Infectious Disease
Fungi/Yeasts
Bacteria
Spirochetes
Viruses
Parasites

Claire Babcock O’Connell, MPH, PA-C
Associate Professor
Physician Assistant Program
June, 2015

Topics to cover today:

- Fungi/Yeasts
  - candida
  - cryptococcus
  - histoplasmosis
  - pneumocystis

- Bacteria
  - botulism
  - cholera
  - diphtheria
  - pertussis
  - salmonella
  - shigella
  - tetanus
  - Rocky Mtn Spotted Fever

- Spirochetes
  - Syphilis
  - Lyme

- Viruses
  - CMV
  - EBV
  - Rabies
  - HIV

- Parasites
  - helminths
  - malaria
  - toxoplasmosis
  - pinworms

Fungi/Yeast

1. candida

2. cryptococcus

3. histoplasmosis

4. pneumocystis
Risk Factors: fungal infections

- neutropenia, cellular immunodeficiency
- diabetes mellitus
- renal failure
- post transplant patients
- injection drug use
- chemotherapy, corticosteroids
- parenteral nutrition
- recent surgery
- broad spectrum antibiotic use
- intensive care unit stay

Candida, mucous membranes

<table>
<thead>
<tr>
<th>Location</th>
<th>Symptoms</th>
</tr>
</thead>
</table>
| Oral (most common) | - angular cheilitis  
- white plaques, underlying erythema  
- red, painful plaques (dentures) |
| GI (esophagus in immunocompromised) | - odynophagia  
- GERD  
- biopsy to confirm |
| GU (vulva, vagina) | - irritation  
- discharge (white, curd-like)  
- scaly plaques  
- dyspareunia  
- KOH: pseudo-hyphae, budding |
| Cutaneous (balanitis) | - red, pruritic lesions  
- distinct borders  
- satellites, pustules  
- intertrigo—skin folds  
- onychomycosis, paronychia |
| Chronic infection | - variable presentations, atypical  
- specific defect in T cell response  
- possible endocrinopathies |
| Contiguous spread | - trauma, burns, surgery |
| Focal, invasive | - local inoculation, anatomic defects, instrumentation |
**Candidiasis, disseminated**

<table>
<thead>
<tr>
<th>Risk/cause</th>
<th>S&amp;S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidemia (mortality 40%)</td>
<td>Catheters, invasive instrumentation, septic shock multiple organ failure</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>IDU, prosthetic valves, central catheters, murmur, splenomegaly, palpitations, large vegetations, large vessel embolization</td>
</tr>
<tr>
<td>Chronic disseminated (hepatosplenic candidiasis)</td>
<td>Leukemia pts undergoing aggressive treatment, fever, nausea, RUQ tenderness, splenomegaly, hemorrhagic petechiae, splenic septicity, CT: punched out lesions in liver</td>
</tr>
</tbody>
</table>

**Candida, treatment**

- Remove any nidus, instruments; treat underlying disease
- Azoles: Inhibit formation of cell membrane
  - Topical: clotrimazole, miconazole
  - Systemic: fluconazole, itraconazole
- Echinocandins: Inhibit fungal cell wall
  - Caspofungin, micafungin, anidulafungin
- Polyenes: Fungicidal—Increase permeability of cell membrane
  - Amphotericin B (with prednisone or Benadryl to reduce side effects)
- Antimetabolites: Inhibit fungal DNA synthesis, protein formation
  - Flucytosine
- Allylamines: Changes to cell wall leading to cell death
  - Terbinafine (paronychia only)

**Cryptococcus**

- Encapsulated budding yeast; soil, pigeon feces; inhalation (cellular immunodeficiency states)

<table>
<thead>
<tr>
<th>S&amp;S</th>
<th>Diagnostics</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, cough, dyspnea, nodules, pneumonitis</td>
<td>Culture, India ink stain, methenamine silver</td>
<td>Fluconazole (10 weeks)</td>
</tr>
<tr>
<td>Respiratory infection (COPD, steroid use, post-transplant)</td>
<td></td>
<td>Resistance: amphotericin</td>
</tr>
<tr>
<td>H/A, N/V, confusion, lethargy, visual changes, cryptococcomas</td>
<td>CSF: inc protein, inc WBC (lymphs), inc glucose, CT or MRI, cryptococcomas, hydrocephalus</td>
<td>Untreated: severe dz:</td>
</tr>
<tr>
<td>Meningitis (CD4&lt;50)</td>
<td></td>
<td>1) Induction: amphotericin B PLUS flucytosine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) Maintenance: fluconazole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lifelong</td>
</tr>
</tbody>
</table>

---
### Histoplasma

**PANCE/PANRE Review Course**

<table>
<thead>
<tr>
<th>3 Types</th>
<th>S&amp;S</th>
</tr>
</thead>
<tbody>
<tr>
<td>chronic progressive pulmonary dz (elderly, COPD)</td>
<td>apical cavities; calcified nodes; pericarditis</td>
</tr>
<tr>
<td>progressive disseminated disease (HIV; CD4&lt;300)</td>
<td>fever; dyspnea, cough; ulcers (mouth, pharynx); weight loss, prostration; hepatosplenomegaly; adrenal insufficiency</td>
</tr>
<tr>
<td>disseminated disease (AIDS; CD4&lt;100) (or other immunocompromised states)</td>
<td>fever; multiple organ involvement; septic shock, death; miliary pattern on CXR</td>
</tr>
</tbody>
</table>

### Labs

<table>
<thead>
<tr>
<th>S&amp;S (very variable)</th>
<th>diagnostics</th>
<th>treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>fairly abrupt onset</td>
<td>diffuse interstitial infiltrates (most common)</td>
<td><em>TMP-SMX</em></td>
</tr>
<tr>
<td>tachypnea, dyspnea</td>
<td>diffuse or focal consolidation</td>
<td>• clindamycin/primaquine</td>
</tr>
<tr>
<td>cough (usually nonproductive)</td>
<td>cysts, nodules, cavities</td>
<td>• dapsone/TMP</td>
</tr>
<tr>
<td>bibasilar crackles</td>
<td>PFTS:</td>
<td>• pentamidine</td>
</tr>
</tbody>
</table>

### Pneumocystis jiroveci *(nee carinii)*

**UBC**

ubiquitous, airborne; premature or debilitated infants; immunodeficiency states

<table>
<thead>
<tr>
<th>S&amp;S (very variable)</th>
<th>diagnostics</th>
<th>treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>fairly abrupt onset</td>
<td>diffuse interstitial infiltrates (most common)</td>
<td><em>TMP-SMX</em></td>
</tr>
<tr>
<td>tachypnea, dyspnea</td>
<td>diffuse or focal consolidation</td>
<td>• clindamycin/primaquine</td>
</tr>
<tr>
<td>cough (usually nonproductive)</td>
<td>cysts, nodules, cavities</td>
<td>• dapsone/TMP</td>
</tr>
<tr>
<td>bibasilar crackles</td>
<td>PFTS:</td>
<td>• pentamidine</td>
</tr>
</tbody>
</table>

### Prophylaxis:

- *CD4<200; hx PJP*  
- TMP-SMX, daily
Bacteria
- Botulism
- Cholera
- Diptheria
- Pertussis
- Salmonella
- Shigella
- Tetanus
- Rocky Mountain Spotted Fever

**Botulism; *Clostridium botulinum***

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Manifestations</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ubiquitous in soil</td>
<td>- 12-36 hours post ingestion</td>
<td>- Report to health department, CDC</td>
</tr>
<tr>
<td>Strictly anaerobic</td>
<td>- Diplopia, loss of accommodation</td>
<td>- Botulinum antitoxin (within 24 hrs is best)</td>
</tr>
<tr>
<td>Spore-forming</td>
<td>- Dry mouth, dysphagia, dysphonia</td>
<td>- Manage respiratory failure</td>
</tr>
<tr>
<td>Inhibits release of</td>
<td>- Respiratory paralysis</td>
<td>- Parenteral fluids, alimentation</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>- No sensory changes</td>
<td></td>
</tr>
<tr>
<td>Food-borne botulism</td>
<td>- No fever</td>
<td></td>
</tr>
<tr>
<td>Infant botulism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound botulism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biohazard potential</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Cholera; *Vibrio cholerae***

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Manifestations</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activates adenyl cyclase in intestinal epithelial</td>
<td>- Acute onset</td>
<td>Fluid replacement [1/2 tsp salt, 8 tsp sugar/1 liter water]</td>
</tr>
<tr>
<td>Hypersecretion of water and chloride</td>
<td>- &quot;Rice water&quot; stool</td>
<td>- NS, Ringer's IV</td>
</tr>
<tr>
<td>Ingestion of contaminated water or food</td>
<td>- Gray, turid</td>
<td>- +/- antibiotics (may shorten course)</td>
</tr>
<tr>
<td>Epidemics</td>
<td>- Dehydration</td>
<td>Tetracycline, ampicillin, chloramphenicol, TMP-SMZ, quinolones</td>
</tr>
<tr>
<td>Natural disasters</td>
<td>- Hypotension</td>
<td>prevention:</td>
</tr>
</tbody>
</table>

Vaccine: short lived, limited
2 doses, 1-4 wks apart, booster every 6 mos
### Diphtheria; Corynebacterium diphtheriae

- **Characteristics**: Gram-positive bacillus; resp transmission
- **Manifestations**:
  1. Nasal: discharge
  2. Laryngeal: obstruction
  3. Pharyngeal:
     - Tenacious gray membrane
     - Tonsils and pharynx
     - Mild sore throat
     - Lymphadenopathy
     - Fever, malaise
     - Ixemia, prostration
     - Confirm with culture
- **Treatment**:
  - Reportable disease
  - Antitoxin: all suspects
  - Remove membrane
  - Antibiotics: penicillin, erythromycin, azithromycin, clarithromycin
  - Case: till 3 consecutive neg cultures
  - Contacts: erythromycin x 7 days
  - Prevention
    - DTap, Td

### Pertussis; Bordetella pertussis

- **Characteristics**: Gram-negative aerobic coccobacillus; resp transmission
- **Incubation period**: 7-17 days
- **Manifestations**:
  - Catarrhal: insidious; lacrimation, sneezing, coryza, anorexia, malaise, hacking night cough
  - Paroxysmal: bursts of rapid, consecutive coughs followed by “whoop”
  - Convalescent: 4 wks after onset; decrease in frequency and severity of cough
  - Lymphocytosis
  - Culture nasopharynx: Bordet-Gengou agar
  - PCR available
- **Treatment**:
  - Erythromycin X 7 days
  - Alternatives (may be better tolerated): azithromycin, clarithromycin, TMP-SMX
  - No lasting immunity (disease nor immunization)
  - Culture nasopharynx: Bordet-Gengou agar
  - PCR available
  - Contacts: same
  - Prevention
    - DTaP: infants
    - Tdap: adolescents, adults; at least one booster should contain pertussis!

### Tetanus; Clostridium tetani

- **Characteristics**: Gram-positive anaerobic rod; soil; local inoculation
- **Neurotoxin (tetanospasmin)**
  - Cleaves synaptobrevin
  - Incubation 5-15 days
  - Elderly, migrant workers, IDUs
- **Manifestations**:
  - Progressive:
    - Pain and tingling at site
    - Muscle spasms
    - Stiffness of jaw, neck, dysphagia, irritability
    - Painful tonic convulsions—trismus
    - Acute asphyxia
    - Remain conscious
    - No sensory deficits
    - No fever
- **Treatment**:
  - Tetanus immune globulin
  - Full course of immunization once recovered
  - Sedation, induced paralysis, mechanical ventilation
  - Penicillin—eradicate any toxin-producing organisms
### Tetanus prophylaxis, wound management:

<table>
<thead>
<tr>
<th></th>
<th>Clean, minor wound</th>
<th>All other wounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tdap or Td</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>TIG</td>
<td>no</td>
<td>yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>yes if &gt; 10 years since last booster</th>
<th>yes if &gt; 5 years since last booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tdap or Td</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>TIG</td>
<td>yes if &gt; 5 years since last booster</td>
<td>no</td>
</tr>
</tbody>
</table>

### Salmonella; *S. enterica* spp

**Gram-negative facultative anaerobic rod; fecal/oral**

<table>
<thead>
<tr>
<th>Gastroenteritis</th>
<th>Bacteremia</th>
<th>Enteric fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation 8-48 hrs</td>
<td>Immunosuppressed, Prolonged or recurrent fever</td>
<td>Incubation 5-14 days</td>
</tr>
<tr>
<td>Contaminated food or liquid</td>
<td>Distant seeding, Bones, joints, pleura, pericardium, endocardium, lungs, other</td>
<td>Malaise, h/a, cough, s/t</td>
</tr>
<tr>
<td>Fever, chills, N/V, crampy abd pain</td>
<td>Treatment: Fluids, Fluoroquinolones</td>
<td>Abx: Poorly effective</td>
</tr>
<tr>
<td>Diarrhea (+/- bloody), 5-5 days</td>
<td>TMP-SMX, Amoxicillin, Ciprofloxacin</td>
<td>Adequate waste disposal, Protect food and water</td>
</tr>
<tr>
<td>Self-limited</td>
<td>Treatment: Fluids, Fluoroquinolones</td>
<td>Treatment: Fluids, Fluoroquinolones or Ceftriaxone</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>Blood culture</td>
<td>Carrier state 1-4%</td>
</tr>
<tr>
<td>Abx: Malnourished, Severely ill, Sicker</td>
<td>Blood culture</td>
<td>Prevention</td>
</tr>
<tr>
<td>TMP-SMX, Amoxicillin, Ciprofloxacin</td>
<td>Sigmoidoscopy</td>
<td>Vaccine: Poorly effective</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Shigella; *S. sonnei, S. dysenteriae*

**Gram-negative non-spore forming rod; fecal-oral**

<table>
<thead>
<tr>
<th>Manifestations</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrupt onset</td>
<td>Leukocytes, RBCs</td>
<td>Hydration</td>
</tr>
<tr>
<td>Diarrhea with blood and mucus</td>
<td>Blood culture</td>
<td>Most pts require Abx: TMP-SMZ, Fluoroquinolones</td>
</tr>
<tr>
<td>Lower abdominal cramps</td>
<td>Sigmoidoscopy</td>
<td>Very resistant to Amoxicillin and Amphenicol</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>Inflamed engorged mucosa</td>
<td></td>
</tr>
<tr>
<td>Fever, chills, malaise, anorexia, h/a</td>
<td>Punctate lesions</td>
<td></td>
</tr>
<tr>
<td>Temp. Disaccharidase deficiency—reactive arthritis (Reiter’s)</td>
<td>Ulcers</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Rocky Mountain Spotted Fever

- *Rickettsia rickettsii*
- Middle and Southern Atlantic, Miss. Valley
- wood tick, dog tick
- late spring, summer
- 1000 cases/yr USA
- 3-5% mortality (age, chronic diseases, delay tx)
- prevention: avoid ticks; chemoprophylaxis not recommended

## Rocky Mountain Spotted Fever (RMSF)

### Manifestations

- 7 (2-14) days after bite
  - fever, chills, l/v, N/V, myalgias
  - restless, insomnia, irritable
  - cough, pneumonitis
  - delirium, lethargy, seizures, stupor
  - faint macules to papules (day 2-6)
  - wrists/ankles (inc palms and soles), spreads
  - rare: hepatosplenomegaly, jaundice, vasculitis, ARDS, uremia, myocardiitis

### Labs

- thrombocytopenia
- hyponatremia
- elevated liver enzymes
- CSF: hypoglycorrhachia, mild pleocytosis

### Treatment

- **doxycycline** — all ages
  - pregnant, if mild case: chloramphenicol
  - prognosis: good with tx
  - without tx: 70% fatality rate in elderly; 25% fatality rate in children

- **immunohistologic testing, serology to confirm**
Lyme disease

- *Borrelia burgdorferi*
- most common tick-borne illness in US
- Ixodes tick (blacklegged or deer tick)
  - larvae (late summer); nymph (most abundant); adult
- must feed 24-36 hrs to transmit
- drops off in 2-4 days
- best removal: fine tipped tweezers

http://www.cdc.gov/ncidod/dvbid/lyme/index.htm
**Lyme, clinical stages**

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>.3-30 days after bite</td>
<td>early disseminated</td>
<td>late persistent infection</td>
</tr>
<tr>
<td>flu-like sx</td>
<td>days to weeks</td>
<td>mos to yrs</td>
</tr>
<tr>
<td>erythema migrans</td>
<td>fatigue, malaise</td>
<td>-MSS: variable arthritis, synovitis</td>
</tr>
<tr>
<td>flat or raised</td>
<td>skin: smaller, multiple</td>
<td>NS: subacute encephalopathy, axonal polyneuropathy, leukoencephalitis</td>
</tr>
<tr>
<td>expands</td>
<td>CNS: h/a, neck pain</td>
<td>less common:</td>
</tr>
<tr>
<td>bull’s eye clearing</td>
<td>MSS: migratory arthritis</td>
<td>-cardiac: pericarditis, arrhythmias, block</td>
</tr>
<tr>
<td>single or multiple</td>
<td></td>
<td>-focal neuro: aseptic meningitis, Bell’s palsy, other</td>
</tr>
<tr>
<td>atypicals occur</td>
<td></td>
<td>-skin: Europe, acrodermatitis chronicum atrophicans (B. afzelii)</td>
</tr>
</tbody>
</table>

**Lyme testing**

*early dz: unreliable* [50% will be Ab neg]; late dz: evidence required

<table>
<thead>
<tr>
<th>Ab: IFA or ELISA, confirm with Western blot</th>
<th>other diagnostics</th>
</tr>
</thead>
<tbody>
<tr>
<td>serum</td>
<td>IgG 6-8 wks; peak 4-6 mos; decline 4-6 mos</td>
</tr>
<tr>
<td>IgM 2-4 wks; peak 6-8 wks; decline 4-6 mos</td>
<td>culture: 30-60% yield</td>
</tr>
<tr>
<td>acute/conv titers: 4X rise</td>
<td>PCR for Borrelia DNA</td>
</tr>
<tr>
<td></td>
<td>CSF: pleocytosis, increased protein</td>
</tr>
<tr>
<td>False Pos: RA, SLE, mono, endocarditis, syphilis, gingival dz, other</td>
<td>other:</td>
</tr>
<tr>
<td>False Neg: early illness; early antibiotic use</td>
<td>increased ESR (&gt;20)</td>
</tr>
<tr>
<td></td>
<td>liver enzymes</td>
</tr>
<tr>
<td></td>
<td>anemia</td>
</tr>
<tr>
<td></td>
<td>leukocytosis</td>
</tr>
<tr>
<td></td>
<td>micro hematuria</td>
</tr>
</tbody>
</table>

**Lyme, treatment**

<table>
<thead>
<tr>
<th>treatment</th>
<th>doxycycline, 2-3 wks (longer for arthritis) symptomatic relief as needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>alternatives</td>
<td>amoxicillin (peds), cefuroxine, penicillin IM (preg), ceftriaxone IV, cefotaxime IV</td>
</tr>
<tr>
<td>prevention</td>
<td>avoid tick areas; use repellent</td>
</tr>
<tr>
<td></td>
<td>cover skin, light colored clothing; inspect often</td>
</tr>
<tr>
<td></td>
<td>environmental controls</td>
</tr>
<tr>
<td></td>
<td>chemoprophylaxis: (200 mg doxy once)</td>
</tr>
<tr>
<td></td>
<td>endemic area, tick embedded &gt;36 hrs, tx begins within 72 hrs, no contraindications to doxycycline</td>
</tr>
<tr>
<td></td>
<td>LYMErix: gone!</td>
</tr>
</tbody>
</table>
**Treponema pallidum**

- **Transmission:** Sexual contact
- **Sensitive to heat and drying**

**Syphilis, testing**

<table>
<thead>
<tr>
<th><strong>non-treponemal tests</strong></th>
<th><strong>treponemal tests</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>VDRL, RPR</td>
<td>FTA-ABS, TPHA, TPPA</td>
</tr>
<tr>
<td>- cardiolipin-cholesterol and lecithin Abs</td>
<td>- Abs reacting to killed T pallidum; (+) in most primary, all secondary and beyond</td>
</tr>
<tr>
<td>- screens evaluate treatment</td>
<td>- false pos: SLE, malaria, leprosy</td>
</tr>
<tr>
<td>- (+) 4-6 wks after inoculation or 1-3 wks after lesion</td>
<td>- dark field microscopy</td>
</tr>
<tr>
<td>- almost 100% (+) in secondary syphilis</td>
<td>- immunofluorescent staining</td>
</tr>
<tr>
<td>- false pos: CT dz (SLE, others), mono, malaria, febrile dz, leprosy, IDU, endocarditis, older ages, hep C, pregnancy</td>
<td>- CSF (neurosyphilis): increased protein, lymphocytic pleocytosis, (+) VDRL</td>
</tr>
</tbody>
</table>

**Syphilis, clinical manifestations**

<table>
<thead>
<tr>
<th></th>
<th>30-60 days after inoculation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td>painless chancre, rapid progression; clean base, firm margins</td>
</tr>
<tr>
<td></td>
<td>large lymph nodes, non or mildly tender</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>wks to mos after chancre; highly infectious</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary</strong></td>
<td>fever, LN, maculopapular rash; includes palms and soles</td>
</tr>
<tr>
<td></td>
<td>condylomata lata: fused, weeping papules in moist areas</td>
</tr>
<tr>
<td></td>
<td>less common: atopy, meningitis, jaundice, nephrotic syndrome, periostitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>anytime after secondary; 1/3 of untreated pts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tertiary</strong></td>
<td>localized gummatous reactions</td>
</tr>
<tr>
<td></td>
<td>diffuse inflammation with myriad presentations</td>
</tr>
<tr>
<td></td>
<td>mucous membranes, bones (Charcot joints), eyes, lungs, GI, cardiovascular</td>
</tr>
<tr>
<td></td>
<td>neurosyphilis: (+) CSF alone; meningovascular; general paresis</td>
</tr>
<tr>
<td></td>
<td>tabes dorsalis: progressive degeneration of parenchyma, posterior columns; impaired proprioception, Argyll Robertson pupils, hypotonia, hyporeflexia, shooting pains, TD crises</td>
</tr>
</tbody>
</table>
Syphilis, treatment

- **penicillin** -- drug of choice, all stages
  - pen allergic: tetracycline
  - alternatives: ceftriaxone, azithromycin
  - Jarish-Herxheimer reaction: fever within 24 hours of treatment
    - more likely with bx of early syphilis
    - sudden destruction of spirochetes, toxins produced
  - stop bx ONLY if: laryngitis/impending obstruction, auditory neuritis or labyrinthitis (risk permanent hearing loss)

- post-exposure prophylaxis
  - any known intimate exposure within past 3 mos
  - if greater than 3 mos, treat only if (+) serology

Syphilis, special considerations

- pregnancy
  - screen all prenatal pts, repeat in 3rd trimester
  - any (+) serology, tx with penicillin

- congenital syphilis
  - maculopapular rash, mucous membrane patches
  - serous nasal d/c ("snuffles")
  - hepatosplenomegaly, anemia, osteochondritis
  - isolate newborn (infectious), tx with penicillin
  - if untreated: interstitial keratitis, Hutchinson teeth, saddle nose, saber shins, deafness, CNS defects

Viruses

- CMV (cytomegalovirus)
- EBV (Epstein Barr virus)
- Rabies
- HIV (Human immunodeficiency virus)
Cytomegalovirus (CMV)

- common infection, most are asymptomatic
- seroprevalence increases with age group
- virus remains latent
- serious disease: immunocompromised
- transmission: sexual, congenital, blood products, transplanted organs, person to person

CMV, primary disease

<table>
<thead>
<tr>
<th>Perinatal disease</th>
<th>Immunocompetent host</th>
</tr>
</thead>
<tbody>
<tr>
<td>In utero or via breast milk</td>
<td>Fever, malaise, mono-like</td>
</tr>
<tr>
<td>Jaundice, hepatosplenomegaly</td>
<td>Myalgias, arthralgias</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Spleen/liver defects</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>Leukopenia, then leukocytosis</td>
</tr>
<tr>
<td>CNS calcifications</td>
<td>Complications: GI, encephalitis, pericarditis, myocarditis, thrombocytopenia, Guillain Barre syndrome</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>Associations: IBD, atherosclerosis, breast cancer</td>
</tr>
<tr>
<td>Motor disability</td>
<td>Leukopenia, then leukocytosis</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>Complications: GI, encephalitis, pericarditis, myocarditis, thrombocytopenia, Guillain Barre syndrome</td>
</tr>
</tbody>
</table>

CMV reactive disease, immunocompromised CD4<100

<table>
<thead>
<tr>
<th>Retinitis</th>
<th>Neovascular proliferative lesions, &quot;pizza pie&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI/biliary</td>
<td>Esophagitis, IBD-like syndrome, ulceration, perforation, diarrhea, hematochezia, abd pain, fever, weight loss, cholangiopathy</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Pneumonitis (dry cough, dyspnea)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Polyradiculopathy, transverse myelitis, encephalitis, disseminated disease</td>
</tr>
</tbody>
</table>

CD4 count typically <50

High mortality
CMV

**Diagnosis**
- Tissue confirmation; bx: "owl's eyes" intracytoplasmic inclusions
- Leukopenia—lymphocytosis—ataypical lymphs
- IgM; follow IgG titers; viral loads
- PCR: Ags—blood, urine, CSF

**Treatment**
- Ganciclovir IV, intravenous +/- foscarinet
- If resistant: valganciclovir PO, foscarinet IV, switch to PO, cidofovir IV
- Maintenance: ganciclovir + foscarinet daily

**Prevention**
- HIV: HAART, ganciclovir or valganciclovir
- Transplant: antiviral agents and CMV immunoglobulin

---

**Epstein Barr Virus (EBV)**

- Human herpesvirus 4
- Any age; most common in 10-35 year old
- Sporadic cases or epidemics
- Transmission—probably saliva
- Incubation period several weeks

*Associated with:* Burkitt’s lymphoma, nasopharyngeal carcinoma, chronic fatigue, oral hairy leukoplakia, Hodgkin’s, SLE, MS, rheumatoid arthritis, others . . .

**EBV, clinical manifestations**

<table>
<thead>
<tr>
<th>More Common</th>
<th>Common</th>
<th>Less Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Lymphadenopathy (posterior chain)</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Sore throat</td>
<td>Spleenomegaly</td>
<td>Gall bladder</td>
</tr>
<tr>
<td>Malaise</td>
<td>Maculopapular rash (15% give ampicillin-90%)</td>
<td>Mononeuropathy</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Exudative pharyngitis</td>
<td>Aseptic meningitis, encephalitis</td>
</tr>
<tr>
<td>Myalgia</td>
<td>Soft palate petechiae</td>
<td>Interstitial nephritis</td>
</tr>
</tbody>
</table>

*Coarse cough, "pseudocroup" myocarditis*
**EBV**

**labs**
- granulocytopenia, then leukocytosis, atypical lymphocytes
- hemolytic anemia; thrombocytopenia
- heterophil antibodies (monospot) [4 wks]
- increased liver enzymes, bilirubin
- meningitis: high pressure, lymphocytosis, increased protein

**treatment**
- asymptomatic, supportive
  - acyclovir: decrease viral shedding, no effect on course of illness, give if pneumonitis or underlying immune disorders
  - steroids: if impending airway obstruction, hemolytic anemia, severe thrombocytopenia

**prognosis**
- 95% recover without specific treatment
- fever ends in about 10 days
- lymphadenopathy, splenomegaly ~4 wks
- debility may linger 2-3 mos

---

**Rabies**

**characteristics**
- raccoons, skunks, bats, foxes, coyotes
- incubation period ~3-7 wks
- virus travels along nerves, multiplies in brain, migrates to salivary glands

**manifestations**
- pain at site, fever, malaise, N/V
- CNS stage: relentlessly progressive
  - "furious" encephalitis: delirium, spasm, hydrophobia
  - "dumb" paralytic: ascending paralysis

**prognosis**
- 95% recover without specific treatment
- fever ends in about 10 days
- lymphadenopathy, splenomegaly ~4 wks
- debility may linger 2-3 mos

---

**Rabies, prevention and treatment**

**primary prevention**
- immunization of domestic animals
- local care of bites

**post exposure immunization**
- rabies immune globulin [HRIG] (IM, to wound PLUS a distant site; separate syringes)
- human diploid cell rabies vaccine (HDCV)
  - 5 injections days 0, 3, 7, 14
  - (add dose on day 28 if immunocompromised)
- if previously immunized—day 0 and day 3

**pre-exposure immunization**
- HDCV, 3 doses IM: day 0, 7, 21 or 28
- boosters if titers wane

**treatment:** (almost) universally fatal; ICU, ventilation, multi-drug approach—one known survivor
Human Immunodeficiency virus (HIV/AIDS)

- first recognized 1981
- human retrovirus, requires reverse transcriptase for replication
- targets all cells with T4 antigen, primarily the CD4 helper lymphocyte
- currently >40 million people infected worldwide
- 5 million new cases and 3 million deaths/year
- sexual contact, parenteral exposure, perinatal transmission

HIV, diagnosis

<table>
<thead>
<tr>
<th>screening</th>
<th>ELISA (1 or 2), confirmatory Western blot or HIV antigen assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>viral load</td>
<td>actively replicating virus</td>
</tr>
<tr>
<td>CD4 count</td>
<td>decreases with illness progression</td>
</tr>
<tr>
<td></td>
<td>CD4&lt; 200 OR CD4% &lt;20% highest risk of poor outcome (OIs, malignancies)</td>
</tr>
<tr>
<td>other labs</td>
<td>anemia, leukopenia, thrombocytopenia, hypergammaglobulinemia, hypercholesterolemia</td>
</tr>
</tbody>
</table>

HIV, clinical manifestations

<table>
<thead>
<tr>
<th>acute HIV syndrome</th>
<th>HIV disease</th>
<th>AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>infrequently identified</td>
<td>systemic manifestations</td>
<td>indicator conditions</td>
</tr>
<tr>
<td>flu or EBV-like illness</td>
<td>fever, night sweats, weight loss, dementia specific manifestations</td>
<td></td>
</tr>
<tr>
<td>persistent lymphadenopathy</td>
<td>opportunistic infections, malignancies</td>
<td></td>
</tr>
</tbody>
</table>
**AIDS indicator conditions**

http://www.aids-ed.org/aetc?page=cm-105_disease

- Bacterial pneumonia, recurrent (≥ 2 episodes in 12 months)
- Candidiasis of the bronchi, trachea, or lungs
- Candidiasis, esophageal
- Cervical carcinoma, invasive, confirmed by biopsy
- Coccidiodomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1-month duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Herpes simplex: chronic ulcers (>1-month duration), or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1-month duration)
- Kaposi sarcoma
- Lymphoma, Burkitt, immunoblastic, or primary central nervous system
- Mycobacterium avium complex (MAC) or M kansasii, disseminated or extrapulmonary
- Mycobacterium tuberculosis, pulmonary or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- Pneumocystis jiroveci pneumonia (PCP)
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent (nontyphoid)
- Toxoplasmosis of brain
- Wasting syndrome due to HIV (involuntary weight loss >10% of baseline body weight) associated with either chronic diarrhea (≥2 loose stools per day ≥1 month) or chronic weakness and documented fever ≥1 month

**HIV/AIDS prevention**

| primary | safer sex, harm reduction, drug rehab, screening blood products, universal precautions |
| secondary | screening programs, prevention of opportunistic infections and malignancies in those infected |
| post-exposure | counseling, testing now, 6 wks, 3 mos, 6 mos, antiretroviral therapy (AZT alone or in combination-preferred), begin within 72 hours for best outcome, continue 4-6 weeks |
| perinatal | antiretrovirals during pregnancy, L&D, and to newborn, avoid breast feeding |

**HIV/AIDS, treatment**

- antiretroviral therapy, HAART
- treatment of or chemoprophylaxis against opportunistic infections and malignancies
- goal: suppression of viral load
- combination therapy preferred
- monitor CD4, viral load, overall patient health status
- adherence, effectiveness, resistance, and adverse effects
### anti-HIV drugs

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTIs (nucleoside reverse transcriptase inhibitors)</td>
<td>abacavir (Ziagen), didanosine (ddI), emtricitabine (FTC), lamivudine (3TC), stavudine (d4T), tenofovir (TDF, TFV), zidovudine (AZT, ZDV)</td>
<td>anemia, neutropenia, GI distress, hepatitis, pancreatitis, renal insufficiency, headache, myopathy, peripheral neuropathy, aphthous ulcers, rash</td>
</tr>
<tr>
<td>NNRTIs (non-nucleoside reverse transcriptase inhibitors)</td>
<td>delavirdine (Rescriptor), efavirenz (EFV), etravirine (Incivir), nevirapine (NVP), rilpivirine (Edurant)</td>
<td>rash, neurologic manifestations, anxiety</td>
</tr>
<tr>
<td>Fusion inhibitor</td>
<td>enfuvirtide (T-20)</td>
<td>injection site pain, pruritis, allergic reactions, flu-like</td>
</tr>
<tr>
<td>CCR5 antagonist</td>
<td>maraviroc (Selzentry)</td>
<td>cough, fatigue, abdominal pain, dizziness</td>
</tr>
</tbody>
</table>

### protease inhibitors

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>protease inhibitors</td>
<td>atazanavir (Reyataz), darunavir (Prezista), fosamprenavir (Lexiva), indinavir (Crixivan), lopinavir/ritonavir (Kaletra), nelfinavir (Viracept), ritonavir (Norvir), saquinavir (Invirase), tranavir (Aptivus)</td>
<td>headache, GI upset, peripheral neuropathies, renal calculi (indinavir), depression, arrhythmias, lipid abnormalities</td>
</tr>
<tr>
<td>INSTIs (integrase strand transfer inhibitors)</td>
<td>dolutegravir (Tivicay), elvitegravir/cobicistat/emericitabine/tenofovir (Stribild), raltegravir (Isentress)</td>
<td>headache, dizziness, nausea, insomnia</td>
</tr>
<tr>
<td>Combination drugs</td>
<td>abacavir/lamivudine (Epzicom), abacavir/lamivudine/zidovudine (Triziv), lamivudine/zidovudine (Combivir)</td>
<td></td>
</tr>
</tbody>
</table>

### Parasites

- Helminths
- Malaria
- Toxoplasma
- Pinworm
Helminths

- 3 general categories
  - Nematodes (roundworms)
    - Filaria, ascariasis, hookworm, pinworm, trichinosis, whipworm, others
  - Trematodes (flukes)
    - Shistosomes
  - Tapeworms
    - Cysticerocosis
  - Hermaphroditic

Helminth infestations

- Intestinal infestations (mild—severe)
  - Inflammation, fibrosis, ulcers, obstruction, penetration
  - Malnutrition, growth disruption, anemia
  - Skin signs: red, serpiginous, pruritic (hookworm)
  - Lymphatic obstruction
    - Disfigurement, disability, elephantiasis (filaria)
  - Renal disease, splenic infarction
  - Absenteeism: school, work
  - Treatment: albendazole
  - Deworming programs: stop transmission

Malaria

*Plasmodium vivax; P falciparum; P ovale; P malariae*

<table>
<thead>
<tr>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endemic to tropics, subtropics</td>
</tr>
<tr>
<td>300-500 million cases/year</td>
</tr>
<tr>
<td>1 million deaths/year</td>
</tr>
<tr>
<td>Most cases in US are imported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lifecycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anopheles mosquito ingests gametocytes, become sporozoites</td>
</tr>
<tr>
<td>Mosquito inoculates human</td>
</tr>
<tr>
<td>Sporozoites travel to liver, become merozoites</td>
</tr>
<tr>
<td>Released into blood stream, enter RBCs and become gametocytes</td>
</tr>
<tr>
<td>Invade new cells, repeat cycle</td>
</tr>
</tbody>
</table>
### Malaria, clinical manifestations

- attacks last 4-6 hrs; recurrence common
- every other day; every third day (*P. malariae*)
  - shaking chill (cold stage)
  - fever (hot stage)
  - diaphoresis (sweating stage)
- malaise, h/a, dizziness
- anorexia, N/V, diarrhea, cramps
- myalgia, arthralgia, cough, splenomegaly
- *P. falciparum*: severe disease, poorest prognosis

### Malaria, labs and treatment

#### Labs
- peripheral smear, fresh blood
- quantify parasitemia
- antibodies persist 10+ years
- transient leukocytosis, then leukopenia
- anemia, hemolytic

#### Treatment
- chloroquine remains drug of choice
- safe in pregnancy, well tolerated
- transient GI sxs, h/a, pruritus, other
- resistance growing: add doxy, clindamycin or tetracycline in areas of resistance
- alternatives: malarone, mefloquine, atovaquone/doxy, others

### Malaria, peripheral smear
Malaria, prognosis and prevention

**prognosis**
- 2-4 weeks uncomplicated, untreated
- good prognosis if treated
- P falciparum: 14-17% mortality despite treatment

**prevention**
- chemoprophylaxis: chloroquine, malarone, mefloquine, doxycycline
- education
- mosquito control: bed nets, screens, clothing, DEET

Toxoplasmosis; *Toxoplasma gondii*

**characteristics**
- humans, animals (cats), birds
- 80% of primary infections are asymptomatic
- trophozoite: body tissue and fluids
- cysts: latent form, muscle and nerve tissue, persist indefinitely
- oocyst: passed in feces, remain infective wks- yrs

**transmission**
- ingest cysts: raw or uncooked meat
- ingest oocysts: food water, cat litter, soil
- become sporozoites, invade cells, become trophozoites in tissue
- transplacental transmission
- direct inoculation

Toxoplasmosis, 4 clinical syndromes

**primary infection, immunocompetent**
- acute, mild, febrile, multisystem, mono-like
- lymphadenopathy, nontender

**congenital infection**
- maternal primary infection during pregnancy
- rare cause of stillbirth or abortion
- <15% with eye or brain damage at birth
- >85% will develop, within week or so

**retinochoroiditis**
- wks to mos after congenital infection
- OR acquired infection in very young child
- persistent inflammation
- focally necrotic lesions

**reactivated disease, immunocompromised**
- focal infection
- brain: encephalitis
- lungs, eye, heart, skin, GI, liver
- disseminated infection
### Toxoplasma

**diagnosis**
- Histology: cysts, trophozoites
- Serology (Abs): ELISA, Western blot, PCR, IgG
- Leukocytes: normal or high
- CT: ring enhancing lesions, usually multiple

**treatment**
- Immunocompetent: tx only if severe disease
- Immunocompromised: pyrimethamine PLUS folic acid
- Treat 4-6 wks, then prophylaxis (TMP-SMX, dapsone)

**prevention**
- Irritate meat, fully cook meats
- Protect from cat feces
- Clean litter box
- Screen all pregnant woman for Abs, if neg—avoid exposure

### Pinworms; *Enterobius vermicularis*

**characteristics**
- Humans only host, fecal-oral transmission
- Adult worms reside in colon
- Gravid females deposit eggs in perianal area
- Ingest eggs, hatch in duodenum, migrate to cecum

**diagnosis**
- Scotch tape test, wash with toluene, see eggs or worms
- Anoscopy rarely necessary

**treatment**
- Albendazole, mebendazole, pyrantel
- Treat all members of household
- Repeat treatment in 2 weeks
- Hygiene, linens, etc.
The END!

Good Luck to All