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

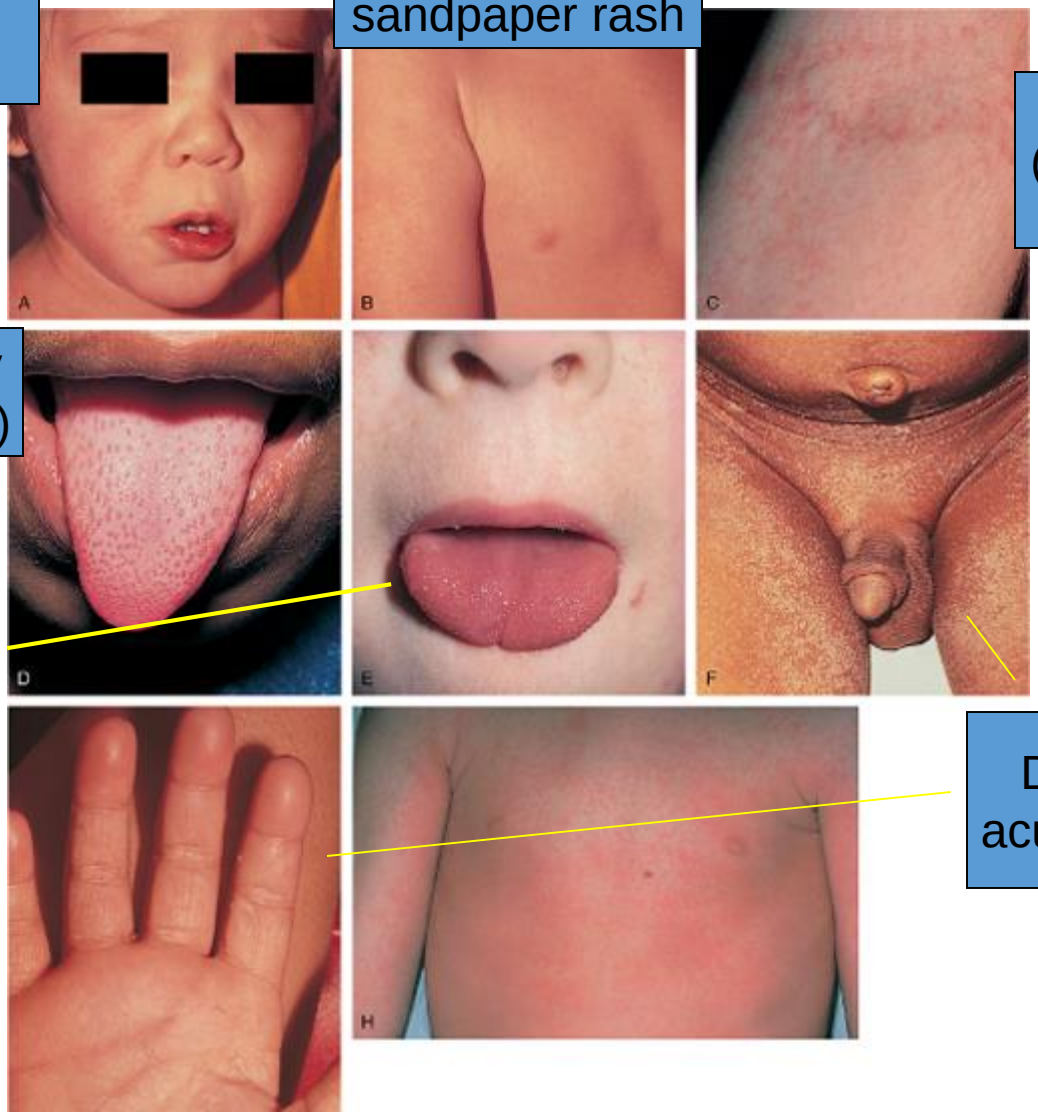
Blanching, sandpaper rash

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 ß-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)

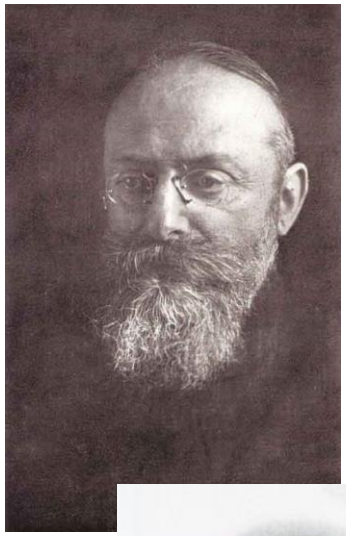
- Staphylococcal exfoliatins
- Desquamation
  - Nikolsky's sign
- May have edema at areas of erythema
- Localized infection +/- bacteremia
- Anti-staphylococcal antibiotic

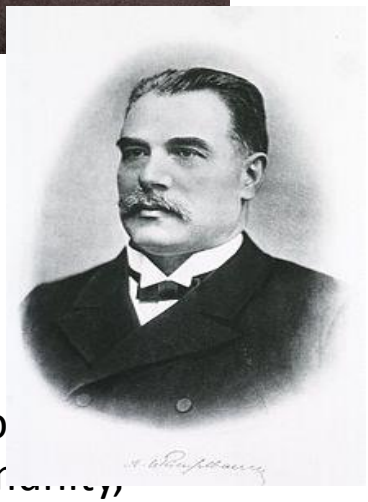
Mixed Streptococcal & Staphylococcal Skin Infection Complicating Varicella

A Case…

- 8 year old boy
- Acute onset of fever, prostration
- Progesses 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
  - Predisoposing factors: crowding, poverty, cigarette smoke (active o
    prior viral respiratory infxn, winter/dry season, move to new comm
    impaired phagocytosis

Rickettsial causes of rash

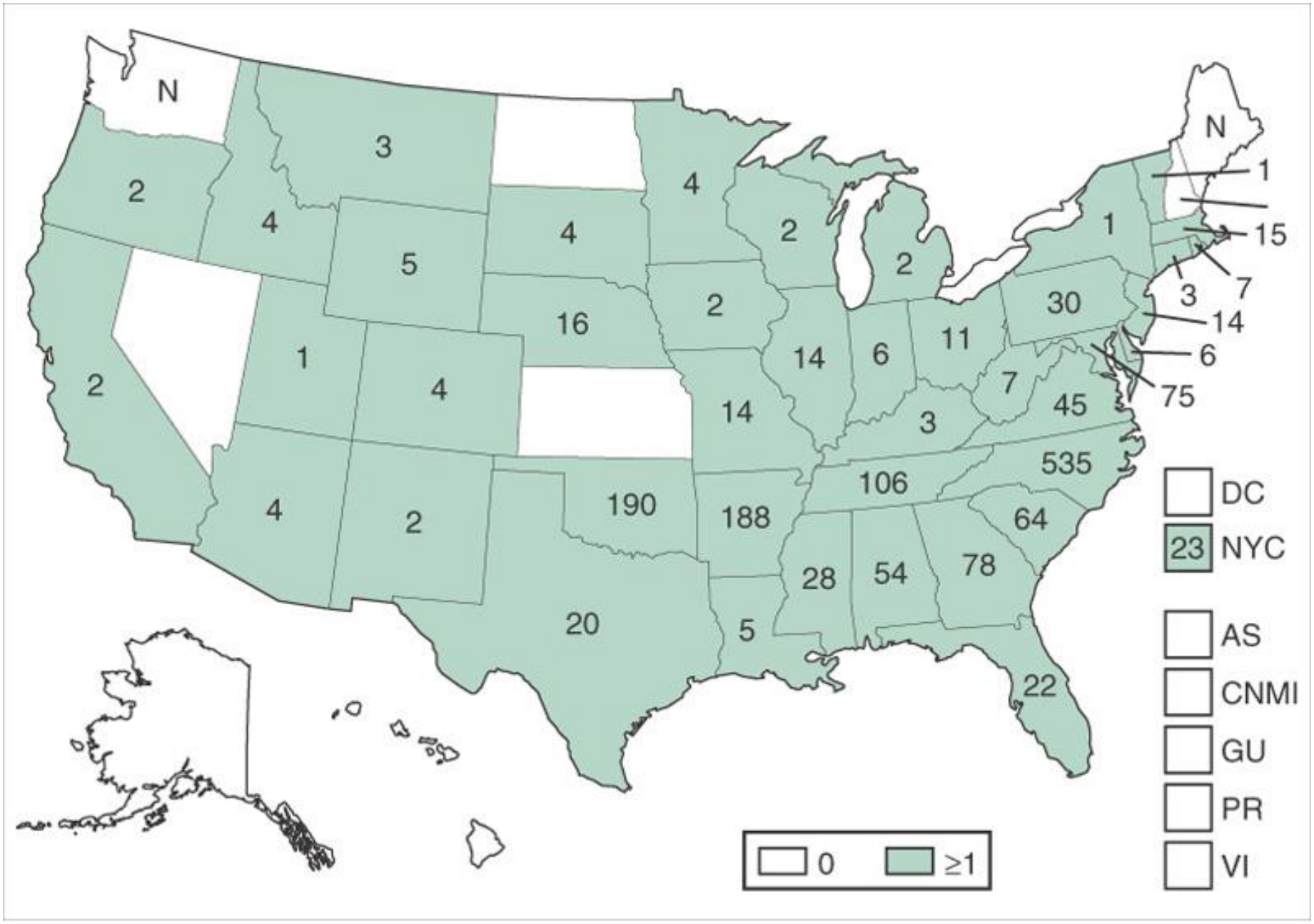
- *Rickettsia rickettsii:* Rocky Mountain Spotted Fever
- *Ehrlicia chaffeensis:* Human monocytic ehrlichiosis (HME)
- *Anaplasma phagocytophilum:* Human granulocytic anaplasmosis (HGA) [formerly HGE]
- *E. ewingii* infection

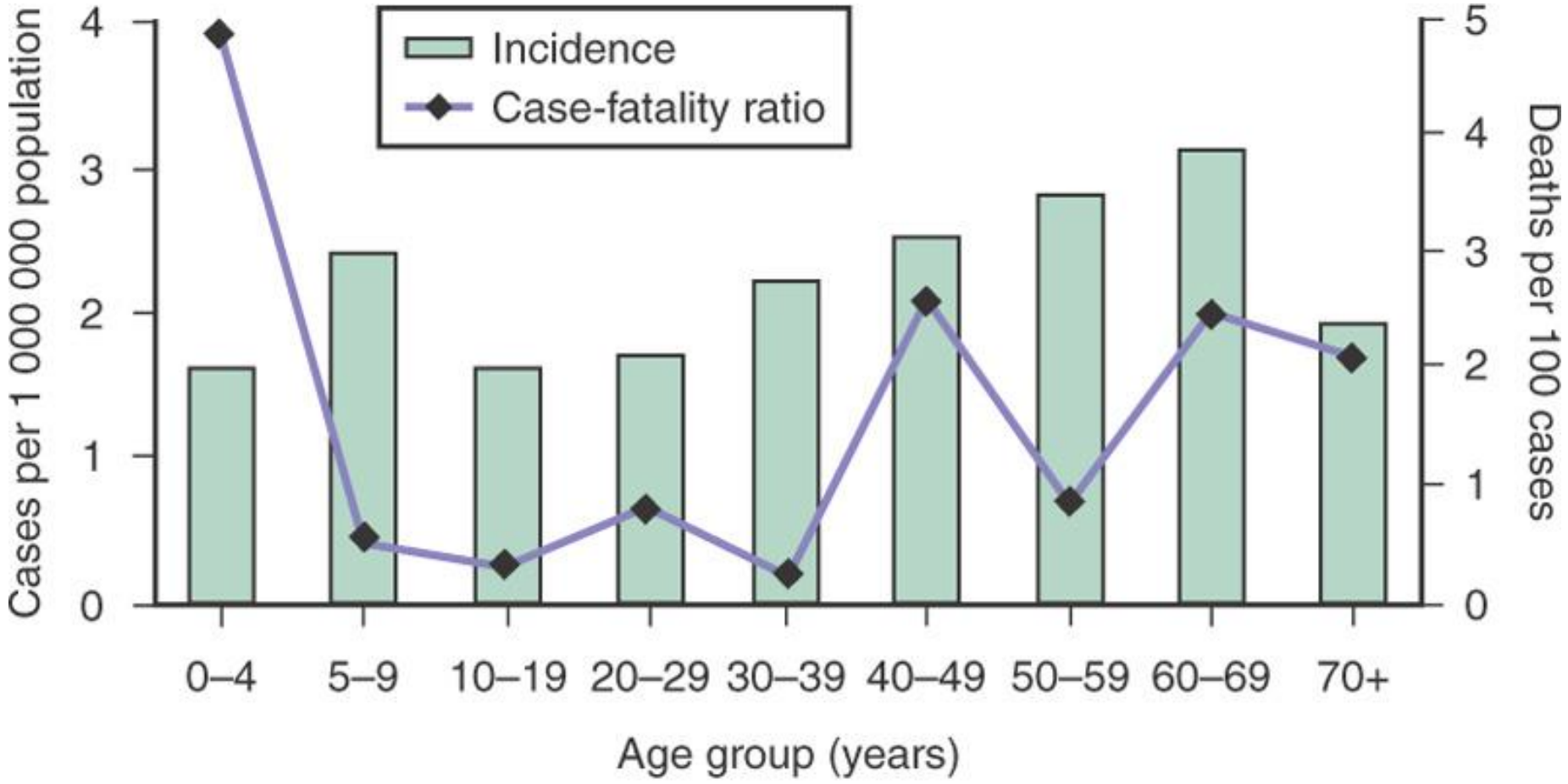
- 2 year old girl admitted with fever and rash
- Crying, cranky, appears to “hurt everywhere”
- 3rd day of illness, faint rash at wrists, ankles, which blanched on pressure
- Family went on picnic in forest preserve about 10 days ago

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

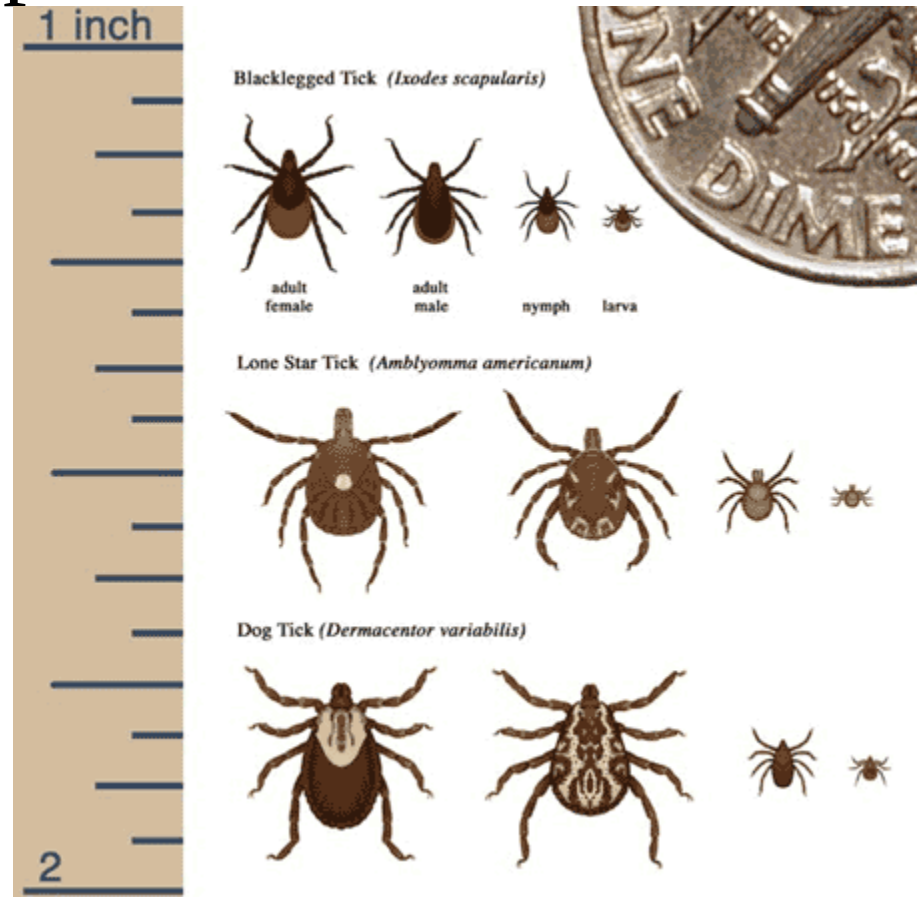
- *Borrelia burgdorferi* spirochete
- Ixodid tick vectors (*Ixodes scapularis*, *I pacificus*)
- Early (single EM), early disseminated, late stages
- Doxycycline for early/early dissem, > 8 yo
- Amoxicillin for < 8 yrs old
- Ceftriaxone or penicillin for late disease

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



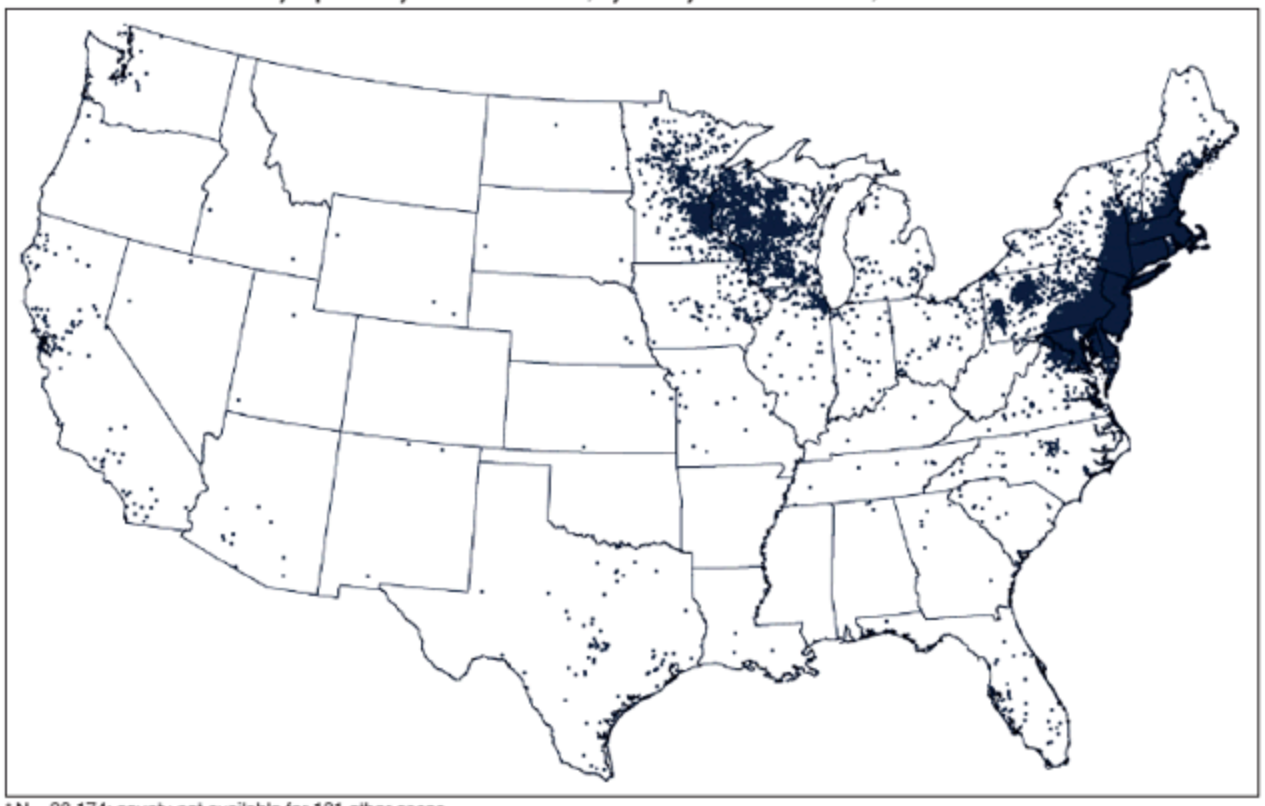
- Source: CDC

Ixodes ticks, unengorged and engorged

- Source: *Red Book Online*®, "Image of the Week," February 13, 2006.

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

FIGURE 1. Number* of newly reported Lyme disease cases, by county† — United States, 2005



* N = 23,174; county not available for 131 other cases.
† One dot was placed randomly within the county of patient residence for each reported case.

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

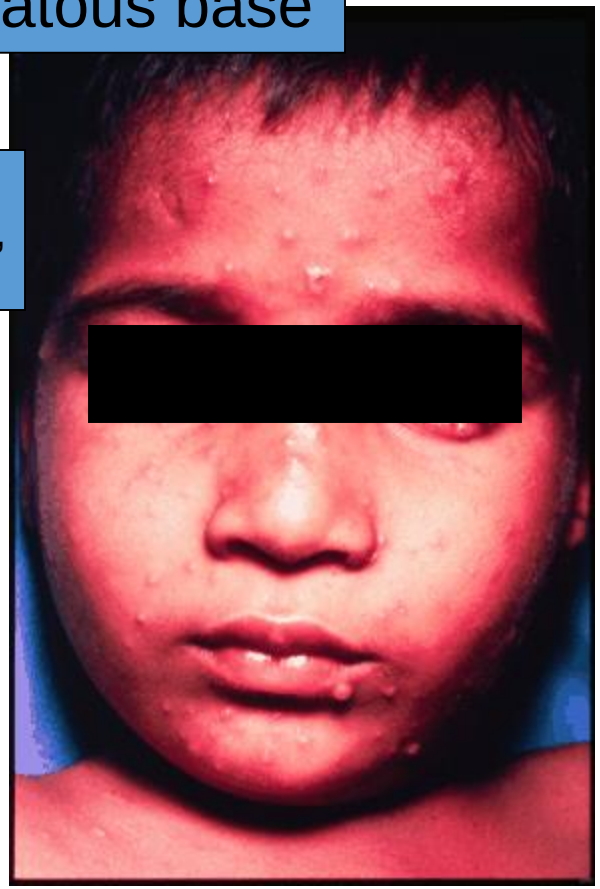
Viral causes of rash

- 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

- From Fenner, F., et al. Smallpox and Its Eradication. 1988.

SMALLPOX: PROGRESS OF LESIONS—DAYS 1 THROUGH 4

- From Fenner, F., et al. Smallpox and Its Eradication. 1988.

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

From Fenner, F., et al. Smallpox and Its Eradication. 1988

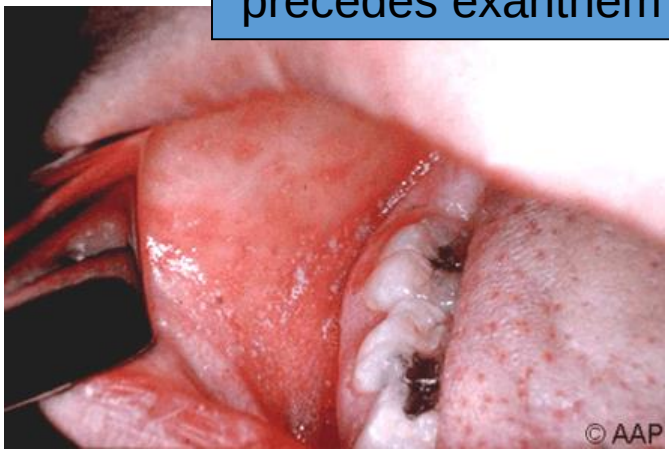
Measles

Blotchy, erythematous, maculopapular

Starts at hairline & postauricular; spreads cephalocaudally

Koplik Spots: bluish white w/red halo on buccal mucosa; precedes exanthem

Involves palms and soles



Conjunctivitis with watery discharge

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, hemagluttination, 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 ≈ 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

- 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
- Polyarthralgia and arthritis common in adolescents

Congenital Rubella Syndrome

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

Cataracts

Microcephaly

"Blueberry muffin rash" from dermal erythropoesis

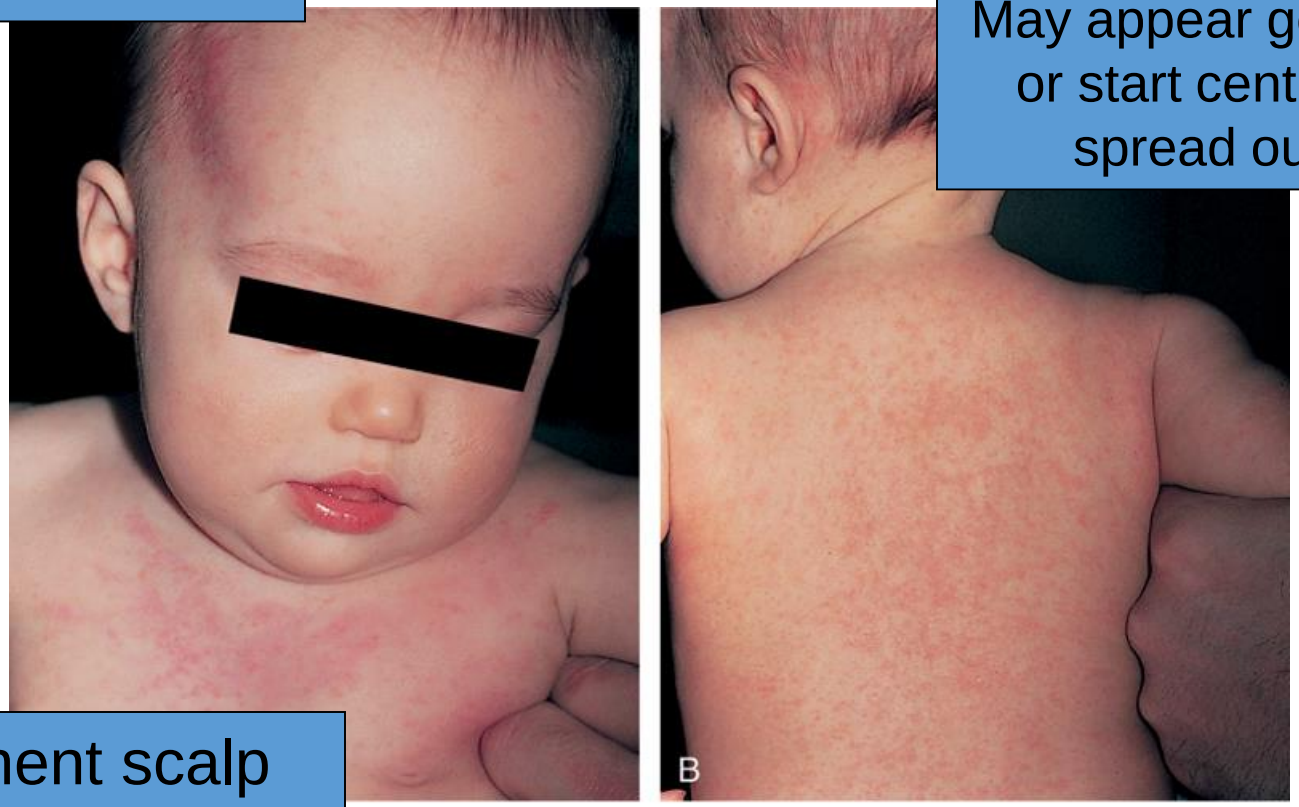
Also:
Deafness
Congenital heart ds
Thrombocytopenia

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

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

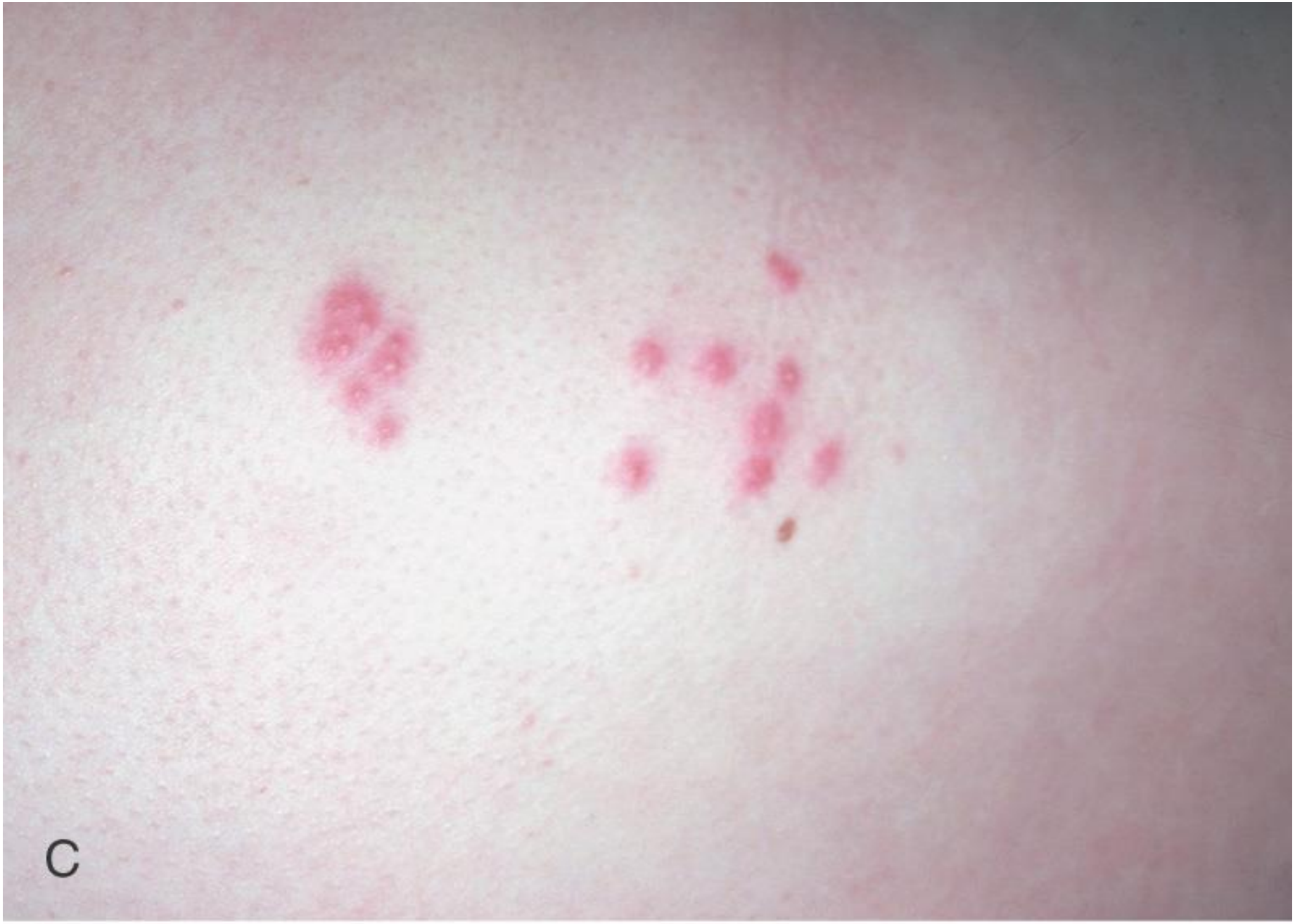
Thick-walled vesicles on erythematous base on peri-oral skin

Ocular Herpes

- Primary herpetic infection of eye
- Keratoconjunctivitis
- Can cause permanent visual impairment
- Urgent ophthalmology evaluation
  - Topical (ophthalmic) Trifluridine or Idoxuridine gtt
  - +/- topical steroids

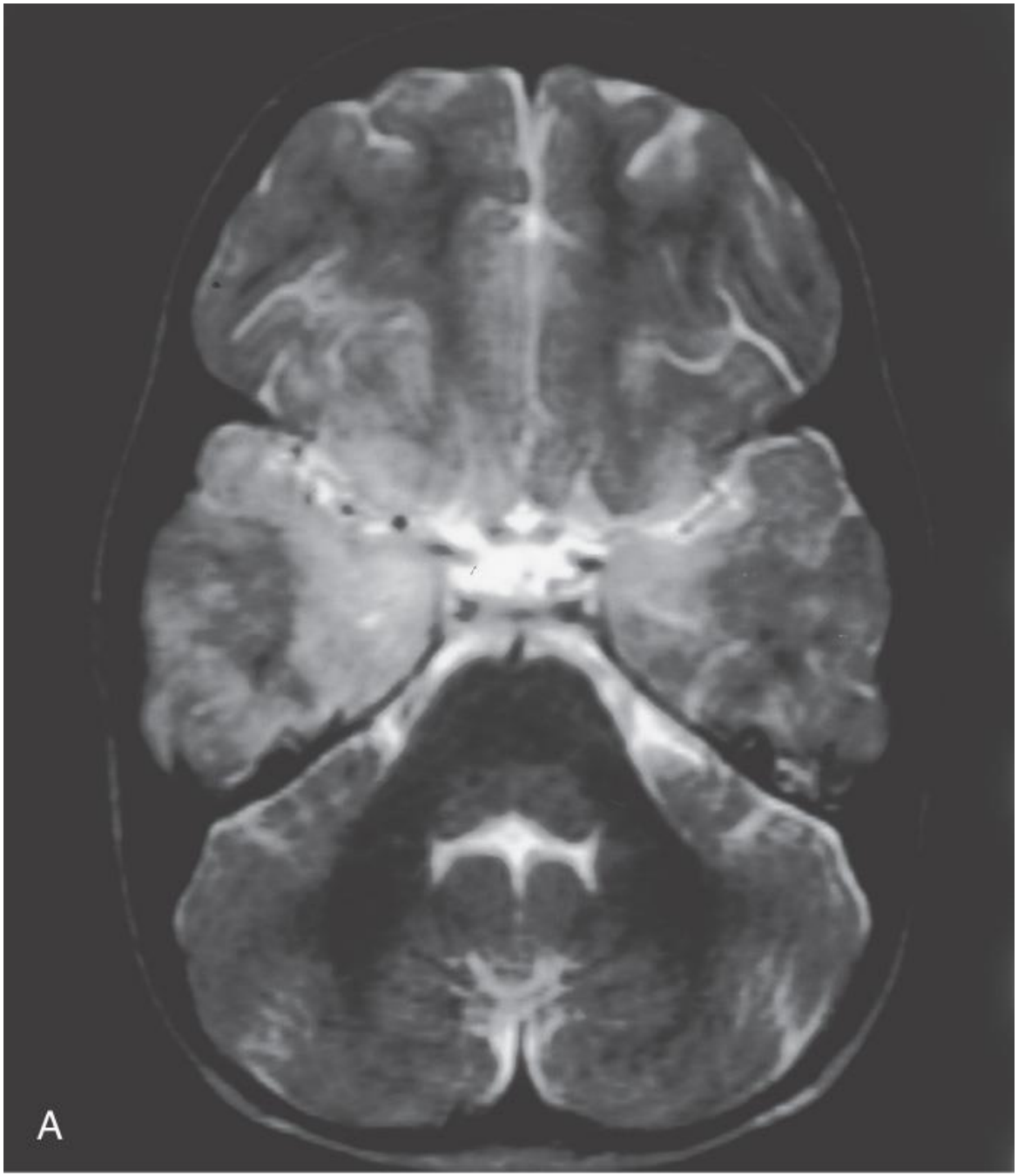
5 day old infant admitted with these skin lesions

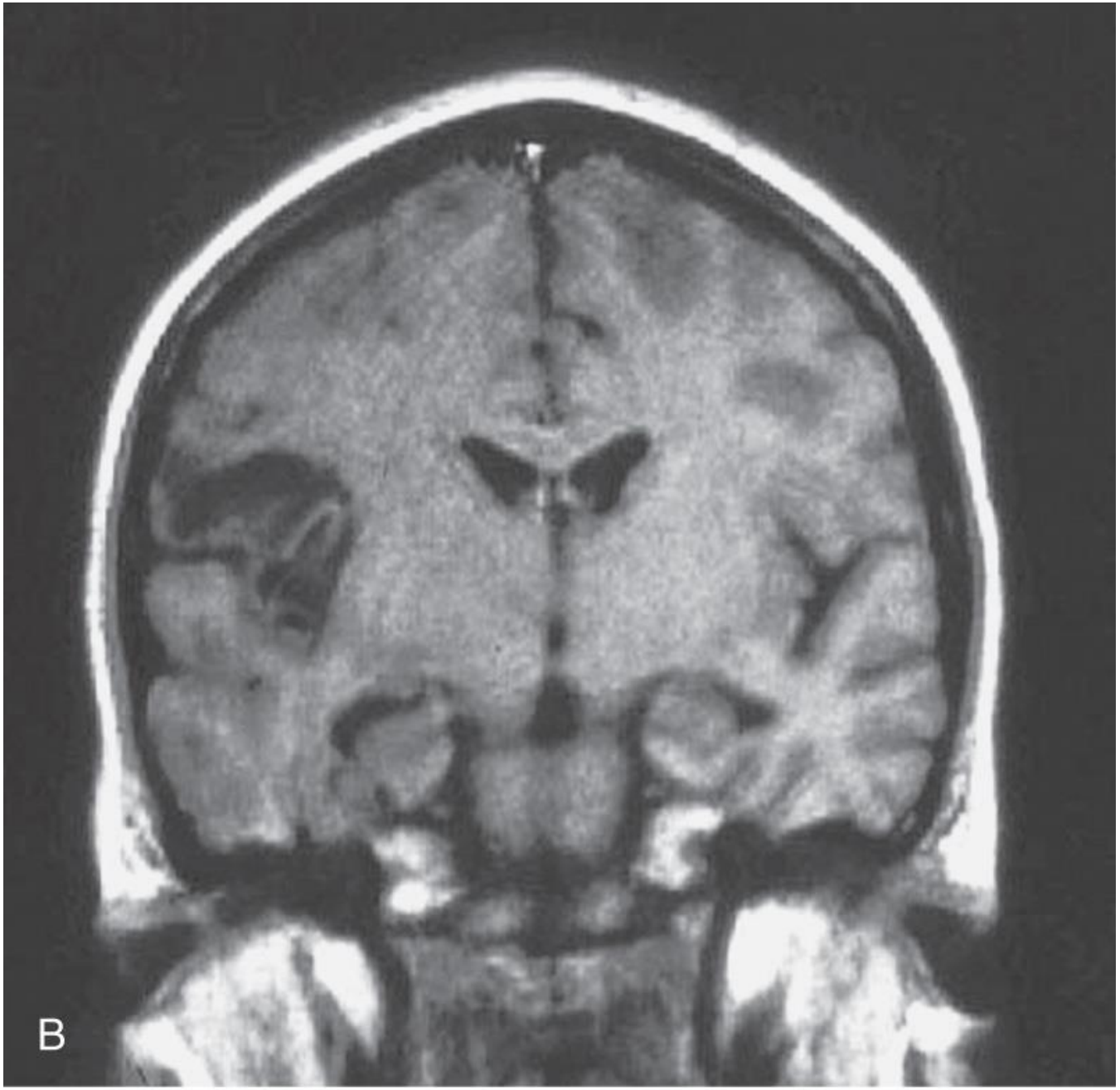
- Had fetal scalp electrode during delivery



Neonatal HSV infections

- Skin-eye-mucous membrane; 7 – 14 d
- Disseminated; 5 – 10 d
  - Multisystem involvement, including CNS
  - Shock, hepatomegaly, jaundice, bleeding, resp distress
  - Acylcovir 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…

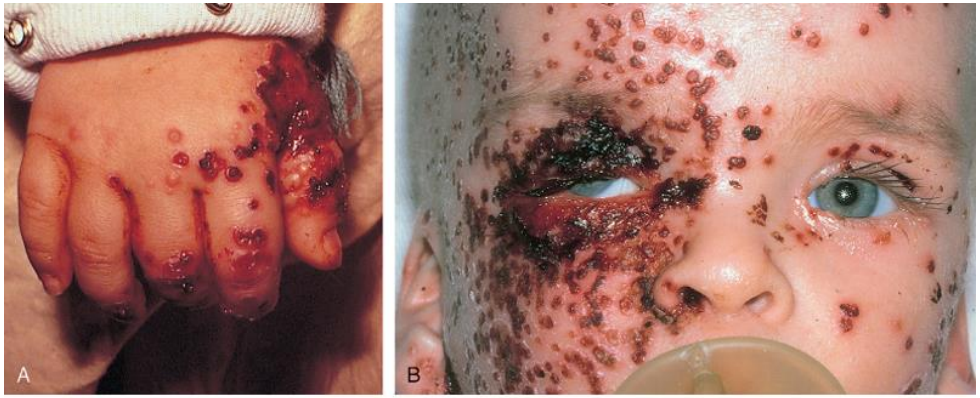
Herpetic Whitlow

- 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

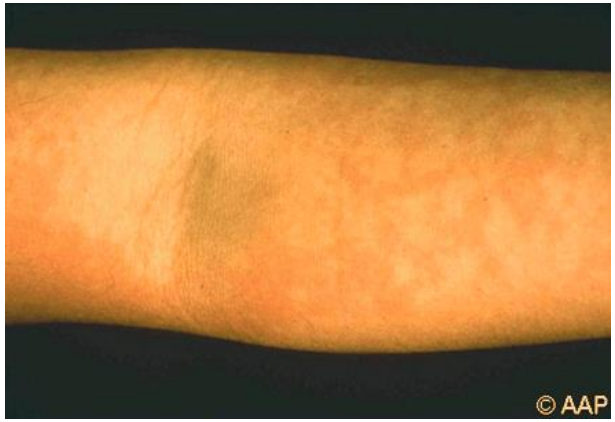
Erythema infectiosum

- “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

© AAP

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

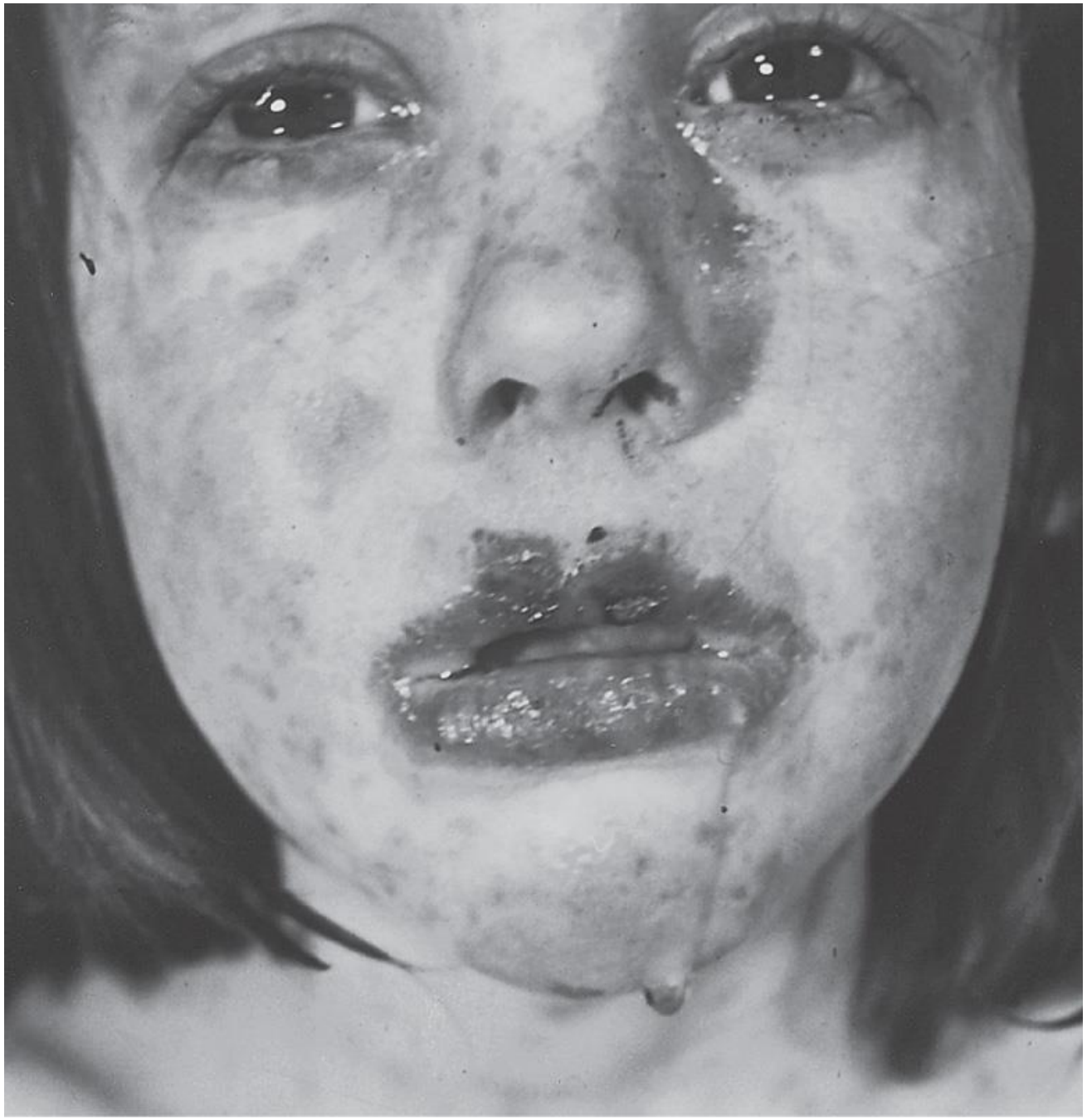
- 1st – Measles—rubeola
- 2nd – Scarlet Fever—*S. pyogenes*
- 3rd – Rubella, German measles—*Rubivirus*
- 4th – Dukes' Disease—echovirus, enterovirus, coxsackie
- 5th – Fifth Disease—parvovirus B19
- 6th – Exanthema subitum ("sudden"), roseola infantum—human herpesvirus 6

Kawasaki Disease

- "Classical": Fever ≥ 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

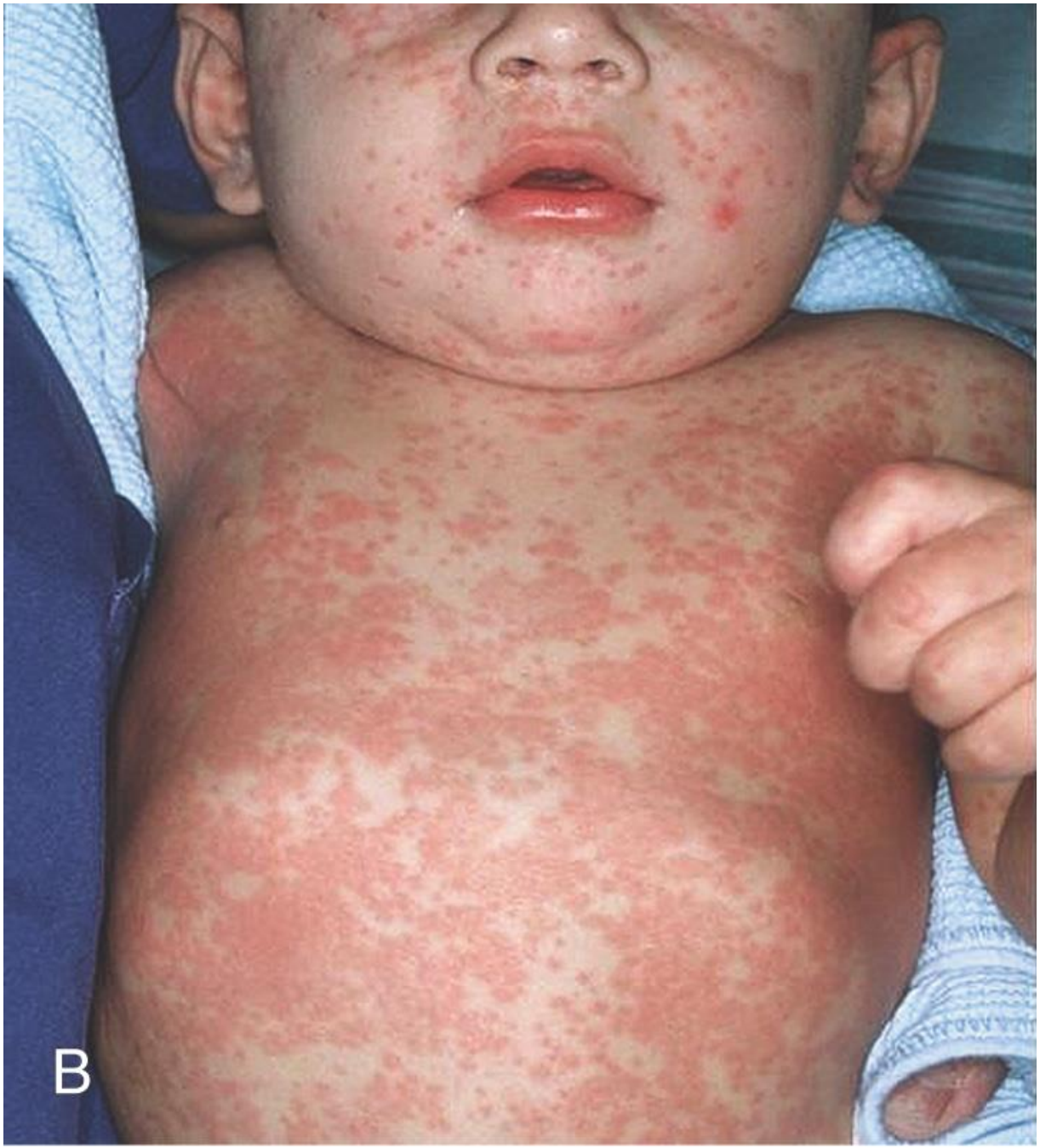


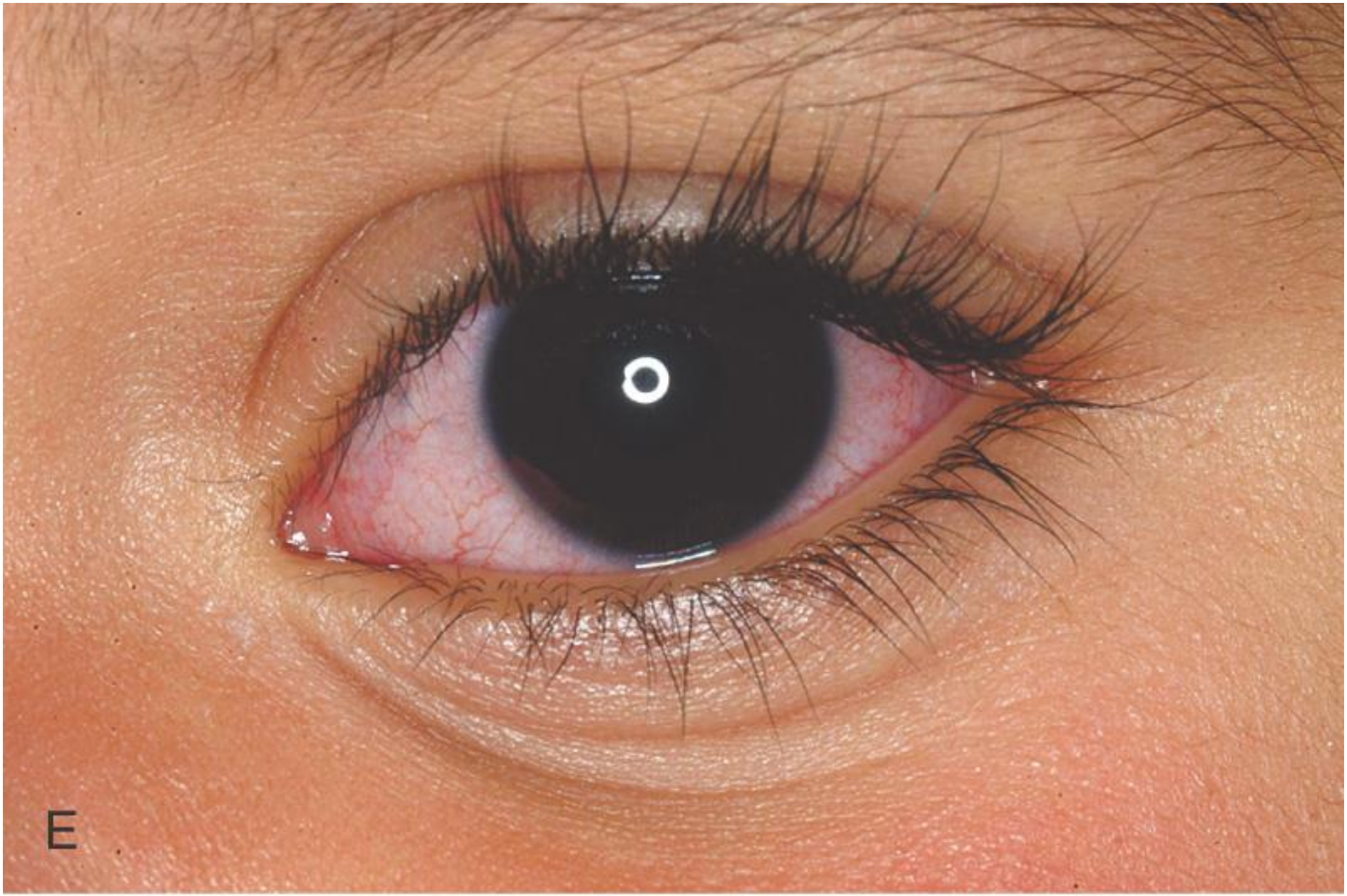
Stevens-Johnson Syndrome

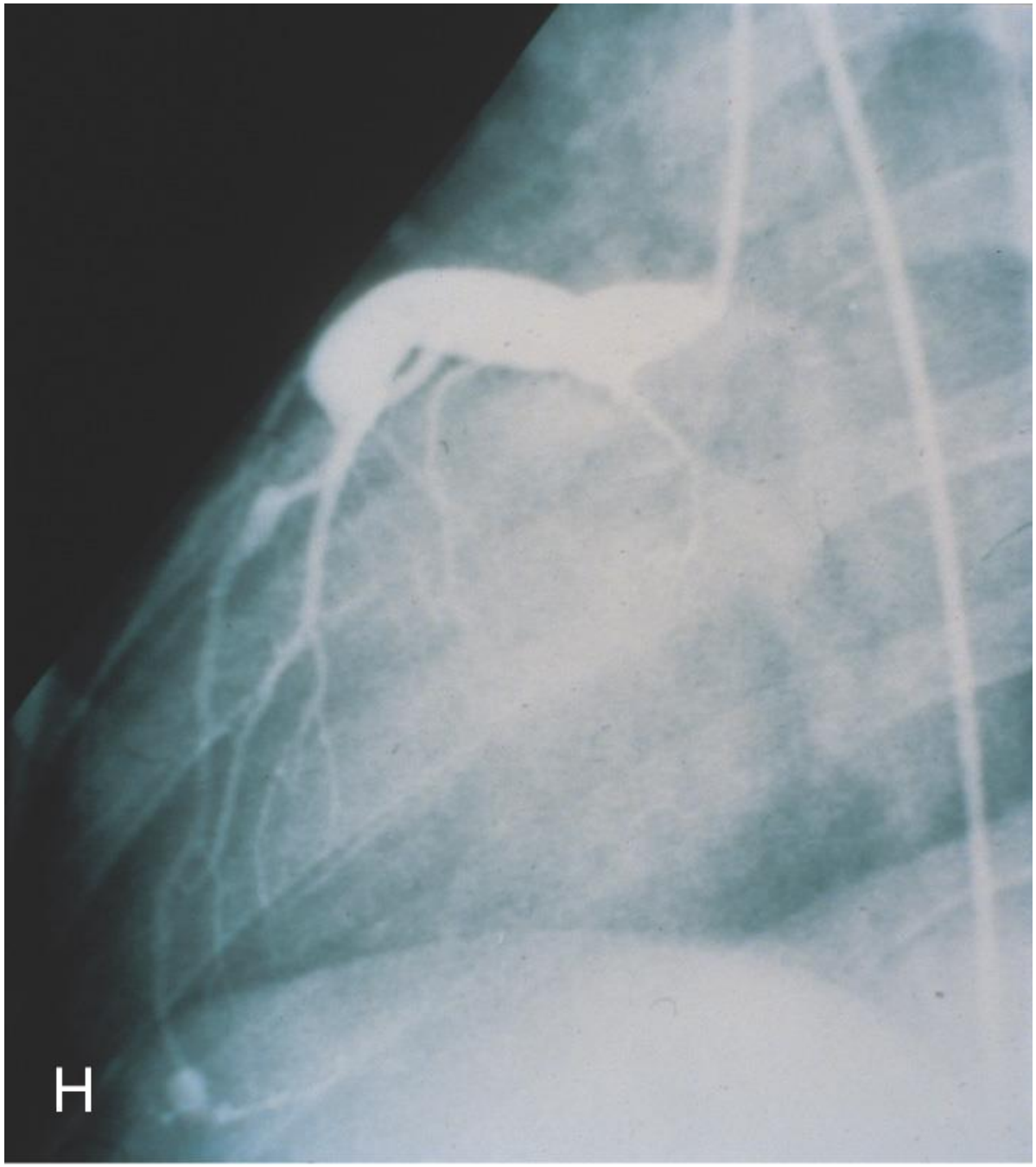
- Erythema multiforme with bullous lesions of mouth, oropharynx
- Skin lesions may become bullous
- Supportive fluid & electrolyte therapy

Kawasaki Disease

- Mainly in children 1 – 8 yrs of age
  - 80% of cases, $\leq$ 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