I. General Considerations and Terms
   A. Exanthem - a generalized cutaneous eruption associated with a systemic disease
   B. Enanthem - an eruption on a mucus membrane associated with a systemic disease
   C. Differential Dx based on:
      1. Past history of infection, exposure, immunization
      2. Type of prodromal period
      3. Features of the rash
      4. Presence of pathognomonic or diagnostic signs
      5. Laboratory diagnostic tests

II. Scarlet Fever
   A. Etiologic agent: Group A β-hemolytic streptococci (GABS), S. pyogenes, which produce erythrogenic exotoxins
      1. Usually associated with exudative pharyngitis
      2. GABS infections at other sites (e.g. skin) can also produce scarlet fever ("surgical scarlet fever")
   B. Clinical manifestations
      1. Acute onset of fever, malaise, sore throat, and tender cervical nodes.
      2. Rash appears 12-48 hours later
      3. Abdominal pain, sometimes with emesis, is not uncommon
      4. Typical enanthem: enlarged beefy red exudative tonsillitis, palatal petechiae and a "strawberry tongue"
      5. Features of the exanthem:
         a. Generalized orange-red punctate eruption with rough, sandpaper-like texture
         b. Flushed face with perioral pallor
         c. Increased intensity in groin, axillae
         d. Linear erythema in skin folds (Pastia's lines)
         e. Desquamation after 4-5 days
      6. Milder versions sometimes referred to as “scarlatina”
   C. Epidemiology
      1. More common in children but infection can occur at any age
      2. Strep pharyngitis is uncommon in children <3 years old as is rheumatic fever
      3. Person to person spread by respiratory secretion contact -- enhanced by crowding and close contact
   D. Diagnosis
      1. Characteristic clinical features
      2. Positive throat culture or strep antigen screen
      3. Rising antibody titer to strep toxins (e.g., anti-streptolysin O [ASO])
         a. Usually only necessary to confirm prior infection
E. Differential Dx
1. Viral pharyngitis with rash
2. "Staphylococcal scarlet fever"
3. Corynebacterium hemolyticum pharyngitis with rash
4. Kawasaki syndrome
5. Staphylococcal toxic shock syndrome
6. Infectious mononucleosis

F. Complications
1. Suppurative: cervical adenitis, peritonsillar abscess, etc.
2. Non-suppurative: rheumatic fever (RF) and acute glomerulonephritis
   a. RF does not occur after skin infection
   b. RF is preventable with antibiotic Rx; nephritis

G. Treatment and infection control
1. Penicillin - high dose not necessary but need sustained blood levels to eradicate
   NP strep and prevent RF
   a. PO - 10 full days
   b. IM benzathine penicillin
2. Isolation of patient indicated for 24 hrs after initiation of effective therapy

III. Measles (rubeola)
A. Etiologic agent: measles virus, a paramyxovirus (RNA)
B. Epidemiology (pre-vaccine)
   1. Highly infectious respiratory illness
   2. Peak age incidence was in preschool and early school-age children
   3. Infection was almost universal
C. Clinical manifestations
   1. Fever and malaise 8-12 days after exposure
   2. Coryza, conjunctivitis and cough 24 hrs later
   3. Pathognomonic enanthem on buccal mucosa: Koplick spots
   4. Rash: red-purple maculo-papules starting on the forehead and gradually spreading down to feet
      a. Coalescence of lesions is common on upper body
      b. Rash clears in 6-7 days in same sequence
D. Differential Dx
   1. Other viral infections (enteroviruses, adenovirus, etc.)
   2. Infectious mono, esp. with ampicillin Rx
   3. Mycoplasma pneumoniae infection
   4. Drug eruption
E. Complications
   1. OM
   2. Laryngotracheitis (croup)
   3. Bronchopneumonia
   4. Encephalitis
   5. SSPE
F. Treatment and infection control
   1. No specific antiviral Rx is recommended
2. Patients are infectious at the onset of symptoms through the first day of rash; isolation is indicated until 5 days after onset of rash.
3. Active immunization with live attenuated measles virus - 2 dose schedule
   a. First dose at 12-15 months (as MMR)
   b. Second dose at school entrance or middle school (MMR or monovalent measles vaccine)

IV. Rubella (German measles)
   A. Etiologic agent: rubella virus, a togavirus (RNA)
   B. Epidemiology - pre-vaccine data is limited because rubella is generally a mild illness and was not reportable
      1. Peak age incidence 5-9 years
      2. Peak seasons are winter and spring
      3. Incubation period is relatively long, 14-21 days
      4. Infections often subclinical
      5. Introduction of vaccine in 1969 caused dramatic decline in cases
   C. Clinical manifestations (postnatal)
      1. 1-5 day prodrome of low grade fever, mild constitutional symptoms and lymphadenopathy
         a. Typically posterior cervical and suboccipital nodes
      2. Exanthem: discrete rose-pink maculo-papules starting on the face with rapid spread to the trunk
         a. Rash lasts only 1-3 days
         b. Infections without rash are common
         c. Rash is often pruritic in adolescents and adults
      3. Enanthem: pinpoint red macules on soft palate early in course - Forchheimer spots (suggestive but not pathognomonic)
   D. Differential Dx
      1. Enteroviral infections (different seasons)
      2. Erythema infectiosum (fifth disease)
      3. Infectious mono
      4. Toxoplasmosis
   E. Complications
      1. Joint involvement - more common in adults than children
      2. Thrombocytopenia
      3. Encephalitis (rare)
      4. Fetal infection
         a. Teratogenicity recognized in 1941
         b. Congenital rubella syndrome
   F. Treatment and prevention
      1. Rubella vaccine (live, attenuated) introduced in 1969
      2. Vaccine given at 12-15 months (MMR)

V. Erythema Infectiosum (fifth disease)
   A. Etiologic agent: human parvovirus B19 (ssDNA)
      1. EI is the most common of several distinct syndromes caused by this virus
B. Epidemiology  
1. Peak age incidence is early school-age  
2. Incubation period 4-21 days  
3. Peak seasons are late winter and early spring  
4. Patients are infectious only in the few days before the rash appears  

C. Clinical manifestations  
1. Mild prodromal phase of low grade fever, sore throat, coryza and malaise  
2. Rash typically evolves through 3 stages:  
   a. Facial erythema, "slapped-cheek appearance"  
   b. Erythematous macular eruption spreading from trunk to extremities (palms and soles spared)  
   c. Central clearing of lesions leaving a reticular pattern  
3. Rash tends to recur over the course of weeks  
4. Other symptoms have resolved by the time rash appears  

D. Differential Dx  
1. Rubella  
2. Enteroviral infection  
3. Measles  
4. Drug eruptions  

E. Complications  
1. Arthritis - more common in adults  
2. Fetal infection - associated with nonimmune hydrops (uncommonly)  

F. Treatment and infection control  
1. There is no antiviral Rx and no vaccine available  
2. Isolation of patients with EI is ineffective - patients are generally noninfectious when rash appears  

VI. Roseola (Exanthem subitum)  
A. Etiologic agent: human herpesvirus-6 (HHV-6, dsDNA)  
B. Epidemiology  
1. Primarily a disease of young children: peak age incidence is 7-13 months  
C. Clinical manifestations  
1. Basic pattern is high fever for 3-5 days, then defervescence with appearance of rash  
   a. Child may be mildly irritable but often appears well despite the high fever  
2. Rash occurs as the fever subsides: discrete erythematous maculopapules on the neck and trunk; rash duration is brief, usually 24-48 hours  
3. Leukopenia is a common finding  
D. Differential Dx  
1. Other viral infections  
2. Occult bacteremia  
3. Drug eruptions  
E. Complications  
1. Febrile seizures  
2. Nonspecific febrile illness in infants may be confused with more serious
conditions such as pneumococcal sepsis, meningitis, etc.

F. Treatment - none specific

VII. Varicella (chickenpox)
A. Etiologic agent: Varicella-zoster virus (VZV, dsDNA, herpesvirus)
B. Epidemiology
   1. Most common infectious exanthem in the US (prior to vaccine)
   2. Highly contagious with respiratory transmission
      a. 96% of household contacts will become infected
   3. Patients are considered infectious from 24 hours prior to onset of rash until all
      lesions have crusted.
   4. Late winter and early spring are peak seasons
   5. Incubation period 7-21 days
C. Clinical manifestations
   1. Fever and rash usually begin together
      a. Fever subsides 3-4 days after the eruption
   2. Rash starts on the scalp or trunk with clear vesicles on an erythematous base
      a. Lesions extremely pruritic
      b. Vesicles progress to form crusts
      c. Lesions spread centrifugally
      d. Mucus membranes commonly involved
   3. Vesicles typically erupt in crops so lesions of varying ages will be present
      together
D. Differential Dx
   1. Disseminated herpes simplex
   2. Coxsackie virus infections (i.e., hand-foot-and-mouth syndrome)
   3. Bullous impetigo
   4. Scabies
   5. Eczema herpeticum
E. Complications
   1. Bacterial superinfection
   2. Neurologic complications
      a. Cerebellar ataxia
      b. Encephalitis
   3. Thrombocytopenia
   4. Varicella pneumonia
   5. Reyes syndrome
F. Diagnostic tests
   1. Viral isolation from vesicular fluid - low yield
   2. Tzanck prep on scraping from lesions - multinucleated giant cells with
      intranuclear inclusions (not specific for VZV)
   3. Immunofluorescent staining of vesicle scrapings using VZV-specific mab
   4. Acute and convalescent serology- laboratory confirmation usually not
      necessary
G. Treatment and control
   1. IV acyclovir and vidarabine are effective
a. Treatment reserved for severe disease with complications or for immunocompromised host
2. PO acyclovir approved for use in chickenpox but is not recommended as routine
3. V-Z immune globulin (V-ZIG) - post-exposure prophylaxis
4. Live attenuated varicella vaccine licensed for general use in the US
   a. Vaccine recommended for universal use in early childhood and in susceptible older children and adolescents
   b. Age-specific recommendations:
      12 months-13th birthday: one dose
      Adolescents beyond 13th birthday: 2 doses 4-8 weeks apart

VIII. Enteroviral Infections
A. Virology
   1. ss RNA viruses of the Picornavirus family
   2. Genus contains 6 major groups: polioviruses, echoviruses, coxsackieviruses A and B, enteroviruses and hepatitis A virus.
      a. Each group has multiple serotypes (except hepA)
   3. So named because all replicate in, and are shed into, the GI tract
      a. Viral spread by fecal-oral route
B. Clinical Features
   1. Associated with a variety of febrile illnesses
   2. Over 30 of the non-polio strains have been associated with exanthems
      a. Rashes are most frequently erythematous, maculopapular (rubelliform) but can be urticarial, petechial, purpuric, vesicular, morbilliform, or scarlatiniform.
   3. Peak season is summer and early fall
C. Hand-Foot-and-Mouth Syndrome
   1. Distinct illness characterized by fever, small vesicles/shallow ulcers in the anterior mouth and similar small vesicles on the hands and feet; rash occasionally spreads to distal arms and legs, buttocks
   2. Caused mainly by Coxsackie A16 (other serotypes also possible)
   3. Self-limited illness; vesicles heal rapidly without crusts or scars

VIII. Rocky Mountain Spotted Fever
A. Étiologic agent: Rickettsia rickettsii
B. Epidemiology
   1. Transmitted by bite of tick (vector-borne)
   2. Most cases reported in the southeastern and south central regions
   3. Incubation period is approx. 1 week
C. Clinical manifestations
   1. Abrupt onset of fever, headache and myalgias
   2. Rash develops in 2-5 days: initially blanching macules that become petechial within 1-3 days
      a. Distribution: begins distally on flexural areas of wrists and ankles, spreading centrally
b. Palms and soles may be involved
c. About 20% of cases may never develop rash
3. If untreated, lesions can become confluent and hemorrhagic with severe organ system involvement, DIC, and death

D. Differential Dx
1. Meningococcemia
2. Enteroviral infection
3. Other rickettsial infections (e.g. ehrlichiosis)
4. Other bacterial sepsis
5. Noninfectious vasculitis

E. Diagnosis
1. Acute and convalescent serology
2. Immunoflourescent staining of skin biopsy (not widely available)
3. Cultures are not practical
4. Dx usually based on history and clinical presentation with a high index of suspicion

F. Treatment and control
1. Chloramphenicol or tetracycline will shorten the course
2. Treatment must be initiated early in the course to be most effective
3. No person-to-person transmission so isolation not indicated

IX. Meningococcemia
A. Etiologic agent: *Neisseria meningitidis*
B. Clinical manifestations
1. Abrupt onset of fever, chills and malaise
2. Rash initially may be maculopapular and becomes petechial; distribution is variable
3. In fulminant cases, purpura, DIC, shock and death can ensue in a matter of hours

C. Differential Dx
1. RMSF
2. Gram negative sepsis
3. Enteroviral infection (early on)

D. Diagnostic tests
1. Isolation of *N. meningitidis* from blood or CSF
2. Gram stain of CSF or buffy coat
3. Culture and gram stain of petechial skin lesions

E. Treatment and control
1. IV penicillin is still drug of choice; ceftriaxone and cefotaxime are effective alternatives
2. Isolation of patient is indicated for 24 hours after initiation of effective therapy
3. Antibiotic prophylaxis for close/household contacts
4. Vaccine available - serogroups A, C, Y, and W-135 (not for group B)
   a. Not immunogenic enough for general use in young children
   b. Current recommendation for college students
   c. Often used to help control outbreaks
X. Fever and Petechiae
A. Differential Dx includes several life-threatening conditions:
   1. RMSF
   2. Meningococcemia
   3. Other overwhelming bacterial sepsis (*H. influenzae*, *E. coli*, etc.)
   4. Viral infection, esp. enteroviruses
   5. Trauma
B. This finding should prompt w/u for serious infection and presumptive Rx pending culture results

XI. Kawasaki Disease
A. Etiologic agent: unknown (presumed infectious)
B. Epidemiology
   1. Most cases in children 1-5 years old
   2. No evidence for person-to-person spread
C. Clinical manifestations and diagnostic criteria
   1. Fever lasting at least 5 days; other features usually begin by day 3
   2. Presence of 4 of the 5 following:
      a. Bilateral conjunctival injection
      b. Changes in the oral mucosa including pharyngeal injection, dry fissured lips and strawberry tongue
      c. Changes of the peripheral extremities, such as edema or erythema of hands and feet, desquamation
      d. Rash, primarily truncal; quite variable, often morbilliform, sometimes scarlatiniform, but non-vesicular
      e. Cervical lymphadenopathy
   3. Illness not explained by other known disease process
D. Atypical (incomplete) KD
   1. Coronary artery abnormalities plus some of the KD criteria
E. Differential Dx
   1. Major conditions to exclude
      a. Scarlet fever (strep infection)
      b. Toxic shock syndrome (staph infection)
      c. RMSF
      d. Measles
      e. Drug reactions
      f. Systemic-onset JRA, other vasculitides
F. Complications
   1. Carditis/coronary aneurysms
   2. Arthritis
   3. Gall bladder hydrops
G. Treatment - therapy is aimed at prevention of coronary artery disease and its complications
   1. IVIG
   2. Aspirin: high dose (anti-inflammatory) followed by low dose (thrombolytic)
Infectious Exanthems of Childhood - Clinical Case Vignettes

Case #1: 7y/o with 2 day hx of fever, sore throat and abdominal discomfort, and 1 day hx of a generalized rash. 
PE: alert but ill; erythematous, finely papular rash; exudative pharyngitis; tender cervical nodes.

1. Differential dx
2. Therapy- duration?
3. Period of infectivity - when can he return to school?
4. Immunity - can this recur?

Case #2: 10y/o with hx of URI 4-5 days ago, now with rash on face spreading to trunk. Mother worried about measles because she thinks he “missed a shot”. Attends public school.
PE: afebrile, doesn’t appear ill except for prominent rash: flushed appearance to face with diffuse, erythematous, maculopapular rash on trunk and proximal extremities. Palms and soles are spared.
HEENT exam is normal.

1. Differential dx
2. Could this be measles?
3. When can he return to school?

Case #3: 3y/o with a 2-3 day hx of fever, decreased activity and complaints of headache. Presents during the month of July. Lives in rural area but no history of tick bite.
PE: Ill-appearing but alert and cooperative. Neck is supple. Faint petechial rash on distal extremities, including palms and soles; none on trunk. Rest of exam is unremarkable.

1. Differential dx
2. Therapy - outpatient vs. inpatient?
3. Contagious?

Case #4: 4y/o with 2 day hx of sores in his mouth and on his hands associated with low grade fever. Attends daycare center where chickenpox has been noted (last case 1 month ago). Pt has never had chickenpox but had varicella vaccine 2 months ago (one dose).
PE: febrile, unhappy but not in distress. Small, shallow ulcers on buccal mucosa and gums. Small, clear vesicles noted on hands and feet without crusts. Shotty cervical adenopathy. Rest of exam normal.

1. Differential dx
2. Acyclovir rx?
3. When can he return to daycare?