Vesicles on an erythematous base
- "Dewdrop on a rose petal"
- In different stages of healing
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)

Herpes zoster
- Virus establishes latency in dorsal root ganglia during primary infection
- Grouped vesicular lesions in dermatomal distribution
- Rash may be preceded by pain

Complications of varicella
- Necrotizing fasciitis
- Hemorrhagic varicella
- Also: Pneumonia, Acute cerebellar ataxia, Encephalitis

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 7 OF RASH

ECZEMA VACCINATUM

ECZEMA VACCINATUM

GENERALIZED VACCINIA

Measles

- Blotchy, erythematous, maculopapular
- Conjunctivitis with watery discharge
- Involves palms and soles
- Koplik Spots: bluish white with red halo on buccal mucosa, precedes exanthem

Measles

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

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 diagnosis
- Primarily clinical
- Reportable disease
- CBC: leukopenia & lymphopenia
- Serologies preferred for confirmation of Dx
  - complement fixation, hemaglutination, 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
- 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
- Vaccine-era in U.S.
  - peak in 1990 with ≈ 28,000 cases
  - record low in 2004 with 37 cases
- Of ≈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

- 12 – 15 mo of age, and ≥1 month after
- 2nd dose usually 4 – 6 yo
- Effective as post-exposure prophylaxis w/in 72 hours in susceptible person
- If vaccinating infant 6 – 12 months of age, needs usual primary series anyway
- Passive immunization

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

Rubella

- Fine, pink-red maculopapular rash
- Morbilliform, but less red
- Posterior auricular or occipital LAD

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
Rubella (German measles)
- Many cases are subclinical
- Mild disease with rash, LAD, and slight fever
- Polyarthritis and arthritis common in adolescents

Congenital Rubella Syndrome
- Maternal rubella during pregnancy can result in miscarriage, fetal death, or congenital anomalies
- Microcephaly
- Cataracts
- "Blueberry muffin rash" from dermal erythropoiesis
- 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
- May appear generalized or start centrally and spread outward
- Prominent scalp involvement
- Usually appears abruptly after 3 days of fever and irritability

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 erythematosus base
- On hands, feet, and buttocks

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

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

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

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

Scarlet Fever
- Pastia lines (linear petechiae along creases)
- White strawberry tongue (days 1-2)
- Red strawberry tongue
- Flushed face with perioral pallor
- 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

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

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

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
- Doxycycline is treatment of choice
  - Benefits far outweigh risk
  - Chloramphenicol is only other treatment, may be inferior
  - Treat at least 5 – 7 days, and at least 3 d beyond clear clinical improvement
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

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

Source: www.cdc.gov/mmwr/preview/mmwrhtml/mm5623a1.htm?s_cid:mm5623a1_e