

# Infectious Disease Review

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NORTH CAROLINA  
Academy of Physician Assistants

- I have no financial or other fiduciary relationship with any pharmaceutical or medical device manufacturing companies or corporations. I have not received stipends for promotion of any specific drugs or medical devices.
- Thanks to Erich Grant, MMS, PA-C - who graciously allowed me to use his previous lecture as a template for developing the presentation for the past two years' conferences. Many updates have been made since then.

# Objectives

- Describe key aspects of the **clinical presentation** of blueprint infectious diseases.
- List significant **risk factors** for each disease.
- State most common and reliable **laboratory tests** for diagnosing each disease.
- Name the preferred **treatments** for each disease.
- State **prophylactic measures** for applicable diseases.
- Describe any significant risks to **immunocompromised** individuals that these diseases pose.
- List the **“TORCH” infections** that carry significant risk for severe neonatal infection.

# **VIRAL DISEASE**

# Cytomegalovirus

- Herpes family
- Neonatal infections - **TORCH**
  - Hepatosplenomegaly, purpura, CNS changes, hearing loss
  - Thought to be **#1 cause of congenital neurologic sequelae**
- Immunocompetent patients
  - Usually **asymptomatic**, can have **Mono-like illness** (most common cause of “heterophile negative” mono)
  - IgM antibody is diagnostic, IgG takes 1-6 weeks.
- Immunocompromised patients
  - **AIDS retinitis, pneumonia, meningoencephalitis, chronic diarrhea**
    - **Leading cause of blindness in AIDS patients**

# CMV Infections

- Diagnosis
  - Gold standard in **neonates** is viral culture of the urine and saliva obtained within the first two weeks of life. PCR
  - In **HIV**: real-time PCR, tissue Bx demonstrating viral inclusions + clinical evidence
- Treatment
  - Supportive care
    - Prophylactic treatment in HIV patients
  - IV Ganciclovir
    - Used in children and adults with severe disease
  - **Oral valganciclovir**
  - Foscarnet, Cidofovir check for resistance mutations

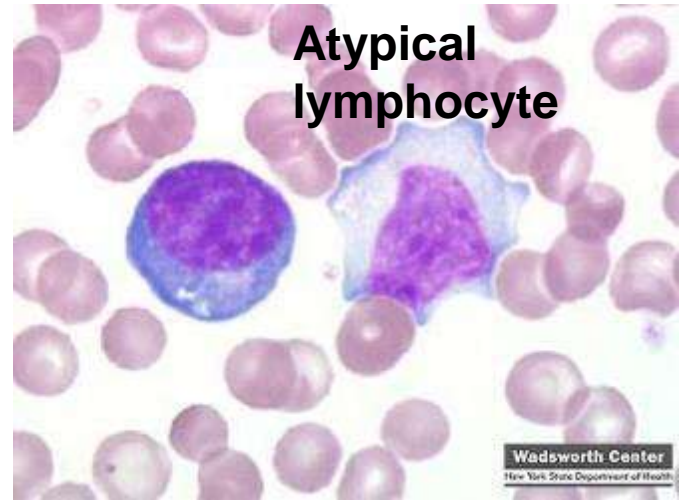


# Epstein Barr Infection

- Member of Herpes family
- Causes **infectious mononucleosis**
- Transmitted by saliva, incubation period 5-15 days
- Peak age 14-18 years old
- Signs/Symptoms
  - **Fever, pharyngitis, malaise, lymphadenopathy (Posterior cervical), rash, splenomegaly**
- **Consider in strep neg pts sick for > 1 wk**

# Epstein Barr Infection

- Labs
  - Lymphocytosis with **atypical lymphs**
  - Elevated liver function tests
  - Positive **heterophile antibody**
    - **Monospot**
      - 25% false neg in first week
      - Ok to recheck
  - Positive EBV specific serology, **IgM**
  - If negative, consider HIV, CMV, Hep
- Complications
  - Splenic rupture – **avoid contact sports**
  - Hepatitis, Myocarditis, Thrombocytopenia, Encephalitis
- Treatment
  - Supportive care
  - **Ampicillin/amoxicillin may cause a rash**
  - Cochrane review: minimal evidence for benefit of steroids; low quality studies





# Herpes Simplex Virus

- Transmission by direct contact with infected secretions
- Recurrent grouped **small vesicles on a erythematous base**
- Peri-oral (type 1) or peri-genital (type 2)
- Primary Infection
  - **Fever, regional lymphadenopathy**, aseptic meningitis
  - Recurrences: precipitated by stress, trauma, sun
- Systemic Infection
  - Immunosuppressed patients
  - Proctitis, esophagitis, keratitis
- Neonatal infection: severe sequelae (**TORCH**)

# HSV type 1

- Primary infection (gingivostomatitis) usually in early childhood
- Painful and last 5-10 days
- May become latent in sensory nerve root ganglion – recurrent disease
- Herpetic whitlow - HSV of finger or nail region
- Oral acyclovir and pain control



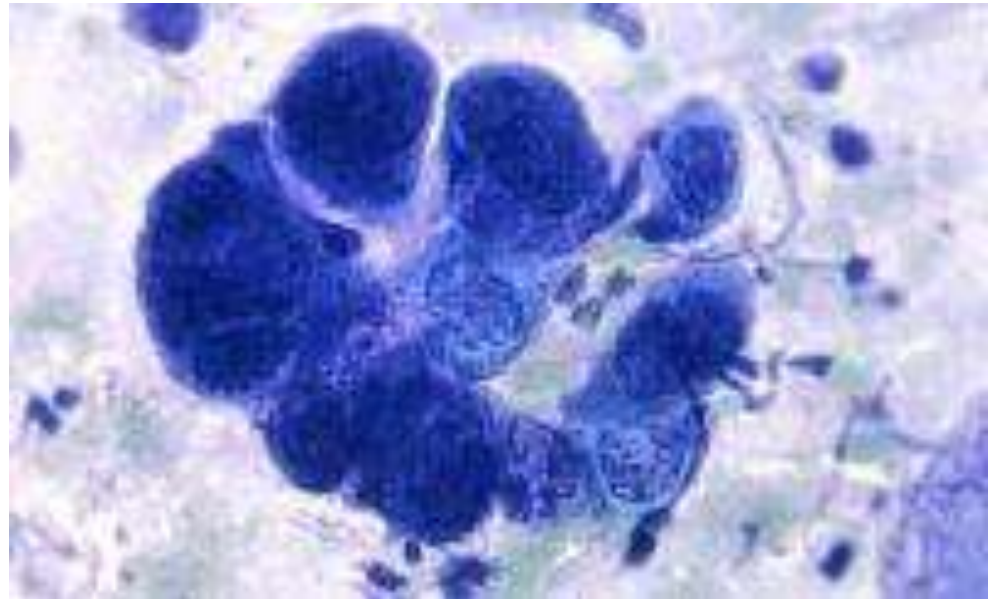
# HSV type 2

- Genital herpes
- Incubation period 5 days after sexual contact
- Painful, multiple lesions
- May have **systemic symptoms such as fever and myalgias**
- **Prodromal paresthesias in recurrent disease** may be noted 12-24 hours prior to lesions



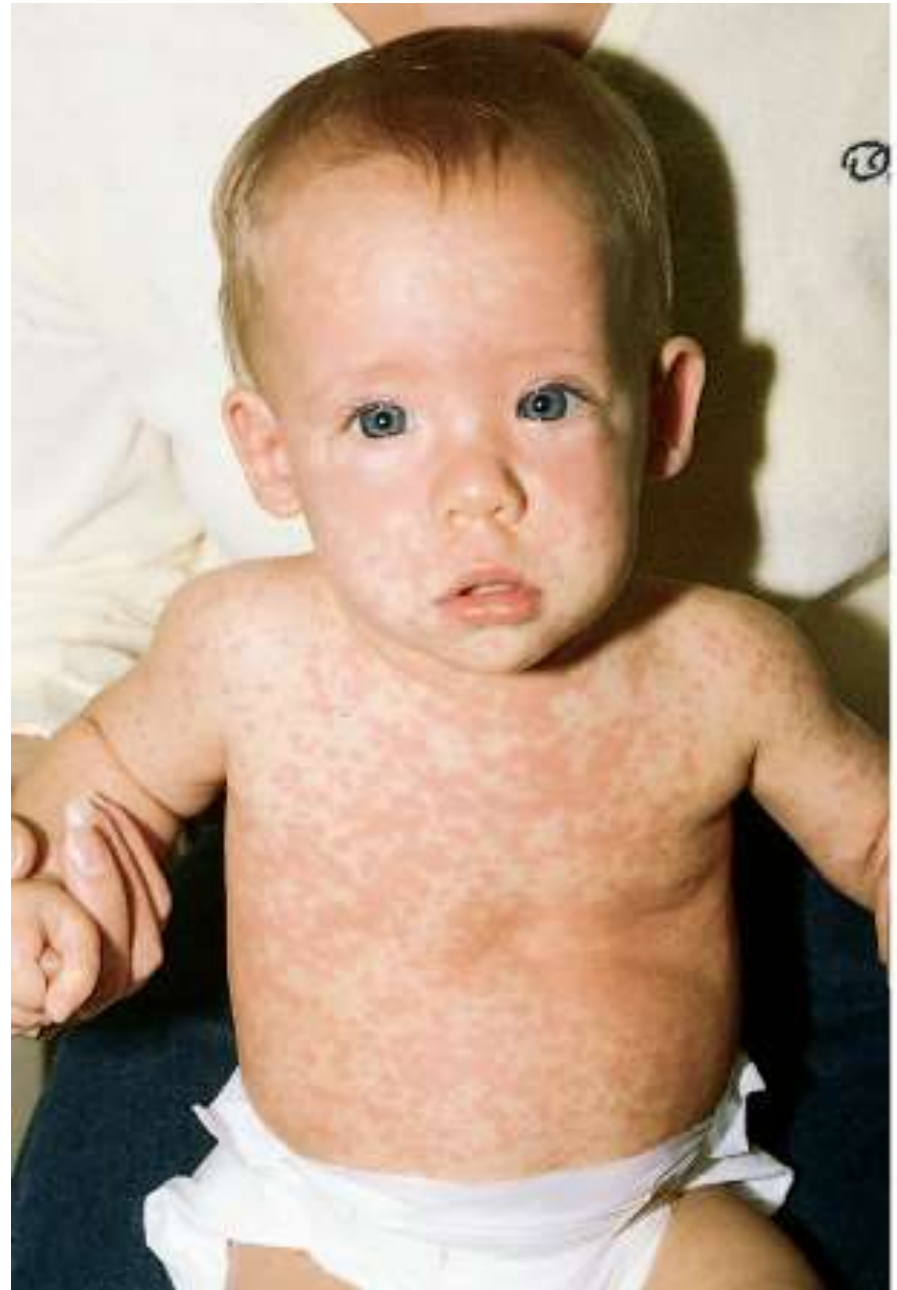
# Herpes Simplex Virus

- Diagnosis
  - Tzanck smear – old; look for multi-nucleated giant cells
  - Direct fluorescent antibody - newer
  - Culture (**high** false neg)
  - **HSV 2 serology**
- Treatment
  - Acyclovir
    - IV for encephalitis
  - Famciclovir
  - Valacyclovir
    - Generic now available



# Roseola – HSV6, 7

- 6-24 months
- Incubation 9-10 days
- **High fever 3+ days, otherwise well-appearing**
- **Crisis, Then rash**
- +/- URI sx, nodes, fussiness, appetite
- Febrile seizures



# HUMAN PAPILLOMA VIRUS (HPV)

- DNA virus
- Classified by type and risk:
  - 6, 11 = Low risk → dysplasia / respiratory papillomatosis
  - 16, 18 = High risk → cervical / anogenital cancer
  - **General rule: types that cause cancer usually don't cause warts!**
  - Vaccination is recommended in boys and girls ages 9-12. Catch up till age 26 for quadrivalent (Gardasil).
  - **Nonavalent vaccine preferred**
- Most infections are transient and resolve on their own, as do cervical abnormalities.

# Human Papilloma Virus (HPV)

- Clinical manifestations of genital HPV infection include:
  - **Genital warts**
  - **Cervical cell abnormalities**
  - Anogenital cancer
  - Penile cancer (35%)
  - Recurrent respiratory papillomatosis – juvenile disease
- Condylomata acuminata
  - Cauliflower-like appearance
  - Skin-colored, pink, or hyperpigmented
  - May be keratotic on skin; generally non-keratinized on mucosal surfaces
- Smooth papules – **beware condylomata lata; molluscum contagiosum**
- Flat papules - More commonly found on mucosal surfaces
- Keratotic warts - Thick horny layer that can resemble common warts or seborrheic keratosis



*Source:* Seattle STD/HIV Prevention Training Center at the University of Washington/ UW HSCER Slide Bank



*Source:* Cincinnati STD/HIV Prevention Training Center



# HPV Diagnosis

- Usually made via **visual inspection**
- Cytologic evaluation:
  - Cervical = Pap smear, colposcopy, biopsy
  - Anal = Pap smear, biopsy
  - Respiratory = biopsy
  - Biopsies are recommended with recurrent disease, ulcerating/bleeding lesions, **immunocompromised host**, pigmented lesions
- **Direct testing**
  - Women 21-24 – no HPV co-testing; reflex to HPV if + LSIL, HSIL
  - Women 24-29 – no consensus (ACOG and USPSTF recommend using best clinical judgment; should always reflex if LSIL/HSIL)
  - Women 30-65 – co-testing recommended

# Treatments

## Patient-Applied

- Podofilox 0.5% solution or gel
  - Twice daily for 3 days, then 4 days off
  - May do 4 cycles
- Imiquimod 5% cream (Aldara)
  - One application, 3 times weekly for 16 weeks
  - Wash area 8-10 hours after application

**Avoid the above agents (cytotoxic) in pregnancy**

**2 doses nonavalent vaccine current preferred prevention**

## Provider applied

- **Cryotherapy**
  - Repeat applications every 1-2 weeks
- **Podophyllin resin**
  - Apply a small amount to each wart and allow to air dry
  - Treatment may be repeated weekly if needed
- **Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90%**
  - Apply small amount only to warts and allow to dry
  - Treatment may be repeated weekly if needed
- Surgery (laser ablation)

# Influenza

- RNA virus
- **Influenza A (subtypes based on hemagglutinin/neuraminidase) and B (two currently circulating lineages)**
  - Influenzae A highly infectious, institutional settings
  - Influenzae B noted in schools and military
- Spread by respiratory droplets
- Incubation 1-3 days
- Outbreaks every winter
- **Endemic vs epidemic; antigenic drift, shift**

# Influenza

- Clinical
  - Abrupt onset **fever** (101-106F)
  - **Myalgias, headache, nonproductive cough**
  - **Coryza and sore throat**
  - Exam usually normal
- Labs
  - Leukopenia or normal WBC
  - CXR normal
  - **PCR, direct antigen**

# Influenza

- Treatment
  - Symptomatic
  - Influenza A > **Oseltamivir, Zanamivir**
  - Influenza A or B > Oseltamivir, Zanamivir
    - Antivirals reduce duration of symptoms if **given within 48 hours** (<15% of patient present within 48 hours)
  - Antibiotics if secondary bacterial infection
  - Immunization: (everybody!) elderly, respiratory disease, pregnant women, cardiac disease, health care workers, immunosuppressed; **avoid FluMist w/ asthma history**
- Complications
  - Reye syndrome (Aspirin)
  - Secondary bacterial infections: Pneumonia

# Rabies

- Rhabdovirus
- Transmitted by infected saliva
- History of animal bites
  - **Bats, bears, skunks, foxes, raccoons**
  - Dogs and cats in developing countries
- **Bites closest to brain progress most quickly – retrograde axonal transport**
- Signs/Symptoms
  - Encephalitic – **rage, hyperactivity, hydrophobia, pharyngeal spasms (80%)**
  - Paralytic – paresis, sphincter deficit

# Distribution of Rabies



400-500 cases per year in NC

## Rabies postexposure prophylaxis



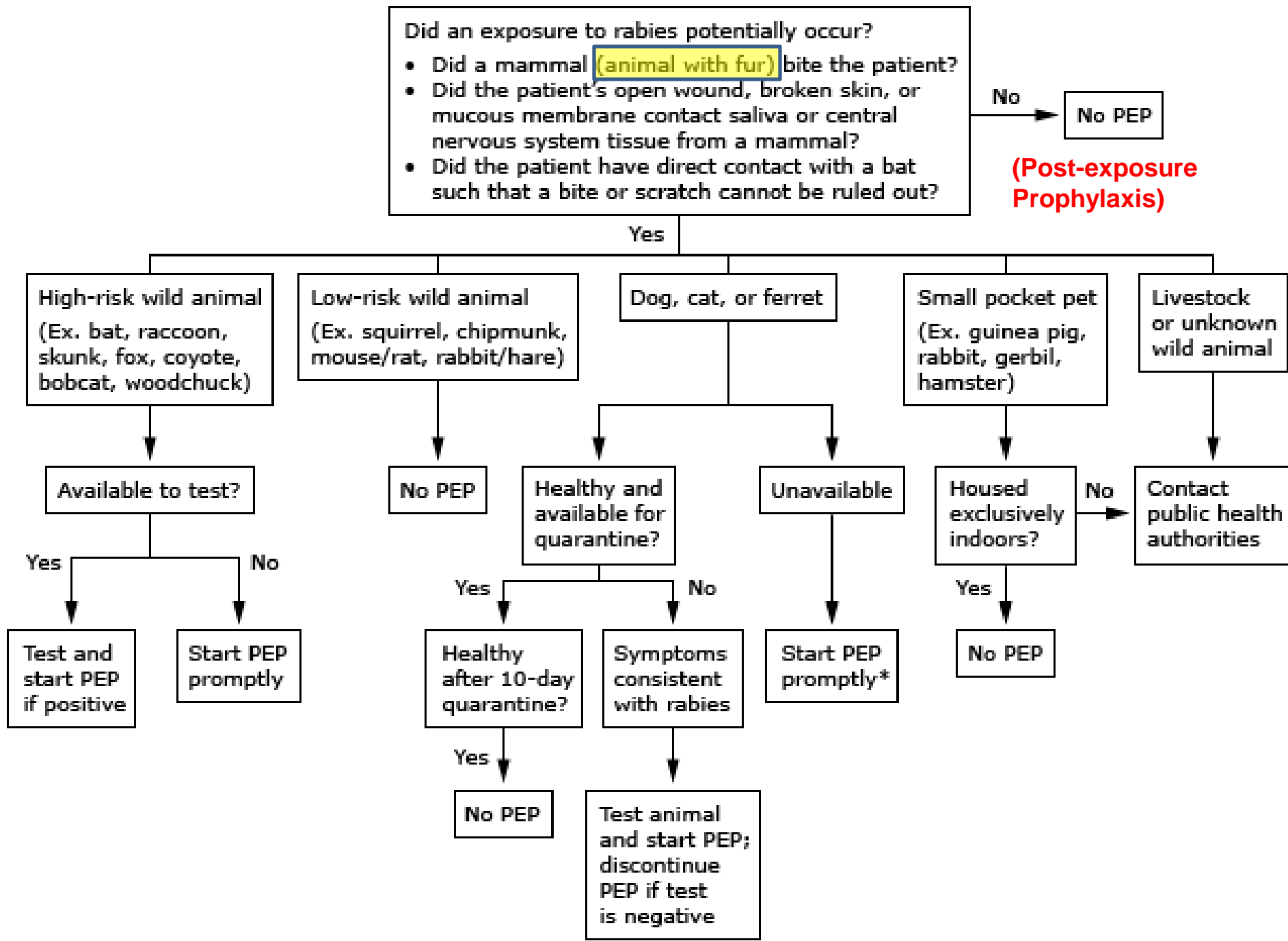
Vaccination category	Biologic	Schedule
<b>Not previously vaccinated</b>	RIG	Total dose is 20 units/kg body weight. As much of the full dose as feasible should be infiltrated around the wound(s) and any remaining given IM.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1 mL, IM (deltoid area), 1 each on days 0, 3, 7 and 14*
<b>Previously vaccinated</b>	RIG	Not indicated
	Vaccine	HDCV or PCECV 1 mL, IM (deltoid area), 1 each on days 0 and 3

RIG: rabies immune globulin.

\* For persons with immunosuppression, rabies postexposure prophylaxis should be administered using all five doses of vaccine on days 0, 3, 7, 14, and 28.

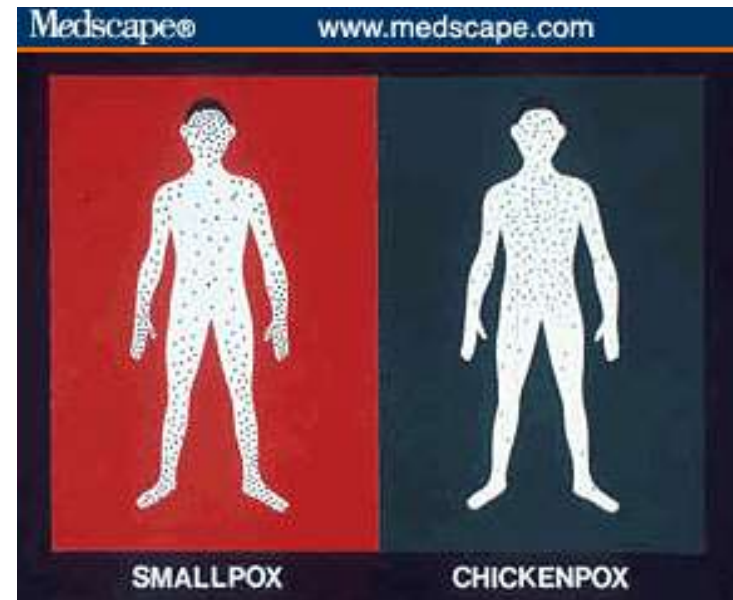
*Rupprecht CE, Briggs D, Brown CM, et al. Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies: recommendations of the advisory committee on immunization practices. MMWR Recomm Rep 2010; 59:1.*





# Varicella-Zoster Infections

- Acute Varicella (Chicken Pox)
  - Fever, malaise
  - Rash
    - **Pruritic, centripetal, papular rash, vesicular and pustular before crusting**
    - First lesion is a “drop on rose petal”
    - **Lesions in all stages at any given time**
  - Incubation period 14-21 days
  - Vaccine – live virus
- Reactivation (Zoster/Shingles)
  - **Dermatomal distribution**
  - Vesicular rash with preceding pain



# Varicella-Zoster



# Varicella-Zoster Infections

- Complications
  - Bacterial infection
  - **Pneumonia – older patients**
  - Encephalitis
  - **Post-herpetic neuralgia**
  - **TORCH (“other”)**
- Treatment
  - Supportive: lotions, antihistamines
  - Antivirals: Acyclovir (**for primary only if >12 yo, chronic skin/lung disease, steroid therapy, ?pregnancy**), valacyclovir, famciclovir
  - **Immune globulin ? availability in US**: pregnancy, immunosuppressed
  - ACIP recommends routine **vaccination** of all persons aged  $\geq 60$  years with 1 dose of zoster **vaccine**.
    - Persons who report a previous episode of zoster and persons with chronic medical conditions (e.g., chronic renal failure, diabetes mellitus, rheumatoid arthritis, and chronic pulmonary disease) can be vaccinated unless those conditions are contraindications or precautions.

# Erythema Infectiosum (Fifth Disease)

- **Parvo B-19 - virus**
- Vasculitis, **slapped cheek appearance, mild or no other Sx**
- Lacy rash O/O x 6 mo
- Fairly benign except:
  - **Sickle cell anemia** – virus can affect RBC production
  - Impaired immune system – anemia
  - 1. AIDS**
  - 2. Cancer treatments**
  - 3. Anti-rejection drugs** used after organ transplants
- Pregnancy-hemolysis in fetus/newborn – **TORCH** (“other”)
- myocarditis

Erythema Infectiosum



# Measles (Rubeola)

- Contagious before rash appears
- Contagion by aerosol
- **Cough, coryza, conjunctivitis**
- **Fever, photophobia**
- **Rash - morbilliform**
- **Kopliks spots**
- **Complication: encephalitis, thrombocytopenia, pneumonia, OM, SSPE**

## *Atypical measles*

- Centripetal rash
- Pneumonia
- Abdominal pain, myalgias
- RISK – incomplete vaccination or killed virus vaccine – waning immunity and exposure to wt



Measles



# MUMPS

- **Parotid predilection; usually bilateral**
- Transmission by saliva
- Incub: 2-3 wks
- **Orchitis – 30%;** tunica albuginea becomes stiff **w/ age**; pressure necrosis
- **Meningitis**
- Live virus vaccine



# Rubella (German measles)

- Benign illness – immunize because of threat to neonates (**Blueberry muffin**) - **TORCH**
- Respiratory transmission
- Incub: 2-3 wks
- **Post-auricular nodes**
- **3 day rash; arthralgia in females**
- **Live virus vaccine – do not give if pregnant or immunocompromised**

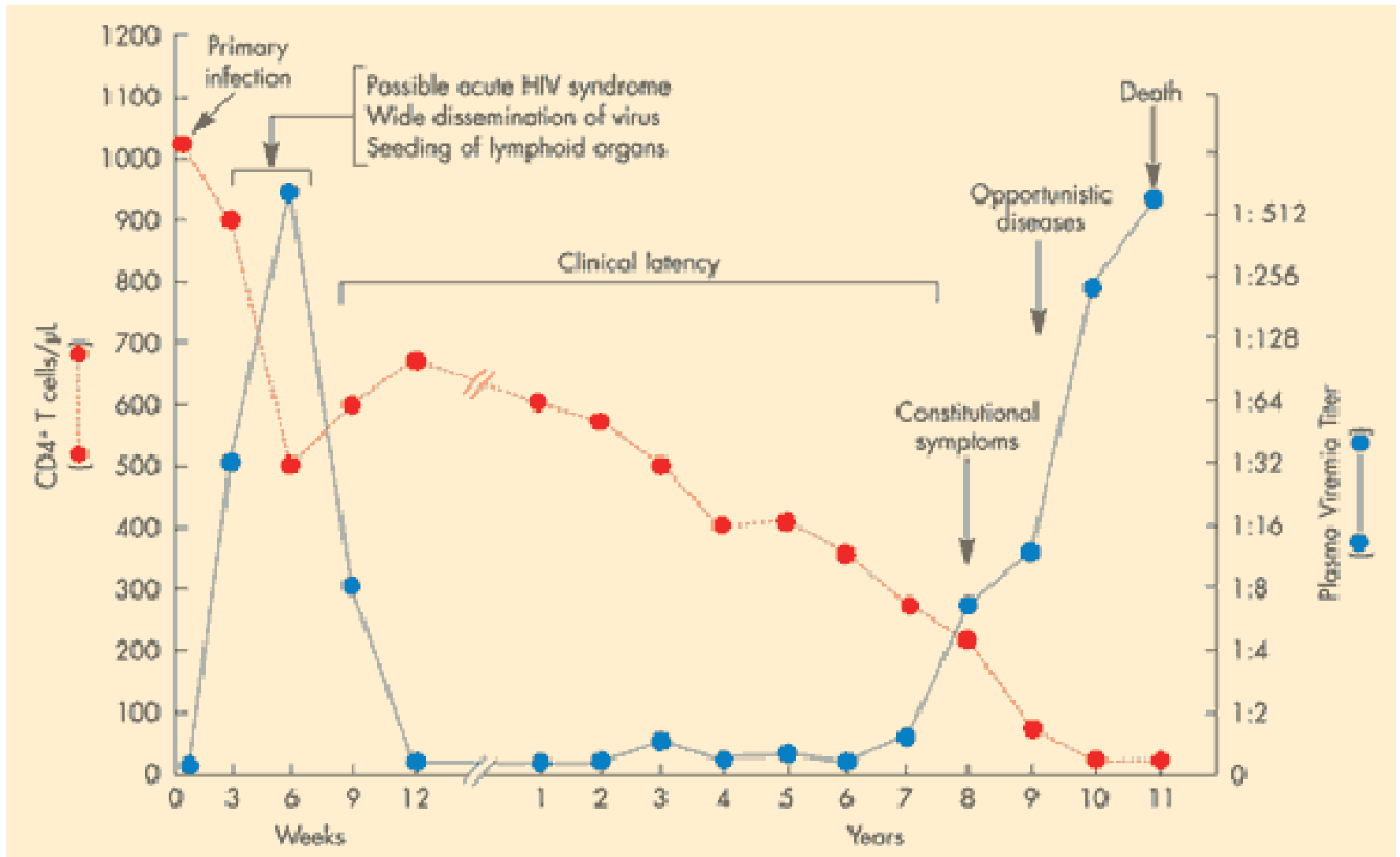




# HIV

- Epidemiology
  - Risk factors: **sex, injection drug use**, transfusions (before screening)
  - CDC rec's testing age 13-64.
- Etiology
  - Retrovirus
  - Changes viral RNA to viral DNA with aid of **reverse transcriptase**
- **Acute HIV syndrome**
  - **flu-like illness**
- Predilection for CD4 lymphs which express CCR5 and CXCR4

# HIV Infection Course



# HIV

- Labs

- Screening **HIV 1,2 Ab and HIV 1 p24 Ag** – early disease
- If screening + need differentiating Ab test
- If + on screen and neg on differentiation, proceed w/ NAT
- Reactive NAT w/ neg or indeterminate Ab differentiation signifies infection w/ HIV 1
- neg NAT w/ neg or indeterminate Ab differentiation signifies false +
- **Western no longer considered reliable due to frequent misclassification but may still be on test!**
- HIV RNA viral load
- CD4 count
- ART resistance assay

# “AIDS-indicator” diseases

- Candidiasis (esophagus)
- Coccidioides (extrapulmonary)
- Cryptococcus (extrapulmonary)
- Pneumocystis
- CMV (retinitis, colitis, esophagitis, etc.)
- Herpes simplex (chronic/severe)
- Kaposi's sarcoma; other malignancies
- Cryptosporidium, isospora (chronic)
- Toxoplasma (cerebral)
- Progressive multifocal leukoencephalopathy
- Tuberculosis
- Invasive cervical cancer
- HIV encephalopathy
- Histoplasmosis, disseminated
- Isosporiasis
- Lymphoma
- Lymphoid interstitial pneumonia
- Atypical mycobacterial infection, disseminated
- Recurrent pneumonia
- Salmonella septicemia
- Wasting syndrome

# Prophylaxis: Opportunistic Infections

All CD4 counts

- **Tuberculosis – INH+B6 or rifampin**

CD4 counts  $\leq 250$  cells/microL

- **Coccidioides** (if sero+ in endemic areas) - **fluconazole**

CD4 counts  $\leq 200$  cells/microL

- **Pneumocystis jiroveci – TMP-SMX**

CD4 counts  $\leq 150$  cells/microL

- **Histoplasma** (high risk exposure) - **itraconazole**

CD4 counts  $\leq 100$  cells/microL

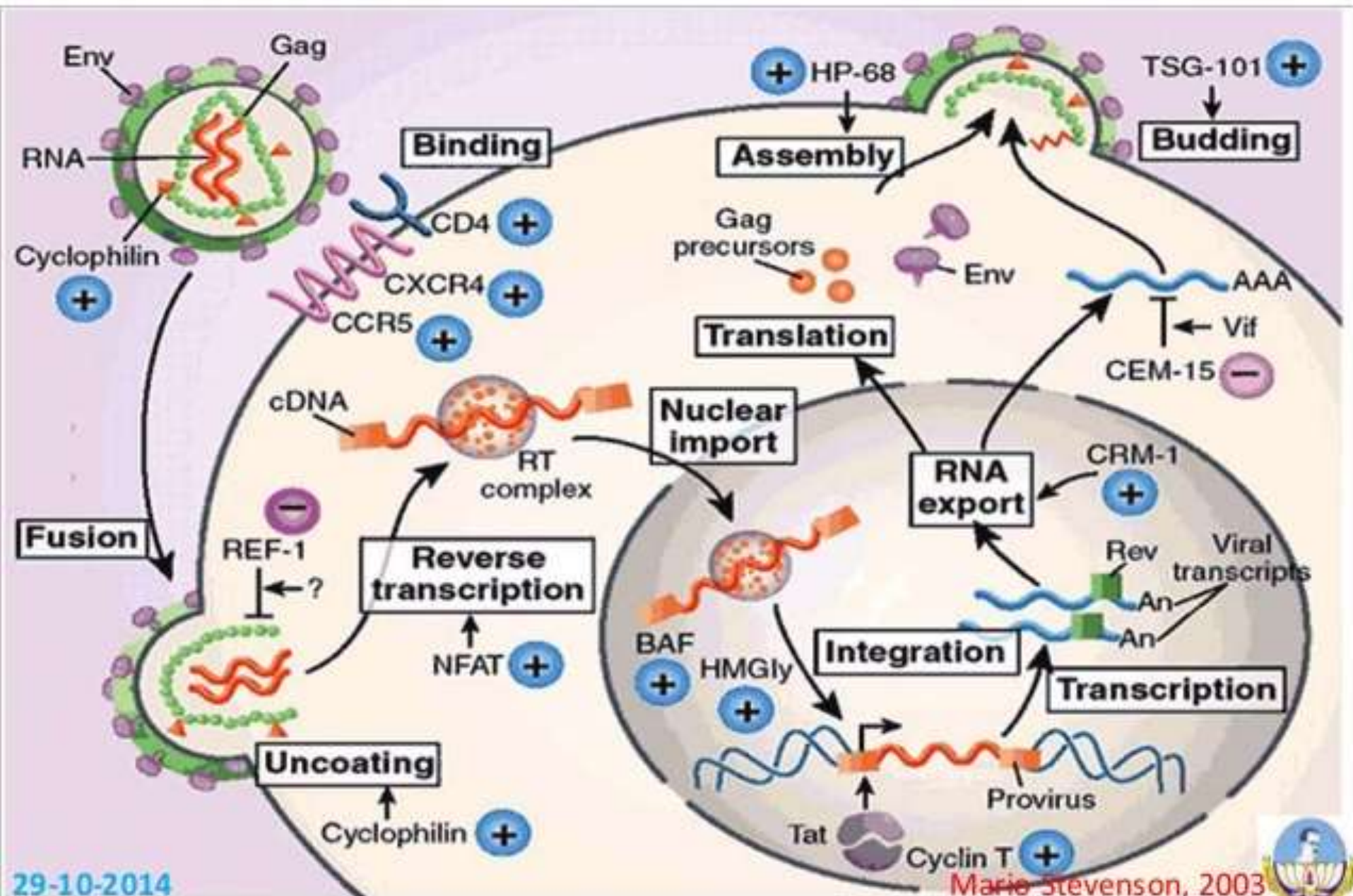
- **Toxoplasma** (if sero+) – **TMP-SMX**
- **Cryptococcus**

CD4 counts  $\leq 50$  cells/microL

- **Mycobacterium avium complex** (MAC) – **azithromycin**

<https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5108a1.htm>

# HIV-1 PATHOGENESIS



# HIV Drugs - ART

- **Non-nucleoside reverse transcriptase inhibitors (NNRTIs)**
- **Nucleoside reverse transcriptase inhibitors (NRTIs)**
- **Protease inhibitors (PIs)**
- Fusion inhibitors
- CCR5 antagonists (CCR5s) (also called entry inhibitors)
- Integrase strand transfer inhibitors (INSTIs)
- Choice of regimen is made on individual basis; many are available in combinations

# HIV Drugs - ART

- Nucleoside reverse transcriptase inhibitors (NRTIs)
  - Zidovudine (AZT)
  - Lamivudine (3TC)
  - Didanosine (ddI)
  - Stavudine (d4T)
  - Tenofovir (TDF)
  - Abacavir (ABC)
  - Emtricitabine (FTC)
- Side Effects
  - **AZT- bone marrow suppression**
  - **ddI, d4T- peripheral neuropathy, pancreatitis**
  - **ABC – cardiovascular disease**
  - **TDF – renal damage**



# HIV Drugs

- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
  - Nevirapine
  - Delavirdine
  - Efavirenz
  - Etravirine
- Side Effects
  - **All can cause a rash**
  - **Efavirenz causes vivid dreams and is contraindicated in pregnancy**

# HIV Drugs

- Protease Inhibitors (PIs)
  - Saquinavir
  - Ritonavir
  - Indinavir
  - Nelfinavir
  - Darunavir
  - Tipranavir
  - Lopinavir
  - Atazanavir
- Side Effects
  - **All can cause nausea, vomiting, and diarrhea**
  - **Lipodystrophy**
  - **Indinavir- nephrolithiasis**
  - **Atazanavir - hyperbilirubinemia**

# HIV Drugs

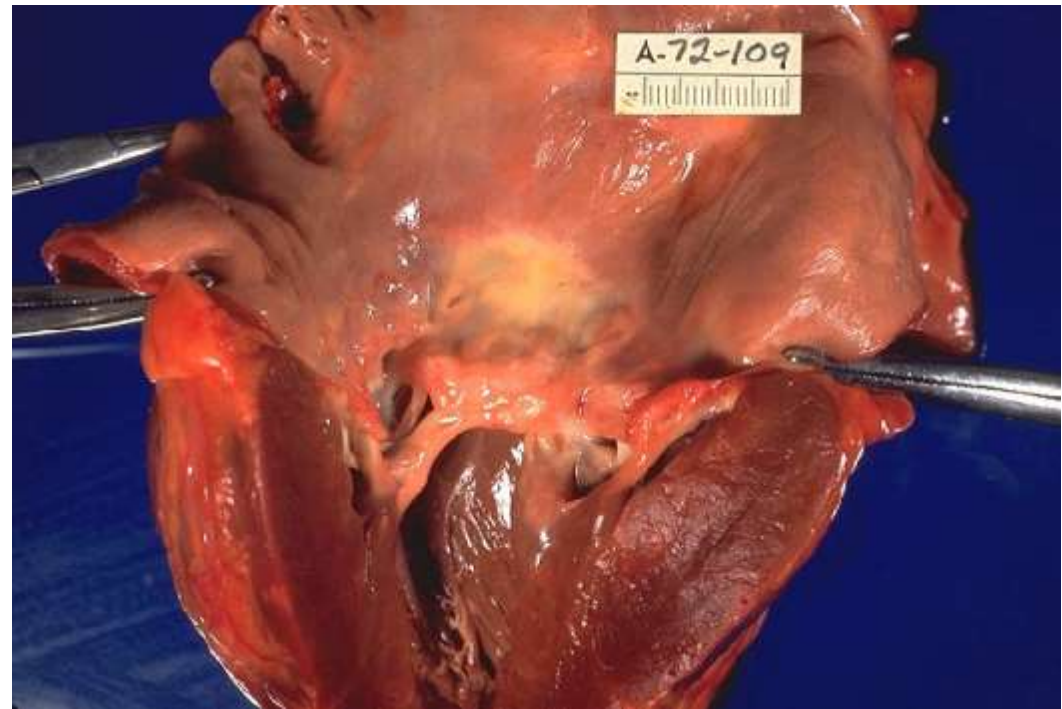
- Integrase Inhibitors
  - Raltegravir
  
- Entry Inhibitors
  - Enfuvirtide
  - Maraviroc
  - Vicriviroc

**Newer agents with fewer side effects**

# **BACTERIAL DISEASE**

# Acute Rheumatic Fever

- Attack against heart valves - most common cause of valve pathology (**Molecular mimicry**)
- **Mitral valve most common valve affected – almost always RF, also aortic, tricuspid**
- **Group A beta hemolytic streptococci (*S. pyogenes*) – un/undertreated**



# Jones criteria

## Major Criteria

Carditis

Polyarthritits

Sydenham's chorea

Erythema marginatum

Subcutaneous nodules

**Need: two of the major criteria, Or one major criterion plus two minor criteria**, are present

along with **evidence of**

**streptococcal infection** (Anti-

Streptolysin-O titer, anti-DNAseB or antihyaluronidase); or direct detection

## Minor Criteria:

Fever

Arthralgia

Previous rheumatic fever or rheumatic heart disease

Acute phase reactants: Leukocytosis, elevated sed rate (ESR) and C-reactive protein (CRP)

Prolonged P-R interval on electrocardiogram (ECG)

# Rheumatic fever treatment and prevention

- **Treatment of acute disease: anti-inflammatory (ASA, naproxen), antibiotics to eradicate GAS carriage or active disease, mgmt of heart failure**
- **Prophylaxis: benzathine PCN monthly;** azithromycin, sulfadiazine if PCN allergic
  - x10 yrs or to age 40, whichever is longer as long as no recurrence