# INFECTIOUS DISEASES

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Esther Bui and Sharmistha Mishra, chapter editors  
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## BACTERIA

Glossary of Bacterial Terms

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## ANTIBACTERIALS

Cell Wall Synthesis Inhibitors (Bactericidal)
- Protein Synthesis Inhibitors
  - Via 50S Ribosome (-static)
  - Via 30S Ribosome (-cidal)
  - Via 30S Ribosome (-static)
- Folic Acid Metabolism Inhibitors (-static)
- DNA Gyrase Inhibitors (-cidal)
- DNA-Directed RNA Polymerase Inhibitors (-cidal)
- DNA Complex Damaging Agents (-cidal)

## ANTIMYCOBACTERIALS

Anti-Tuberculosis (TB) Drugs
- Anti-M. Avium-Intracellulare Complex Drugs
- Anti-Leprosy Drugs

## ANTIVIRALS

- Non-Nucleoside Polymerase Inhibitors
- Nucleoside Analogs

## ANTIFUNGALS

- Polynes
- Imidazoles
- Triazoles

## ANTIPARASITICS

- Anti-Protozoal Drugs
- Anti-Malarial Drugs
- Anti-Helminthic Drugs

## INFECTIONS IN THE COMPROMISED HOST

- HIV and AIDS
- Febrile Neutropenia
- Transplant or Leukemia/Lymphoma
- Infections in a Diabetic Patient

## FEVER OF UNKNOWN ORIGIN

## HIV AND AIDS

## COMMON INFECTIONS

## REFERENCES
BACTERIA

Figure 1. General Schematic of Bacterial Structure

Figure 2. Bacterial Morphology

Illustrations by Miyuki Fukuma

GLOSSARY OF BACTERIAL TERMS

Virulence Factors
- Flagella
  - protein filament tails that propel the bacteria (motility)
- Pili
  - shorter than flagella, serve as adherence factors
  - some bacteria use sex pili for reproduction
- Capsules
  - protective layer surrounding cell membranes, usually made of secreted carbohydrate residues, helps to evade host immune response

Endospores
- metabolically dormant forms of bacteria, may lie dormant for years
  - only Bacillus and Clostridium

Toxins
- Exotoxins
  - proteins released by bacteria that cause disease independent of the bacteria
    - neurotoxins act on nerves or motor endplates
    - enterotoxins act on the GI, etc.
- Endotoxins
  - normal part of the bacterium that may be shed while living, or released during cell lysis causing disease processes (i.e. septic shock)
### Table 1. Bacterial Classification

<table>
<thead>
<tr>
<th>Gram Stain</th>
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<th>Aerobes</th>
<th>Rods</th>
<th>Anaerobes</th>
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<tr>
<td>Gram +ve</td>
<td>Staphylococcus -S.aureus -S.epidermidis -S.saprophyticus Streptococcus -S.pyogenes (Group A) -S.agalactiae (Group B) -Group D Strep (S. bovis) -S.viridans -S.pneumoniae Enterococcus</td>
<td>Corynebacterium diphtheriae Listeria monocytogenes Bacillus cereus Nocardia</td>
<td>Streptococci/Peptostreptococci</td>
<td>Clostridium -C.tetani -C.botulinum -C.perfringens -C.difficile</td>
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<td></td>
<td>Un-detectable</td>
<td>Mycobacterium, Spirochetes, Chlamydia, Bartonella, &amp; Mycoplasma spp. (due to lack of cell wall)</td>
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### AEROBIC BACTERIA

#### GRAM POSITIVE COCCI

**Staphylococcus aureus (S. aureus)**

- **microbiology**
  - Gram positive, catalase-positive cocci in grape-like clusters/tetrads
  - its production of catalase differentiates it from Streptococcus
  - coagulase-positive more virulent; coagulase-negative strains only cause disease in the setting of prosthesis/foreign body
- **mode of transmission**
  - normal flora of human skin, respiratory and gastrointestinal tracts
  - 25% of healthy adults are colonized in anterior nares
  - person-to-person transmission and via contaminated fomites
  - important cause of hospital-acquired infections
  - risk factors for infection include: broken skin, young, old, foreign bodies
- **clinical features**
  - **EXOTOXIN DEPENDENT**
    - staphylococcal gastroenteritis (enterotoxin)
      - sudden onset of vomiting and diarrhea
      - associated with cream, ham, poultry
      - heat stable therefore not destroyed by cooking
    - toxic shock syndrome (TSS toxin-1)
      - from focal infections and/or colonization
      - acute onset of high fever, nausea and vomiting, watery diarrhea
      - desquamation of skin (palms and soles)
      - hypotension, renal/liver dysfunction
      - associated with tampon use (rare), nasal packing, wound infections
AEROBIC BACTERIA . . . CONT.

- scalded skin syndrome (exfoliative toxin)
- extensive desquamation and bullae formation
- resembles massive scalding
- predominately affects children i.e. neonates with infected severed umbilicus or skin infections

DIRECT INVASION
- skin, soft tissue infections (most common especially boils)
- furuncles (boils), carbuncles (clusters of boils)
- cellulitis, wound infections (most common), mastitis, folliculitis,
- impetigo (contagious pyoderma)
- abscess formation
  - acute focal inflammation involving many extracellular toxins (e.g. coagulase, hemolysin, leucocidin, staphylokinase, etc.) and host production of thick walled fibrin capsule forming an abscess
- bacteremia
  - metastatic focal infection in 15% if undertreated
  - endocarditis is a complication because tends to colonize previously traumatized or highly vascular tissue
- endocarditis
  - can affect normal valves
  - tricuspid valve involvement unique to IV drug users or people with IV lines
- osteomyelitis
  - often history of preceding skin infection (50%), or trauma
- septic arthritis
- pneumonia (uncommon but severe)
  - often occurs after influenza infection
  - increase occurrence if history of COPD or chronic bronchitis
- acute bacterial meningitis (uncommon)

- diagnosis (applicable to all Staphylococcus strains)
  - specimens: surface swab, blood, pus, tracheal aspirate or CSF for culture
  - smears of pus or sputum
  - catalase and coagulase tests

- treatment
  - drugs of choice: beta-lactamase-resistant penicillins (e.g. cloxacillin), cephalosporins, macrolides, or clindamycin (95% penicillin-resistant - beta-lactamase production)
  - minor skin infections may be treated without oral/IV antibiotics (i.e. drainage, warm saline soaks +/- topical bacitracin or fusidic acid)
  - drain abscess/wound debridement

Methicillin-Resistant Staphylococcus aureus (MRSA)
- resistance to methicillin and nafcillin via change in penicillin-binding proteins (PBP 2a)
  - often in hospitals, transmitted by health-care workers
- treatment
  - IV vancomycin
  - eradication of colonization with topical mupirocin to nares and washing with chlorhexidine soap +/- oral septran and rifampin
  - contact isolation should be enforced to prevent intra-patient spread

Staphylococcus epidermidis (S. epidermidis)
- microbiology
  - Gram positive cocci, catalase-positive, coagulase negative, sensitive to novobiocin
- mode of transmission
  - ubiquitous normal flora of human skin, GI tract
- pathogenic mechanisms
  - adheres to prosthetic surfaces using slime layer
  - highly resistant to antibiotics
- clinical features
  - commonly infects foreign bodies: prosthetic joints, prosthetic heart valves, shunts, catheters, intravenous lines, intravascular grafts
  - frequent contaminant in blood cultures
- treatment
  - drug of choice: vancomycin since resistant to multiple antibiotics

Staphylococcus saprophyticus (S. saprophyticus)
- microbiology
  - coagulase-negative, urease-positive, novobiocin-resistant
- clinical features
  - UTIs
  - second most common cause of simple cystitis in sexually active women (after E. coli)
- treatment
  - penicillin
AEROBIC BACTERIA . . . CONT.

**Streptococci** (Common features of all groups)

- **microbiology**
  - cocci in chains or pairs
  - catalase-negative (vs. Staph. catalase-positive)
  - hemolytic patterns on sheep blood agar:
    - alpha (green partially-hemolyzed), beta (clear-hemolyzed), or gamma (non-hemolytic)
  - also grouped based on cell-wall carbohydrates (Lancefield groups A, B, D, etc.)

- **diagnosis**
  - specimens: throat swab, pus, blood for culture
  - smears from pus; smears from throat swabs are never helpful because S. viridans, endogenous flora have the same appearance as GAS
  - serological tests: antibodies to GAS antigen - antistreptolysin O (ASO) indicates recent infection

**Group A Streptococci** (GAS or *S. pyogenes*)

- **microbiology**
  - beta-hemolytic
  - sensitive to bacitracin

- **mode of transmission**
  - colonizes pharynx (15% of children are carriers)
  - person-to-person transmission

- **pathogenic mechanisms**
  - pil for attachment to epithelial cells
  - M protein on cell wall resists phagocytosis
  - production of toxic enzymes such as DNAse, hyaluronidase, streptokinases, streptolysins

- **clinical features**
  - **MILD INFECTIONS**
    - tonsillo-pharyngitis (Strep throat)
      - purulent exudate on tonsils, fever $>38^\circ C$, tender swollen anterior cervical lymph nodes, and absence of cough
      - 40-60% of patients with all 4 criteria have GAS pharyngitis
      - clinical criteria not reliable must swab throat if suspicious
      - diagnose with throat culture or rapid antigen test (specificity 95%, sensitivity 85%)
      - follow-up negative rapid test with culture
    - skin, soft tissue, and wound infections *(see Colour Atlas ID5 and ID8)*
      - erysipelas, impetigo, cellulitis, lymphangitis
  - **SEVERE INFECTIONS**
    - scarlet fever (erythrogenic/pyrogenic toxin)
      - pharyngitis, fever, erythema, desquamation of palms and soles, strawberry tongue
    - necrotizing fasciitis
      - severe pain out of proportion to lesion in early stages
      - fever, well-demarcated expanding area of erythema, hemorrhages, blisters, bullous and gangrenous skin lesions
      - rapid progression
      - renal failure
    - streptococcal toxic shock syndrome (TSS toxin)
      - fever, shock, rash or bullous skin lesion
      - early renal failure, thrombocytopenia
      - risk factors: minor trauma, surgery, preceding viral illness (chicken pox)
    - bacteremia (rare)

- **complications**
  - SUPPURATIVE
    - local extension and invasion
    - cervical adenitis, sinusitis, otitis media, pneumonia
  - NON-SUPPURATIVE (AB-MEDIATED) - specific to GAS
    - rheumatic fever (RF)
      - presents 2-4 weeks post strep infection
      - diagnosed clinically (2 major criteria or 1 major & 2 minor criteria)
      - Jones revised major criteria:
        - carditis, polyarthritis, chorea, erythema marginatum, subcutaneous nodules
      - Minor criteria
        - fever, arthralgia, known rheumatic heart disease, previous hx of rheumatic fever
      - 10-20 years after infection, may develop permanent heart valve damage
    - acute post-streptococcal glomerulonephritis (PSGN)
      - presents 1-4 weeks post strep infection
      - causes acute nephritic syndrome
        - malaise, tea-colored urine, hypertension, proteinuria, periortibial edema
      - only complication not prevented by antibiotics
      - occurs frequently in summer and fall
      - diagnose histologically

- **treatment**
  - penicillin V or G
  - erythromycin if allergic to penicillin
  - treatment of pharyngitis reduces the chance of rheumatic fever but not PSGN
AEROBIC BACTERIA... CONT.

**Group B Streptococci (S. agalactiae)**
- **Microbiology**
  - beta-hemolytic
- **Mode of Transmission**
  - Colonizes large intestine, vagina (20% of women)
  - Person-to-person and vertical transmission
- **Clinical Features**
  - Perinatal infections (leading cause: Group B for BABY)
    - Maternal puerperal sepsis
    - Septic abortion, chorioamnionitis
    - Neonatal sepsis (<10 days old), neonatal meningitis (>10 days old), neonatal pneumonia
  - Adults (elderly, diabetics, alcoholics) develop cellulites, arthritis, meningitis
- **Diagnosis**
  - Routine vaginal/rectal cultures in late third trimester (36-37 weeks)
  - If positive culture or high-risk mother, give prophylactic antibiotics during labour
- **Treatment**
  - Penicillin or ampicillin

**Viridans Streptococci (S. mutans, S. mitis)**
- **Microbiology**
  - Non-Lancefield Group Streptococci
  - Alpha-hemolytic
- **Mode of Transmission**
  - Normal oropharyngeal flora
- **Pathogenic Mechanisms**
  - Seeds the bloodstream during dental manipulation (tooth brushing, chewing)
  - Produces sticky dextrans that help it adhere to surfaces
- **Clinical Features**
  - Most common cause of subacute bacterial endocarditis
  - Affects abnormal heart valves
  - S. mutans causes dental caries
- **Treatment**
  - Penicillin +/- aminoglycoside

**S. pneumoniae (pneumococcus)**
- **Microbiology**
  - Non-Lancefield Group Streptococci
  - Alpha-hemolytic
  - Diplococci (grows in pairs)
  - Growth inhibited by optochin on agar (to differentiate from S. viridans)
  - 84 serotypes based on capsular antigen, all are pathogenic
  - Immunity to one type not cross-protective
- **Mode of Transmission**
  - Colonizes nasopharynx, person-to-person, respiratory droplets
- **Pathogenic Mechanisms**
  - Polysaccharide capsule resists phagocytosis
  - Capsule induces strong inflammatory reaction
- **Risk Factors**
  - Alcoholics, splenectomy, sickle-cell anemia, HIV, hypogammaglobulinemia, multiple myeloma, Hodgkin's Disease
- **Clinical Features**
  - Pneumonia
    - Most common cause of community acquired pneumonia
    - Often preceded by upper respiratory tract infection (e.g. influenza virus)
    - Sudden onset of shaking chills, pleuritic pain, rusty sputum, lobar involvement (dense consolidation on CXR)
    - Sterile pleural effusion (50%)
  - Meningitis
    - Second most common cause of bacterial meningitis in adults
    - Can occur after pneumonia, sinusitis, or skull fracture
  - Bacteremia (25%)
  - Otitis media (in children)
- **Prevention**
  - Polysaccharide vaccine ("pneumovax")
    - Protective against the 23 most common serotypes
    - Recommended for elderly, immunocompromised, splenectomized and those with cardiopulmonary, liver or kidney disease, or sickle-cell anemia
- **Treatment**
  - Penicillin or erythromycin; second generation cephalosporin (e.g. cefuroxime)

**Penicillin-Resistant S. pneumoniae**
- In Toronto: 7% resistance in adults, 20% resistance in children
- Resistance via change in penicillin-binding proteins
- For CNS infection: combine vancomycin and cefotaxime until sensitivities available
AEROBIC BACTERIA . . . CONT.

Enterococcus (E. faecalis, E. faecium)
- **microbiology**
  - beta-, alpha-, or gamma-hemolytic
  - once included in streptococcus; now own genus
  - major species: Enterococcus faecalis and Enterococcus faecium
- **reservoir/mode of transmission**
  - colonize intestinal and genitourinary tracts
  - person-to-person transmission
- **clinical features**
  - subacute bacterial endocarditis
  - urinary tract, hepatobiliary tract, intra-abdominal infections
  - wound and decubitus ulcer infection
- **treatment**
  - enterococci killed by penicillin and aminoglycoside combination (synergy)
  - enterococci only inhibited, not killed by penicillin only
  - resistant to cephalosporins
  - minor infections (UTIs, soft tissue) use ampicillin or quinolone
  - severe infections use ampicillin/gentamycin

Vancomycin-Resistant Enterococci (VRE)
- resistance via change in peptidoglycan component from D-alanine to D-lactate
  - consider synercid, linazolid
  - drugs of choice still ampicillin and gentamicin
  - sensitivity to teicoplanin depends on phenotype
  - new streptogramin therapy under investigation

GRAM POSITIVE BACILLI

Corynebacterium diphtheriae
- **microbiology**
  - club-shaped rods with beaded or barred appearance
  - non-spore-forming
- **mode of transmission**
  - colonizes pharynx
  - person-to-person transmission via airborne respiratory droplets
- **pathogenic mechanisms**
  - pseudomembrane forms in the upper respiratory tract
  - serves as a base from which organism secretes exotoxin
  - disease caused by airway obstruction or effect of exotoxin
    - on heart and nervous system (not invasion)
- **clinical features**
  - pharyngitis, fever, nasal discharge, hoarseness
  - tenacious gray membrane over the tonsils and pharynx
  - myocarditis (10%)
  - neural involvement (peripheral nerve palsies, Guillain-Barré-like syndrome)
  - cellulitis
- **diagnosis**
  - immunity detected by Schick skin test
- **treatment**
  - antitoxin + penicillin or erythromycin
  - prevent by immunization with diphtheria toxoid at ages 2, 4, 6, 18 months and 6 years

Listeria monocytogenes
- **microbiology**
  - non-spore-forming, tumbling motility
  - beta-hemolytic
  - “cold concentrating” (not inhibited by refrigeration)
- **mode of transmission**
  - most commonly foodborne (milk, soft cheese, raw coleslaw)
  - also from soil, decaying matter, feces
  - vertical transmission (vaginal delivery)
- **pathogenic mechanisms**
  - facultative intracellular parasite
- **clinical features**
  - usually < 1 or > 55 years of age
- **ANTENATAL/NEONATAL POPULATION**
  - associated with spontaneous abortions and premature deliveries
  - neonatal meningitis and bacteremia
- **ADULT POPULATION**
  - 3rd most common cause of adult meningitis
  - meningitis in immunosuppressed patients (e.g. alcoholics, pregnancy, diabetics, steroid or immunosuppressive medication users)
  - also bacteremia, gastroenteritis
- **treatment**
  - ampicillin or TMP/SMX
**AEROBIC BACTERIA . . . CONT.**

**Bacillus cereus**
- **microbiology**
  - spore-forming, motile
- **mode of transmission**
  - ubiquitous organism
- **transmission** food contaminated with endospores (fried rice)
- **pathogenic mechanisms**
  - enterotoxins and pyrogenic toxin
- **clinical features**
  - vomiting syndrome
    - occurs 2-3 hrs post infection
    - nausea, vomiting (100%), and diarrhea (33%), fever uncommon
  - diarrheal illness
    - occurs 6-14 hrs post infection
    - diarrhea (100%), vomiting (23%)
  - endophthalmitis (IV heroin users)
- **diagnosis**
  - culture specimen from suspected food source
- **treatment**
  - clindamycin or vancomycin
  - resistant to beta-lactam antibiotics
  - no antibiotic treatment for food poisoning since caused by the pre-formed enterotoxin

**Nocardia asteroides, Nocardia farcinica**
- **microbiology**
  - elongated rods, branched at acute angles, showing irregular staining
  - weakly acid-fast
- **mode of transmission**
  - commonly found in the environment (soil)
  - transmitted by inhalation
  - not person-to-person transmission
- **clinical features**
  - pulmonary nocardiosis
    - ~50% have underlying disease or compromised immunity due to treatment (e.g. leukemia, lymphoma, COPD, chronic steroid use, HIV)
    - can disseminate to distant organs forming multifocal abscesses (brain, lymph nodes, lung)
- **diagnosis**
  - Gram stain, acid-fast stain, cultures
- **treatment**
  - TMP/SMX and surgical drainage

**GRAM NEGATIVE COCCI**

**Neisseria meningitidis (Meningococcus)**
- **microbiology**
  - diplococci
  - 9 serogroups based on capsular polysaccharides (A, B, C, W, Y)
  - obligate human pathogen
- **mode of transmission**
  - colonizes pharynx (15%)
  - droplet transmission
  - periodic epidemics; most cases occur in winter and spring involving children < 5 yrs
  - risk factors: splenectomy, complement deficiency (C8, C9) Hypogammaglobulinemia
  - high risk people: closed populations, e.g. army recruits (carrier rates > 40%)
- **pathogenic mechanisms**
  - capsule is antiphagocytic
  - pili for attachment to epithelial cells
  - toxic effects of lipopolysaccharide
- **clinical features**
  - asymptomatic colonization in the nasopharynx
  - meningitis
    - fever, vomiting, nuchal rigidity, headache lethargy
    - petechial rash, hemorrhages, thrombocytopenia
  - meningococcemia (see Colour Atlas ID1)
    - fever, petechial rash, hemorrhages, thrombocytopenia
    - palpable purpura strongly suggests N. meningitidis
    - hypotension, shock
    - fulminant meningococcemia (Waterhouse-Friedrichsen Syndrome)
      - bilateral adrenal hemorrhage
      - petechial rash, hemorrhages, thrombocytopenia, purpura
      - hypotension, gangrene
- **diagnosis**
  - Gram stain and culture of CSF necessary
  - bacterial meningitis has CSF with high number of cells
  - antigen detection (latex agglutination in CSF)
- **treatment**
  - polysaccharide vaccine (used in epidemics); A, C, Y, W, B135 covered
  - antibiotics
    - penicillin, third generation cephalosporins
    - rifampin, minocycline, ciprofloxacin used prophylactically for close contacts
AEROCBIC BACTERIA... CONT.

**Neisseria gonorrhea** (Gonococcus/GC)
- **microbiology**
  - diplococci
  - obligate human pathogen
- **mode of transmission**
  - transmitted sexually via contact with secretions (asymptomatic carriers), vertical transmission
- **pathogenic mechanisms**
  - pili: antigenic variation
  - endotoxin, IgA protease
- **clinical features**
  - asymptomatic (but still infectious)
  - local infection in men
    - urethritis (purulent discharge and dysuria), epididymitis, proctitis, pharyngitis
  - local infection in women
    - cervicitis (copious yellow discharge)
    - urethra, anus, and pharynx can be infected
    - can progress to pelvic inflammatory disease with complications including sterility, ectopic pregnancy, abscess, peritonitis, Fitz-Hugh Curtis syndrome (gonococcal perihepatitis)
    - disseminated infection in both men and women
      - gonococcal bacteremia
      - pustular skin rash (dermatitis/arthritis syndrome)
      - tenosynovitis
      - septic arthritis: GC arthritis is the most common cause in sexually active individuals
    - neonatal infection
      - ophthalmia neonatorum (usually within the first 5 days)
- **risk factors for disseminated disease**
  - menstruation
  - complement deficiency (C8, C9)
- **diagnosis**
  - Gram stain, culture
  - in smears of exudate, GC is typically found in PMN cells
  - + microscopic finding must be confirmed with culture
- **treatment**
  - erythromycin eye drops immediately following birth for neonatal GC and *Chlamydia* conjunctivitis prophylaxis
  - 1st line: third generation cephalosporin (ceftriaxone IM or cefixime PO x 1 dose unless disseminated)
  - second line: spectinomycin, fluoroquinolone
  - always treat with doxycycline to cover coinfecting *Chlamydia trachomatis*
  - report to public health, treat partner
  - follow-up cultures to ensure for cure

**Moraxella catarrhalis**
- Gram negative diplococci
- obligate human pathogen
- recently recognized as an important human pathogen in immunocompromised patients
- upper respiratory tract acts as reservoir and portal of entry for infection
- causes acute otitis media, sinusitis, bronchopneumonia
- 75% of strains produce beta-lactamase
- drugs of choice: amoxicillin-clavulanate, cephalosporins

**GRAM NEGATIVE BACILLI**

**Enterobacteriaceae**
- Includes *E. coli, Shigella, Salmonella, Proteus, Klebsiella, enterobacter, Serratia, Citrobacter, Yersinia*
- reservoir in GI tract; fecal-oral transmission
- ascending migration up the urethra
- colonization of catheters in hospitalized patients
- cause urinary tract infections, pneumonia, sepsis, nosocomial infections
- diagnosis by culture

**Escherichia coli**
- microbiology
  - normal gut flora, lactose-fermenter
- pathogenic mechanisms
  - capsule, flagella, pili, adhesins, enterotoxin
AEROBIC BACTERIA... CONT.

- **clinical features**
  1. enterotoxigenic (ETEC)
     - watery traveller's diarrhea, non-bloody
     - produces heat-labile and heat-stable enterotoxins
     - treatment: cipro +/- immodium (do not use Imodium if fever or blood)
  2. enterohemorrhagic (EHEC)
     - bloody diarrhea, no pus in stool, no fever
     - strain O157:H7 causes hemorrhagic colitis, hemolytic uremic syndrome due to verocytotoxins (Walkerton crisis)
     - treatment: none because antibiotics may enhance toxin release and increased risk of HUS
  3. enteroinvasive (EIEC)
     - bloody diarrhea, pus in stool, fever
     - urinary tract infections (most common cause)
     - newborn meningitis
     - sepsis
     - treatment: cipro, TMP/SMX, cephalosporin

**Klebsiella pneumoniae**
- microbiology
  - lactose-fermenter, mucoid colonies on culture
- mode of transmission
  - inhabits gut of humans/animals and in soil/water
  - infection either endogenous or acquired by contact
- pathogenic mechanisms
  - encapsulated and resistant to phagocytosis
- clinical features
  - pneumonia
  - significant lung necrosis, bloody sputum
  - risk factors: alcoholic, diabetics, elderly, lung disease
  - hospital-acquired urinary tract infections
  - nosocomial sepsis and wound infections
- treatment
  - imipenem, meropenem, fluoroquinolones (cipro), third-generation cephalosporins, aminoglycoside

**Enterobacter spp.**
- lactose-fermenting, encapsulated
- part of normal human gut flora, on plants
- causes nosocomial UTI, ICU infections, sepsis
- treatment
  - fluoroquinolones (cipro) or imipenem, TMP-SMX, may be resistant to third-generation cephalosporins

**Proteus mirabilis**
- microbiology
  - indole-negative, non lactose-fermenting, urease-positive, swimming motility seen as concentric rings on culture plates
- mode of transmission
  - endogenous infection, fecal contamination
- clinical features
  - urinary tract infection
  - turns urine alkaline due to urease (splits urea into NH₃ and CO₂)
  - associated with urinary calculi (struvite stones)
  - sepsis
- treatment
  - fluoroquinolones, cephalosporins (second/third generation), aminoglycoside

**Shigella**
- microbiology
  - several species differing in pathogenicity
  - nonmotile, non lactose-fermenter
- mode of transmission
  - obligate human pathogen, not part of normal human flora
  - highly communicable
  - fecal-oral contamination
- pathogenic mechanisms
  - invasion of small intestine mucosa helped by Shiga toxin and adhesins
- clinical features
  - bloody diarrhea with mucus, pus, tenesmus (similar to EIEC)
  - self-limited (3-4 days)
  - neurotoxic effects of Shiga toxin including meningismus, coma
  - severe illness at extremes of age
  - Reiter's syndrome may develop in HLA B27 hosts
- treatment
  - fluoroquinolones, TMP/SMX
**Salmonella typhi**

- **Mode of transmission**
  - Obligate human pathogen
  - Motile, non lactose-fermenter
  - Canadian cases are imported
  - Fecal-oral contamination, genital/anal-oral transmission

- **Pathogenic mechanisms**
  - Encapsulated/slime wall resists phagocytosis
  - Able to multiply in macrophages
  - Diarrhea possibly due to altered electrolyte transport by toxin-like molecule
  - Antigenic variation of flagellae

- **Clinical features**
  - Typhoid fever
    - Insidious onset with headache, malaise, anorexia
    - High fever (stepwise increase in temperature), abdominal pain, diarrhea, hepatosplenomegaly
    - Rose spots on abdomen
    - Cholecystitis characterizes asymptomatic carrier state
  - Complications
    - GI hemorrhage and perforation (1%)
    - Relapses due to chronic carrier state with biliary tract colonization (5-10%)

- **Diagnosis**
  - Blood or stool for C&S, serology

- **Treatment**
  - Preventable with vaccine
  - TMP/SMX, ciprofloxacin, third-generation cephalosporin

**Non-typhoidal Salmonella spp. (S. enteritidis, S. typhimurium)**

- **Mode of transmission**
  - Zoonotic (pet turtles, indoor aquaria, chickens, uncooked eggs)
  - One of the most prevalent communicable bacterial infections

- **Pathogenic mechanisms**
  - Encapsulated; able to multiply in macrophages
  - Diarrhea likely due to toxins

- **Clinical features**
  - Gastroenteritis - self-limited (2-5 days); no treatment
  - Paratyphoid fever - similar to typhoid fever
  - Osteomyelitis - especially in sickle-cell patients
  - Bacteremia
  - Risk factors: abnormal cell-mediated immunity (in AIDS patients, bacteremia can be recurrent)

- **Diagnosis**
  - Stool for C&S

- **Treatment**
  - Prevent with adequate cooking, hygiene practices

**Pseudomonas aeruginosa**

- **Microbiology**
  - Non lactose-fermenter, oxidase-positive, motile

- **Mode of transmission**
  - Commonly found free living in moist environments
  - Can be cultured from sinks, showers, hot tubs
  - Pathogen of plants, animals, and humans
  - Transmission via water, soils, foods, inhalation, ingestion, penetration through breaks in epithelium

- **Clinical features**
  - Opportunistic infection
  - Pneumonia in cystic fibrosis along with *Burkholderia cepacia* and in immunocompromised patients
  - Nosocomial infections
  - Burn wound infections, urinary tract infections
  - Endocarditis (IV drug users), sepsis
  - Malignant otitis externa (diabetics)
  - Corneal infections (contact lens wearers, post trauma or surgery)

- **Treatment**
  - Piperacillin + tobramycin, cefazidime, ciprofloxacin, imipenem

**Campylobacter jejuni**

- **Microbiology**
  - Comma-shaped rods, motile, oxidase-positive

- **Mode of transmission**
  - Zoonotic (animals, fowl)
  - Consumption of contaminated food, water, unpasteurized milk

- **Pathogenic mechanisms**
  - Motile, enterotoxins, adhesins

- **Clinical features**
  - Gastroenteritis
    - Usually self-limiting
    - Fever, abdominal pain, secretory or bloody diarrhea
    - Most common cause of bloody diarrhea in children
    - Responsible for 10% of acute diarrhea worldwide

- **Treatment**
  - Unclear role antimicrobials because the disease is usually self-limiting
  - Erythromycin, azithromycin, clarithromycin
  - Resistance to fluoroquinolone increasing
**Helicobacter pylori**
- **microbiology**
  - small curved rods, urease-positive
- **mode of transmission**
  - person-to-person transmission (oral-oral and fecal-oral)
  - prevalence of infection increases with age (about 1% per year) in developed countries
  - higher prevalence in developing countries, lower socioeconomic groups
- **exclusive to humans**
- **pathogenic mechanisms**
  - flagella
  - urease aids survival in extreme acid environment of stomach
  - urease and cytotoxin cause injury to stomach
- **clinical features**
  - causally associated with gastric ulcer (80%), duodenal ulcer (90%), gastric adenocarcinoma and MALT lymphoma
  - infection is commonly asymptomatic
  - causal association with non-ulcer dyspepsia has not been established
- **diagnosis**
  - gastric biopsy, culture, serology and saliva antibody tests
  - urease tests: ¹⁴C-urea breath test
- **treatment**
  - indicated only if ulcer is present
  - triple therapy: “OAC” omeprazole, amoxil/metronidazole clarithromycin (90% eradication)

**Vibrio cholerae**
- **microbiology**
  - short comma-shaped rods, oxidase-positive, thrives in alkaline medium
- **mode of transmission**
  - fecal-oral, contaminated food, only in human beings
  - 1991 Latin America epidemic, 1993 epidemic in Bangladesh and India
- **pathogenic mechanisms**
  - flagella, fimbriae help with attachment to cells
  - enterotoxin (A and B subunits) causes secretion of fluid into the intestinal tract
- **clinical features**
  - cholera
    - nausea, vomiting, abdominal cramping
    - massive watery diarrhea (rice water stools)
    - no pus in stools, no tissue invasion
- **diagnosis**
  - stool culture
- **treatment**
  - fluid, electrolyte replacement
  - doxycycline, fluoroquinolones, TMP/SMX
  - vaccine of limited benefit

**Haemophilus influenzae**
- **microbiology**
  - pleomorphic coccobacillus
  - type B (based on capsule) is most virulent
- **mode of transmission**
  - a human commensal
  - type B colonizes pharynx (5%), especially young children
  - transmitted via respiratory route
  - secondary household cases occur in contacts
- **pathogenic mechanisms**
  - capsule, IgA protease, slows beating of cilia
- **clinical features**
  - meningitis
    - was most common cause of meningitis in children (1-3 years)
    - Hib vaccine in Canada has led to decreasing incidence of invasive Hib disease
  - pneumonia
    - especially in children, alcoholics, COPD
  - acute epiglottitis
  - conjunctivitis
  - septic arthritis in infants
  - cellulitis in children
  - sepsis (especially if asplenic)
  - osteomyelitis in sickle-cell patients
  - nonencapsulated (nontypable) H. influenzae causes otitis media, sinusitis
- **diagnosis**
  - Gram stain, culture
- **treatment**
  - prevention of invasive disease: Hib polysaccharide vaccine
  - prophylaxis with rifampin for household contacts of meningitis
  - second or third generation cephalosporins since H. influenzae can acquire ampicillin resistance by plasmids
  - steroids in children with H. influenzae meningitis may decrease complications (i.e. deafness)
**Haemophilus ducreyi**
- sexually transmitted
- chancroid: painful genital ulcer often associated with unilateral swollen lymph nodes
- treatment
  - azithromycin, erythromycin, ceftriaxone IM, ciprofloxacin

**Bordetella pertussis**
- microbiology
  - Gram negative coccobacillus
- mode of transmission
  - colonizes pharynx; transmitted via respiratory route
  - highly contagious
  - high risk groups: infants < 1 year; adults (since immunity acquired from vaccine wears off)
- pathogenic mechanisms
  - capsule, adherent fimbriae, phase variation
  - pertussis toxin, tracheal cytotoxin
  - attachment to and immobilization of cilia; not invasive
- clinical features
  - whooping cough
    - catarrhal phase (1-2 weeks - highly contagious)
    - low grade fever, runny nose, mild cough
    - antibiotic susceptible
    - paroxysmal phase (2-10 weeks)
      - whoop on inhalation (nonproductive cough), vomiting, cyanosis
      - antibiotics ineffective during this stage
    - convalescent stage
- diagnosis
  - culture, ELISA, identification by immunofluorescence
- treatment
  - prevent with new acellular pertussis vaccine
  - erythromycin (catarrhal phase)

**Legionella pneumophila**
- microbiology
  - small, nutritionally fastidious pleomorphic rods/coccobacilli
  - weakly acid-fast
  - facultative intracellular parasite
- mode of transmission
  - thrives in non-maintained water environments (air conditioning systems, cooling towers)
  - transmitted via inhalation of airborne organisms, not person-to-person
  - risk factors: cell-mediated immunodeficiency, chronic steroid usage, nursing homes, elderly, smoking
- pathogenic mechanisms
  - capsule, motile, cytotoxin, multiplies in macrophages
- clinical features
  - Legionnaire’s disease
    - pneumonia, fever, non-productive cough
    - multilobar pneumonia and diarrhea
  - Pontiac fever
    - headache, fever, muscle aches and fatigue
    - self-limited acute febrile illness
- diagnosis
  - culture, serology, direct fluorescent antibody, DNA probes
- treatment
  - erythromycin +/- rifampin, or ciprofloxacin

**Yersinia enterocolitica**
- mode of transmission
  - reservoir in wild and domestic animals
  - ingestion of contaminated food, water or unpasteurized milk
- pathogenic mechanisms
  - motile, enterotoxin
- clinical features
  - acute enterocolitis (usually in infants and young children)
  - fever, diarrhea, abdominal pain
  - bacteremia
- diagnosis
  - stool C&S
- treatment
  - antibiotics do not alter the course of the diarrhea
  - if bacteremic, treat with fluoroquinolone
**AEROBIC BACTERIA . . . CONT.**

*Yersinia pestis*
- mode of transmission
  - reservoir mainly in squirrels, prairie dogs, rats in southwest U.S.
  - fleas serve as vectors between rodents and humans
- pathogenic mechanisms
  - virulence factors allow organism to resist phagocytosis
  - reproduce intracellularly
- clinical features
  - swollen, hot, painful lymph node (usually inguinal)
  - fever, headache, general malaise
  - hemorrhages under skin turn blackish: “Black Death”
  - death in a few days if untreated
- diagnosis
  - C&S
- treatment
  - TMP/SMX or quinolone

*Pasteurella multocida*
- mode of transmission
  - part of normal flora of domestic and wild animals (cat or dog bite)
- pathogenic mechanisms
  - capsule
- clinical features
  - wound infections may progress to nearby bones and joints
- diagnosis
  - culture
- treatment
  - amoxicillin-clavulinic acid, cefuroxime

**ANAEROBIC BACTERIA**

**GRAM POSITIVE COCCI**

*Anaerobic Streptococci/ Peptostreptococci/ Peptococci*
- microbiology
  - Gram positive cocci in chains
- mode of transmission
  - normal colonization of oral cavity, GI tract, vagina
- clinical features
  - sinusitis, dental, abdominal, lung, brain abscesses, postpartum endometritis
- diagnosis
  - culture
- treatment
  - penicillin, clindamycin

**GRAM POSITIVE BACILLI**

*Clostridium tetani*
- microbiology
  - large Gram positive rods, spore-former
- mode of transmission
  - reservoir: soil, splinters, rusty nails, GI tract (humans and animals)
  - endospores introduced through wound, germinate under anaerobic conditions
  - 50% of wounds can have history of minor or no environmental contamination
  - neonatal tetanus: contamination of umbilical cord at delivery
- pathogenic mechanisms
  - exotoxin: tetanospsasmin attaches to peripheral nerves in region of wound and transmitted to cranial nerve nuclei (via involved motor neurons or hematogenously)
  - inhibits release of GABA from nerve cells leading to sustained muscle contraction (spastic paralysis)
- clinical features
  - tetanus
    - symptoms after approximately 14 days
      - muscle spasms, lockjaw (trismus), risus sardonicus (facial spasm)
      - respiratory muscle paralysis
      - mentally alert, fever rare
      - mortality 50%
  - diagnosis
    - clinical (ddx: stiff man syndrome, malignant neuroleptic syndrome)
    - Gram stain, culture
Clostridium botulinum

- **mode of transmission**
  - reservoir: soil, stored vegetables (home-canned/zip-lock storage), fresh honey
  - ingestion of heat-resistant endospores

- **pathogenic mechanism**
  - neurotoxin inhibits release of acetylcholine from peripheral cholinergic nerves
  - flaccid paralysis occurs 12-36 hours post ingestion
  - exotoxin heat-labile

- **clinical features**
  - food-borne botulism
    - toxin-contaminated food – no colonization and invasion by organism
    - severe dryness of mouth and pharynx
    - progressive descending paralysis: cranial nerves (diplopia and blurred vision) -> dysphagia -> striated muscle weakness -> respiratory paralysis
    - no systemic signs of fever or sepsis
  - infant botulism (< 6 months)
    - traumatic wound contaminated by spores – toxins produced at wound site
    - severe neurological disease similar to food borne botulism
    - constipation, flaccid paralysis (“floppy baby”) -> cry becomes feeble and suck reflex weakens

- **diagnosis**
  - Gram stain, culture, toxin in serum
  - ddx: myasthenia Guillain-Barré, diphtheria

- **treatment**
  - antitoxin
    - administer ASAP
    - acquired from horses therefore high incidence of hypersensitivity
  - penicillin
  - supportive therapy (respiratory support, parenteral nutrition)

- **outcome**
  - may last weeks with treatment (however individual muscles may be paralysed for months or permanently)
  - mortality rate with supportive care 25%

Clostridium perfringens

- **mode of transmission**
  - reservoir: ubiquitous in dust, soil, air and GI tract (humans and mammals)
  - wound contamination or ingestion of endospores
  - germinate under anaerobic conditions

- **pathogenic mechanism**
  - alpha toxin acts as a lecithinase (leading to cell necrosis – gas gangrene)
  - collagenase facilitates spread
  - beta toxin destroys neutrophils

- **clinical features**
  - food poisoning
    - mediated by enterotoxin
    - symptoms within 24 hours
    - self-limited diarrhea (lasting 24 hours)
  - soft tissue infections
    - simple wound contamination without disease
    - superficial skin ulcers/bed sores, not systemically ill
    - necrotizing fascitis
      - cellulitis with fascitis and gas in fat layer
    - gas gangrene
      - clostridial myonecrosis: sudden pain around wound, frothy discharge, edema, fatal if untreated
      - systemic: fever, sweating, hypotension, decrease U/O, shock, renal failure
    - uterine infections
      - following instrumentation
      - septic abortion

- **diagnosis**
  - Gram stain, culture, x-rays

- **treatment**
  - radical surgery (may require amputation)
  - penicillin, clindamycin +/- hyperbaric oxygen (inhibits production of α-toxin and suppresses growth of organism)
  - antitoxin not recommended
**ANAEROBIC BACTERIA . . . CONT.**

**Clostridium difficile**

- **mode of transmission**
  - reservoir: intestinal tract, endospores contaminate environment (hospitals, nursing homes)
  - ingestion of endospores
- **pathogenic mechanism**
  - toxin A: induces watery fluid secretion
  - toxin B: cytotoxic to colonic epithelial cells
- **clinical features**
  - variable severity
  - pseudomembranous colitis (antibiotic-associated diarrhea)
    - usual suspect antibiotics: clindamycin, ampicillin, cephalosporins
  - occasionally fever, abdominal pain
- **diagnosis**
  - immunoassay test for C. difficile toxin B
  - colonoscopy to look for pseudomembranous colitis (raised plaques - "swollen rice grains", bleed when scraped)
- **treatment**
  - terminate use of the causative antibiotic (when possible)
  - metronidazole PO/IV; or vancomycin PO
  - metronidazole-resistant C. difficile strains isolated

**GRAM NEGATIVE BACILLI**

**Bacteroides fragilis**

- **microbiology**
  - non-spore-forming, slender rods
- **mode of transmission**
  - normal flora of GI tract and vagina
- **clinical features**
  - abscesses in abdomen, pelvis, and lungs, often as part of mixed infection
  - breach of bowel wall —> to peritoneal cavity —> abscess
- **diagnosis**
  - Gram stain, culture
- **treatment**
  - penicillin resistant
  - metronidazole, clindamycin, cefoxitin or piperacillin
  - surgically drain abscesses

**Clinical Pearl**

- **Suspect anaerobic infections when there is foul smelling pus or gas**
  - with both gram-positive and gram-negative organisms on Gram stain.

**OTHER BACTERIA UNDETECTABLE BY GRAM STAIN**

**ACID-FAST**

**Mycobacterium tuberculosis (TB)**

- **microbiology**
  - slow growing aerobe
  - resistant to drying and chemicals
  - intracellular survival and replication in macrophages
- **mode of transmission**
  - inhalation, ingestion of droplets
- **most disease is reactivated latent infections years after primary infection**

**Pathophysiology**

Alveolar macrophages (infections)

macrophages activated (move to hilar nodes: CD4 response, inflammation within 30 days, PPD positive, CXR-opacities)

- tubercules (small granulomas in tissue) ——> caseation ——> heal spontaneously (infection contained)
  - invade blood stream (1 miliary TB)
  - reactivation (2º)
risk factors for infection
- travel to or born in country with high prevalence of TB
- First Nations people, homeless, correctional facility, personal or occupational contact with infected person
- substance abuse, older age

risk factors for progression from infection to disease (Primary or Secondary)
- immunocompromised: HIV, DM, chemotherapy, lymphoma, long-term steroid use
- alcohol abuse, IV drug abuse, gastrectomy, malnutrition
- ESRD
- silicosis (pulmonary)
- pregnancy or immediately post-partum
- recent TB conversion; old, healed, untreated TB

clinical features
- primary TB
  - asymptomatic (self-limited pneumonitis)
  - overt disease (lower lungs, miliary TB, meningitis)
- secondary TB (reactivation) – majority occur within first 2 years after infection
  - insidious onset, chronic in nature
- pulmonary
  - constitutional symptoms common (fatigue, anorexia, night sweats, weight loss)
  - chronic productive cough, +/- hemoptysis
  - apical, posterior upper and superior lower lobe pneumonia
  - caseating necrosis/cavitiation
- miliary TB
  - wide-spread dissemination – especially to spleen, liver, bone marrow, kidneys, adrenals, lungs
  - multiple nodules in lung (small, millet seeds)
- extrapulmonary TB
  - lymph nodes (common)
  - pleura, pericardial, intra-abdominal, CNS (meningitis most common), GU, bone (spine most common)
  - eyes, skin, soft tissue (infrequent)

diagnosis
- positive PPD skin test indicates infection but not necessarily disease (test may be negative due to anergy if patient has impaired cellular immunity)
- microbiology: sputum, bronchoscopy, gastric aspiration, or needle aspiration to obtain sample (1) microscopy (sensitivity 40-60%, specificity 99%) employing acid-fast stain (report in 1 day), Ziehl-Neelsen stain; (2) culture (sensitivity 82%, specificity 98%) - definitive diagnosis, report in 2-3 weeks
- rapid PCR tests to confirm species
- CXR
  - parenchyma - nodular or alveolar infiltrates in upper lung zones, cavituation
  - pleural effusion – usually unilateral and exudative
  - hilar/mediastinal adenopathy – usually unilateral (90%)
  - tuberculoma – solitary coin lesion (0.5-4 cm), well-defined border, with calcification and adjacent ‘satellite’ lesions (can represent active or healed lesion)
  - miliary TB – discrete nodules (1-5 mm diameter) scattered throughout lungs
  - normal CXR – rare; can occur with endobronchial or laryngeal disease
  - evidence of past disease: calcified hilar and mediastinal nodes, calcified focus, pleural thickening with calcification, scarring in upper lung zones (note: if any are present with a new pulmonary process, suspect active TB)

prevention
- BCG (Bacille-Calmette-Guérin) vaccine – questionable efficacy
- INH prophylaxis for positive skin test (if converted within 2 years), age < 35, HIV

treatment
- initial phase Rx: isoniazid, rifampin, pyrazinamide +/- ethambutol (in combination to kill bacteria and prevent emergence of drug resistance) x 2 months
- continuation phase Rx: isoniazid, rifampin x 4 months
- suspected drug resistance: add ethambutol or IM streptomycin for 12 months

Mycobacterium leprae (Hansen’s Disease)
microbiology
- uncultivable, grows very slow at low temperatures
- survives and multiplies in macrophages

mode of transmission
- low infectivity
- transmission via contamination of nasal mucosa or minor skin lesions with infected nasal secretions
- most individuals have innate immunity

clinical features
- spectrum of disease determined by host immune response to infection
- chronic granulomatous disease
- tuberculoid leprosy
  - red blotchy lesions with anesthetic areas on face, trunk, extremities
  - palpable thickening in peripheral nerves
  - high cell mediated immune response
  - self-limiting or progression to lepromatous form
- lepromatous leprosy
  - diminished delayed hypersensitivity (low cell diated immunity)
  - leonine facies (loss of eyebrows, thickened enlarged nares, ears, cheeks)
  - skin and nerves involved
  - systemic progressive disease
OTHER BACTERIA UNDETECTABLE BY GRAM STAIN . . . CONT.

- **diagnosis**
  - skin biopsy or split skin smears
- **treatment**
  - rifampin, dapsone, clofazimine, ofloxacin, doxycycline

*Nocardia* (see Aerobic Gram Positive Bacilli section)
- Gram positive but weakly acid-fast

**SPIROCHETES**

*Treponema pallidum*
- **microbiology**
  - detectable by dark-field microscopy
  - thick, rigid, spiral-shaped, and motile
  - extremely sensitive to heat and drying
- **mode of transmission**
  - humans only
  - transmitted sexually, vertically, or by blood
- **clinical features**
  - primary syphilis *(see Colour Atlas ID11)*
    - painless genital chancre at ~ 21 days following infection
    - acute disease, 9-90 day duration, 50% develop secondary syphilis
    - regional lymphadenopathy
  - secondary syphilis *(see Colour Atlas ID13)*
    - subacute disease, occurs at 4-8 weeks after infection
    - rash on palms and soles, macular/papular, scaly, non-pruritic
    - bacteraemia - systemic spread
    - generalized lymphadenopathy
    - condyloma lata: painless, wart-like lesion in warm, moist places (vulva or scrotum)
    - CNS, eyes, bones, kidneys, and/or joints can be involved
  - latent syphilis
    - asymptomatic disease > 1 year
    - 2/3 of patients with secondary syphilis
  - tertiary syphilis
    - chronic disease
    - occurs 15-20 years after initial infection
    - gummas (nodular granulomas) of skin, bone, liver, testis
    - cardiovascular syphilis (aortitis, aneurysms)
    - neurosyphilis due to vasculitis or direct invasion (strokes, dementia, personality changes, Argyll-Robertson pupils, tabes dorsalis -“Charcot joint”)
  - congenital syphilis
    - causes spontaneous abortion, stillbirths, congenital malformations, mental retardation
    - infant presents with rhinitis, fever, lymphadenopathy, bone and cartilage degeneration, hepatosplenomegaly, rash
    - Jarisch-Herxheimer reaction: acute worsening of symptoms after antibiotics are started (release of endotoxin) (e.g. hypotension)
- **diagnosis**
  - screening tests (VDRL or RPR) - high false positive rate
  - confirmatory tests (TP, FTA-ABS, MHA-TP)
  - cutaneous lesions examined by dark-field microscopy, silver stain
- **treatment**
  - IM benzathine penicillin (drug of choice)/erythromycin/doxycycline
  - neurosyphilis: penicillin G (IV for 10 days)

*Borrelia burgdorferi*
- **microbiology**
  - motile, spiral organism
- **mode of transmission**
  - reservoir: white-footed mouse, white-tailed deer
  - carried and transmitted by tick bite (Ixodes) in wooded areas in summer and fall
- **clinical features**
  - Lyme disease
    - stage 1 (early localized stage)
      - erythema chronicum migrans (ECM)
      - flu-like symptoms (malaise, fatigue, H/A, myalgias, etc.)
      - large expanding bull’s eye lesion at site of tick bite
    - stage 2 (early disseminated stage)
      - days to weeks post stage 1
      - multiple smaller ECM
      - CNS: aseptic meningitis, CN palsies, peripheral neuropathy, cerebellar ataxia
      - cardiac: transient heart block or myocarditis
      - MSK: brief attacks of arthritis of large joints (esp. knee)
    - stage 3 (chronic)
      - chronic arthritis
      - encephalopathy, meningitis, neuropathy
OTHER BACTERIA UNDETECTABLE BY GRAM STAIN . . . CONT.

- diagnosis
  - PCR (synovial fluid), culture (biopsy erythema), ELISA, western immunoblotting
- treatment
  - doxycycline, amoxicillin, or cefuroxime
- prevention
  - insect repellent, inspecting for ticks after exposure
  - vaccination available 15-70 year olds who live or visit high risk areas

INTRACELLULAR PARASITIC BACTERIA

Chlamydia trachomatis

- microbiology
  - not detectable by Gram stain
  - grown in cell culture
  - multiply in macrophages
- mode of transmission
  - human reservoir only
  - sexually transmitted (commonly occurs with GC)
  - vertical transmission
- clinical features
  - sexually transmitted disease
  - women: urethritis, cervicitis, PID, perihepatitis (Fitz Hugh Curtis Syndrome)
  - men: nongonococcal urethritis, epididymitis, prostatitis
  - trachoma (Chronic Follicular Keratoconjunctivitis)
  - organism grows in conjunctival cells, causes inflammation and scarring of the inside of the eyelid
  - redirection of the eyelashes onto the cornea resulting in scarring and blindness
  - worldwide most common cause of blindness
  - lymphogranuloma venereum
    - STD characterized by painless papules on external genitalia and inguinal lymphadenopathy
    - leads to genital enlargement and swelling
  - neonatal pneumonia and conjunctivitis
  - reactive arthritis
- diagnosis
  - serology: swab or urine sample, ELISA (poor sensitivity)
- treatment
  - doxycycline or azithromycin (see Gynecology Chapter)

Chlamydia pneumoniae (strain TWAR)

- human reservoir with respiratory person-to-person transmission
- causes atypical pneumonia in young adults
  - viral-like, similar to mycoplasma-induced pneumonia
- diagnosis by serology
- treat with erythromycin or doxycycline

Bartonella henselae

- Gram negative pleomorphic rods
- seen on Warthin-Starry stain
- transmitted via cat scratch or dog contact
- causes Cat-Scratch disease
- primary papule, regional lymphadenopathy, hepatosplenic involvement, fever
- diagnosis by suggestive history and physical, skin test, lymph node histopathology, serology
- usually self-limited

MISCELLANEOUS

Mycoplasma pneumoniae

- microbiology
  - smallest known bacteria capable of growth and reproduction outside a living cell
  - no cell wall, therefore not detectable by Gram stain
  - highly pleomorphic
  - small colonies resembling ‘fried eggs’ on culture
- mode of transmission
  - reservoirs: human carriers, animals, environment
  - person-to-person via inhaled droplets
- clinical features
  - classic atypical pneumonia (walking pneumonia)
    - fever with a dry, non-productive hacking cough
    - headache prominent, sore throat, myalgias
    - occasionally, hemolytic anemia (with cold agglutins)
    - most common in 15-40 year old age group
    - clinical findings and CXR are much worse than symptoms
- diagnosis
  - 60-80% by presentation and CXR (typically bronchopneumonia)
  - cold agglutinins, complement fixation test, culture (requires 2-3 weeks), DNA probes
- treatment
  - self-resolving
  - can use erythromycin, doxycycline, or levofloxacin
VIRUSES

- Viruses are composed of an internal core containing single or double-stranded DNA or RNA, covered by a protein coat, and may have a surrounding envelope of glycoprotein.
- Virion is a single virus particle.
- Classification of human viruses based on:
  - Nature of nucleic acid (DNA vs. RNA, double-stranded (ds) vs. single-stranded (ss))
  - Structure of virion (symmetry)
  - Presence or absence of a viral envelope.
- Persistent vs. latent viral infections:
  - Persistent: virus continues to replicate
  - Latent: no replication, genome incorporated (latency important in retrovirus, herpes virus, adenovirus, papillomavirus).

**Table 2. Families of Viruses**

<table>
<thead>
<tr>
<th>Genome</th>
<th>Non-Enveloped</th>
<th>Enveloped</th>
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<tr>
<td>DNA</td>
<td>ds</td>
<td>ss</td>
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<tr>
<td>Adenovirus</td>
<td>Parovirus</td>
<td>Herpesvirus</td>
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<td>Papovavirus</td>
<td>Picornavirus</td>
<td>Hepadnavirus</td>
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<td>RNA</td>
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<td>Deltavirus</td>
<td>Retrovirus</td>
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</tbody>
</table>

**Figure 3. Stages of Viral Growth Cycle**

- Attachment and penetration by parental virion
- Uncoating of viral genome
- Synthesis of early viral mRNA
- Replication of viral genome
- Possible integration into host DNA
- Synthesis of late viral mRNA
- Assembly of progeny virion
- Release of virion from cell
**HERPES VIRUSES**

- large, enveloped viruses with double-stranded, linear DNA genome that are capable of establishing latent infections
- 8 herpes viruses: HSV1, HSV 2, VZV, EBV, CMV, HHV6, HHV7, HHV8 (causes Kaposi's sarcoma)

**Herpes Simplex Virus (HSV) Types 1 and 2**

- **modes of transmission**
  - HSV 1 or 2 transmitted via saliva, mouth-to-skin contact, autoinoculation of eyes, sexual intercourse, and birth canal
- **pathogenic mechanisms**
  - dormant in nerve root ganglion
  - reactivation associated with UV light, immunosuppression, trauma to skin, illness, fever, change in temperature
- **clinical features**
  - vesicular lesions in clusters with a erythematous base
  - HSV 1: oral herpes (gingivostomatitis/cold sores), ocular herpes (keratitis), encephalitis, disseminated herpes (see Colour Atlas ID12)
  - HSV 2: genital/anal herpes, neonatal herpes, meningoencephalitis
  - with exception of ocular herpes, meningoencephalitis, and encephalitis, any other herpes associated infections can be caused by both HSV 1 and HSV 2
- **diagnosis**
  - viral culture: “gold standard”
  - Tzanck smear - specimen scraped from base of lesion reveals multinucleated giant cells (syncytia) and intranuclear inclusion bodies
  - serology (retrospective diagnosis), immunofluorescence, PCR
- **treatment and prevention**
  - acyclovir, valacyclovir or famciclovir for primary episode of genital infection, neonatal infection, encephalitis
  - chronic suppressive treatment in severe or frequent recurrent genital disease, or in compromised host
  - virus can be shed even in the absence of visible lesions
  - avoid contact with vesicular lesions or ulcers
  - Cesarean section for pregnant women who have genital lesions and ruptured membranes for less than 4 hours, especially if a primary infection

**Varicella-Zoster Virus (VZV)**

- **mode of transmission**
  - highly contagious (infection rate 85% among household contacts)
  - transmitted via aerosolized droplets and contact with ruptured vesicles
- **pathogenic mechanisms**
  - zoster (shingles) is reactivation of dormant virus in dorsal root ganglion
- **clinical features**
  - varicella (chicken pox) (see Pediatrics Chapter)
  - primary infection usually in childhood
  - incubation period 10-21 days, average 14 days
  - fever and headache (2 days prior to skin rash)
  - rash is the simultaneous presence of different stages of eruption
  - infectious 48 hrs before lesions appear to several days after scab formation
  - complications include secondary bacterial skin infection (including GAS), thrombocytopenia, interstitial pneumonia (adults), acute cerebellar ataxia, encephalitis and death in neonates and immunocompromised patients
  - zoster (shingles)
  - pain may precede eruption by 48-72 hrs
  - unilateral painful vesicular eruption usually confined to a single dermatome (however, may involve adjacent or multiple dermatomes)
  - if involves CN V1 dermatome, high risk of corneal involvement (see Colour Atlas ID9)
  - vesicles form crusts that disappear in 3 weeks
  - complications: post-herpetic neuralgia
- **diagnosis**
  - clinical presentation (most important)
  - culture and immuno fluorescent stains
  - Tzanck smear reveals multinucleated giant cells and intranuclear inclusion bodies
- **treatment**
  - normal host (child 2-12 years)
  - only symptomatic treatment
  - fever: acetaminophen for fever (avoid ASA in children because of association with Reye's syndrome)
  - pruritus: antihistamine, calamine lotion, oatmeal colloid bath, baking soda baths
  - adolescents, adults, and immunocompromised hosts: antiviral medication within 24 hours of onset to shorten illness duration and to decrease post-herpetic neuralgia
  - acyclovir IV to prevent visceral disseminated zoster, does not prevent viral entry into nerve ganglia
  - famciclovir and valacyclovir have higher bioavailability and lower dosing frequency
- **prevention**
  - vaccine effective and available in Canada (recommended by Canadian Pediatrics Association)
  - VZIG post-exposure for high risk patients
Clinical Pearl


Epstein-Barr Virus (EBV)

- **mode of transmission**
  - transmitted via saliva, bodily secretions, organ/blood donation, intimate contact (e.g. kissing)
- **clinical features**
  - infection acquired early and usually asymptomatic
  - infectious mononucleosis (see Pediatrics Chapter)
    - triad of fever, lymphadenopathy, and exudative pharyngitis (50% of patients)
    - splenomegaly, palatal petechiae, hepatomegaly (10% of patients)
  - complications: rash if given ampicillin, neurologic complications
  - cancers associated with EBV include lymphoproliferative diseases: Burkitt’s lymphoma, nasopharyngeal carcinoma, transplant-associated lymphomas, Hodgkin’s disease
  - EBV associated with opportunistic infections in AIDS (hairy oral leukoplakia)
- **diagnosis**
  - lymphocytosis with atypical lymphocytes (see Colour Atlas ID1)
  - monospot test to detect presence of heterophile antibodies (false negative common in children, false positive with lymphoma, hepatitis)
  - EBV-specific antibodies
- **treatment and prevention**
  - only supportive
  - avoid contact sports for one month (risk of splenic rupture)
  - steroids indicated for pharyngeal swelling causing airway obstruction, severe thrombocytopenia, hemolytic anemia
  - antibiotics for secondary bacterial infection

Cytomegalovirus (CMV)

- **mode of transmission**
  - transmitted via all bodily fluids (including tears and breast milk), vertically (TORCH infection), organ/blood donation
  - most adults have been infected with CMV
- **clinical features**
  - infection acquired early and usually asymptomatic
  - congenital disease (severity ranging from rash and hearing loss to microcephaly and mental retardation)
  - reactivation in immunocompromised patients
  - can affect a number of organs causing retinitis, hepatitis, pneumonitis, esophagitis etc.
  - CMV “mononucleosis” syndrome - fever, splenomegaly, abnormal LFTs, lymphocytosis
  - differentiate from EBV infection via age (older, mean age 29), milder disease, typhoidal (fever with minimal adenopathy)
- **diagnosis**
  - isolation of virus in urine culture (or culture of other secretions)
  - cytology (owl’s eye inclusion bodies)
  - screen for antibodies
  - antigen detection, PCR
- **treatment and prevention**
  - normal host and congenital CMV ruled out
  - no treatment indicated
  - immunocompromised host
    - ganciclovir, foscarnet for CMV related complications (colitis, esophagitis, pneumonia)
  - transplant patients
    - CMV IG, acyclovir to decrease infections
    - matching donor and recipient of blood, bone marrow or organs based on CMV serology

Human Herpes Virus 6 (HHV6)

- **mode of transmission**
  - transmitted via saliva
- **clinical features**
  - roseola (exanthem subitum)
    - most common in children under two years of age
    - high fever (non-toxic, child looks well) lasting 3-5 days, post-auricular lymphadenopathy
    - followed by rose-pink rash as fever subsides, mostly on the trunk, lasting 1-2 days
- **diagnosis**
  - clinical presentation
- **treatment and prevention**
  - supportive only
PAPOVAVIRUS
- small non-enveloped viruses with double-stranded, circular DNA genome that is capable of integrating into host genome or existing as an episome
- family members include human papilloma virus and JC virus (causing progressive-multifocal leukoencephalopathy in HIV patients)

Human Papilloma Virus (HPV)
- microbiology
  - over 50 antigenic types
- mode of transmission
  - transmitted via sexual contact (genital, oral warts) or skin-skin contact (plantar, hand warts) *(see Colour Atlas ID4)*
- clinical features
  - common warts, genital warts, laryngeal warts (recurrence common)
  - cervical dysplasia and cancer (types 16, 18), anal dysplasia
- diagnosis
  - clinical
  - PAP smear
  - ELISA, PCR
- treatment and prevention
  - wart removal by: liquid nitrogen, excision, electrocautery, podophyllin, alpha-interferon, trichloroacetic acid, aldera
  - many warts resolve spontaneously in 1-2 years
  - relapses are common after treatment because HPV DNA is found in normal appearing tissue around the wart
  - avoid contact with lesions

ADENOVIRUSES
- microbiology
  - non-enveloped viruses with linear, double-stranded DNA genome
  - almost 100 different serotypes, 47 affecting humans and subdivided into 6 subgroups
- mode of transmission
  - transmitted via aerosol, direct contact, sexual contact, and fecal-oral route
- clinical features
  - potential for prolonged infection without disease
  - respiratory: URTI, pneumonia, pharyngitis
  - ocular: epidemic keratoconjunctivitis, pharyngoconjunctival fever
  - GU: acute hemorrhagic cystitis in children, cervicitis, urethritis
  - GI: gastroenteritis
- diagnosis
  - virus isolates from lung biopsy, urine, conjunctival or NP swabs
- treatment and prevention
  - no specific therapy
  - live, non-attenuated vaccine used in military but no vaccine for civilian use

OTHER DNA VIRUSES
- Parvovirus: non-enveloped viruses with single-stranded, linear DNA genome *(e.g. parvovirus B19 - erythema infectiosum)*
- Hepadnavirus: enveloped viruses with double-stranded, partly circular DNA genome *(e.g. Hepatitis B) *(see Gastroenterology Chapter)*
- Poxvirus: large, enveloped viruses with double-stranded, linear DNA genome *(e.g. smallpox, cowpox)*
RNA VIRUSES

RETROVIRUSES
HIV (see Infections in the Compromised Host section)

Human T-Cell Lymphotropic Virus (HTLV) Types I and II
- HTLV Type I: causative agent of certain cutaneous adult T-cell leukemia/lymphoma; implicated in HTLV-I myelopathy (tropical spastic paraparesis)
- transmission by blood, breast milk, and sexual intercourse
- increased incidence in those of Japanese or Caribbean descent

PICORNA VIRUSES
- 5 genera (enterovirus, rhinovirus, aphthovirus, cardiovirus, hepatovirus)
- small, naked virus with single-stranded RNA genome

Enteroviruses
- microbiology
  - includes poliovirus, coxsackie A and B, echoviruses
- mode of transmission
  - transmitted via fecal-oral route
  - replicate in lymphoid tissue of pharynx and GI tract resulting in transient viremia (to CNS, PNS in polio)
  - humans are the only natural host
- clinical features
  - poliovirus: poliomyelitis (flaccid paralysis)
  - coxsackie A: hemorrhagic conjunctivitis, aseptic meningitis, herpangina, URTI, hand-foot-and-mouth disease
  - coxsackie B: myocarditis, pleurodynia, aseptic meningitis, orchitis
  - echovirus: aseptic meningitis, maculopapular rash, febrile illness
- diagnosis
  - CSF: high lymphocytosis, normal to slightly decreased glucose, normal to slightly increased protein
  - culture (pharynx, feces)
  - serology
- treatment and prevention
  - supportive treatment
  - poliomyelitis can be prevented by killed (Salk) and live-attenuated vaccine (Sabin)
  - no vaccine available for echovirus, coxsackie
  - good personal hygiene

Rhinoviruses
- microbiology
  - more than 100 serological types
  - also known as common cold viruses
- mode of transmission
  - transmitted via large and small particle aerosols and fomites
  - replication in upper respiratory tract
- clinical features
  - major causes of mild URTI syndromes in all age groups, especially older children and adults
  - incubation period 2-4 days followed by rhinorrhea, sneezing, cough, sore throat and headache lasting for 2-3 days
  - complications: sinusitis, OM, COPD exacerbation
- diagnosis
  - clinical presentation
  - serological tests are not done
- treatment and prevention
  - no specific therapy but zinc lozenges may shorten symptomatic period
  - no vaccine available
  - hand washing and disinfecting contaminated objects

ORTHOMYXOVIRUSES
- includes influenza A, B
- enveloped viruses with segmented, negative-sense RNA genome, capable of genetic reassortment

Influenza Virus
- microbiology
  - type A has greatest virulence and potential epidemic and pandemic spread
  - antigenic drift occurs every few years in type A and B, antigenic shift in type A only
- mode of transmission
  - transmitted via aerosols
  - human and animal reservoirs (birds, pigs)
- clinical features
  - incubation period 1-4 days followed by "the flu": fever, coryza, cough, myalgias, arthralgias, headache, malaise lasting 3-7 days
  - complications: secondary bacterial pneumonia in the elderly and chronically ill
- diagnosis
  - clinical presentation, culture, IFA of nasopharyngeal swabs, serology
RNA VIRUSES . . . CONT.

- treatment and prevention
  - supportive treatment
  - zanamivir and oseltamivir for decreasing the duration and severity of symptoms (if initiate < 48 hours)
  - amantadine prophylaxis (in outbreaks or for prophylaxis of type A)
  - vaccine consisting of killed influenza A and B viruses is recommended annually for everyone
  - vaccine is reformulated each year to contain current serotypes of influenza A and B

PARAMYXO VIRUSES
- enveloped viruses with single-stranded, -ve sense, RNA genome
- family includes parainfluenza, RSV, measles and mumps

Parainfluenza Virus
- microbiology
  - four subtypes (1-4)
- mode of transmission
  - transmitted via respiratory droplets
- clinical features
  - type 1: acute croup (laryngotracheobronchitis)
  - type 2: associated with croup and mild URI and occasionally with acute lower respiratory disease; outbreaks usually in fall months
  - type 3: major cause of severe lower respiratory disease in infants and young children; often causes bronchiolitis, pneumonia, croup in those < 1 year; infections are common and can occur in any season
  - type 4: least common; generally associated with mild URTI
- diagnosis
  - serology
  - virus isolation
  - direct immunofluorescence for antigen detection
- treatment and prevention
  - supportive treatment (see Pediatrics Chapter)
  - live-attenuated vaccine given to children at 15 months of age

Respiratory Syncytial Virus (RSV)
- mode of transmission
  - transmitted via contact with nasal secretions, fomites and by inhalation of aerosols
- clinical features
  - most children infected by age 4
  - incubation period of 4-5 days followed by bronchiolitis and pneumonia lasting up to 2 weeks in infants
  - children and adults have milder illness: febrile rhinitis, pharyngitis, bronchitis
- diagnosis
  - virus isolation, direct immunofluorescence of nasopharyngeal (NP) swab
- treatment and prevention
  - supportive treatment
  - ribavirin aerosol treatment might be effective in some circumstances (e.g. patient with underlying chronic heart/lung disease or immunodeficiency)
  - no vaccine available

Measles (Rubeola)
- microbiology
  - also known as morbillivirus
- mode of transmission
  - epidemics in nonimmunized groups
  - transmitted via respiratory route
  - highly communicable
- clinical features
  - incubation period 10 days (range 5-21)
  - symptoms: high fever, cough, coryza and conjunctivitis (the 3Cs)
  - 1-3 days after onset, pinpoint gray-white spots surrounded by erythema appear on oral mucosa (Koplik's spots)
  - 12-24 hours later the maculopapular and confluent measles rash starts on the head and progresses to the trunk and extremities (descending pattern)
  - typical illness lasts 7-11 days (more severe in adults)
  - complications
    - Respiratory: otitis media, sinusitis, pneumonia (2nd bacterial infection)
    - Hematological: thrombocytopenic purpura (rare)
    - CNS: encephalitis, meningoencephalitis (1/1000), subacute sclerosing panencephalitis (1/500 000)
    - GI: gastroenteritis, hepatitis
- diagnosis
  - usually clinical diagnosis
  - virus isolation from oropharynx or urine only required in atypical cases
  - rapid diagnosis by immunofluorescence
RNA VIRUSES . . . CONT.

Treatment and prevention
- Supportive measures and close observation for development of complications
- High-dose vitamin A in severe measles in kids <2 years
- Live-attenuated vaccine given to children after 12 months of age and at 4-6 years of age (see Pediatrics Chapter)
- Vaccine not given to pregnant women and immunocompromised patients

Clinical Pearl
- Koplik's spots are pathognomonic for measles. They are blue-grey lesions with erythematous base on buccal mucosa often next to second molars.

Mumps
- Microbiology
  - 1 serotype
- Mode of transmission
  - Transmitted via respiratory route and contact with infected saliva
  - Life-long immunity follows infection
- Clinical features
  - Incubation period of 12 to 29 days followed typically by fever and tender swelling of the salivary glands, especially the parotid glands
  - Swelling may be unilateral or bilateral and persists for 7-10 days
  - Complications
    - Develop within 1-3 weeks of onset of illness
    - Epididymoorchitis, meningitis, encephalitis, transverse myelitis, pancreatitis, oophoritis, nephritis, arthritis
- Diagnosis
  - Cell culture from saliva, throat swab, CSF, urine
  - Immunofluorescence
  - Serology
- Treatment and prevention
  - Supportive measures: Analgesia, warm and cold compresses
  - Live-attenuated vaccine given to children after 12 months of age and at 4-6 years (see Pediatrics Chapter)
  - Vaccine not given to pregnant women and immunocompromised patients

TOGA VIRUSES
- Enveloped viruses with single-stranded, +ve sense RNA genome

Rubella (German Measles)
- Microbiology
  - Also known as rubivirus
- Mode of transmission
  - Transmitted via respiratory route and transplacentally
- Clinical features
  - Mild URTI with lymphadenopathy (usually sub-occipital)
  - Macular rash prominent over the head, neck, and trunk; may be quite faint and last 1-3 days
  - Arthralgia, arthritis most common in women
  - Complications: Include thrombocytopenic purpura, post-infectious encephalitis, progressive rubella encephalitis (all rare)
  - Congenital rubella syndrome
    - Fetal damage with infection in first trimester
    - Visual defects, neurosensory hearing impairment, congenital heart disease, small for gestational age, microcephaly with mental retardation
    - Increases in utero mortality
- Diagnosis
  - Hemagglutination inhibition test, EIA or latex particle agglutination for serodiagnosis
  - Presence of IgG is evidence of immunity; rising IgG titer or presence of IgM is evidence of infection
- Treatment and prevention
  - Supportive treatment
  - Live-attenuated vaccine given after 12 months and at 4-6 years (see Pediatrics Chapter)
  - Prenatal counseling and screening for rubella status

RHABDO VIRUSES
- Bullet-shaped, enveloped virus containing single-stranded, -ve sense RNA

Rabies Virus
- Mode of transmission
  - Zoonotic infection, i.e., transmitted via animal bites
  - Reservoirs: All warm-blooded animals (dogs, cats, skunks, coyotes, foxes, raccoon, bats) but not rodents
RNA VIRUSES... CONT.

- clinical features
  - incubation can be from 2 weeks to years then travels to PNS and CNS
  - prodrome: fever, headache, sore throat, increased sensitivity around the healed wound site (duration of 2-10 days)
  - acute encephalitis (duration of 2-10 days)
  - hyperactivity, agitation, confusion, seizures, hypotonia
  - classic brainstem encephalitis (duration of 2-10 days)
    - cranial nerve dysfunction, painful contraction of pharyngeal muscles when swallowing liquids, resulting in hydrophobia and foaming of the mouth
    - coma and death due to respiratory centre dysfunction
  - fatal unless treated with post-exposure vaccine and immunoglobulin

- diagnosis
  - ante-mortem: immunofluorescence or PCR on skin biopsy, corneal impression, saliva; viral isolation; serology
  - post-mortem: direct immunofluorescence in nerve tissue; presence of Negri bodies (inclusion bodies in neurons)

- treatment and prevention (see Emergency Medicine Chapter)
  - post-exposure vaccine is effective
  - treatment depends on regional prevalence (contact Public Health)
  - if bitten by a possibly rabid animal (i.e. unusual behavior or wild animals)
    - capture animal and observe for 10 days
    - sacrifice animal and examine brain for Negri bodies
    - treat immediately if the animal cannot be captured, or if the animal is found to have rabies
  - clean wound
  - passive immunization with Human Rabies Ig
  - active immunization with killed rabies virus vaccine (human diploid cell vaccine x 5 doses over 1 month)
    - available for persons at high risk of exposure
    - vaccinate animals

SOME OTHER RNA VIRUSES
- Calicivirus: non-enveloped, +ve ssRNA viruses (Hepatitis E, Norwalk)
- Reovirus: non-enveloped, dsRNA viruses (Reovirus, Rotavirus)
- Flavivirus: enveloped, +ve ssRNA viruses (Hepatitis C, Yellow Fever, Dengue)
- Coronavirus: enveloped, +ve ssRNA viruses (Coronavirus)

Fungi

- mechanisms by which fungi cause disease:
  - mycotoxicoses e.g. aflatoxin, hallucinogenic mushrooms
  - hypersensitivity disease
  - colonization of host and resulting diseases

Yeast    Mold    Puff Balls    Mushroom

septal hyphae non-septal hyphae

Figure 4. Common Fungus Morphology

Illustration by Miyuki Fukuma

PRIMARY PATHOGENIC FUNGI

Histoplasma capsulatum

- microbiology
  - dimorphic (both yeast and mycelial forms)
  - mycelium in the environment
  - in tissue, a budding yeast usually found within macrophages

- mode of transmission
  - endemic in central USA, Ohio and Mississippi River Valleys
  - exposure to bird/bat excrement
  - inhalation of airborne spores in environment
  - present in soil of endemic regions
FUNGI . . . CONT.

- **clinical features**
  - acute primary (pulmonary): fever, cough, pneumonia
  - chronic cavitory (pulmonary): sputum, night sweats, calcified lesions can be seen on CXR (may look similar to TB)
  - disseminated infection in immunocompromised - especially in lung, spleen, liver, lymph node
  - complications: fibrosing syndromes of mediastinum, meningitis

- **diagnosis**
  - biopsy, serology, culture, exoantigen test

- **treatment**
  - itraconazole
  - amphotericin B (if immunocompromised patient, treatment failure, or rapidly progressive disease)

**Blastomyces dermatitidis**

- **microbiology**
  - dimorphic (mycelial and yeast forms)
  - big, broad, budding yeast in tissue

- **mode of transmission**
  - outbreaks primarily in midwest USA
  - Red River Valley, St. Lawrence Valley, Northern Ontario (Timmins)
  - inhalation of airborne spores in environment
  - infects and causes disease in humans, horses and dogs

- **clinical features**
  - also known as Chicago disease or Gilchrist’s disease
  - pulmonary infection: symptoms may resemble TB – fever, cough, weight loss
  - characteristically forms microabscesses and granulomata
  - associated bone lesions and skin lesions

- **diagnosis**
  - CXR: non-specific pulmonary infiltrates without calcification
  - bronchoalveolar lavage, skin biopsy
  - serology, culture

- **treatment**
  - itraconazole, amphotericin B

**Coccidioides immitis**

- **microbiology**
  - dimorphic (sporangia and mycelial forms)

- **mode of transmission**
  - desert areas of the southwest USA (San Joaquin Valley) and northern Mexico
  - epidemics associated with dust storms
  - inhalation of airborne arthrospores from environment (e.g. soil)

- **clinical features**
  - also known as desert rheumatism, and San Joaquin Valley fever
  - acute, self-limiting, benign respiratory infection in most persons (60%)
  - influenza-like syndrome: fever, chills, cough, chest pain, sore throat
  - disseminated - can affect the lungs, skin, bones and meninges
  - common opportunistic infection in AIDS patients

- **diagnosis**
  - KOH preparation and microscopy of specimen looking for doubly refractile spherules
  - culture, serology

- **treatment**
  - amphotericin B, ketoconazole, fluconazole

**OPPORTUNISTIC FUNGI**

- fungi which become pathogens due to an immunocompromised state (e.g. HIV infection, hematologic malignancies, transplantation, use of corticosteroids or cytotoxic drugs)

**Pneumocystis carinii**

- **microbiology**
  - previously classified as a protozoan
  - unicellular fungi

- **mechanism of transmission**
  - acquired at an early age by the respiratory route
  - remains latent in immunocompetent hosts
  - common opportunistic infection in AIDS patients
    - occurs when CD4 count < 200 x 10^6/L
    - 80% lifetime risk without prophylaxis

- **clinical features**
  - interstitial pneumonia (PCP)
    - bilateral interstitial disease
    - may also present with pneumothorax
    - fever, nonproductive cough, progressive dyspnea
  - elevated LDH in about 90% of patients
FUNGI . . . CONT.

- **diagnosis**
  - monoclonal staining of induced sputum or bronchoalveolar lavage
  - CXR: diffuse interstitial infiltrate, starts perihilar (98% bilateral)

- **treatment and prevention**
  - oxygen to keep SaO2 > 90%
  - TMP/SMX (PO or IV), TMP-dapsone (PO), pentamidine (IV), trimetrexate (IV), clindamycin + primaquine (PO), atovaquone (PO)
  - corticosteroids used as adjuvant therapy in those with severe hypoxia (pO2 < 60 mmHg or A-a O2 gradient > 35 mmHg)
  - prophylactic TMP/SMX or dapsone, aerosolized pentamidine, atovaquone for those at risk (see HIV section)

**Cryptococcus neoformans**

- **microbiology**
  - encapsulated yeast
  - serotypes A, B, C, D

- **mode of transmission**
  - long survival in pigeon droppings
  - inhalation of airborne yeast from environment
  - risk factor: immunocompromised state

- **clinical features**
  - primary pulmonary infection: pneumonitis, usually asymptomatic and self-limited
  - subacute or chronic meningitis
  - skin lesions - resembles *Molluscum contagiosum*
  - osteolytic bone lesions

- **diagnosis**
  - CSF: India-ink stain for oval budding cells surrounded by thick gelatinous capsule; cryptococcal antigen test
  - fungal culture (blood, urine, sputum, CSF)

- **treatment**
  - amphotericin B, fluconazole

**Candida albicans**

- **microbiology**
  - pseudohyphae and yeast forms
  - grows readily on ordinary culture media

- **mode of transmission**
  - normal flora of skin, mouth, vagina and GI tract
  - risk factors: immunocompromised state, broad-spectrum antibiotics, diabetes, corticosteroids

- **clinical features**
  - oral thrush, vulvovaginal candidiasis (see Gynecology Chapter), cutaneous (diaper rash, skin folds) *(see Colour Atlas ID10)*
  - immunocompromised host:
    - thrush, vaginitis and/or cutaneous
    - esophageal (retrosternal chest pain, odynophagia, fever)
    - endophthalmitis, endocarditis, UTI, hepatosplenic abscess
    - chronic mucocutaneous candidiasis

- **diagnosis**
  - mount scrapings in 10% KOH
  - Gram stain and culture

- **treatment**
  - thrush: swish and swallow nystatin or imidazole
  - vulvovaginal candidiasis: topical imidazole or nystatin; oral fluconazole
  - cutaneous infection: topical imidazole
  - AIDS opportunistic infections (thrush, esophageal, vaginal): fluconazole, itraconazole, ketoconazole
  - systemic candidiasis: amphotericin B, fluconazole
  - chronic mucocutaneous candidiasis: ketoconazole, fluconazole, itraconazole, or amphotericin B

**Aspergillus spp.**

- **microbiology**
  - branching septate hyphae
  - common species causing disease include *A. fumigatus, A. flavus*

- **mode of transmission**
  - ubiquitous in environment

- **clinical features**
  - risk of respiratory distress increases with age
  - allergic bronchopulmonary aspergillosis
    - IgE-mediated asthma-type reaction with dyspnea, high fever, and transient pulmonary infiltrates
  - secondary colonization - aspergilloma formation
    - fungus ball formation in pre-existing cavity (i.e. from old TB)
**FUNGI . . CONT.**

- invasive aspergillosis
  - associated with AIDS and leukopenic patients
  - necrotizing pneumonia
  - may disseminate to other organs in immunocompromised patients:
    - intracerebral abscess, necrotic ulcers in (skin, bone, liver, breast)
  - fatal if not treated early and aggressively
- mycotoxicosis
  - aflatoxin produced by A. flavus
  - toxin contaminates nuts, grains, rice
  - results in liver hemorrhage, necrosis, and hepatoma formation

- diagnosis
  - tissue biopsy with silver staining, culture (often negative)
  - CXR, CT

- treatment
  - itraconazole, amphotericin B
  - oral prednisone for allergic bronchopulmonary aspergillosis (no antifungal)
  - surgical resection for aspergilloma and hemorrhage

**PARASITES**

<table>
<thead>
<tr>
<th>Table 3. Comparison of Protozoa and Helminths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protozoa</strong></td>
</tr>
<tr>
<td>- unicellular</td>
</tr>
<tr>
<td>- trophozoite→ cyst</td>
</tr>
<tr>
<td>- multiplication</td>
</tr>
<tr>
<td>- no eosinophilia</td>
</tr>
<tr>
<td>- indefinite life span; i.e. will continue to multiply in host</td>
</tr>
</tbody>
</table>

* exceptions *Strongyloides stercoralis, Hymenolepis nana*
** highest eosinophilias are associated with tissue invading parasitic infections such as trichinosis, toxocariasis and filariasis
** helminths which do not invade (adult *Ascaris, tapeworms*) do not produce eosinophilia

**PARASITES (PROTOZOA)**

<table>
<thead>
<tr>
<th>amoeba</th>
<th>coccidia</th>
</tr>
</thead>
<tbody>
<tr>
<td>ciliate</td>
<td>apicomplex sporozite</td>
</tr>
<tr>
<td>flagellate</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 5. Representative Protozoa**

*Illustration by Miyuki Fukuma*
PARASITES (PROTOZOA) … CONT.

INTESTINAL AND VAGINAL

**Flagellates**
- protozoa with flagella for motility
- commonly cause disease via mechanical irritation and inflammation

**Giardia lamblia**
- mechanism of transmission
  - reservoir is infected humans and other mammals
  - waterborne transmission (especially in the Rockies) and fecal-oral transmission of infectious cysts
  - risk factors: institutions, daycare centres, homosexual men
- clinical features (Beaver Fever, giardiasis)
  - asymptomatic intestinal infection
  - watery diarrhea; may rarely cause steatorrhea and malabsorption
  - nausea, abdominal cramps, bloating, flatulence, fatigue, weight loss
- diagnosis
  - multiple stool samples (1 per day x 3 days)
  - occasionally, small bowel aspirate or biopsy for diagnosis
  - antigen detection in stool
- treatment and prevention
  - metronidazole, furazolidone, paromomycin, albendazole, atabrine
  - good personal hygiene and sanitation
  - municipal water should be filtered
  - avoid contaminated food

**Trichomonas vaginalis**
- mechanism of transmission
  - sexually transmitted
  - via birth canal
- clinical features (see Gynecology Chapter)
  - painful vaginal itching
  - burning on urination; males often asymptomatic
  - yellow-green, malodorous, frothy vaginal discharge (pH > 4.5)
- diagnosis
  - highly motile flagellated protozoa on examination of vaginal discharge or urine
- treatment
  - metronidazole to patient and partner

**Coccidia**
- part of Apicomplexa phylum
- intracellular parasite
- capable of asexual and sexual reproduction

**Cryptosporidium spp.**
- mechanism of transmission
  - reservoir: infected humans and a wide variety of young animals
  - fecal-oral transmission by the ingestion of feces containing infectious cysts; waterborne
  - risk factors: summer and fall, young children, homosexual men, contact with farm animals, HIV infection
- clinical features
  - asymptomatic carrier
  - immunocompetent patients: self-limited (within 10 days) watery diarrhea
  - immunocompromised patients: severe, large volume diarrhea with cachexia, weight loss and possible death
- diagnosis
  - modified acid-fast or acridine orange stain of stool specimen
- treatment and prevention
  - not usually effective
  - no treatment usually required for immunocompetent hosts
  - paromomycin partially effective in AIDS
  - good hygiene, sanitation
  - municipal water filtered

**Cyclospora spp.**
- mechanism of transmission
  - fecal-oral route
  - seen in travelers, sporadic cases elsewhere
  - recent outbreaks associated with contaminated water sources, Central American raspberries, and basil
  - parasite requires period of time outside host for maturation
- clinical features
  - clinically indistinguishable from giardiasis
  - often waxes and wanes
  - self-limited diarrheal illness, frequent watery stools, anorexia, fatigue, bloating
  - asymptomatic biliary tract disease
Parasites (Protozoa) … cont.

- Diagnosis
  - stool specimen
  - acid-fast stain of stool
  - parasite fluoresces under UV light

- Treatment and prevention
  - TMP/SMX
  - wash produce, filter municipal water
  - good hygiene and sanitation

Amoebae
- primitive unicellular parasites which reproduce via binary fission
- motility via pseudopod (false foot)

Entamoeba histolytica
- mechanism of transmission
  - reservoir: infected humans
  - fecal-oral transmission by the ingestion of feces containing infectious cysts or by insects carrying cysts (e.g. flies, cockroaches); waterborne
  - seen in immigrants, travellers, institutionalized individuals, Native Canadians
  - most strains are noninvasive and nonpathogenic, now designated Entamoeba dispar, indistinguishable microscopically from E. histolytica

- Clinical features
  - asymptomatic carrier state (most often)
  - intestinal amoebiasis: abdominal pain, cramping, colitis, dysentery, low grade fever with bloody diarrhea secondary to local tissue destruction of large intestine
  - extraintestinal amoebiasis: liver abscesses, leukocytosis, fever

- Diagnosis
  - stool exam
  - serology when invasive disease suspected
  - E. dispar distinguished from E. histolytica by stool antigen detection and PCR
  - serology usually negative in E. dispar infections

- Treatment and prevention
  - invasive: metronidazole plus iodoquinol or paromomycin
  - cyst/trophozoite passer: iodoquinol or paromomycin alone
  - good personal hygiene
  - purification of water supply

Blood and Tissue

Apicomplexa
- phyla consisting of coccidia and sporozoan protozoa
- intracellular, unicellular parasites with organelles at apex

Plasmodium spp.
- Microbiology
  - species include: P. falciparum, P. vivax, P. ovale, P. malariae
  - require two hosts for reproduction cycle: human host for asexual reproduction and mosquito for sexual reproduction

- Mechanism of transmission
  - reservoir: infected human
  - transmission by the night-biting female Anopheles mosquito, congenital, and blood transfusion
  - P. vivax and P. falciparum most frequently imported malarials

- Clinical features
  - malaria
    - headache, myalgia
    - periodic episodes (that occur with red cell lysis) of high fever and shaking chills, followed by diaphoresis
      - tertian malaria: episodes occur every 48 hours (P. vivax, P. ovale)
      - quartan malaria: episodes occur every 72 hours (P. malariae)
      - P. falciparum (most deadly): irregular fever spikes
      - anemia, thrombocytopenia, hepatosplenomegaly
  - complications of P. falciparum malaria
    - cerebral malaria, jaundice, hemoglobinuria, renal failure, ARDS
    - P. falciparum parasitemia > 5% fatal, often within several days
    - only P. vivax and P. ovale have dormant relapsing forms in liver

- Diagnosis
  - thick films: sensitive
  - thin films: to distinguish species
  - blood should be examined at 12-24 hour intervals (x 3) to rule out infection
PARASITES (PROTOZOA) . . . CONT.

Treatment

- *P. vivax*, *P. ovale*: chloroquine plus primaquine to eradicate liver forms
- *P. malariae*: chloroquine
- *P. falciparum*
  - most areas of world show drug resistance
  - quinine plus doxycycline, or atovaquone/proguanil (Malaxone) combination
  - alternative is mefloquine alone
  - if severe illness (> 10% parasitemia), then consider exchange transfusion

Prophylaxis/prevention

- chloroquine (in chloroquine-sensitive areas)
- if chloroquine resistance: mefloquine, doxycycline, primaquine, atovaquone/proguanil
- mosquito repellants, bed nets, screens

Toxoplasma gondii

- mechanism of transmission
  - 1/3 of Ontario population infected
  - acquired from ingestion of cat feces or poorly cooked meat from animals which are intermediate hosts (e.g. sheep, goats, cattle)
  - congenital infections only with a primary maternal infection (TORCH infection); as pregnancy progresses morbidity of fetus decreases but likelihood of infection increases

Clinical features

- congenital disease
  - stillbirth, chorioretinitis, blindness, seizures, mental retardation, microcephaly
  - normal appearing infant may develop reactivation of chorioretinitis as adolescent or adult
- acquired disease
  - usually asymptomatic
  - mononucleosis-like syndrome in immunocompetent patient
  - infection remains latent for life unless reactivation due to immunosuppression
  - immunocompromised patients (most commonly AIDS)
    - encephalitis with multiple ring enhancing masses on CT
    - lymph node, liver, and spleen enlargement and pneumonia

Diagnosis

- serology, histopathology, antigen or DNA detection (PCR)

Treatment and prevention

- pyrimethamine + sulfadiazine (add folinic acid), clindamycin
- spiramycin in early pregnancy; pyrimethamine/sulfadiazine in late pregnancy
- corticosteroids for eye disease
- cook meat thoroughly
- pregnant women to avoid undercooked meat and refrain from emptying cat litter boxes

Flagellates

Trypanosoma cruzi

- South and Central America
- vector-borne - reduviid bug, congenital and blood transfusion
- Chagas' Disease (American trypanosomiasis)
  - chronic cardiomyopathy +/- achalasia and constipation 10-25 years after acute, flu-like illness

Treatment

- treat acute cases with nifurtimox, benznidazole
- no treatment for chronic manifestations

Prevention

- insect control, bed nets when sleeping in adobe huts (mud walls, thatched roof)

Trypanosoma rhodesiense, T. gambiense

- East and West Africa
- vector-borne - tsetse fly bite and contaminated blood transfusion
- causes sleeping sickness (African trypanosomiasis)
  - systemic illness progresses to CNS involvement and coma
- treat with suramin, melarsoprol (for CNS involvement) or eflornithine (T. gambiense)

Leishmania spp.

- Africa, Middle East, and Latin America
- vector-borne - sandfly bite
- clinical picture depends on species and on patient's cell-mediated immune response
  - cutaneous --> single ulcer
  - diffuse cutaneous --> nodules all over body
  - mucocutaneous --> erodes nasal septum, lips, soft palate
  - visceral (Kala Azar) --> hepatosplenomegaly, fever, often fatal
- important opportunistic infection in AIDS patients, especially in southern Europe

Treatment

- efficacy and choice of treatment depends on infecting species
- treat cutaneous disease with stibogluconate, pentamidine, itraconazole, local heat or nothing
- treat visceral disease with stibogluconate, pentamidine, amphotericin B
### Table 4. General Features of Helminths

<table>
<thead>
<tr>
<th>Helminth</th>
<th>Shape</th>
<th>Reproduction</th>
</tr>
</thead>
</table>
| Nematode | • roundworm  
• large, cylindrical, unsegmented  
• filariae form (slender, long worm) in blood, lymph and subcutaneous tissue | male and female worms |
| Cestodes | • flatworms  
• flat, segmented, ribbonlike  
• each segment is called a proglottid  
• head comprised of four suckers and a crown of hooklets | hermaphroditic |
| Trematodes | • flukes  
• flat, fleshy, leaf-shaped  
• two muscular suckers  
• require intermediate hosts (e.g. snails) for asexual reproduction | hermaphroditic (except Schistosoma) |

### INTESTINAL

**Nematodes (Roundworms)**

*Strongyloides stercoralis (roundworm)*

- **mechanism of transmission**
  - transmission through unbroken skin, barefoot walking  
  - adult worms live embedded in mucosa of small intestine  
  - one of the only worms capable of multiplying in human host  
  - source of infection: fecal contamination of soil, autoinfection (larvae penetrate skin, enter circulation, migrate through lungs to the trachea, and are swallowed; adults reside in the small intestine)

- **clinical features**
  - mostly asymptomatic  
  - pruritic dermatitis at site of larval penetration  
  - transient pulmonary symptoms during pulmonary migration of larvae  
  - epigastric pain, rash, pruritus ani  
  - vomiting, diarrhea uncommon  
  - occasional fatal cases caused by massive auto-infection in immunocompromised host: triad of pneumonia, diarrhea and Gram negative bacteremia
PARASITES (HELMINTHS) . . . CONT.

- **diagnosis**
  - fecal exam for larvae (no eggs), larval culture on agar
  - small bowel biopsy
  - serology most sensitive (88%)
  - eosinophilia common

- **treatment**
  - albendazole, ivermectin, thiabendazole

*Ascaris lumbricoides* (roundworm)

- **mechanism of transmission**
  - ingestion of eggs
  - source of infection: fecal contamination of soil and vegetables, particularly in regions using human feces as fertilizer

- **clinical features**
  - asymptomatic in many individuals
  - adult worms live in small intestine and may exit nose or mouth of infected person
  - occasional obstruction of pancreatic or bile duct, appendix, or small bowel
  - dry cough, fever, transient pulmonary infiltrates (Loffler's syndrome), eosinophilia while larvae migrate in the lungs
  - children may develop malnutrition due to protein loss

- **diagnosis**
  - stool exam for eggs
  - dead adult worms in feces or vomitus
  - eosinophilia during migration phase, none during adult phase

- **treatment and prevention**
  - mebendazole, pyrantel pamoate, albendazole
  - good hygiene and sanitation

*Necator americanus, Ancylostoma duodenale* (hookworms)

- **mechanism of transmission**
  - through unbroken skin (barefoot walking)
  - source of infection is fecal contamination, ingestion of larvae

- **clinical features**
  - usually asymptomatic in light infections
  - itching at site of skin penetration
  - GI symptoms
  - worms attach to and suck blood from mucosa of small intestine leading to iron-deficiency anemia, peptic ulcer-like symptoms in heavy infections

- **diagnosis**
  - stool exam for eggs
  - mild eosinophilia

- **treatment**
  - mebendazole, pyrantel pamoate, albendazole

*Enterobius vermicularis* (pinworm)

- **mechanism of transmission**
  - humans only host
  - adult worms live in cecum and migrate at night to perianal skin to deposit eggs
  - self-inoculation by fecal contaminated hand-to-mouth, person to person contact, autoinfection

- **clinical features**
  - asymptomatic carrier state
  - severe nocturnal perianal itching
  - occasionally vaginitis

- **diagnosis**
  - sticky tape test (5-7 tests required to rule out infection)
    - examination of perianal area at night may reveal adult worms seen with unaided eye
    - no eosinophilia usually

- **treatment and prevention**
  - mebendazole, pyrantel pamoate, albendazole, pyrvinium pamoate
  - clean underwear change, pajamas to sleep, bathe in morning, wash hands after BM
  - treat all members of family simultaneously
  - reinfection common
Trichuris trichiura (whipworm)
- mechanism of transmission
  - ingestion of eggs in soil or on vegetables
  - large bowel parasite
- clinical features
  - rarely symptomatic
  - heavy infections: diarrhea, abdominal pain, rectal prolapse, stunted growth
- diagnosis
  - stool exam for eggs
  - mild/no eosinophilia
- treatment: mebendazole, albendazole

Cestodes (flatworms)

Taenia solium (pork tapeworm)
- mechanism of transmission
  - ingestion of cestode eggs or undercooked pork containing larvae
- clinical features
  - ingestion of larval cestode in pork leads to intestinal adult tapeworm infection
  - usually asymptomatic
  - ingestion of eggs (results in cysticercosis)
  - eggs hatch within the small intestine and larvae travel to subcutaneous tissue, muscle, CNS, and/or the eye, where they eventually form cysts to which the host responds with an inflammatory response as they die (after 4-5 years)
    - can develop blindness or neurological manifestations
    - neurocysticercosis is most frequent
    - headache, seizures, focal neurologic deficits, hydrocephalus
- diagnosis
  - stool exam for eggs or gravid proglottids to diagnose adult tapeworm
  - CT scan, MRI, biopsy of brain or soft tissue X-ray of muscle may reveal multiple cysts
  - serology is the most important diagnostic test for cysticercosis (no need to examine CSF serology)
  - no eosinophilia
- treatment and prevention
  - cysticercosis: albendazole is treatment of choice, praziquantel alternative
  - corticosteroids to treat “dead worm” reaction (inflammatory response due to larval death), associated with treatment of neurocysticercosis
  - treat tapeworm with albendazole or praziquantel
  - good sanitation and personal hygiene
  - avoid uncooked pork

Taenia saginata (beef tapeworm)
- mechanism of transmission
  - ingestion of undercooked beef containing larvae
- clinical features
  - can grow to 25 m in length in the small bowel
  - usually asymptomatic
  - occasionally develop abdominal discomfort, weight loss, and diarrhea; segments (proglottids) can crawl out of anus
- diagnosis
  - fecal exam for eggs or gravid proglottids
  - no eosinophilia
- treatment
  - praziquantel

Diphyllobothrium latum (fish tapeworm)
- mechanism of transmission
  - ingestion of raw freshwater fish containing larvae
- clinical features
  - can grow to 15 m in length in the small bowel
  - nonspecific abdominal symptoms
  - vitamin B12 deficiency, leading to macrocytic anemia and neurological findings
- diagnosis
  - fecal exam for eggs or gravid proglottids
  - no eosinophilia
- treatment and prevention
  - praziquantel
  - cook fish well before consumption
  - good sanitation
Trematodes (Flukes)

*Clonorchis sinensis*
- **mechanism of transmission**: ingestion of raw fish
- **clinical features**: mostly asymptomatic, worms reside in biliary tree
- **complications**: bile duct stones, recurrent pyogenic cholangitis, association with cholangiocarcinoma
- **diagnosis**: fecal exam for eggs, no eosinophilia
- **treatment**: praziquantel

BLOOD AND TISSUE

Nematodes

*Wuchereria bancrofti, Brugia malayi*
- adult worms produce larvae called microfilaria
- **mechanism of transmission**: transmitted through mosquito bite, migrate from bite site to lymphatic system
- **clinical features**: disease caused by inflammatory response to adult worms living in lymphatics, and in TPE, to microfilaria
  - febrile episodes associated with headache and painful, enlarged lymph nodes, and lymphangitis spreading distally in affected limbs
  - elephantiasis
    - following repeated infections, dying worms cause lymphadenitis and damage to lymphatics (dilatation and flow impediment)
    - results in swelling of the legs and genitals; damaged lymphatics lead to recurrent bacterial cellulitis
    - thick, scaly skin covers the edematous lower extremities, giving the appearance of elephant legs
  - tropical pulmonary eosinophilia (TPE)
    - hypersensitivity reaction with bouts of wheezing and coughing, associated with hypereosinophilia due to hyperimmune response to dying microfilariae in lungs
- **diagnosis**: look for microfilariae in blood drawn at nighttime, biopsy not optimal because nodes already damaged, serology (nonspecific but very sensitive), negative serology excludes viable infection, TPE shows marked increase in filaria antibodies, hypereosinophilia, reticular-nodular pattern on CXR, restrictive pattern on PFTs
- **treatment and prevention**: diethylcarbamazine, albendazole, insect repellants, protective clothing, mosquito control

*Onchocerca volvulus*
- **mechanism of transmission**: transmitted through blackfly bite (breeds in fast moving rivers and streams)
- **clinical features**: disease caused by inflammatory response to microfilariae
  - skin nodules contain adult worms
  - allergic reaction to microfilariae migrating through the dermis causes pruritic rash with depigmentation and thin scaly skin called “leopard skin” which may hang in folds
  - river blindness (onchocerciasis)
    - microfilariae migrate across the cornea or retina
    - an inflammatory response occurs with their death, which can lead to blindness due to keratitis or chorioretinitis
- **diagnosis**: skin snips reveal microfilariae, nodulectomy shows adult worms, eosinophilia common
- **treatment and prevention**: ivermectin; kills only microfilariae; need to repeat treatment every 6-12 months until adult dies in 10-20 years, excise nodules containing adult worms, protective clothing against insect bites, insect repellant
Cestodes

*Echinococcus granulosus* (canine tapeworm)

- **mechanism of transmission**
  - through ingestion of fertilized eggs
  - adults found in canines' intestines and pass in feces

- **clinical features**
  - hydatid disease
  - larval cysts bud internally to produce daughter cysts
  - hydatid cysts form most often in the liver, lung, and peritoneal cavity
  - the cysts slowly enlarge over 5 to 20 years
  - symptoms secondary to pressure effects of growing cyst
  - leakage of hydatid cyst fluid can cause an anaphylactic reaction (rare) or bile duct obstruction if leakage into biliary tree

- **diagnosis**
  - CT scan or U/S reveals cysts in the liver or lung
  - serology (very sensitive and specific)
  - eosinophilia (in 25% of cases)

- **treatment and prevention**
  - surgical evacuation of cysts: extreme caution is required, as leakage of cystic fluid can induce an anaphylactic reaction or give rise to new cysts in pleural or peritoneal cavities
  - cyst aspiration with scolicide instillation
  - albendazole used adjunctively or for cure (40% cure rate with albendazole alone)
  - protect sites of food preparation or animal slaughter against canines, particularly dogs

Trematodes

*Schistosoma* spp.

- **species**
  - *S. mansoni*, *S. hematobium*, *S. japonicum*, *S. mekongi*, *S. intercalatum*

- **mechanism of transmission**
  - found in tropics
  - through unbroken skin
  - acquired when larvae, released from snail, penetrate unbroken skin during exposure in slow-moving infested fresh water
  - adult worms live in terminal venules of bladder/bowel passing eggs into urine/stool
  - eggs must reach freshwater to hatch; schistosomes cannot multiply in humans
  - no person-to-person transmission because snail intermediate host is required

- **immunology**
  - molecular mimicry: incorporation of host antigens onto the surface of the schistosomes to mask themselves from host immune system
  - disease results from granulomatous response and fibrosis secondary to egg deposition in tissues

- **clinical features**
  - pruritic skin rash at site of penetration (cercarial dermatitis)
  - acute schistosomiasis (Katayama fever) at time of egg deposition (4-8 weeks after infection)
    - fever, hives, headache, weight loss, cough, abdominal pain, diarrhea (lasts up to 3 months), eosinophilia
  - complications
    - caused by granulomatous response and fibrosis secondary to egg deposition by adults in the veins surrounding the intestine or bladder
    - *S. mansoni*, *S. japonicum*
      - worms in mesenteric vein; eggs in portal tracts of liver and bowel
      - mostly asymptomatic
      - heavy infections: intestinal polyps, portal and pulmonary hypertension
    - *S. hematobium*
      - worms in vesical plexus; eggs in distal ureter and bladder
      - terminal hematuria and rarely obstructive uropathy
      - associated with bladder cancer

- **diagnosis**
  - serology (very sensitive and specific)
  - rectal biopsy for *S. mansoni* and *S. japonicum*
  - eosinophilia often
  - *S. mansoni*, *S. japonicum*: eggs in stool, liver U/S shows fibrosis
  - *S. hematobium*: bladder biopsy (eggs in urine and bladder wall)

- **treatment**
  - praziquantel
  - control with proper disposal of human fecal waste, mass chemotherapy and reduced exposure to infested water
ANTIMICROBIALS

GENERAL PRINCIPLES
- bactericidal vs. bacteriostatic therapy
- bacteriostatic = nonlethal inhibition of growth
- bactericidal therapy is indicated for patients with immunologic compromise, impaired regional defences or life-threatening infection (e.g. endocarditis and meningitis)
- most other infections can be treated effectively with either bactericidal or bacteriostatic drugs

ANTIBACTERIALS

CELL WALL SYNTHESIS INHIBITORS (BACTERICIDAL)

Beta-Lactams (e.g. Penicillins, Cephalosporins, Carbapenems)
- mechanism of action
  - competitively inhibit penicillin binding proteins (PBPs) which prevents cross linking of peptidoglycan strands normally needed for cell wall integrity → osmotic lysis of the bacterium
- mechanisms of beta-lactam resistance
  - altered PBP
  - production of beta-lactamase (cleaves beta-lactam ring)
  - decreased outer membrane permeability

Penicillins
- benzyl penicillin (susceptibility)
  - benzyl penicillin (narrow spectrum, resistance by beta-lactamase production)
    - e.g. penicillin G (IV or IM), penicillin V (PO)
    - effective against Streptococci, (PSSA), most anaerobes (not B. fragilis), Neisseria, and T. pallidum (syphilis)
  - isoxazoyl penicillin (narrow spectrum, beta-lactamase resistant)
    - e.g. methicillin, cloxacillin, oxacillin, nafcillin
    - effective against Staphylococci and some Streptococci; drug of choice for penicillin-resistant S. aureus (PRSA)
- aminopenicillins (broad spectrum, resistance by beta-lactamase production)
  - e.g. ampicillin, amoxicillin
  - effective against most Gram positives including Enterococci, some Gram negatives
- ureidopenicillins (extended spectrum, beta-lactamase sensitive)
  - e.g. piperacillin, carbencillin, ticarcillin
- combination of beta-lactam with beta-lactamase inhibitors (extended spectrum, beta-lactamase resistant)
  - e.g. amoxicillin-clavulanic acid, piperacillin-tazobactam, ampicillin-sulbactam
- side-effects
  - hypersensitivity reactions as described for penicillin
  - 15% cross-reactivity in setting of penicillin allergy
  - dose-related nephrotoxicity

Cephalosporins
- susceptibility
  - note: cephalosporins are ineffective against Enterococci, Listeria
  - 1st generation (e.g. cefazolin, cephalexin)
    - Gram positive cocci (except MRSA and Enterococci), Gram negative bacilli (mainly E. coli, Klebsiella, P. mirabilis)
  - 2nd generation (e.g. cefuroxime, cefetetan)
    - less Gram positive activity but more Gram negative coverage than 1st generation (H. influenzae, E. coli, Klebsiella, Proteus)
    - cefotetan has anaerobic activity and is used in intra-abdominal and pelvic infections
  - 3rd generation (e.g. cefotaxime, ceftriaxone, ceftazidime)
    - broad spectrum activity against Gram negatives, less Gram positive coverage than 1st generation
    - crosses blood-brain barrier ( unlike 1st and 2nd generation)
    - ceftazidime should be used if Pseudomonas coverage is required
  - 4th generation (e.g. ceftepime, ceftipirome)
    - broad spectrum activity against Gram negatives (including P. aeruginosa) and good coverage of Gram positive cocci (MRSA and Strep. pneumoniae)
    - useful in severe hospital or community-acquired infections (pneumonia, bacteremia)
- side-effects
  - hypersensitivity reactions as described for penicillin
  - 15% cross-reactivity in setting of penicillin allergy
  - dose-related nephrotoxicity
**ANTIBACTERIALS . . . CONT.**

**Carbapenems (e.g. Imipenem, Meropenem)**
- **mechanism of action**
  - imipenem inhibits cell wall synthesis
  - cilastin protects the kidney from toxicity and inhibits a renal enzyme that metabolizes imipenem, increasing its half-life
- **susceptibility**
  - broadest spectrum of activity against anaerobes, Gram positives (except *Enterococcus faecium* and MRSA), and Gram negatives, including *P. aeruginosa*
- **side-effects**
  - seizures (less likely with Meropenem)
  - cross-reactivity in patients with anaphylaxis to penicillin

**Glycopeptides (e.g. Vancomycin)**
- **mechanism of action**
  - blocks cell wall peptidoglycan polymerization resulting in loss of cell wall integrity and osmotic rupture of the bacterium
- **susceptibility**
  - only active against Gram positive organisms (e.g. *S. aureus*)
- **side-effects**
  - red person syndrome: histamine-mediated reaction with erythematous flushing of the trunk, neck, and face during infusion +/- associated hypotension
  - nephrotoxicity, ototoxicity, neutropenia, thrombocytopenia, rash, hypersensitivity
- **clinical indications**
  - true major penicillin allergic patients (e.g. anaphylaxis, exfoliative dermatitis, vasculitis, or severe urticaria)
  - MRSA infection
  - coagulase-negative *Staphylococcus* (e.g. *S. epidermidis*) in patients with prosthetic valves with joint or line infections
  - infections due to ampicillin-resistant *Enterococci*
  - 2nd line treatment for antibiotic-associated pseudomembranous colitis (C. difficile)

**PROTEIN SYNTHESIS INHIBITORS - VIA THE 50S RIBOSOME (BACTERIOSTATIC)**

**Chloramphenicol**
- **mechanism of action**
  - inhibits protein synthesis by binding to the ribosomal 50S subunit, which prevents the aminoacyl end of tRNA from associating with peptidyl transferase
- **susceptibility**
  - excellent coverage of most Gram positives and Gram negatives, including anaerobes
- **side-effects**
  - reversible or irreversible bone marrow depression, leukopenia, aplastic anemia, gray baby syndrome (toxic levels in newborns unable to conjugate drug; symptoms include abdominal distension, vomiting, cyanosis, hypothermia, death)

**Macrolides (e.g. Erythromycin, Clarithromycin, Azithromycin)**
- **mechanism of action**
  - inhibit protein synthesis by binding to the P site of the ribosomal 50S subunit, which prevents translocation of polypeptide chain
- **susceptibility**
  - cover *Mycoplasma, Legionella, Chlamydia, Treponema, Helicobacter pylori, Staphylococci, Streptococci, Gram positives*
- **side-effects**
  - GI upset, hepatotoxicity
- **clinical indications**
  - staphylococcal and streptococcal infections in patients allergic to penicillin

**Lincosamides (e.g. Clindamycin)**
- **mechanism of action**
  - inhibit protein synthesis by binding to 50S ribosomal subunit
- **susceptibility**
  - covers Gram positives and most anaerobes
- **side-effects**
  - pseudomembranous colitis, rashes, thrombophlebitis, reversible elevation of liver enzymes, blood dyscrasias (rare)
- **clinical indications**
  - anaerobic infections
~ VIA THE 30S RIBOSOME (BACTERICIDAL)

**Aminoglycosides (e.g. Gentamicin, Tobramycin, Amikacin, Streptomycin, Neomycin)**

- **mechanism of action**
  - Inhibit protein synthesis initiation by binding to the 30S ribosomal subunit thereby causing misreading of mRNA
- **susceptibility**
  - Primarily active against Gram negative aerobes and mycobacteria
  - Tobramycin is most active against *Pseudomonas aeruginosa*
  - Synergistic with penicillins against *Enterococci* and *Pseudomonas*
- **side-effects**
  - Nephrotoxicity, ototoxicity, vertigo, neurotoxicity

~ VIA THE 30S RIBOSOME (BACTERIOSTATIC)

**Tetracyclines (e.g. Tetracycline, Doxycycline)**

- **mechanism of action**
  - Inhibit protein synthesis by binding to the 30S ribosomal subunit thereby blocking amino acid linked tRNA from binding to the A site of the ribosome
- **susceptibility**
  - *Chlamydia, Mycoplasma, Rickettsia*, Gram positive cocci
- **side-effects**
  - GI upset, hepatotoxicity
  - Photosensitivity, dental staining (contraindicated in pregnancy, neonates, children)
- **clinical indications**
  - Used for acne and chlamydial infections
  - Doxycycline used for malaria prophylaxis and treatment

**FOLIC ACID METABOLISM INHIBITORS (BACTERIOSTATIC)**

**Co-Trimoxazole (Trimethoprim-Sulfamethoxazole, TMP/SMX)**

- **mechanism of action**
  - 2 mechanisms of interfering with folic acid synthesis as described for TMP and SMX (synergistic)
    - TMP inhibits dihydrofolate reductase which inhibits nucleic acid synthesis and bacterial growth
    - SMX competes with paraaminobenzoic acid for incorporation into folic acid which also inhibits nucleic acid synthesis and bacterial growth
- **susceptibility**
  - Broad spectrum Gram positives and Gram negatives
  - *Pneumocystis carinii*
  - *Isospora* and *Cyclospora* spp.
- **side-effects**
  - Kernicterus (sulfonamides compete with bilirubin for albumin sites), renal toxicity, photosensitivity, hemolysis, hepatotoxicity, fever, Stevens-Johnson Syndrome
- **clinical indications**
  - UTI, traveller’s diarrhea
  - *Pneumocystis carinii* pneumonia, *Isospora*, *Nocardia*, *Toxoplasma* infections

**DNA GYRASE INHIBITORS (BACTERICIDAL)**

**Quinolones (Ciprofloxacin, Levofloxacin, Moxifloxacin, Norfloxacin, Ofloxacin, Nalidixic Acid)**

- **mechanism of action**
  - Prevents supercoiling of nucleic acids
- **susceptibility**
  - Enteric Gram negative bacilli, limited Gram positive coverage
  - Levofloxacin has more activity against resp pathogens (*Legionella, Chlamydia, Pseudomonas, Mycoplasma*)
  - Unreliable activity against *S. pneumoniae*
  - No anaerobic coverage
- **side-effects**
  - CNS: seizures, headache, dizziness, ophthalmologic changes
  - Nausea, rash, pruritus, photosensitivity
  - Not recommended for children and pregnant women
- **clinical indications**
  - Mainly for UTI, pneumonia
  - Levofloxacin is first-line agent for community acquired pneumonia
  - Ciprofloxacin most active quinolone against *Pseudomonas*
ANTIBACTERIALS... CONT.

DNA-DIRECTED RNA POLYMERASE INHIBITORS (BACTERICIDAL)

Rifampin
- mechanism of action
  - inhibits bacterial protein synthesis by interacting with the DNA-dependent RNA polymerase, thus preventing chain initiation
- susceptibility
  - covers Gram positive cocci, many Gram negative bacilli, most Mycobacterium species
- side-effects
  - dizziness, abdominal pain, nausea, vomiting, diarrhea, visual changes, pruritus, rash, renal dysfunction
  - transient abnormalities in liver function, jaundice
  - turns tears, saliva, and urine orange-red
  - induces P450 enzymes and alters metabolism of oral contraceptives, oral hypoglycemics, coumadin, corticosteroids, digoxin, methadone

DNA COMPLEX DAMAGING AGENTS (BACTERICIDAL)

Metronidazole
- mechanism of action
  - intrabacterial activation of the drug leads to release of toxic metabolites that cause damage to the microbial DNA
- susceptibility
  - covers strictly anaerobic bacteria and several protozoan parasites (Giardia lamblia, Entamoeba histolytica, Trichomonas vaginalis) “G.E.T. MET”
- side-effects
  - major: disulfiram type reaction with alcohol, peripheral neuropathy
  - minor: anorexia, nausea, diarrhea, reversible neutropenia, metallic taste, dark or red-brown urine, rash
- clinical indications
  - anaerobic infections “below the diaphragm”
  - Trichomonas vaginits
  - invasive amoebiasis including liver abscesses
  - giardiasis
  - first line for pseudomembranous colitis (C. difficile)

ANTIMYCOBACTERIALS

ANTI-TUBERCULOSIS DRUGS

1ST LINE DRUGS (e.g. Isoniazid, Rifampin)

Isoniazid (INH)
- bactericidal agent that inhibits mycolic acid synthesis in mycobacterial cell walls
- side-effects include hepatitis, drug-induced lupus, peripheral neuropathies (prevent by pretreating with pyridoxine Vitamin B6)

Rifampin (see Antibacterials section)

2ND LINE DRUGS (e.g. Ethambutol, Pyrazinamide)

Ethambutol
- bactericidal agent that inhibits mycolic acid synthesis in mycobacterial cell walls
- side-effects include retrobulbar neuritis resulting in loss of central vision

Pyrazinamide (PZA)
- unknown mechanism of action
- side-effects include hepatotoxicity, gout, gastric irritation

Streptomycin (aminoglycoside) (see Antibacterials section)

3RD LINE DRUGS (e.g. Ethionamide, Cycloserine, Clofazimine)
- see below
ANTIMYCOBACTERIALS . . . CONT.

ANTI-M. AVIUM-INTRACELLULARE COMPLEX DRUGS

Clarithromycin, Azithromycin, Ethambutol (see Antibacterials section)

Rifabutin, Ethambutol

ANTI-LEPROSY DRUGS

Sulfones (e.g. Dapsone, Sulfoxone)
- action similar to that of sulfonamides (see Antibacterials Sulfonamides section)
- side-effects include skin rash, drug fever, agranulocytosis

Clofazimine
- functions by binding to Mycobacterium leprae DNA
- also has anti-inflammatory actions for treating the leprosy reactions
- major toxicity: skin discoloration

Rifampin (see Antibacterials section)

ANTIVIRALS

NON-NUCLEOSIDE POLYMERASE INHIBITORS

Interferon-alpha 2B
- mechanism of action
  - induces production of immune proteins that inhibit RNA synthesis
  - inhibits viral mRNA
  - available for subcutaneous injection
- susceptibility
  - used for chronic Hepatitis B and C, condyloma acuminatum (caused by HPV), Kaposi's sarcoma
- side-effects
  - flu-like syndrome: fever, headache, nausea, myalgias
  - neutropenia, thrombocytopenia
  - neurotoxicity, confusion

Amantadine/Rimantadine
- mechanism of action
  - inhibits the viral uncoating after entering the cell thereby blocking the release of viral genome into the cell
- susceptibility
  - orthomyxo viruses (influenza A)
  - paramyxo viruses
  - toga virus (rubella)
- side-effects
  - anticholinergic effects: blurred vision, dry mouth, flushed faces, urinary retention, psychosis
  - CNS (rare): confusion, anxiety, insomnia
  - teratogenicity: pregnant women should not use

Phosphonoformate
- mechanism of action
  - pyrophosphate analog inhibits viral DNA polymerase and reverse transcriptase by competing for pyrophosphate sites
- susceptibility
  - all Herpes viruses (including CMV), HIV related CMV retinitis, encephalitis + HSV esophagitis in AIDS
- side-effects
  - reversible nephrotoxicity
  - nausea, headache, fatigue, tremor
  - anemia, hypocalcemia, hypomagnesemia, hypophosphatemia
ANTIVIRALS...CONT.

NUCLEOSIDE ANALOGUES

- chemically modified nucleosides that are incorporated into growing viral DNA chains, thereby preventing elongation of the chains and inhibiting DNA polymerase
- new formulations of pro-drugs lead to increased serum concentrations

Anti-Retrovirals (see HIV/AIDS section)

Acyclovir

- mechanism of action
  - guanosine analogue uses viral thymidine kinase for phosphorylation into its active form
- susceptibility
  - highly potent, highly specific anti-herpetic agent
  - very potent against HSV 1, HSV 2, and VZV infections
  - only minor activity against EBV and CMV (use ganciclovir)
- side-effects
  - inflammation at injection site
  - crystalline nephropathy if drug is infused rapidly without adequate hydration
  - neurotoxic at high doses: confusion, lethargy, seizures

Ganciclovir

- mechanism of action
  - guanosine analog, activated by host cell thymidine kinase
  - induced by CMV infection
- susceptibility
  - CMV: retinitis, pneumonitis, esophagitis, prophylaxis in organ transplant patients
  - also effective against HSV, VZV, EBV but not used due to its high toxicity
- side-effects
  - hematologic: neutropenia, thrombocytopenia, anemia
  - rash, CNS toxicity, confusion, GI upset

Ribavirin

- mechanism of action
  - guanosine analog
- susceptibility
  - RSV bronchiolitis or pneumonia, influenza A or B infections
  - used with Interferon for Hep C
  - Lassa fever, Hanta virus pulmonary syndrome
- side-effects
  - little toxicity when given via aerosol (conjunctivitis)
  - extremely expensive
  - teratogenic

Table 5. Specific Viruses Targeted by Available Antiviral Drugs

<table>
<thead>
<tr>
<th>Virus</th>
<th>Antiviral Drug (Generic/Trade Name)</th>
<th>Class of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV, VZV</td>
<td>acyclovir/Zovirax</td>
<td>nucleoside analog</td>
</tr>
<tr>
<td></td>
<td>valacyclovir/Valtrex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>famciclovir/Famvir</td>
<td></td>
</tr>
<tr>
<td>CMV</td>
<td>phosphonoformate/Foscarnet</td>
<td>non-nucleoside polymerase inhibitor</td>
</tr>
<tr>
<td></td>
<td>ganciclovir/Cytovene</td>
<td>nucleoside analog</td>
</tr>
<tr>
<td>Influenza A</td>
<td>ribavirin/Virazole</td>
<td>nucleoside analog</td>
</tr>
<tr>
<td></td>
<td>amantadine/Symmetrel</td>
<td>non-nucleoside polymerase inhibitor</td>
</tr>
<tr>
<td>RSV</td>
<td>ribavirin/Virazole</td>
<td>nucleoside analog</td>
</tr>
<tr>
<td>HPV, Hep B/C</td>
<td>interferon alpha</td>
<td>immune system modulation</td>
</tr>
</tbody>
</table>
ANTIFUNGALS

POLYENES
- Bind to fungal cytoplasmic membrane sterols, particularly ergosterol, and change membrane permeability, resulting in cell death

Amphotericin B
- side-effects
  - acute: hypotension, fever, chills, nausea, vomiting, thrombophlebitis
  - reversible nephrotoxicity resulting in hypokalemia, hypomagnesemia, anemia, headache, thrombocytopenia, anaphylaxis, burning sensation in hands and feet
- clinical indications
  - systemic fungal infections: candidiasis, cryptococcosis, blastomycosis, histoplasmosis, coccidioidomycosis, aspergillosis, sporotrichosis, mucormycosis

Nystatin
- used for mucocutaneous candidiasis
- side-effects
  - few adverse effects when administered orally
  - large doses cause occasional GI distress and diarrhea

IMIDAZOLES
- mechanism of action
  - inhibit fungal cytochrome P450-dependent 14-alpha-demethylase
  - abnormal ergosterol synthesis
  - altered membrane permeability
  - cell death

Clotrimazole
- side-effects
  - insignificant toxicity when used topically
- clinical indications
  - topical fungal infections: Tinea versicolor, cutaneous candidiasis, dermatophytosis, vaginal candidiasis

Miconazole
- used topically for vaginal candidiasis
- side-effects include phlebitis, pruritus, nausea, fever, rash, vomiting

Ketoconazole
- pharmacokinetics
  - available in topical and oral forms (requires stomach acid for systemic absorption)
  - poor CSF penetration
- side-effects
  - GI: anorexia, nausea, vomiting, diarrhea, fatal hepatic necrosis (rare)
  - endocrine: dose-dependent increased serum testosterone and cortisol which can be manifested as gynecomastia, breast pain
  - skin: rash, pruritus
  - other: headache, dizziness
- clinical indications
  - chronic mucocutaneous candidiasis
  - ringworm, Tinea versicolor
  - nonmeningeal histoplasmosis and blastomycosis infections in immunocompetent hosts

TRIAZOLES
- mechanism of action as described for imidazoles

Fluconazole
- available in oral and IV forms
  - excellent CSF penetration (80% of serum levels)
- side-effects
  - less toxic than ketoconazole with no effect on testosterone or cortisol levels in serum
  - nausea, headache, rash, vomiting, diarrhea
- clinical indications
  - mucocutaneous candidiasis (including esophageal)
  - alternative to amphotericin B for treatment of systemic candidiasis, cryptococcal meningitis, coccidioidomycosis

Itraconazole
- available in oral form (requires stomach acid for absorption)
- side-effects
  - less toxic than ketoconazole with no effect on testosterone or cortisol levels
  - nausea, hepatitis, edema (rare)
- clinical indications
  - mucocutaneous candidiasis (including esophageal)
  - local Tinea versicolor and Tinea corporis
  - shows promise in treating severe systemic fungal infections (a safer alternative to amphotericin B)
  - active against Aspergillus spp.

MCCQE 2002 Review Notes
Infectious Diseases – ID45
ANTIPARASITICS

ANTI-PROTOZOAL DRUGS

Iodoquinol (see Amoebiasis section)
Metronidazole (see Antibacterials section)
TMP/SMX (see Antibacterials section)
Pentamidine
- unknown mechanism of action
- side-effects include dangerous hypotension, hypoglycemia, hypocalcemia if administered rapidly by IV, renal insufficiency
- used against Pneumocystis carinii and leishmaniasis

ANTI-MALARIAL DRUGS

Chloroquine
- mechanism of action
  - inhibition of heme polymerase causing build-up of toxic heme products
  - kills erythrocyte form but not liver form of Plasmodium vivax and P. ovale
- side-effects
  - ophthalmologic: colour vision changes, central visual loss, and retinal damage (do not occur in doses used to prevent malaria)
  - Gl disturbances, dizziness, headache, non-allergic pruritus (in black skin)
- clinical indications
  - treatment and prophylaxis against malaria caused by non-resistant species
  - used in combination with primaquine for nonresistant P. vivax and P. ovale

Primaquine
- mechanism of action
  - kills liver hypnozoites of P. vivax and P. ovale
  - mechanism unclear but likely to involve crosslinking of glutathione
- side-effects
  - acute hemolytic anemia if G6PD deficient, GI upset
- clinical indications
  - use in combination with chloroquine for liver stage of P. vivax and P. ovale; prophylaxis of all malaria species including chloroquine-resistant P. falciparum

Quinine
- mechanism of action
  - cinchonism = quinine adverse effects = ears (tinnitus, vertigo), eyes (visual disturbances), Gl (nausea, vomiting, diarrhea), CNS (headache, fever); occurs in most users
  - acute hemolytic anemia if G6PD deficient (rare)
  - hypotension when given IV too rapidly
  - blackwater fever (rare): massive lysis of RBC causing dark urine with hemoglobinuria, renal failure, DIC, and possibly death
  - hypoglycemia due to insulin release from pancreas
- clinical indications
  - use in combination with Fansidar, clindamycin or doxycycline for chloroquine-resistant P. falciparum or parenterally for those who cannot tolerate oral medication

Mefloquine
- mechanism of action
  - mechanism as for chloroquine; kills erythrocytic forms
- side-effects
  - GI upset, headache, nightmares, irritability, depression (moderately severe 1:200)
  - seizures and psychosis (1/250 for treatment, 1/3 000 for prophylaxis)
- clinical indications
  - used for treatment of chloroquine-resistant P. falciparum as second line drug
  - drug of choice for prophylaxis when entering regions of chloroquine resistance

Pyrimethamine/Sulfadoxine (Fansidar)
- competitive inhibitor of folic acid production thereby inhibiting synthesis of DNA
- side-effects include severe cutaneous reactions (Stevens-Johnson syndrome 1/25 000)
- used with quinine in areas of chloroquine-resistant P. falciparum (Africa only)
**ANTIPARASITICS ... CONT.**

**Doxycycline**
- inhibits protein synthesis
- side-effects include GI upset, UVA photodermatitis, Candidal vaginitis
- prophylaxis in areas of multi-drug resistant *P. falciparum* malaria and treatment in combination with quinine
- drug of choice to prevent mefloquine-resistant *P. falciparum* malaria on the borders of Thailand

**Atovaquone/Proguanil**
- cause mitochondrial damage
- side-effects mostly GI upset
- prophylaxis in areas of resistant *P. falciparum*
- a drug of choice to treat and prevent chloroquine-resistant *P. falciparum*

**ANTI-HELMINTHIC DRUGS**

**Mebendazole, Thiabendazole, Albendazole**
- mechanism of action
  - paralyzes worms by inhibiting glucose uptake and microtubule synthesis
- side-effects
  - mild abdominal pain
  - thia bendazole very toxic, causes nausea, vomiting, headache, dizziness
- clinical indications
  - albendazole: useful against intestinal nematodes: *Ascaris lumbricoides*, *Necator americanus* (hookworm), *Strongyloides stercoralis*, *Trichinella spiralis*, *Enterobius vermicularis* (pinworm), *Trichuris trichiura* (whipworm)
  - adjunctive therapy for hydatid disease and treatment for cysticercosis
  - mebendazole: drug of choice to treat pinworm, roundworm, hookworm and whipworm
  - thiabendazole: strongyloidiasis only

**Praziquantel**
- mechanism of action
  - increases calcium permeability across cell membranes resulting in calcium loss and paralysis of worms
- side-effects
  - abdominal pain, lethargy, headache, dizziness
- clinical indications
  - all trematodes, e.g. Schistosomes, except *Fasciola hepatica* (liver fluke)
  - cestodes (tapeworms)

**Pyrantel Pamoate**
- paralysis of worm, allowing expulsion by body
- causes mild GI upset
- used for roundworm (Ascaris), hookworm or pinworm

**INFECTIONS IN THE COMPROMISED HOST**

**HIV AND AIDS** (see HIV AND AIDS section)

**FEBRILE NEUTROPENIA**
- definition
  - fever (single oral temp. > 38.3°C or > 38.0°C for greater than 1 hour)
  - neutropenia (< 500/mm³)
- risk of bacterial infection increases significantly if peripheral neutrophil count falls below 1.0 x 10⁹/L but is greatly increased with levels below 0.5 x 10⁹/L, duration of neutropenia > 10 days or hematologic malignancies
- most commonly due to chemotherapy-induced marrow suppression
- other potential causes of neutropenia
  - decreased production
    - hematologic ( aplastic anemia, leukemia, myelodysplastic syndromes
    - drug-induced (procainamide, propranolol, chloramphenicol, pencillins, sulfonamides, rifampin, vancomycin, clozapine)
    - infectious (TB, mononucleosis, viral hepatitis, HIV, measles, malaria, brucellosis, histoplasmosis
    - nutritional deficiencies (vit B12, folate, copper, protein malnutrition)
    - others (bone marrow invasion, autoimmune destruction, radiation)
  - peripheral destruction
    - autoimmune (Felty's syndrome, SLE)
    - splenic sequestration
    - antineutrophil antibodies
    - peripheral margination
    - overwhelming bacterial infection
    - hemodialysis
    - cardiopulmonary bypass
- infecting organisms may be normally nonpathogenic flora for the given anatomic site
the usual signs and symptoms of infection may be diminished or absent in neutropenia because leukocytes that mediate much of the inflammatory response to infection are absent

changing epidemiology of infections in febrile neutropenics

- recent increase in serious Gram positive infections (especially in patients with indwelling catheters)

history

- recent medication/drug use
- recurrent infections, travel, disease exposure

physical

- complete skin inspection including visible evaluation for perirectal abscess; however AVOID rectal exam
- erythema gangrenosum; emboli of Gram negative bacilli (e.g. *Pseudomonas aeruginosa*)
- fungal colonization (opharynx, rectum, vagina)
- mental status, meningeal signs, focal deficits
- new heart murmurs
- signs of respiratory infection

labs

- CBC with differential, blood cultures (x 2)
- urine R&M, C&S
- CXR
- sputum Gram stain and C&S, acid-fast stain (if indicated)
- C&S and Gram stain of skin lesions
- lumbar puncture if indicated clinically

treatment

- may vary with local organisms and sensitivity patterns
- if no documented organism, can start empiric treatment IV antibiotics to cover Gram negative and positive organisms
- initial: piperacillin/tazobactam and tobramycin or ceftazidime monotherapy
- if high incidence of Gram positive organisms in the hospital population, add cloxacillin, cefazolin, or vancomycin
- if no improvement after 4 days and all cultures negative add amphotericin B to cover possible fungal pathogens

### Table 6. Types of infections in Febrile neutropenics

<table>
<thead>
<tr>
<th>Sites</th>
<th>Organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peridontium</td>
<td>HSV, gram negative rods, Captnocytophaga</td>
</tr>
<tr>
<td>Gingiva</td>
<td><em>Streptococc</em></td>
</tr>
<tr>
<td>Buccal mucosa</td>
<td>anaerobes, <em>Candida</em></td>
</tr>
<tr>
<td>Post pharynx</td>
<td><em>Klebsiella, Pseudomonas, Enterobacteriaceae</em>, Candida, Aspergillus, <em>S. aureus</em></td>
</tr>
<tr>
<td>Lungs</td>
<td><em>S. aureus</em></td>
</tr>
<tr>
<td>Skin and soft tissue</td>
<td>anaerobes, Group D Strep, gram negative rods</td>
</tr>
<tr>
<td>Perirectum</td>
<td>*S. aureus, <em>S. epidermidis</em></td>
</tr>
<tr>
<td>Indwelling catheter</td>
<td></td>
</tr>
</tbody>
</table>

### TRANSPLANT OR LEUKEMIA/LYMPHOMA

- patients are often neutropenic: nature of infections depends on the degree and duration of neutropenia, depression of cell-mediated immunity
- days to weeks post transplant
  - gram positive bacteria (*Staphylococcus, Streptococcus, Listeria*)
  - gram negative bacteria (*Enterobacteriaceae, Pseudomonas, Legionella*)
- viruses (HSV, VZV, CMV, EBV, hepB, hepC)
- months post-transplant
  - fungal infections, (if neutropenic > 21 days), such as histoplasmosis, cryptococcus
  - pneumococcal bacteremia, skin/soft tissue/bone infections, and mycobacteriosis
  - parasites (*Toxoplasma gondii, Strongyloides stercoralis*), PCP
- empiric treatment (may vary according to sensitivity of local pathogens)
  - cefazolin or piperacillin/tazobactam + tobramycin (first line)
  - ceftazidime + vancomycin (alternative)
  - amphotericin B (if first and second lines fail and TB/MAC not suspected)
- specific therapy based on sensitivities

### INFECTIONS IN A DIABETIC PATIENT

- altered immunity
  - PMN function is depressed (especially with acidosis): adherence, chemotaxis, phagocytosis may be affected
  - peripheral vascular disease: change in delivery to and extravasation of leukocytes to sites
Table 7. Infections with increased prevalence in diabetics

<table>
<thead>
<tr>
<th>Site of Infection</th>
<th>Organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin and connective tissue</td>
<td><em>Candida albicans</em> and other dermatophytes</td>
</tr>
<tr>
<td></td>
<td><em>Staphylococci, streptococci</em>, Gram negative bacilli</td>
</tr>
<tr>
<td></td>
<td>Anaerobes (e.g. <em>B. fragilis</em>)</td>
</tr>
<tr>
<td>Foot infections</td>
<td>mixed gram +/–, anaerobes, r/o osteomyelitis</td>
</tr>
<tr>
<td>Nasal mucosa</td>
<td>Fungi of genera <em>Mucor, Rhizopus, Absidia</em> (rhinocerebral mucormycosis)</td>
</tr>
<tr>
<td>Ears</td>
<td><em>P. aeruginosa</em> (malignant otitis externa)</td>
</tr>
<tr>
<td>Lungs</td>
<td><em>Staphylococci, Klebsiella sp</em></td>
</tr>
<tr>
<td></td>
<td><em>Mycobacterium tuberculosis</em></td>
</tr>
<tr>
<td>Gallbladder</td>
<td><em>Clostridium sp</em> and other anaerobic and aerobic organisms (emphysematous cholecystitis)</td>
</tr>
<tr>
<td>Urinary tract</td>
<td><em>E. coli, staphylococci, Torulopsis glabrata</em></td>
</tr>
<tr>
<td>Vagina</td>
<td><em>C. albicans</em> (vaginal moniliasis)</td>
</tr>
</tbody>
</table>

FEVER OF UNKNOWN ORIGIN

- **definition:** documented fever for at least 3 weeks, with temperature > 38.3°C and of undetermined etiology after 1 week of investigation as outpatient or in hospital
- **etiologies:** infectious, neoplastic, collagen vascular disease, miscellaneous e.g. drug induced, granulomatous disease, undiagnosed (does not imply a worse prognosis)
- **infectious causes**
  - localized: UTI, infective endocarditis, abscess, empyema, osteomyelitis
  - generalized: TB, histoplasmosis, typhoid, CMV, EBV, HIV, Qfever
  - top fevers in a traveller: malaria, typhoid fever, hepatitis A, dengue
- **neoplastic causes**
  - solid tumours (hypernephroma, hepatoma)
  - lymphoreticular malignancy (Hodgkin’s, non-Hodgkin’s lymphoma)
- **collagen vascular disease**
  - adult-onset Still’s disease
  - temporal arteritis/polymyalgia rheumatica
  - vasculitic syndromes (PAN, Wegener’s, GCA)
  - seropositive diseases (SLE, rheumatoid arthritis)
- **miscellaneous**
  - factitious fever
  - drug fever (antibiotics, barbiturates, antiarrhythmics, phenytoin)
  - recurrent pulmonary emboli
  - sarcoidosis
  - IBD
- **clinical approach**
  - history: including travel, occupation, hobbies, exposure to animals
  - known infectious contacts, drug use, family history, previous surgery
  - physical
    - confirm actual fever and assess fever pattern (sometimes just circadian temperature elevation i.e. in the evening)
    - complete physical, always examine skin, eyes, lymph nodes, abdomen, chest, heart, MSK, oral cavity
  - investigations
    - CBC and smear
    - lytes and LFTs
    - blood C&S, urine C&S, U/A
    - CXR (rule out pneumonia, TB, neoplasm etc.)
    - abdominal U/S
    - further investigation depends on results of initial tests
      - liver biopsy
      - bone marrow examination
      - temporal artery biopsy if ESR elevated
      - CT chest and abdomen, GI endoscopy
      - gallium scan
      - 2D-Echo, transesophageal echocardiography

**Clinical Pearls**

- **Major causes of FUO are infection (30-40%), neoplasms (20-30%), collagen vascular disease (10-15%), and misc. (10-20%).**
- **Most common infections for FUO include TB, intraabdominal infections, bacterial endocarditis, pyelonephritis.**
- **Common neoplastic causes include lymphomas, leukemias, solid tumours, disseminated carcinomatosis.**
HIV AND AIDS

Immunopathogenesis

microbiology
- retrovirus
- HIV I: predominant type in N. America
- HIV II: has a longer latent period, restricted mainly to W. Africa

pathogenesis
- target cell preference for HIV infection is determined by interaction between the host cell surface molecule, CD4, along with a co-receptor molecule (CCR5 or CXCR4), and the HIV envelope (env) glycoprotein (gp160) as the virus binds to and enters the host cell
- target cells of HIV include CD4 T helper cells, macrophages, monocytes, microglial cells
- once HIV enters a cell, HIV can replicate and cause cell fusion (syncytium formation) or death
- follicular dendritic cells and other antigen-presenting cells (macrophages, B cells) are involved in the initiation and propagation of HIV infection in CD4 T cells, and can act as viral reservoirs
- after primary infection, acute viremia occurs with wide-spread dissemination of HIV
- inappropriate immune activation and increased secretion of certain proinflammatory cytokines upregulate HIV expression in tissues, paradoxically propagating HIV infection
- key element in HIV pathogenesis is the high level of productive infection, which is characterized by a high level of virion turnover (10 billion virions produced daily)
- viral replication is partially contained by an appropriate immune response, resulting in a markedly decreased amount of virus in the blood to a "set point" which has prognostic significance (i.e. higher the load, the faster the clinical progression to AIDS and death)
- virus is not completely eliminated from the body, and a state of chronic, persistent viral replication ensues

mechanism of immunocompromise
- the damage inflicted by HIV infection is mainly the direct active viral replication resulting in CD4 T cell lysis
- causes immunodeficiency, patient becomes susceptible to opportunistic infections and malignancies
- decline in CD4 T cell levels and the rise in viral load vary considerably throughout the stages of HIV infection and from person to person

lymphoid tissue and the CNS are the major reservoir for and possible sites of persistent viral replication

mode of transmission
- sexual intercourse
- contaminated blood or blood products (IV drug users, transfusion recipients before 1985, occupational exposure through needles)
- organ or tissue transplantation
- vertical transmission from mother to child in utero, during delivery or through breast milk (25% risk without treatment, reduced to 8% or less with antiretrovirals)
- infection is NOT transmitted by casual contact, kissing, mosquitoes, toilet seats, shared utensils

Epidemiology (Health Canada, 1998)
- in 2000, estimated 55,000 Canadians living with HIV
- number of cases of AIDS (1999): 252, marking a dramatic decline in AIDS incidence in Canada
- males and females represent approximately 86.7% and 13.3%, respectively, of total positive HIV test reports with known gender - proportion of women among HIV positive population increasing
- percentage of positive HIV test reports by exposure category (1999)
  - sexual contact with person at risk (11.0%)
  - origin in a pattern 11 country (3.2%)
  - men who have sex with men (48.9%)
  - injection drug use (22.9%)
  - blood product/transfusion recipient (1.4%)

Clinical Perspective

clinical features
- 90% to 70% of persons with primary HIV infection have a clinical syndrome of “flu-like” symptoms and signs (fever, sore throat, skin rash, lymphadenopathy, neutropenia, splenomegaly, myalgia, arthritis)
- acute syndrome occurs 3-6 weeks after primary infection and is associated with high level plasma viremia
- immune response curtails viremia 1 week to 3 months after onset of acute syndrome
- many individuals with HIV infection remain asymptomatic for years
- in adults, the average time to development of AIDS after initial HIV infection is approximately 10 years without antiretroviral therapy
- systemic complaints such as fever, night sweats, weight loss, anorexia, and muscle weakness are common

Clinical Pearl

Whenever the condition of a patient with HIV/AIDS deteriorates consider:
- opportunistic infections
- neoplasms
- effects of medications
- the disease itself
- coinfection - in Hepatitis C
HIV AND AIDS... CONT.

- **diagnosis of HIV infection**
  - two or more reactive screening tests (i.e. ELISA) that detect serum HIV antibodies followed by a confirmatory test (i.e. Western blot or recombinant ELISA) that detect specific antibodies against HIV antigens
  - false negatives possible in recently exposed patients therefore repeat ELISA at 6 weeks and 3 months to avoid “window period” if highly suspicious
  - false positives rare
  - other tests that can be used to identify HIV include viral culture, p24 antigen detection, DNA PCR

- **diagnosis of AIDS**
  - 1993 revised CDC HIV classification system and expanded AIDS surveillance definition
  - CD4 count <200 x 10⁶/L or
  - opportunistic infection (PCP, cryptococcal meningitis, CNS toxoplasmosis) or malignancy (e.g. Kaposi’s sarcoma, CNS lymphoma), HIV wasting syndrome, HIV encephalopathy
  - other infections suggestive (not diagnostic) of early HIV infection include oral candidiasis, oral hairy leukoplakia, ITP, cervical dysplasia, and multidermatomal Herpes Zoster

- **evaluation of newly diagnosed HIV infection**
  - HIV viral load
  - CD4 cell count
  - CBC, liver transaminases, creatinine, creatine kinase
  - serologies for hepatitis B and C, Toxoplasma, CMV, syphilis
  - G6PD assay
  - TB skin test
  - pap smear
  - assess for depression

- **predictors of progression**
  - plasma HIV RNA levels, CD4 cell count
  - onset of HIV-related symptoms, HLA genes, age, and environmental factors
  - after an AIDS diagnosis, survival is usually 1-2 years in an untreated patient due to the opportunistic infections and neoplasms

- **prevention**
  - education, safer sex
  - screening pregnant women
  - screening blood donations, heat treatment of coagulation factors
  - needle exchange programs

- **prophylaxis**
  - prevention of neonatal transmission
  - post-exposure (e.g. occupational, post-sexual)
GI Tract Complications in HIV and AIDS

Odynophagia
- Candida (most common cause)
  - treatment: nystatin swish and swallow, ketoconazole, fluconazole
  - if oral thrush concomitantly present, diagnosis of Candida esophagitis probable, established by history of odynophagia; otherwise need gastroscopy and biopsy
- ulcers from CMV
- herpes
  - treatment = acyclovir
- idiopathic HIV-related
  - treatment = prednisone, thalidomide

Chronic Diarrhea
- commonly idiopathic, associated with weight loss
- frequently drug related, i.e. protease inhibitors
- common infectious causes: Cryptosporidium, Mycobacterium avium complex, CMV (causes mucosal ulcers), C. difficile, Salmonella, Campylobacter
- most useful test is stool examination: O&H, C&S, modified acid-fast stain for Cryptosporidium + Isospora, C. difficile toxin
- colonoscopy and small bowel biopsy only if loperamide is not helpful and other tests are normal

Abdominal Pain
- "HIV cholangiopathy" = sclerosing cholangitis due to CMV, Cryptosporidium, Mycobacterium avium infection of bile ducts
  - increased ALP
  - diagnosis established by ERCP (biliary strictures)
  - endoscopic sphincterotomy helps in 1/3 of cases
- bowel obstruction from lymphoma, Kaposi's sarcoma, CMV
- peritonitis
  - perforated bowel from CMV ulcer
  - acalculous cholecystitis
- lymphoma
- pancreatitis
  - alcohol
  - antiretroviral drugs
  - hypertryglyceridemia
  - peptic ulcer rare in AIDS because gastric acid level is low

Liver Disease
- most common
  - fatty liver (presumably from malnutrition)
  - drugs (especially TMP/SMX, anti-TB, antiretroviral drugs)
  - co-morbid with chronic Hep B or C
- Mycobacterium avium complex and CMV cause increase in serum ALP

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**Figure 8. Evaluation of Abnormal Liver Enzymes in HIV Infection**

- abdominal ultrasound
- focal abnormality
- isotope-tagged red cell scan
  - normal
  - hemangioma
  - (hemangioma alone does not cause abnormal liver enzymes)
  - biopsy
  - serum HBsAg, anti-HCV
  - +ve
  - -ve
  - disproportionate rise in AST/ALT
  - disproportionate rise in ALP

- trial of stopping meds, consider liver biopsy if CMV hepatitis, etc are real possibilities
- ERCP
- counsel, treat, implications

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ID52 – Infectious Diseases

MCCQE 2002 Review Notes
HIV AND AIDS ... CONT.

CNS complications in HIV and AIDS
- HIV infection can present with abnormalities anywhere in the nervous system
- brain involvement occurs in over 90% of HIV infected individuals
- 1/3 of people with AIDS have signs and/or symptoms of nervous system involvement
- HIV with neurological disease means “AIDS-Related Complex”
- Cerebral Toxoplasmosis
  - opportunistic infection
  - most common cause of intracerebral mass lesion
  - signs and symptoms
    - headache, fever, confusion, lethargy, seizures
    - dementia, ataxia, hemiparesis
    - choroidoretinitis occasionally occurs
  - diagnosis
    - CT with contrast: multiple ring-enhancing lesions
  - treatment: sulfadiazine + pyrimethamine + folate (replace sulfadiazine with clindamycin if allergic)
- Progressive Multifocal Leukoencephalopathy
  - opportunistic infection
  - pathophysiology
    - reactivation of HPV causing widespread hemispheric demyelination
  - signs and symptoms
    - often clinically normal (i.e. with normal mental status functioning)
    - presents with dementia, ataxia, dysphagia, visual disturbance
    - death in weeks/months
  - diagnosis: CT shows multiple, nonenhancing, white matter lesions
  - treatment: high dose zidovudine (no proven effective treatment) or combination ARV
- CMV Encephalitis
  - opportunistic infection
  - signs and symptoms
    - presents with acute onset of headache (+/- fever), progressing to alterations in cognitive function; may also cause acute myelopathy and cranial neuropathies
  - diagnosis
    - tissue culture or serology (must be done with CBC and differential, metabolic screen, CT, EEG)
  - treatment: ganciclovir and/or foscamet to help limit extent of disease
- Herpes Encephalitis (see Neurology Chapter)
  - opportunistic infection
- Fungal Encephalitis
  - opportunistic infection
  - caused by Candida, Aspergillus, Cryptococcus, Coccidiomycosis, Histoplasmosis
- Cryptococcal Meningitis
  - commonest CNS fungal opportunistic infection
  - diagnosis
    - CSF - India ink stain (see halos), culture; serum cryptococcus antigen
    - radiology often normal
  - treatment: amphotericin B or fluconazole
- Tuberculous Meningitis
  - opportunistic infection
  - signs and symptoms
    - meningeal involvement is most marked at base of brain (i.e. CN V-XII)
    - may also produce spinal abscess (causing an acute myelopathy)
  - diagnosis
    - CSF - serology, Ziehl-Neelsen stain (acid fast bacilli), culture (takes ~ 2 months)
    - high mortality rate due to delayed diagnosis
  - treatment
    - INH, rifampin, pyrazinamide (give pyridoxine supplement), streptomycin
- Neurosyphilis
  - opportunistic infection
  - signs and symptoms
    - atypical presentations: usually is asymptomatic/meningovascular/GPI (dementia or tabes dorsalis)
  - treatment
    - aqueous procaine penicillin G x 10 days IV
- Dementia-Encephalopathy
  - due to direct effect of HIV
  - signs and symptoms
    - cognitive, behavioral, and motor involvement (especially mental slowing, apathy, and social withdrawal)
    - often hyperreflexic, with upgoing toes and primitive reflexes (e.g. glabellar tap)
  - depression is a common presentation
  - diagnosis
    - clinical: rule out infections/malignancies
    - CT/MRI: atrophy, white matter abnormalities
  - treatment
    - supportive, ARV
HIV AND AIDS . . . CONT.

- **Myelopathy**
  - due to direct effect of HIV, occasionally CMV
  - signs and symptoms
    - presents in a fashion similar to subacute combined degeneration of the cord
    - muscle weakness, myalgia, weight loss
    - also consider compression by abscess, systemic lymphoma
  - diagnosis
    - increased CK, EMG, muscle biopsy
  - treatment
    - ARV

- **Neuropathy**
  - due to direct effect of HIV, or toxic effects of medications
  - acute inflammatory demyelinating neuropathy
  - chronic inflammatory demyelinating neuropathy
  - distal symmetric neuropathy
  - shingles (herpes zoster)
  - multiple and/or frequent lesions means AIDS
  - treatment: analgesics

- **Cerebral Lymphoma**
  - most common CNS neoplasm in AIDS
  - may occur in other locations (i.e. spinal cord)
  - signs and symptoms: headache, lethargy, cognitive changes, hemiparesis, aphasia
  - diagnosis: CT/MRI shows enhancing lesions
  - treatment: radiation

- **Kaposi’s Sarcoma (Herpes Virus 8)**
  - epidemiology
    - believed to be related to sexual transmission
    - most commonly present in homosexual males in US
    - uncommon among other risk groups
  - signs and symptoms
    - predilection for oral cavity and skin, also commonly occurs in GI tract, lungs, lymph nodes, but can occur in any organ, including the brain
  - treatment
    - chemotherapy for systemic/disseminated disease
    - radiation or interferon-a for cutaneous/mucosal lesions

---

**Table 8. Opportunistic Infections**

**Oral**
- Oral thrush - *Candida albicans*
- Oral Hairy Leukoplakia - EBV
- Herpes simplex ulcers
- Kaposi’s sarcoma - HHV(8)-associated malignant vascular neoplasm, predilection for oral cavity and skin

**Dermatological**
- Herpes simplex
- Shingles (VZV)
- Staphylococcal folliculitis
- *Molluscum contagiosum* (see Colour Atlas ID3)
- Candidal rash

**CNS**
- CMV retinitis
- CMV encephalitis - confusion and cranial nerve abnormalities
- Toxoplasmosis encephalitis (T. gondii) - fever + focal neurological defect.
- PML (secondary to a papovavirus) - progressive dementia
- Aseptic meningitis
- Cryptococcal meningitis

**Pulmonary**
- Bacterial pneumonia - *S. pneumoniae*, *H. influenza*, *Legionella sp.*
- CMV pneumonia
- *Pneumocystis carinii* pneumonia
- MAC
- Tuberculosis - higher rate of extrapulmonary TB, multidrug resistance

**GI**
- CMV esophagitis
- Infiltrative disease of the liver - MAC, CMV
- Chronic active Hep B/C - may be secondary to medications
- Diarrhea - *Salmonella sp.*, *Yersinia sp.*, *Campylobacter sp.*, *C. difficile*
- CMV colitis
- Cryptosporidium

At CD4 count > 200, infections respond to routine treatments; < 200 patients require chronic suppressive therapy after treatment of acute infection
**HIV AND AIDS . . . CONT.**

**Treatment**
- recent data strongly support the principle that HIV viral replication should be maximally suppressed throughout the course of HIV infection.
- monotherapy or combination regimens that only partially suppress viral replication allow more rapid selection of resistant variants, and therefore are not used.

<table>
<thead>
<tr>
<th>Status</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic HIV disease*</td>
<td>Therapy recommended for all patients</td>
</tr>
<tr>
<td>RNA levels above 30 000 copies/mL plasma (regardless of CD4 cell count)</td>
<td>Therapy recommended for all patients</td>
</tr>
<tr>
<td>CD4 cell count &lt; 350 X 10^6/L</td>
<td>Therapy recommended for all patients</td>
</tr>
<tr>
<td>RNA levels &gt; 5 000 copies/mL and/or CD4 cell count &lt; 500 x 10^6/L</td>
<td>Therapy should be considered</td>
</tr>
<tr>
<td>Patients at low risk of disease progression (low plasma HIV RNA level and high CD4 cell count)</td>
<td>Therapy may be deferred Re-evaluate every 3 to 6 months</td>
</tr>
</tbody>
</table>

*symptomatic HIV disease includes symptoms such as recurrent mucosal candidiasis, oral hairy leukoplakia, and chronic and unexplained fever, night sweats, and weight loss

- **recommended initial therapy regimens**
  - triple combination therapy options
    1. 1-2 NRTIs + 2 PIs
    2. 2 NRTIs + 1 PI
    3. 2 NRTIs + 1 NNRTI
    4. 3 NRTIs
  - monotherapy is now considered suboptimal
  - effective therapy is indicated by 0.5 log _10_ or more (about 3-fold) decline from pre-treatment viral levels; goal is to suppress to < 50 copies/mL
  - "treatment failure" is defined as return of HIV RNA titer or CD4 cell count to pre-treatment levels
  - may use drugs with greater potency or switch to drugs with different mechanism of action (e.g. adding a protease inhibitor) and those without cross-resistance (e.g. switching nucleoside analogues)
  - when changing regimens, at least two antiviral drugs should be changed to minimize the development of resistant virus

- **nucleoside reverse transcriptase inhibitors (NRTI)**
  - preferentially incorporated into the growing viral DNA chain thereby terminating its growth and inhibiting reverse transcriptase
  - toxicities: anemia, headache, nausea, neutropenia, myopathy, peripheral neuropathy
  - zidovudine (AZT)
    - thymidine analog
    - can cross the blood brain barrier; effective in decreasing vertical transmission from mother to fetus
    - many treatment experienced patients have developed viral resistance to AZT
    - toxicities: anemia, neutropenia, h/a, nausea, myopathies
  - lamivudine (3TC)
    - can potentially reverse or delay viral resistance to AZT
    - weak antiviral medication; resistance to 3TC alone can develop quickly
    - toxicities: anemia, nausea, hair loss
  - combivir (AZT+3TC)
    - advantage: increased adherence to antiviral regimen
  - didanosine (ddI)
    - adenosine analog
    - toxicities: pancreatitis, hepatitis, neuropathy
    - ddI can decrease levels of oral ganciclovir
    - proposed that viral resistance to ddI develops later compared to other nucleoside analogs
  - zalcitabine (ddC)
    - cytosine analog
    - toxicities: peripheral neuropathy, apthous ulcer, pancreatitis, rash
  - stavudine (d4T)
    - can cross the blood brain barrier
    - toxicities: peripheral neuropathy, hepatitis
  - abacavir (1592U89)
    - potent antiviral drug
    - toxicities (hypersensitivity reaction): N/V, fever, rash, hypotension, deaths reported with rechallenge
HIV AND AIDS... CONT.

- protease inhibitors (PI)
  - inhibit maturation of infectious virions by inhibiting the cleavage of gag and gag-pol polyproteins
  - combination therapy with protease inhibitors delays disease progression and prolongs life
  - lipoatrophy syndrome: (common side-effect associated with the use of protease inhibitors): body fat redistribution (increased central, decreased peripheral) increased triglycerides, decreased HDL and increased LDL cholesterol, possible increased risk of cardiac and cerebrovascular diseases, increased levels of insulin and insulin resistance
  - saquinavir
    - limited oral bioavailability but new soft-gel capsule (Fortovase) has better bioavailability
  - ritonavir
    - greatest rate of intolerance
    - ritonavir plus saquinavir combination increases the bioavailability of saquinavir
  - indinavir
    - toxicities include ingrown toenails, nephrolithiasis, asymptomatic hyperbilirubinemia
  - nelfinavir
    - can raise serum levels of soft-gel saquinavir up to 5 x normal level which may increase the side-effects (e.g. diarrhea)
    - adverse effects of initial regimens (nausea, rash, diarrhea)
  - lopinavir
    - increased incidence of increased TG/cholesterol, diarrhea, nausea
    - coformulated with ritonavir
- non-nucleoside reverse-transcriptase inhibitors (NNRTI)
  - inhibit function of reverse-transcriptase by interacting with the enzyme directly, thereby preventing viral RNA replication
  - nevirapine
    - major toxicities: fever, nausea, headache, rash, Stevens-Johnson syndrome, hepatitis
    - may interact with rifampin, rifabutin, and birth control pills
  - efavirenz
    - major toxicities (transient): increased depression, dizziness, insomnia, drowsiness, problems concentrating, rash
    - teratogenic in animal models
    - disadvantages: greatly reduces serum levels of saquinavir and other PI
  - delavirdine
    - advantages: increases levels of protease inhibitors
    - major toxicities: rash, headache, nausea, fever, elevated liver enzymes
    - may greatly increase serum levels of saquinavir
- prophylactic medications for opportunistic infections (see Table 10)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Indication</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pneumocystis carinii</em></td>
<td>CD4 count &lt; 200/mm³ or fever for 2 weeks</td>
<td>TMP/SMX, aerosol pentamidine or dapsone</td>
</tr>
<tr>
<td><em>M. tuberculosis</em></td>
<td>TB skin test &gt; 5mm or contact with active TB</td>
<td>isoniazid; pyridoxine</td>
</tr>
<tr>
<td><em>Toxoplasma gondii</em></td>
<td>IgG antibody to toxoplasma and CD4 count &lt; 100/mm³</td>
<td>TMP/SMX</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>CD4 cell count &lt; 75/mm³</td>
<td>pneumococcal vaccine</td>
</tr>
<tr>
<td>MAC</td>
<td></td>
<td>azithromycin, clarithromycin, rifabutin</td>
</tr>
</tbody>
</table>
Post-Exposure Prophylaxis

- **occupational exposure**
  - Health-care workers have a 0.3% risk of transmission from a percutaneous needlestick injury from a known HIV+ patient.
  - Prophylaxis with zidovudine has been shown to reduce risk of transmission by nearly 80% in case-control studies.
  - Post-exposure prophylaxis is recommended in situations in which there is definite high risk for transmission.
  - Combination therapy (AZT, 3TC and nelfinavir) may be more effective and should be begun as soon as possible after exposure, ideally < 2 hours and not > 48 hours, continued for 1 month.

- **vertical transmission**
  - HIV-infected mothers not on antiretroviral therapy have a 25% chance of vertical transmission.
  - Perinatal prophylaxis with AZT reduces transmission to 8% (and less with combination ARV) is recommended for all HIV-infected women.
  - HIV-infected mothers should be encouraged to bottle-feed.
    - Current practice in developed countries is to treat infected women with triple combination antiviral therapy (except efavirenz).
    - Delivery by Cesarean section can also decrease the risk of transmission.
    - Studies ongoing to determine duration and appropriate timing for perinatal prophylaxis.

### COMMON INFECTIONS

<table>
<thead>
<tr>
<th>CNS Infection</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aseptic Meningitis</td>
<td>Enteroviruses, HSV-2, HIV</td>
<td>None</td>
</tr>
<tr>
<td>Bacterial Meningitis</td>
<td>Group B strep (most common), E. Coli, Listeria</td>
<td>Ceftriaxone IV 200mg/kg/d</td>
</tr>
<tr>
<td>• Newborns</td>
<td>Strep. Pneumonia, meningococci, listeria</td>
<td>Cefotaxime IV 2g q6h and Vancomycin IV 1g q12h  and Ampicillin 2mg IV q4h</td>
</tr>
<tr>
<td>&gt; 1 month - adult</td>
<td></td>
<td>Penicillin and Metronidazole +/- Ceftriaxone</td>
</tr>
<tr>
<td>Brain abscess</td>
<td>Streptococci, bacteroides, enterobacteriaceae, S. aureus, toxoplasma gondii (AIDS)</td>
<td>Acyclovir IV (if HSV)</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>HSV-1 (most frequent), VZV, CMV, rabies, HIV, mumps, measles, echovirus, coxsackievirus</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ENT Infection</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otitis Media</td>
<td>S. pneumonia (40-50%), H. influenza (20-25%), M. catarhalis (10-15%), Viral (48%) (respiratory syncitial virus, rhinovirus)</td>
<td>Amoxicillin 250mg TID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amox/Clavulanate 250mg TID</td>
</tr>
<tr>
<td></td>
<td>Staphylococci, Pseudomonas (swimmer's ear), enterobacteriaceae, proteus sp.</td>
<td>Garamycin eardrops</td>
</tr>
<tr>
<td>Otitis Exerna</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Strep. Pneumoniae (31%), H. influenzae (21%), M. catarhalis (2%)</td>
<td>Amoxicillin 500mg TID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TMP/SMX DS 1 tab BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Azithromycin 250-500mg OD</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>Respiratory viruses (rhinovirus, coronavirus, adenovirus, influenza), EBV, HSV, Coxsackievirus A</td>
<td>Penicillin V 300mg TID</td>
</tr>
<tr>
<td></td>
<td>• Group A Strep</td>
<td></td>
</tr>
</tbody>
</table>

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### COMMON INFECTIONS... CONT.

<table>
<thead>
<tr>
<th>Eye Infection</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbital cellulitis</td>
<td>• Strep. pneumoniae, H. influenza, M. catarrhalis, S. aureus</td>
<td>• Cefuroxime IV 1.5g q8h</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ampicillin/sulbactam IV 1.5g q6h</td>
</tr>
<tr>
<td>Blepharitis</td>
<td>• Unclear etiology, associated with S. aureus, S. epidermis, seborrhea, rosacea</td>
<td>• Wash and topical bacitracin or erythromycin x 2wks</td>
</tr>
<tr>
<td>Hordeolum (Stye)</td>
<td>• S. aureus</td>
<td>• Hot packs +/- topical sulpha</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>• N. gonorrhoea, S. aureus</td>
<td>• Ophthalmic erythromycin, gentamicin, or bacitracin-polymyxin B</td>
</tr>
<tr>
<td></td>
<td>• Adenovirus</td>
<td>• Ceftriaxone 125mg IV/IM x 1 (if gonococcal)</td>
</tr>
<tr>
<td>Keratitis</td>
<td>• P. aeruginosa (contact lense users)</td>
<td>• Tobramycin + piperacillin or ticarcellin eye drops</td>
</tr>
<tr>
<td></td>
<td>• S. aureus</td>
<td>• Cefazolin + gentamycin or tobramycin eye drops</td>
</tr>
<tr>
<td></td>
<td>• HSV-1, HSV-2, Varicella zoster</td>
<td>• Trifluridine or Famciclovir eye drops (if viral)</td>
</tr>
<tr>
<td>Retinitis</td>
<td>• Varicella zoster, CM (immunocompromised)</td>
<td>• Acyclovir IV 10-12mg/kg q8h or gancyclovir</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiac Infection</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infective endocarditis</td>
<td>• Strep. viridans (30-40%), other strep (15-25%), S. aureus (20-35%), Enterococci, HACEK (Haemophilus, Actinobacilus, Cardiobacterium, Eikenlla, Kingella)</td>
<td>• Pen G 12-18 mill u/d x 4-6 wks</td>
</tr>
<tr>
<td>• Native valve</td>
<td></td>
<td>• +/- Aminoglycoside Pen G 12-18 mill u/d x 4-6 wks</td>
</tr>
<tr>
<td>• Prosthetic valve</td>
<td>• S. epidermis, S. aureus, Strep. viridans, GNB</td>
<td>• Ceftriaxone Ig OD x 4-6 wk (if HACEK)</td>
</tr>
<tr>
<td>• IV drug users</td>
<td>• S. aureus, Streptococci, GNB, Enterococci, Fungi (Candida) (oral flora)</td>
<td>• Vancomycin Ig IV q12h +/- Rifampin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• +/- gentamicin x 3-5 day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Vancomycin Ig IV q12h +/- Rifampin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• +/- gentamicin x 3-5 day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Breast Infection</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastitis:</td>
<td>• S. aureus</td>
<td>• Cloxacillin 250-500mg QID</td>
</tr>
<tr>
<td>• Postpartum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone and Joint Infections</td>
<td>Organisms</td>
<td>Empirical Treatment</td>
</tr>
<tr>
<td>---------------------------</td>
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<td>--------------------</td>
</tr>
<tr>
<td>Osteomyelitis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Contiguous</td>
<td>S. aureus, S. epidermis (prosthesis)</td>
<td>Vancomycin 1g q12h +/- Rifampin 600-900 mg PO OD</td>
</tr>
<tr>
<td>• Diabetic</td>
<td>mixed flora (S. aureus, Streptococcus, GNB, anaerobes)</td>
<td>Ceftazidime 2g q8h IV</td>
</tr>
<tr>
<td>• Trauma</td>
<td>S. aureus, GNB</td>
<td>repeat</td>
</tr>
<tr>
<td>- post-surgical</td>
<td>Pasteurella multocida</td>
<td>amoxicillin/clavulanate</td>
</tr>
<tr>
<td>- cat or dog bites</td>
<td>S. aureus</td>
<td>Nafcilin or oxacillin 2g q8h IV or cefazolin 2g IV q8h</td>
</tr>
<tr>
<td>• Hematogenous:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- IV catheters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- IV drug use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-surgical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>post-streptococcal (Group A) infection</td>
<td>None</td>
</tr>
<tr>
<td>Septic bursitis</td>
<td>S. aureus</td>
<td>Cloxacillin</td>
</tr>
<tr>
<td>(olecranon, prepatellar)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic arthritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Adults</td>
<td>N. gonorrhea (sexually active, polyarticular at onset), S. aureus (monoarticular, large joint), streptococci, GNB (elderly with chronic arthritis), viral (polyarticular) – Mumps and rubella (direct invasion), Hepatitis B (immune mediated response)</td>
<td>Cloxacillin (if S. aureus)</td>
</tr>
<tr>
<td>• IV drug users</td>
<td>Pseudomonas (often sternoclavicular joint), S. aureus, Candida</td>
<td>Ceftriaxone (if N. gonorrhoeae)</td>
</tr>
<tr>
<td>• Chronic</td>
<td>Mycobacteria, Fungi, Borrelia burgdorferi (Lyme disease)</td>
<td></td>
</tr>
</tbody>
</table>
### COMMON INFECTIONS... CONT.

<table>
<thead>
<tr>
<th>GI Infections</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
</table>
| **Oral infections:**  
  - Thrush  
  - Herpetic stomatitis  
  - Parotitis | C. albicans, HSV-1, 2, Mumps | Nystatin |
| **Gastric infections:**  
  - Peptic Ulcer Disease | H pylori | Triple therapy  
  Clarithromycin 500mg BID  
  Metronidazole 500mg BID  
  Omeprazole 20mg BID |
| **Hepatobiliary infections:**  
  - Gallbladder infections | enterobacteriaceae (68%), enterococci (14%), bacteroides (10%), Clostridium perfringens (7%) | Piperacillin/Tazobactam  
  Ampicillin + gentamycin + Flagyl |
| - Viral Hepatitis | Hepatitis A, B, C, D (with concomitant Hep B infection), E, G | |
| - Hepatic abscess | enterobacteriaceae, bacteroides, entamoeba histolytica | |
| **Intra-abdominal abscesses:**  
  - Splenic abscess  
  - Pancreatic abscess  
  - Subphrenic, Pelvic abscesses  
  - Perinephric abscess | Staphylococci, Streptococci, GNB  
  GNB, Streptococci  
  GNB, Streptococci, anaerobes  
  GNB, Staphylococci | Ampicillin  
 Gentamycin  
 Flagyl |
| **Intestinal Infections:**  
  - Esophagitis | Candida albicans  
  HSV  
  CMV | Fluconazole  
 Acyclovir  
 Gancyclovir |
| - Gastroenteritis  
  Mild/moderate diarrhea: | viral most likely (rotavirus, norwalk virus), bacterial (see below), parasitic | fluids +/- lactose free diet |
|  
  Severe diarrhea: | shigella, salmonella, campylobacter, E. coli 0157: H7 (severe afebrile bloody diarrhea), toxigenic E. coli (traveler's diarrhea) | Ciprofloxacin 500mg q12h x3-5d  
 or observation  
 +/- Metronidazole 500mg tid PO x10-14d  
 (if C. difficile) |
| - Diverticulitis | enterobacteriaceae, bacteroides, enterococci | Ciprofloxacin 500mg BID + metronidazole 500mg q8h |
| **Peritonitis:**  
  - Primary (Spontaneous Bacterial Peritonitis) | GNB, Enterobacteriaceae, S. pneumonia, enterococci, anaerobes (<1%) | Cefotaxime IV 2g q8h |
| - Secondary (peritoneal soilage) | enterobacteriaceae, bacteroides, enterococci, P aeruginosa | Ampicillin/Gentamycin/Flagyl or Piperacillin/Tazobactam |
### COMMON INFECTIONS . . . CONT.

<table>
<thead>
<tr>
<th>Genital Tract Infections</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
</table>
| ❏ Chancroid             | • H. ducreyi | • Erythromycin 500mg QID x 7 days  
|                         |           | • Ceftriaxone 250mg IM x 1 |
| ❏ Cervicitis/Urethritis | • N. gonorrhea, Chlamydia | • Ceftriaxone 125mg IM or cefixime 400mg PO or Ciprofloxacin 500mg PO x 1 |
| ❏ Anogenital warts      | • HPV     | • Podophyline |
| ❏ Endometritis          | • Bacteroides, Group B, A strep, enterobacteriaceae, C. trachomatis | • Ampicillin/Gentamycin/Flagyl |
| ❏ PID                   | • N. gonorrhea, Chlamydia, bacteroides, enterobacteriaceae, streptococci | • Ceftriaxone IM 250mg x1 and Doxycycline 100mg BID |
| ❏ Vaginitis             | • candida albicans, trichomonas vaginalis, gardnerella vaginalis | • clotrimazole or butoconazole or miconazole suppositories/creams |
| ❏ Prostatitis           | • E.coli, Pseudomonas, S.fecalis | • Ofloxacin 400mg x 1, then 300mg q12h  
|                         |           | • Ciprofloxacin 500mg BID x 4 wks |
| ❏ Epididymitis          | • Gonorrhea, Chlamydia (<35 yo)  
|                         | • Enteric GNB (>35 yo) | • Ceftriaxone 250mg IM x1 + doxycycline 100mg BID x 10d |
| ❏ Orchitis              | • Mumps   | • None |

<table>
<thead>
<tr>
<th>Urinary Tract Infections</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>❏ Uncomplicated Cystitis</td>
<td>• E. coli, Enteric bacilli, S.saprophyticus</td>
<td>• TMP/SMX DS 1 tab BID</td>
</tr>
</tbody>
</table>
| ❏ Cystitis/Pyelonephritis | • Routine (KEEPS): Klebsiella, E.coli, Enterococci (other GNB), Proteus, Pseudomonas, S.saprophyticus, S.fecalis | • TMP/SMX DS 1 tab BID  
|                         |           | • Amox/Clavulanate 500mg TID |
|                         |           | • Ciprofloxacin 500mg BID |

<table>
<thead>
<tr>
<th>Skin and Soft Tissue Infections</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
</table>
| ❏ Superficial (Epidermal)       | • S. aureus, Candida  
| ❏ Folliculitis                   | • S. aureus  
| ❏ Furuncles                      | • Group A strep, S. aureus | • topical clindamycin or erythromycin |
| ❏ Impetigo                       |           |                     |
| ❏ Dermal & Subcutaneous         | • Group A strep | • Penicillin G  
| ❏ Erysipelas                     |           | • Penicillin G  
| ❏ Cellulitis                     | • Group A strep (most common), S. aureus, Clostridium perfringes, other anaerobes (diabetics), GNB (immunocomprimsed), Pasteurella multocida, Erysiperlophrix (fish/meat handlers), Aeromonas (freshwater exposure), Vibrio spp. (saltwater exposure) | • Penicillin/Clindamycin  
| ❏ Fascitis                       |           | • Ampicillin/Gentamycin/Flagyl |
| ❏ Myonecrosis                    | • Clostridium perfringes, streptococci, GNB, mixed anaerobes | • Piperacillin/Tazobactam  
| ❏ Pyomyositis                    | • S. aureus, Group A strep | • Ampicillin/Gentamycin/Flagyl |

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### COMMON INFECTIONS . . . CONT.

<table>
<thead>
<tr>
<th>Respiratory Infections</th>
<th>Organisms</th>
<th>Empirical Treatment</th>
</tr>
</thead>
</table>
| Bronchitis             | • Viral (95%), Mycoplasma pneumoniae  
• Strept. pneumoniae, H. influenzae and M. catarrhalis | • Tetracycline 250mg QID  
• Erythromycin 250mg QID  
• Same as acute bronchitis |
| Pneumonia              | • GBS, E.coli  
• Viral (RSV), Mycoplasma, C. pneumoniae, S. pneumoniae  
• Mycoplasma, C. pneumoniae, S. pneumoniae, H. influenzae, anaerobes, VZV  
• S. pneumoniae, anaerobes, H. influenzae, GN rods, tuberculosis, viral (<10%, influenza virus most common)  
• Staph. aureus, GN rods, Legionella  
• Staph., GN rods, fungi (aspergillosis), P. carinii (HIV) | • Ampicillin and Gentamycin  
• Levofloxacin or Biaxin  
• Ciprofloxacin or 3rd generation Cephalosporin |

### REFERENCES