**Indiana University School of Medicine, Department of Microbiology & Immunology**
**MICROBIOLOGY CORE CURRICULUM**
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# I. General Bacteriology

**1a. <u>Morphology and ultrastructure</u> (overview)**

a. Shapes (cocci, bacilli, fusiform, spiral, curved; concept of pleomophism)
b. Reproduction (binary fission)
c. General cytology (structure and function)
   cell wall; plasma (cytoplasmic) membrane; nucleoid; ribosomes; mesosomes; inclusions; appendages (flagella, pili/fimbriae); capsule/glycocalyx/slime layers; endospores
d. Gram's stain: technique; mechanism of differential staining; implications
e. Gram positive envelope (structure and functions)
   peptidoglycan; teichoic acids; lipoteichoic acids; plasma (cytoplasmic) membrane
f. Gram negative envelope
   outer membrane (lipopolysaccharide; OM proteins [porins and porin-like proteins]); peptidoglycan; periplasmic space; plasma (cytoplasmic) membrane

**1b. <u>Taxonomy</u> (overview)**

a. Domains: *Bacteria* (*Proteobacteria, Fermicutes, Actinobacteria, Bacteroidetes, Spirochaetes, Chlamydiae*), *Archaea, Eucarya*
   (Genus & species example)
b. Basis for classification and identification
   visible features; nutrition; endproducts; surface molecules; molecular techniques for identification (nucleic acid homology, PCR, genetic probes)

**1c. <u>Envelope structures, synthesis, and functions</u>**

a. Peptidoglycan (PG)
   (1) Basic structure (repeating units of β-1,4 linked N-acetyl-D-glucosamine and N-acetyl-D-muramic acid tetra- or pentapeptide; O-acetylated MurNAc resists lysozyme)
   (2) Cross-link options
   (3) Synthesis (soluble precursors; carrier [bactoprenol-P], transglycosylation, transpeptidation; dephospholylation of carrier; sites of antibiotic actions)
   (4) Proinflammatory effects of PG
b. Capsule, glycocalyx, and biofilm
   (1) Properties; structure; and composition (examples)
   (2) Function in virulence
c. Pili/fimbriae (somatic versus sex; structure; function; roles in virulence [esp. adherence])
d. Motility and chemotaxis
   (1) The flagellum (Basic arrangements [monotrichous, peritrichous]; structure [switch and Mot proteins])
   (2) Chemotaxis (molecular mechanisms of directed movement; methylation and phosphorylation reactions; driven by PMF)
e. Plasma (cytoplasmic) membrane
   (1) Structure and function

(2) Transport (facilitated diffusion; primary and secondary active transport; group translocation; periplasmic binding proteins)
(3) Electron transport and generation of ATP (proton motive force)
(4) Secretory mechanisms (Types I, II, III and IV; roles in virulence)

f. Gram positive envelope
(1) PG (many layers; extensive cross-linking)
(2) Teichoic acids (structure, function, role in virulence)
(3) Teichuronic acids (structure and function)
(4) Lipoteichoic acids (structure; function; role in virulence)

g. Acid fast envelopes
(1) The acid-fast stain
(2) Components and their biological activity
(mycolic acids, cord factor, trehalose mycolates and sulfolipids, arabinogalactan; lipoarainomannan, arabinomannan, and wax D)

h. Gram negative envelope
(1) PG (few layers; little cross-linking)
(2) Outer membrane (structure, function)
(a) OM proteins (functions; roles in virulence)
(b) Lipopolysaccharide (O-Ag, Core, Lipid A) and lipooligosaccharide
Biologic activities of Lipid A (endotoxin): LPS binding protein/CD14 interactions; effects on phagocytes and endothelial cells (sepsis syndrome); chemical mediators of sepsis (esp. IL-1, TNF-alpha); LPS assembly (bactoprenol carrier)

**1d. <u>Endospores</u>**

a. Structural and functional aspects of endospores (core; cortex; coats; dipicolinic acid)
b. Sporulation (induction [quorum sensing]; forespore; release)
c. Germination (induction, initiation, outgrowth)
d. Role in epidemiology and virulence
e. Sterilization of material containing spores

**2. <u>Growth and Metabolism</u>**

a. General (nutrient requirements; temperature; pH optimum)
b. Carbohydrate metabolism
(1) Aerobic (EMB; pentose phosphate shunt; Entner-Douderoff pathway)
(2) Fermentative (endproducts resulting from alcoholic, homolactic, mixed acid, butyric, propionic fermentative pathways; purpose [recycling reducing equivalents])
c. Respiration
Anaerobic versus aerobic; TCA (heterotrophic $CO_2$ fixation, reductive TCA cycle)
d. Split TCA cycle for biosynthetic needs under anaerobiosis

**3a. <u>Bacterial genetics, gene transfer, and antibiotic resistance</u>**

a. General characteristics of the bacterial chromosome
b. DNA Replication
c. Endonucleases (function and use in cloning)
d. Quorum sensing (overview of concept, examples [*Pseudomonas aeruginosa*,

*Staphylococcus*])

e. Mechanisms of altering DNA (transposons; gene conversion; site-specific inversion)

d. Mechanisms of gene transfer

(1) Transformation - competence; competence pheromones; quorum sensing; gene activation; DNA uptake and incorporation

(2) Conjugation - F plasmids; Hfr and transfer of chromosomal genes; F' plasmids; R factors; role of transposons

(3) Transduction - mechanisms of generalized and specialized transduction; phage conversion (example: diphtheria toxin)

**3b. <u>Protein synthesis and regulation of gene expression</u>**

a. Review transcription and translation; polycistronic messages; initiation; elongation; termination

b. Transcriptional regulation
operons: regulator proteins and effectors and where they bind mRNA; catabolite-sensitive operons (Lac operon); the Tryp operon and attenuation

**4. <u>Antibiotics</u>**

a. General principles

(1) Desired properties
(broad range; bactericidal versus bacteriostatic; good distribution; selective toxicity; therapeutic margin)

(2) Measurement of antimicrobial activity
(Diffusion [Etest, Kirby-Bauer], macrodilution; microdilution; determination of MIC and MBC)

(3) Antimicrobial combinations
(synergism; antagonism; indifference; indications for combined therapy)

(4) Appropriate prophylactic use of antibiotics
(contacts; preexisting condition; surgery; immunocompromised)

b. Antibiotics that affect cell wall synthesis

(1) Beta-lactam antibiotics (mechanisms of action [inhibit transpeptidation and activate autolytic enzymes]; examples of uses; combinations with beta-lactamase inhibitors [clavulanic acid, sulbactam, tazobactam]; resistance mechanisms; allergic reactions)

(a) Penicillins (natural [Pen G & V]; penicillinase-resistant [methicillin, nafcillin, cloxacillin, oxacillin]; amino-penicillins [ampicillin, amoxacillin]; anti-pseudomonas [azlocillin, ticarcillin]; extended spectrum [mezlocillin, pipercillin])

(b) Cephalosporins (relationship between generations and activity):
($1^{st}$ generation [cephalexin, cefazolin; for non-life threatening infections, surgical prophylaxis]; $2^{nd}$ generation [cefaclor, cefuroxime, cefoxitin; increased activity against gram negatives; more resistant to beta-lactamases]; $3^{rd}$ generation [ceftriaxone, cefpodoxime, cefotaxime, cefoperazone, cefditoren; broad spectrum; good CNS penetration]; $4^{th}$ generation [cefepime; broadest spectrum of activity]

(c) Aztreonam (a monobactam; resistant to beta-lactamases; effective against most gram-negatives but not gram-positives)

(d) Imipenem, meropenem, ertapenem (carbapenems: resistant to most beta-lactamases; used for gram-negative and gram-positive infections; toxicity)

(2) Bacitracin (mechanism of action [blocks dephosphorylation of carrier] and uses)
(3) Vancomycin, teicoplanin and other glycopeptide antibiotics (mechanism of action [blocks transglycosylation]; uses [for resistant staph]; resistance [VanA])
(4) Other
(a) Cycloserine (uses and mechanism of action [D-alanine analog])
(b) Isoniazid (uses and mechanism of action [inhibits mycolic acid synthesis])
(c) Ethambutol (uses and mechanism of action [inhibits arabinogalactan synthesis])
(d) Ethionamide (uses and mechanism of action [inhibits mycolic acid synthesis)
(e) Methenamine (uses and mechanism of action)
(f) Nitrofurantoin (uses and mechanism of action)

c. Antibiotics that affect membrane integrity
(1) Polymyxins (uses and mechanism of action [disrupts plasma membrane])

d. Antibiotics that affect nucleic acid and protein synthesis
(1) Antimetabolites
(a) Sulfonamides (examples [sulfisoxazole, sulfmethoxazole, dapsone]; uses; and mechanism of action [inhibit PABA incorporation into dihydropteroic acid]; resistance mechanisms; allergic reactions)
(b) Trimethoprim (uses and mechanism of action [inhibits dihydrofolate reductase]); resistance)
(c) Synergistic use and TMP and SMX (mechanism of action; uses)
(2) Inhibitors of DNA synthesis
(a) Quinolones and fluoroquinolones (examples [ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, moxifloxicin, gatifloxicin, grepafloxacin, gemifloxacin]; mechanism of action [inhibit DNA gyrase];uses and resistance mechanisms)
(b) Rifamycins (rifampin, rifabutin, rifaximin) (mechanism of action [inhibit RNA polymerase] and uses)
(c) Metronidazole (mechanism of action [damages DNA, not an inhibitor of synthesis] and uses)
(3) Inhibitors of protein synthesis
(a) Aminoglycosides (examples [streptomycin, neomycin, gentamicin, tobramycin, amikacin]; mechanism of action [binds 30S, blocks initiation]; uses; and resistance mechanisms)
(b) Tetracyclines (examples [tetracycline, doxycycline, minocycline, tigecycline], mechanism of action [binds 30S, stops elongation]; uses; toxicity; and resistance mechanisms [efflux])
(c) Chloramphenicol (mechanism of action [binds 50S, inhibits peptide bond formation]; uses; toxicity; and resistance mechanisms)
(d) Macrolides (examples [erythromycin, azithromycin, clarithromycin]; mechanism of action [bind 50S, blocks translocation and/or inhibits peptide bond formation]; uses; and resistance mechanisms)
(e) Lincosamides (clinadamycin)(mechanism of action [binds 50S, inhibits peptide bond formation] and uses)
(f) Mupirosin (topical; inhibits synthesis of isoleucyl-tRNA)
(g) Quinupristin+dalfopristin=Synercid (FDA approved to treat vancomycin-resistant *E. faecium*; also effective against vano-resistant staph; mechanism of

action [30s])

(h) Linezolid (an oxazolidinone: mechanism of action [50s site]; uses [VREF, MRSA and MSSA])

**5. Sterilization and disinfection**

a. Define: antiseptic, disinfectant (high and low levels); germicide; sporicide; bacteriocide; fungicide; virucide; pasteurization

b. Describe: dry and moist heat sterilization; radiation sterilization; sterilization by filtration

c. Describe common methods of disinfection and what microbes survive the following agents: alcohols; halogens; aldehydes; phenols; gases; cationic detergents

d. Describe the following antiseptics and their limitations: iodine compounds; alcohol; chlorhexidine; hexachlorphene

**6. Normal flora**

a. Microbe/host interactions (commensalisms; symbiosis; parasitism; residents; transients; carrier state; effects of the normal flora on the host)

b. Skin (major inhabitants: *S. epidermidis, Micrococcus sp., Corynebacterium sp., P. acnes*; minor: Yeasts, *S. aureus, Lactobacillus sp.*)

c. Nose and nasopharynx (major inhabitants: *S. epidermidis, Corynebacterium sp.*; minor: *S. aureus, Haemophilus sp., Streptococcus sp., Branhamella sp.*)

d. Mouth (major inhabitants: *S. mitis, S. sanguis, S. salivarius, S. mutans* (plaque and caries); other: *S. epidermidis, Peptostreptococcus sp., Lactobacillus sp., Treponema sp., Actinomyces sp., Bacteroides sp., Fusobacterium sp., Veillonella sp.*)

e. Oropharynx (like mouth plus *Corynebacterium* sp.)

f. Stomach (*H. pylori*)

g. Small intestine

Jejunum (*Corynebacterium sp., Lactobacillus sp., Enterococcus sp.*)

Ileum (distal) (*Candida albicans, Enterobacteriaceae*, Gram negative anaerobes)

h. Large intestine (major inhabitants [strict anaerobes]: *Bacteroides sp., Fusobacterium sp., Eubacterium sp., Peptostreptococcus sp., Bifidobacterium sp.*; minor: *Enterococcus sp., Staphylococcus sp., Enterobacteriaceae, C. albicans*)

i. Genitourinary tract

Kidneys, bladder, urethra (sterile except for distal urethra [flora like skin])

Vagina and uterine cervix (*Lactobacillus sp., Bacteriodes sp., Corynebacterium sp., S. epidermidis, Enterococcus sp.*, [*C. albicans, T. vaginalis* in carriers])

**7. Introduction to the pathogens**

a. Definition of a pathogen (strict versus opportunistic; intracellular versus extracellular; definition of virulence and virulence factors)

b. Events associated with infection

(1) Routes of transmission (secretions; stool; skin; blood; zoonotic; arthropod-borne)

(2) Adherence; entry; and dissemination

(3) Incubation; exotoxins; and pathologic change (inflammation, necrosis)

(4) Subclinical infection and carrier state

c. Epidemiology

(1) Define and identify agents; their habitats; reservoirs; modes of transmission; and

define methods of management (treatment and prevention)

(2) Surveillance (disease prevalence and incidence)

(3) Terms that define disease patterns (outbreak; epidemic; pandemic; endemic; relapse; recrudescence)

(4) Terms that define disease severity (mortality and fatality rates; attack or infection rates)

d. Virulence factors and mechanisms of pathogenesis

(1) Pili/fimbriae (adherence; resistance to phagocytosis)

(2) Capsules and slime layers (resistance to phagocytosis; inhibition of C3b deposition)

(3) Exotoxins (type A-B toxins; non A-B toxins; mechanisms of action

(4) Other surface proteins (superantigens; antigenic mimicry; antigenic variation)

(5) Protein secretion

(6) Cell invasion (adherence; entry mechanisms; survival within host cells

# II. BACTERIAL PATHOGENS

(NOTE: Reservoirs and routes of transmission are included under the heading "virulence factors". Characteristics common to all members of a particular genera or group are in parentheses after the name.)

**10.** ***Actinomyces israelli & Nocardia asteroides*** (gram-positive, filamentous bacteria)

***Actinomyces israelli***

Characteristics: filamentous bacteria that fragment; facultative and strict anaerobes; common in soil
Infections: pyogenic abscesses connected by sinus tracts; "sulfur granules" form in tissues; endogenous opportunistic infections (cervicofacial, thoracic, abdominal, and genital infections); cervicofacial the most common (abscess associated with oral trauma or poor oral hygiene)
Control: penicillin, tetracycline, or macrolide

***Nocardia asteroides***

Characteristics: partially acid-fast, aerobic filamentous bacteria that fragment; common in soil
Infections: can survive and replicate in macrophages; cause exogenous bronchopulmonary infections in immunocompromised that often disseminates to the CNS; also cause primary cutaneous and lymphocutaneous infections and brain abscess
Control: trimeth-sulfameth, 3rd gen ceph

**11. Anaerobes, non-spore forming** (all lack cytochromes)

Gram positive cocci: ***Peptostreptococcus, Streptococcus*** (predisposing conditions; proinflammatory cell walls; infections: brain abscess, pulmonary infection, intra-abdominal infection, female pelvic infections, skin and soft tissue infections; control: penicillin, clindamycin, imipenem)
Gram negative rods: ***Bacteroides fragilis*** group (~60% of intra-abdominal infections and ~70% of anaerobic bacteremias)***, Prevotella, Porphromonas, Fusobacterium*** (virulence factors: varies with genus, includes capsule, adhesins, endotoxin, enzymes; infections: brain, oral, URT, dental, sinuses, LRT, female genital tract infections; control: drain, debride, metronidazole, clindamycin, chloramphenicol, imipenem)
Gram positive rods: ***Propionibacterium acnes*** (associated with acne)

**12. The genus *Bacillus*** (gram-positive rods, endospore-formers, common soil inhabitants, fac. anaerobes, catalase pos)

***B. anthracis***

Characteristics: non-motile
Virulence factors: zoonosis; polyglutamic acid capsule; toxins (PA-EF [calmodulin-dependent adenylate cyclase that increases intracellular cAMP], PA-LF [protease that induces apoptosis and disrupts endothelial barrier])
Infections: symptoms associated with toxin & route of entry: intestinal, inhalation, cutaneous anthrax (all may be associated with toxemia)
Control: vaccine (limited use in USA); penicillin, doxycyline, quinolone

***B. cereus***

Characteristics: motile
Virulence factors: heat labile & stable enterotoxins, cereolysin, lecithinase
Infections: emetic and diarrheal diseases (food-borne); other: bacteremia, pneumonia, ophthalmitis, osteomyelitis
Control: proper food storage; supportive and symptomatic; quinolone, gentamicin, serious infections with vancomycin

other *Bacillus sp.*:
***B. subtilis*** (emetic gastroenteritis, septicemia), ***B. licheniformis*** (diarrheal gastroenteritis)

**13. *Bordetella pertussis*** (and ***B. parapertussis***)
Characteristics: gram neg coccobacilli, aerobe, capsule, pili
Virulence factors: human reservoir, aerosol transmission; LPS, capsule, sol PG, pertussis toxin, invasive adenylate cyclase, adhesins (pertactin, filamentous hemagglutinin, pili, pertussis toxin), type III secretion
Infections: pertussis in children, persistent cough in adults
Control: Vaccine; macrolide

**14. The genius *Borrelia*** (motile, microaerophilic, gram-negative spirochete; zoonotic diseases; difficult to culture)
***B. recurrentis*** (lice vector, humans only host), ***B. hermsii*** and others (tick vector, rodents and small mammal are natural hosts)
Virulence factors: LPS, changes antigenic structure (variable major protein), highly invasive, intracellular growth
Infections: Relapsing fever
Control: avoid vectors; tetracyclines, macrolides, chloramphenicol

***B. burgdorferi*** (2 other species in Europe and Asia)
Virulence factors: tick vector; mice, deer, birds reservoirs; LPS, adhesins, invasive
Infections: Lyme disease (early localized [erythema chronicum migrans], early disseminated [secondary skin lesions, facial nerve palsy, meningitis, carditis], late disease [arthritis])
Control: avoid vectors; vaccine (not distributed); doxycycline, ceftriaxone

**15. *Brucella melitensis*** (biovars or species ***melitensis***, ***abortus***, ***suis***, and ***canis***)
Characteristics: gram neg, nonmotile coccobacilli, aerobe, catalase pos, oxidase pos, urease pos
Virulence factors: animal reservoir; transmission by direct contact or ingestion; LPS, facultative intracellular pathogen
Infections: brucellosis; septicemia, granulomas or abscesses in reticuloendothelial tissue (nodes, bone marrow, spleen, liver)

Control: doxycycline + rifampin

**16. The genus *Campylobacter*** (gram-negative, curved bacilli; microaerophilic, motile at 37C, oxidase & catalase positive)

***Campylobacter fetus*** (ssp ***fetus*** & ***venerealis***)
Characteristics: grows at 25C but not at 42C
Virulence factors: zoonotic with many animal reservoirs; transmission by direct contact or food or water; LPS, capsule (S protein that inhibits C3b binding)
Infections: infections in immunocompromised; septicemia following gastroenteritis
Control: avoid undercooked food and contaminated water; tetracyclines, macrolides, quinolones

***C. jejuni*** (ssp ***jejuni***)
Characteristics: grows at 42C but not at 25C
Virulence factors: many animal reservoirs (especially food animals); transmission by contaminated food or water; LPS, invasive, enterotoxin?, cytotoxin?
Infections: the leading cause of bacterial food-borne gastroenteritis (inflammatory); disseminated disease in immunocompromised; secondary complications include Guillain-Barre syndrome and arthitis
(Other species: *C. coli* and *C. upsaliensis*)
Control: avoid undercooked food and contaminated water; tetracyclines, macrolides, quinolones

**17. The genera *Chlamydia* and *Chlamydophila*** (strict intracellular bacteria; life cycle with two morphologic forms: elementary bodies (infectious form) and reticulate bodies (replicative form); gram-negative-like envelope; no peptidoglycan)

***Chlamydia trachomatis***
Virulence factors: intracellular pathogen; human reservoir; transmission (elementary bodies) route depends on syndrome
Infections: trachoma (seros A, B, Ba, C; transmitted by direct contact or flies; keratitis), inclusion conjunctivitis (seros B, Ba, D-K; transmitted by direct contact), STD (seros B, Ba, D-K; urethritis, cervicitis; PID, epididymitis, prostatitis), lymphogranuloma venereum (seros L1-3; STD)
Control: tetracyclines, macrolides

***Chlamydophila (Chlamydia) psittaci***
Virulence factors: intracellular pathogen; bird reservoir; transmission (elementary bodies) by bite or inhalation
Infections: atypical pneumonia
Control: tetracyclines

***Chlamydophila (Chlamydia) pneumoniae***
Virulence factors: intracellular pathogen; human reservoir; transmission (elementary bodies) by aerosols
Infections: (long incubation period) pneumonia, bronchitis, sinusitis, pharyngitis, atherosclerosis (?)
Control: tetracyclines, macrolides

**18. The genus *Clostridium*** (Gram-positive rods, strict anaerobes; produce endospores; common soil inhabitants)

***Clostridium perfringens*** (histotoxic)
Characteristics: aerotolerant and non-motile; found in soil and gastrointestinal tract; 5 strains based on exotoxin profile (A-E); target hemolysis associated with alpha and theta toxins
Virulence factors: exotoxins: alpha (most important) and beta toxin (enteritis necroticans); enterotoxin (super

Ag, heat-labile); infection initiated by traumatic entry of endospores or inoculation of ischemic tissue or consumption of contaminated food (gastroenteritis)
Infections: most associated with A; septicemia, intra-abdominal, biliary tract, genital, pleuropumonary, cellulitis, fasciitis, myonecrosis, gastroenteritis (food poisoning associated with A strains), enteritis necroticans (C strain)
Control: debridement + penicillin or clindamycin (hyperbaric oxygen treatment)

other histotoxic clostridia: ***C. septicum*** (myonecrosis, neutropenic colitis); ***C. novyi, C. sordellii, C. histolyticum*** (myonecrosis); ***C. difficile*** (see below)

***C. difficile***
Virulence factors: human reservoir; survival in hospitals (endospores), adhesins, enterotoxin (toxin A), cytotoxin (toxin B)
Infections: self-limited diarrhea, pseudomembranous enterocolitis (antibiotic-associated)
Control: vancomycin, metronidazole

***C. tetani***
Characteristics: very oxygen sensitive, motile
Virulence factors: traumatic entry of endospores; tetanolysin (hemolysin), tetanospasmin (neurotoxin)
Infections: tetanus (spastic paralysis): generalized, localized, cephalic, neonatal
Control: vaccine (Td); wound management, TIG, Td, penicillin or metronidazole

***C. botulinum***
Characteristics: motile, very resistant endospores
Virulence factors: strain classification: group I (proteolytic, neurotoxins A, B, or F), group II (nonproteolytic, toxins B, E, or F)
Infections: food, wound, infant botulism
Control: anti-toxin (A, B, E), penicillin, metronidazole

**19. *Corynebacterium diphtheriae***
Characteristics: gram-positive pleomorphic bacillus, aerobe, black colonies on tellurite agar
Virulence factors: human reservoir; transmitted by respiratory droplets; diphtheria toxin (ADP-ribosylates EF2 and inhibits protein synthesis)
Infections: related to toxin (myocarditis, neuritis); cutaneous and pharyngeal
Control: vaccine (DPT); anti-toxin + penicillin, macrolide, or tetracycline

20. **The family *Enterobacteriaceae*** (enteric bacteria; >25 genera; gram-negative bacilli; oxidase negative, facultative anaerobes; common inhabitants of GI tract; serological typing based on O-polysaccharide antigens of LPS, K (capsular) antigens, and H (flagellar) antigens)

***Escherichia coli***
Characteristics: lactose fermented
Virulence factors: animal and human resevoir; transmitted by contaminated food or water, direct contact, fecal-oral; adhesins, type III secretion, quorum sensing, cytotoxins, LPS, enterotoxins, capsule/biofilm (see individual syndromes below)
non-GIT Infections & control: UTI (specific adhesins, cytotoxin, LPS; trimeth-sulfmeth, floroquinolone, azithromycin), pneumonia (LPS; 3rd gen ceph + aminoglycoside), sepsis (LPS; 3rd gen ceph + aminoglycoside), meningitis (neonatal; LPS, K-1 strains; 3rd gen ceph + aminoglycoside)
GIT infections: EPEC (bundle-forming pili, type III secretion, intimin-mediated attachment; loss of microvilli in

sm intestine/absorption inhibited; infant diarrhea); ETEC (adhere to sm intestine via pili, secrete heat labile (LT) and/or heat stable (ST) enterotoxins; fluid & electrolyte loss; traveler's diarrhea); EIEC (attaches and invades lg intestine; absorption inhibited; inflammatory diarrhea that is watery to bloody; adult infection); EHEC (adheres to lg intestine epithelial cells via pili; spreads cell to cell via actin tails; secrete Shiga-like toxins I & II; absorption inhibited; watery diarrhea; O157:H7 & SLT-II causes hemolytic uremic syndrome); EAggEC (adheres via bundle-forming pili; noninflammatory diarrhea by unknown mechanism)
Control: avoid contaminated food, water, and animals; symptomatic, trimeth-sulfmeth, quinolone, azithromycin

***Klebsiella pneumoniae*** (spp *pneumoniae*)
Characteristics: non-motile, large capsule
Virulence factors: animal reservoir; transmission by aerosols; LPS, capsule
Infections: lobar pneumonia, UTI, septicemia, meningitis
Control: 3rd gen ceph + aminoglycoside
(other species: ***K. oxytoca***, ***pneumoniae*** spp ***ozaenae***, ***pneumoniae*** spp ***rhinoscleromatis***)

***Proteus mirabilis* and *P. vulgaris***
Characteristics: "swarming" motility; urease pos, $H_2S$ produced,
Virulence factors: animal reservoir; transmission by direct contact; LPS, motility, urease
Infections: UTI, stones (in compromised: pneumonia, septicemia)
Control: 3rd gen ceph + aminoglycoside for life-threatening infections; quinolone, ampicillin or amoxicillin for other

***Shigella sonnei***
Characteristics: nonmotile, no lactose fermentation, no $H_2S$ production
Virulence factors: human reservoir; transmission by direct contact, person to person, food or water; adherence, LPS, type III secretion, intracellular growth, Shiga toxin, actin tails mediate cell to cell spread
Infections: inflammatory diarrhea that is watery or classic dysentery
Control: avoid contaminated food/water; quinolone, trimeth-sulfmeth
(other species: ***S. dysenteriae, flexneri, boydii***)

***Salmonella enterica***
(serotypes ***choleraesuis, paratyphi, typhi, enteritidis, typhimurium, newport, heidelberg***)
Characteristics: motile, no lactose fermentation, produces $H_2S$
Virulence factors: human (typhi and paratyphi) and numerous animal reservoirs; transmission by direct contact, person to person, food or water; adherence, LPS, type III secretion, intracellular growth, enterotoxin, actin rearrangement
Infections: typhoid fever (*S. typhi* & *paratyphi*); inflammatory diarrhea that is watery and mucoid; septicemia
Control: vaccine for typhoid fever; avoid contaminated food/water; quinolone for GIT, ceftriaxone or choramphenicol for septicemia

**Other *Enterobacteriaceae*: *Enterobacter, Hafnia, Serratia, Citrobacter, Providencia, Morganella, Erwinieae, Edwardsiella***
Infections: nosocomial UTI & septicemia in immunocompromised

**21. *Francisella tularensis*** (subsp. ***tularensis***)
Characteristics: gram neg pleomorphic coccobacillus, aerobe, catalase pos, oxidase neg, requires cysteine for growth, capsule

Virulence factors: many animal reservoirs (e.g. rabbits); transmission by ticks, biting flies, direct, ingestion, or inhalation; LPS, capsule, facultative intracellular pathogen, very infectious
Infections: (zoonosis) ulceroglandular, glandular, oculoglandular, pharyngeal, typhoidal, pneumonic
Control: avoid infected animals; doxycycline, quinolone, or gentamicin

**22. The genus *Haemophilus*** (gram negative coccobacilli, facultative anaerobe, catalase pos)
***Haemophilus influenzae***
Characteristics: requires hematin (X-factor) & NAD or NADP (V-factor) for growth, capsule (a-f)
Virulence factors: human reservoir ; aerosol transmission; LOS, capsule, OM proteins (adherence, invasion, intracellular growth), sol PG, IgA peptidase
Infections: pharyngitis, sinusitis, pneumonia, bronchitis, otitis media, conjunctivitis, epiglottitis, septicemia, meningitis (rare with vaccine)
Control: Vaccine; cefuroxime, ceftriaxone, amox for non-life-threatening; rifampin prophylaxis

Other ***Haemophilus*** sp.: non-typeable/unincapsulated ***H. influenzae*** (associated with otitis media, pneumonia, sinusitis, neonatal & postpartum sepsis; treat with macrolide, trimeth-sulfmeth, quinolone); ***H. influenzae*** biotype ***aegypticus*** (associated with conjunctivitis that may disseminate; treat with macrolide or quinolone); ***H. aphrophilus*** (associated with endocarditis; treat with macrolide or quinolone); ***H. ducreyi*** (STD [chancroid]; treat with macrolide or trimeth-sulfmeth)

**23. *Helicobacter pylori***
Characteristics: gram-negative spiral rod, microaerophilic, motile at 37C; urease, oxidase & catalase positive
Virulence factors: human reservoir; route of transmission fecal/oral or direct contact; LPS, urease, acid-inhibitory protein, motility, mucinase, cytotoxin, adhesins (hemagglutinin, sialic acid-binding protein, Lewis blood group adhesin)
Infections: chronic gastritis leading to peptic ulcers; predisposes to carcinoma
Control: improve sanitation; macrolide or tetracycline + metronidazole + bismuth subsalicylate + proton pump inhibitor

**24. *Legionella pneumophila***
Characteristics: gram neg rod, aerobe, catalase pos, oxidase neg, hydrolyzes hippurate, motile, fastidious (requires high cysteine and iron levels)
Virulence factors: aquatic environment the natural reservoir (parasitizes amoebas and ciliated protozoans); transmission by aerosols (point-source); LPS (OM blebs), type II & IV secretion, intracellular growth (internalized by coiling phagocytosis), pili, Th1 response needed
Infections: Pontiac fever (high attack rate, self limiting febrile disease), Legionnaires' disease (low attack rate, predisposing condition, bronchopneumonia with dry cough that becomes productive; GIT, CNS, and kidneys may be involved)
Control: macrolide, quinolones

**25. *Leptospira interrogans***
Characteristics: gram-negative tightly coiled spirochete, hook shaped at one or both ends; motile, aerobe
Virulence factors: many animals are reservoirs; usually transmitted to humans by direct contact with contaminated water; LPS, invasive, intracellular growth
Infections: anicteric leptospirosis (mild syndrome to systemic disease involving aseptic meningitis); icteric leptospirosis (Weil's disease) with liver and kidney failure and vascular collapse
Control: avoid contaminated water; penicillin, tetracyclines, macrolides

**26. *Listeria monocytogenes***

Characteristics: gram positive bacillus, facultative anaerobe, catalase pos, oxidase neg, facultative psychrophile, hydrolyzes esculin, motile at room temperature

Virulence factors: zoonotic, widespread in nature, many foods contaminated; transmitted by ingestion, transplacental (in utero), vaginal; facultative intracellular pathogen (Th1 needed to recover), lysteriolysin, internalin, actin tails, Act A

Infections: pregnancy (septicemia, infection of fetus), neonatal (early and late onset diseases), adults (meningitis and septicemia most important; also gastroenteritis)

Control: avoid processed meats; sulfameth-trimeth prophylaxis; treat with ampicillin+aminoglycoside

**27. Miscellaneous bacteria**

***Pasteurella multocida***

Characteristics: gram neg coccobacilli, facultative anaerobe, catalase pos, oxidase pos, encapsulated Virulence factors: found in the mouth of domestic animals (cats); transmission by bite; LPS, capsule Infections: cellulitis, septicemia

Control: penicillin, ampicillin, tetracycline

***Moraxella catarrhalis***

Characteristics: gram neg diplococcus, aerobe, oxidase pos, catalase pos, grows on most media (not fastidious)

Virulence factors: human reservoir (5-50% colonization); aerosol transmission; LOS (no somatic O-polysacch), adhesins (pili and OM proteins),

Infections: important cause of otitis media, sinusitis, bronchitis, pneumonia

Control: cefaclor, marcrolides, quinolones, trimeth-sulfameth

***Aeromonas hydrophila*** (and ***A. caviae, veronii*** biovar ***sobria***)

Characteristics: gram neg rod, facultative anaerobe, motile, oxidase positive

Virulence factors: aquatic environment the natural reservoir; transmission by trauma, food or water; LPS, enterotoxin, hemolysin

Infections: gastroenteritis (noninflammatory to inflammatory), wound infection (cellulitis, osteomyelitis), sepsis

Control: avoid raw or undercooked food; tetracyclines, aminoglycosides, trimeth-sulfameth

***Plesiomonas shigelloides***

Characteristics: gram neg rod, facultative anaerobe, motile, oxidase positive; aquatic environment the natural reservoir

Infections: inflammatory diarrhea

Control: quinolone, trimeth-sulfameth

***Bartonella henselae***

Characteristics: gram neg rod

Infections: cat scratch disease; bacillary angiomatosis in immunocompromised

Control: rifampin, quinolones, azithromycin

**28. The genus *Mycobacterium*** (gram-positive cytology with high glycolipid [mycolic acids, arabinogalactan, lipoarabinomannan] content in cell wall responsible for acid-fast staining, proinflammatory activities, and resistance to detergents and disinfectants; most slow growing and form serpentine cords; aerobic)

***M. tuberculosis***
Characteristics: produces niacin
Virulence factors: human reservoir; aerosol transmission (prolonged contact needed); facultative intracellular pathogen (Th1 needed to control infection but also responsible for tissue damage); wall gycolipids promote resistance to intracellular killing, inhibit interferon-activation of macrophages, prevent phago-lysosomal membrane fusion, and stimulate cell-mediated inflammatory injury
Infections: pneumonia (hypersensitive reaction to bugs); disseminated disease (bone marrow, nodes, CNS, etc); infection converts to PPD+
Control: vaccine (limited use in USA); rifampin, isoniazid, pyrazinamide, ethambutol first-line drugs
NOTE: ***M. bovis*** causes similar disease. It doesn't produce niacin and many animals serve as reservoirs; transmission by ingestion.

***M. leprae***
Characteristics: intracellular bacterium (no growth on lab media)
Virulence factors: human and armadillo reservoirs; transmission by nasal secretions; intracellular pathogen (Th1 needed but also mediates tissue damage), proinflammatory wall, phenolic glycolipid capsule, phenolase
Infections: Hansen's disease (leprosy): chronic disease of skin, peripheral nerves, & URT; tuberculoid (paucibacillary), borderline, lepromatous (multibacillary); infection converts to lepromin+
Control: dapsone + rifampin; multibacillary: rifampin, clofazimine, dapsone; pauscibacillary: rifampin, dapsone

Other mycobacteria:
***M. kansasii, M. marinum, M. scrofulaceum, M. ulcerans, M. fortuitum, M. avium, intracellulare***
many reservoirs (soil, water, etc); localized to disseminated infections (*M. avium, intracellulare* cause disseminated disease in AIDS); treatments depend on species

**29. The genera *Mycoplasma* and *Ureaplasma*** (no cell wall results in pleomorphic morphology; have sterols in plasma membrane and require exogenous sterols for growth; smallest free-living procaryotes; all extracellular pathogens; membrane induces inflammation)
***Ureaplasma urealyticum***
Characteristics: urease positive, prefers anaerobic growth
Virulence factors: human reservoir; transmission by direct contact
Infections: urethritis, perinatal & postpartum sepsis in women; urethroprostatitis, epididymitis, urinary calculi in men
Control: tetracyclines, macrolides

***Mycoplasma hominis***
Characteristics: prefers aerobic growth
Virulence factors: human reservoir; transmission by direct contact
Infections: vaginitis, cervicitis, PID (endometritis, salpingitis), pyelonephritis, perinatal sepsis, neonatal conjunctivitis, postpartum sepsis
Control: tetracyclines, macrolides

***M. genitalium***
Characteristics: prefers anaerobic growth
Virulence factors: human reservoir; transmission by direct contact
Infections: urethritis (prominent cause of NGU in men and women)
Control: tetracyclines, macrolides

***M. pneumoniae***

Characteristics: aerobic

Virulence factors: human reservoir; transmission by aerosols; adheres to cilitated epithelial cells (kills them with cytotoxic membrane and $H_2O_2$), induces cytokines (IL-1, 6 & TNF) and inflammatory infiltrate

Infections: pneumonia, tracheobronchitis, pharyngitis, otitis, hemorrhagic bullous myringitis

Control: tetracyclines, macrolides

**30. The genus *Neisseria*** (gram-negative, oxidase-positive diplococci; fastidious, requires extra $CO_2$; poor survival on environmental surfaces; human reservoir; high turnover of envelope components (LOS and PG) during growth)

***Neisseria meningitidis***

Virulence factors: aerosol transmission; LOS (blebs, no somatic O-polysacch), capsule (12 serogroups with B, C, and Y most common; A associated with epidemics), adhesins (OM proteins & pili), sol PG, IgA peptidase

Infections: septicemia, meningitis, Waterhouse-Friderichsen syndrome

Control: Vaccine; penicillin, chloramphenicol, ceftriaxone

***N. gonorrhoeae***

Virulence factors: sexual transmission (neonatal infection in utero or during birth); LOS (blebs, no somatic O-polysacch), adhesins (OM proteins [Por mediates complement resistance and intracellular survival, Opa associated with attachment] pili [pili antiphagocytic]), sol PG, beta-lactamase, IgA peptidase

Infections: urethritis in men, urethritis and cervicitis in women (~30% symptomatic); PID, disseminated gonococcal infection (arthritis w/ or w/o skin lesions), gonococcal opthalmia

Control: ceftriaxone or quinolone + doxycycline or azithromycin

**31. *Pseudomonas* and related genera**

***P. aeruginosa***

Characteristics: gram negative rod, aerobic (anaerobic with nitrate), motile, oxidase & catalase pos, non-fermenter, wide temp range, nutritionally versatile, fluorescein pigment (pyocyanin) produced by most

Virulence factors: many environmental reservoirs (including hospitals); transmission by direct contact, food, water; LPS, pili, capsule or biofilm, proteases, cytotoxin, heat stable and labile hemolysins, exotoxin A, exoenzyme (exotoxin) S, Type III secretion, quorum sensing, antibiotic resistance

Infections: mostly opportunistic and nosocomial; endocarditis, respiratory tract infections, pneumonia in cystic fibrosis, septicemia (ecthyma gangrenosum), meningitis, otitis, keratitis, bone and joint infections, UTI, skin (burn infections, generalized folliculitis)

Control: aminoglycoside + anti-Pseudomonas beta-lactam

***Burkholderia cepacia***

Infections: RT infections in cystic fibrosis, catheter-associated UTI & septicemia

Control: trimeth-sulfmeth

***Stenotrophomonas maltophilia***

Infections: nosocomial septicemia, meningitis, UTI, wound infections

Control: trimeth-sulfmeth

**32. The genus *Rickettsia* and related genera (*Ehrlichia, Anaplasma,* and *Coxiella*)** (strict intracellular bacteria)

***Rickettsia rickettsii***

Characteristics: gram neg coccobacilli, strict intracellular pathogen, grows in cytoplasm of host cells, utilizes host ATP, NAD, and intermediates
Virulence factors: animal reservoir; transmission by hard ticks (wood or dog; tick progeny infected); strict intracellular pathogen, weak endotoxin, phospholipase A destroys host membranes, actin tails mediate cell to cell spread
Infections: RMSF (vasculitis, rash)
Control: avoid tick contact; tetracyclines

Other ***Rickettsia*** sp: ***R. akari*** (rickettsialpox; zoonotic in mice; mite transmission; smallpox-like rash); ***R. prowazekii*** (louse-borne or epidemic typhus; human louse transmission; rash); ***R. typhi*** (murine endemic typhus; zoonotic in rodents; flea transmission; rash).

***Ehrlichia chaffeensis***

Characteristics: gram negative cytology, no peptidoglycan or LPS, intracellular pathogen (grows in phagosome=morula), life cycle involves reticulate and elementary - like bodies
Virulence factors: animal reservoir; transmission by tick; strict intracellular pathogen of monocytes; immune response (gamma-interferon and activation of macrophages) associated with pathology
Infections: human monocytic ehrlichiosis
Control: avoid tick contact; tetracyclines

***Anaplasma phagocytophilum***

Characteristics: similar to Ehrlichia
Virulence factors: animal reservoir; transmission by tick; strict intracellular pathogen of myeloid precursors (neutrophils); pathogenesis related to immune response
Infections: human anaplasmosis (formerly human granulocytic ehrlichiosis)
Control: avoid tick contact; tetracyclines, chloramphenical

***Coxiella burnetii***

Characteristics: gram negative pleomorphic bacillus that produces resistant endospore-like structures; obligate intracellular pathogen
Virulence factors: animal reservoir; transmission by tick to animals, to humans by inhalation or ingestion; strict intracellular pathogen of reticuloendothelial cells; antigenic variation of LPS during infection
Infections: Q-fever (acute febrile disease, atypical pneumonia most common; chronic with subacute endocarditis, hepatitis, CNS, and/or pulmonary involvement)
Control: tetracyclines

**33. The genus S*taphylococcus*** (gram-positive cocci that grow in clusters; facultative anaerobes, catalase positive, salt-tolerant)

***S. aureus***

Characteristics: coagulase positive, ferments mannitol
Virulence factors: human reservoir (carriers); transmission by direct contact; capsule and biofilm, quorum sensing; alpha, beta, delta, gamma-toxins, enterotoxins (super antigens), pyrogenic exotoxins (TSST-1), exfoliatins (super antigens), facultative intracellular parasite, proinflammatory cell wall components (induces IL1,

TNF alpha), beta-lactamases, cell wall-bound adhesion molecules (fibrinogen, collagen, & fibronectin-binding proteins), Protein A, extracellular hydrolases
Infections: folliculitis, furuncle, carbuncle, cellulitis, impetigo, scalded skin syndrome, septicemia, endocarditis, pneumonia, osteomyelitis, septic arthritis, purulent meningitis, food poisoning, toxic shock
Control: hand washing; mupirocin, macrolide, beta-lactam (w/ or w/o aminoglycoside), vancomycin

***S. epidermidis***
Characteristics: coagulase negative
Virulence factors: human reservoir, commensal and pathogenic strains; transmission by direct contact; biofilm, quorum sensing, proinflammatory cell wall components (induces IL1, TNF alpha), alpha and delta toxins, beta-lactamases
Infections: neonatal bacteremia, nosocomial bacteremia, prosthetic devise infection, surgical infections, infections associated with peritoneal dialysis, urinary tract infection
Control: hand washing; beta-lactams, vancomycin+rifampin

***S. saprophyticus***
Characteristics: resistant to novobiocin, coagulase negative
Virulence factors: human reservoir; transmission by direct contact; specific adherence to urinary tract epithelial cells; proinflammatory cell wall components
Infections: community-acquired UTI (mostly women)
Control: trimeth-sulfmeth, quinolone, amox+clavulanic acid

**34. The genus *Streptococcus* and *Enterococcus*** (gram-positive cocci occurring in pairs and/or chains; facultative anaerobes; ferment lactic acid; catalase negative; alpha, beta, or gamma-hemolysis)
***Streptococcus pyogenes***
Characteristics: grows in chains, Group A carbohydrate, beta-hemolytic, sensitive to bacitracin
Virulence factors: human reservoir; transmission by aerosols, food, water and direct contact;
M-proteins, fimbriae, proinflammatory cell wall components, hyaluronic acid capsule, Streptolysin O & S, Streptococcal pyrogenic exotoxins (super antigens), intracellular invasion, adhesins (LTA, Protein F, fibrinogen binding protein, collagen binding protein, plasmin binding protein), C5a peptidase
Infections: pharyngitis, scarlet fever, streptococcal toxic shock syndrome, impetigo, cellulitis, erysipela, necrotizing fasciitis, puerperal sepsis, rheumatic fever (antigenic mimicry), postinfectious glomerulonephritis
Control: penicillin, macrolide, quinolone

***S. agalactiae***
Characteristics: grows in chains, Group B carb, weakly beta-hemolytic or gamma hemolytic, hydrolyzes hippurate, posituve CAMP test
Virulence factors: human reservoir; transmitted by direct contact, person to person, transplacental; proinflammatory wall components, capsule, intracellular invasion, C5a peptidase
Infections: neonatal infections (early and late onset); adult infections (septicemia, meningitis, respiratory and urinary tracts)
Control: hand washing, hospital control policies; penicillin, vancomycin, penicillin or ampicillin+aminoglycoside

**Viridans Strep: *S. mutans, mitis, sanguis, bovis*** (considered separately below) **groups**
Characteristics: alpha or gamma hemolytic; most lack group antigen
Virulence factors: proinflammatory wall components, adhesins
Infections: inhabit oral cavity & tooth surfaces; most infections endogenous; associated with dental caries (*S.*

*mutans*) and endocarditis
Control: penicillin (+aminoglycoside), vancomycin for resistant strains

***S. bovis* group**
Characteristics: Group D carb
Virulence factors: animal reservoir or endogenous source (GIT); transmitted by contaminated food or water; proinflammatory wall components
Infections: endocarditis, bacteremia (assoc. with GI malignancy)
Control: penicillin

***S. pneumoniae***
Characteristics: grows in pairs, optochin sensitive, large capsule
Virulence factors: human reservoir; transmitted by aerosols or endogenous; capsule, proinflammatory wall components, adhesins (capsule, choline-binding protein, neuraminidase), pneumococcal surface protein A & C, autolysin, pneomolysin O, hyaluronate lyase, antibiotic resistance
Infections: pneumonia, otitis media, meningitis, sinusitis
Control:Vaccines (adult & child); CAP: macrolide, quinolone, ceftriaxone, cefotaxime; OM, sinusitis: amox+clav; Meningitis: vanco+3rd gen ceph

***Enterococcus faecalis*** and ***faecium***
Characteristics: grows in chains, Group D carbohydrate, hydrolyze esculin, tolerates high salt and bile concentrations
Virulence factors: endogenous (GIT & vagina) or nosocomial source; transmitted by direct contact or person to person; proinflammatory wall components, adhesins, cytolysin (bacteriocin), antibiotic resistance
Infections: catheter-associated UTI, septicemia, endocarditis
Control: hand washing, vancomycin, vanco + aminogly, quinupristin/dalfopristin, linezolid, minocycline+chloramphenicol

**35. *Treponema pallidum* (ssp *pallidum*)**
Characteristics: thin gram negative spirochete (special microscopy needed to observe), microaerophilic, motile, no growth on lab media, cardiolipin in OM
Virulence factors: human reservoir; sexual transmission; LPS, highly invasive, intracellular growth, hyaluronidase, OM proteins associated with adherence, fibronectin coats outer membrane (anti-phagocytic); tissue damage associated with immune/inflammatory response
Infections: Syphilis (primary, secondary, latent, tertiary, congenital)
Control: penicillin

**36. The genus *Vibrio*** (curved gram-negative bacilli, inhabit marine environments, motile by single polar flagellum, facultative anaerobes, oxidase positive)
***Vibrio cholerae***
Characteristics: killed by stomach acid; only seotypes O1 and O139 are associated with cholera
Virulence factors: transmission by food or water; toxin coregulated pili (attachment), cholera toxin (increases intracellular cAMP); other: accessory cholera enterotoxin (increases intestinal fluid secretion), zonnula occludens toxin (increases intestinal permeability), other colonization factors
Infections: noninflammatory watery diarrhea (potentially life threatening)
Control: avoid contaminated food/water; tetracyclines, rehydration

***V. parahaemolyticus***
Characteristics: halophilic
Virulence factors: transmission by food or water; LPS, pili, cytotoxin/hemolysin (has enterotoxin activity)
Infections: noninflammatory watery diarrhea to inflammatory dysentery-like gastroenteritis
Control: avoid raw or undercooked seafood; tetracyclines

***V. vulnificus***
Characteristics: halophilic
Virulence factors: transmission by food or water; LPS, pili, proteases, cytotoxin, antiphagocytic capsule (resistance to complement)
Infections: wound infections (rapidly progressive cellulitis), invasive gastroenteritis, septicemia
Control: avoid raw or undercooked seafood; tetracyclines, aminoglycosides

**37. The genus *Yersinia*** (zoonotic, gram negative coccobacilli, facultative anaerobes; common virulence factors: LPS, facultative intracellular parasite, type III secretion, yadA gene products (adhesins and anti-phagocytic proteins), yop/lcr gene products (OM proteins, toxic secreted proteins), V and W antigens (intracellular growth))

***Yersinia pestis***
Characteristics: bipolar staining, capsule (fraction 1 antigen)
Virulence factors: animal reservoir; transmission by flea bite or aerosols; antiphagocytic capsule (fraction 1 Ag)
Infections: bubonic, pneumonic, septicemic plague
Control: gentamycin, tetracycline

***Y. enterocolitica* (**and ***Y. pseudotuberculosis*****)**
Characteristics: facultative psychrophile, urease positive
Virulence factors: transmission by ingestion
Infections: mesinteric adenitis, gastroenteritis
Control: avoid contaminated food and water; doxycycline, ceftriaxone, trimeth-sulfmeth

# III. Outline of General Virology

**41) Morphology and structure of viruses**

a) Nucleic Acid serving as genome -(DNA or RNA; double-stranded or single-stranded; positive strand RNA, or negative strand RNA)
b) Nucleocapsid
   i) Composition (capsid proteins, enzymes and nucleic acid genome)
   ii) Function of individual components (e.g., capsid proteins- protection of nucleic acids; nucleic acid genome- replication and transcription)
   iii) Types (helical vs icosahedral)
c) Envelope or Membrane
   i) Composition and origin - (trilaminar phospholipid membrane derived from host cell)
   ii) Viral proteins associated with envelope
      (1) Matrix proteins

(2) Glycoproteins
(a) Composition - (viral protein moiety, cellular carbohydrate moiety)
(b) Functions - (enzymatic, serves in attachment of virus to cells, major antigen that gives rise to neutralizing antibodies)

d) Types of Viruses
i) Naked viruses
ii) Enveloped viruses

**42a) Classification of viruses**

a) Epidemiological scheme- based on transmission of viruses (respiratory vs enteric vs arthopod-borne)
b) Biochemical scheme- based on the structure and composition of viruses

**42b) Growth Cycle of Viruses**

c) Attachment (basis of specificity)
d) Penetration (receptor-mediated endocytosis and membrane fusion)
e) Uncoating (location and mechanism)
f) Replication (location of viral protein and of viral nucleic acid biosynthesis)
g) Assembly (location)
h) Release (cell lysis vs budding)

**42c) Types of viral infections** (abortive vs acute vs persistent vs latent)

**43) Replication of viral genomes**

a) **DNA-containing viral genomes** (most replicate within nucleus, synthesize early and late mRNAs, and encode a DNA-dependent DNA polymerase, but not a DNA-dependent RNA polymerase). Notable exceptions are indicated below.
i) Papovaviruses - does not encode a viral DNA-dependent DNA polymerase
ii) Parvoviruses - does not encode a viral DNA-dependent DNA polymerase; no temporal control of translation of viral proteins
iii) Poxviruses - core contains a DNA-dependent RNA polymerase, replicates within core and in cytoplasm
iv) Adenoviruses - no exceptions
v) Herpesviruses - encodes a thymidine kinase, three classes of RNA transcripts - alpha, beta and gamma transcripts.
vi) Hepadnaviruses - replicates in cytoplasm, contains a reverse transcriptase, DNA genome is replicated via a RNA intermediate, DNA replication occurs within cores, no temporal control of translation of viral proteins.

b) **RNA-containing viral genomes** (all encode a RNA-dependent polymerase; most replicate in cytoplasm and synthesize transcripts at the same time). Exceptions and other features are listed below.
i) Double-stranded RNA viruses - early and late transcripts, replication of genome occurs within cores using positive-strand RNA as template.
ii) Positive-stranded viruses - genome is synthesized using negative strand viral RNA as a template; translation results in polyproteins which are cleaved to form RNA polymerases and viral proteases. Togaviruses synthesize early and late RNA transcripts.
iii) Negative-stranded viruses - nucleocapsid contains a RNA-dependent RNA polymerase which synthesizes a positive strand RNA for translation and as a template for synthesis of genome.

Orthomyxoviral genomes replicate in nucleus using cellular RNA as primer and virions assemble in cytoplasm

iv) Retroviruses - nucleocapsid contains a RNA-dependent DNA polymerase and an integrase. The virion RNA is a template for the synthesis of a DNA copy. The viral double-stranded DNA integrates into the host's chromosome. Transcription of the integrated viral DNA results in viral RNA that serves as progeny genomes and is used for translation. Viral polyproteins are cleaved by viral proteases to form virion proteins including the RNA-dependent DNA polymerase and integrase.

**44) Anti-viral agents**

a) Interferon
   i) Types and characteristics (alpha, beta, and gamma interferons)
   ii) Properties of alpha- and beta-interferon
      (1) Encoded by cellular gene
      (2) Transcription occurs upon viral infection, associated with viral nucleic acid replication
      (3) Binds to specific receptor proteins on cell membrane, accounting for species specificity
      (4) Induction of interferon-inducible proteins by signal transduction and phosphorylation of cellular transcription factors
      (5) Activation and functioning of the interferon inducible enzymes requires viral double-stranded RNA and ATP
      (6) Functions of interferon-inducible 2'-5' adenylate synthetase and of the interferon inducible protein kinase

b) Antiviral agents affecting nucleic acid synthesis
   i) Nucleoside analogs
      (1) Inhibits viral polymerase activity by causing chain termination
         (a) Acyclovir (derivatives of acyclovir include valacyclovir, penciclovir, famciclovir)
            (i) Specifically phosphorylated by herpesvirus thymidine kinase.
            (ii) Preferentially inhibits herpesviral DNA-dependent DNA polymerase
         (b) Ganciclovir
            (i) Used in treatment of cytomegaloviral retinitis in AIDS patients. Specific inhibition of viral DDDP
            (ii) Phosphorylated by CMV protein kinase
         (c) Adenine arabinoside
            (i) No preferential phosphorlyation by herpes viral thymidine kinase
            (ii) Preferentially inhibits herpesviral DDDP and is rapidly inactivated by adenosine deaminase to an inactive metabolite
         (d) Azidothymidine (AZT)
            (i) Phosphorylated by cellular enzymes
            (ii) Inhibits HIV reverse transcriptase
            (iii)Other nucleoside analogs that inhibit HIV reverse transcriptase: dideoxyinosine, dideoxycytidine, lamivudine
         (e) Acyclic nucleoside phosphonates (e.g. cidofovir for CMV)
      (2) Causes errors in replication and transcription
         (a) Ribavirin - inhibits respiratory synctial virus; also inhibits nucleoside biosynthesis and formation of the mRNA 5' guanosine cap
         (b) Trifluorothymidine (TFT) - thymidine analog, phosphorylated by cellular enzymes,

topical administration.
(c) Iododeoxyuridine - same as TFT

ii) Non-nucleoside analogs
(1) Foscarnet - Binds to the pyrophosphate binding site of the herpesvirus DNA polymerase and inhibits the viral DNA polymerase activity. Does not require phosphorylation to be active. Treatment of CMV retinitis in AIDS patients.
(2) Nevirapine, and delavirdine - noncompetitively inhibits HIV-1 reverse transciptase by binding to the enzyme. Does not require phosphorylation to be active.

c) Antiviral agents inhibiting uncoating - amantadine and rimantadine (specifically inhibits uncoating of influenza A viruses
d) Antiviral agents affecting enzymatic functions of viral proteins
i) Protease Inhibitors (e.g. saquinavir, indinavir, nelfinavir, ritinavir) - Binds to active site of the HIV protease inhibiting the cleavage of HIV polyproteins.
ii) Neuraminidase Inhibitors (zanamivir, oseltamivir) - competitive inhibitor of sialic acid binding, prevents the functioning of neuraminidase and the formation of infectious progeny virions.
e) Fusion inhibitor (enfuvirtide): blocks HIV fusion with host cell by binding to gp41 (for HIV in combination with other drugs)

# IV. Viruses

(NOTE: Reservoirs and routes of transmission are included under the heading "pathogenesis". Characteristics common to all members of a particular family or group are in parentheses after the name.)

**51. Adenovirus** (family *Adenoviridae*)
Characteristics: naked icosahedral capsid (hexon, hexon-associated proteins, fiber [attachment, hemagglutination] penton base [cytotoxic], core proteins [no enzymes]), genome dsDNA
Replication: in nucleus; early, and late transcripts; release by cell lysis
Pathogenesis: lytic or latent infections; transmission by aerosols, direct contact, fecal/oral; human reservoir
Infections: acute febrile pharyngitis, atypical pneumonia, acute respiratory disease, pertussis-like syndrome, pharyngoconjunctival fever, epidemic keratoconjunctivitis, acute hemorrhagic cystitis, gastroenteritis (diarrhea in infants)
Control/prevention: none

**52. *Bunyaviridae*: Bunyavirus, Hantavirus** (envelope with 2 types of glycoproteins (G1 & G2); genome composed of 3 neg pol RNA strands (large [L], medium [M], small [S]); L codes for RNS-dep-RNA pol (found in nucleocapsid), M codes for envelope glycoproteins and a nonstructural protein, S codes for nucleocapsid and a nonstructural proteinenvelope; replication in cytoplasm; bud into golgi and released by exocytosis or cell lysis)

**Bunyavirus** (major strains: California encephalitis virus, La Crosse encephalitis virus)
Pathogenesis: Replicates in (transovarian transmission) and transmitted by mosquito (vector); squirrels, chipmunks major reservoirs
Infections: subclinical, mild febrile disease, meningitis, encephalitis
Control/prevention: control vector

**Hantavirus** (major strain: Sin Nombre)
Pathogenesis: mice major reservoir (strains are species-specific); transmitted by mouse saliva, urine, feces
Infections: pulmonary syndrome (pulmonary edema), hemorrhagic fever renal syndrome (not in U.S.)

Control/prevention: control reservoir

**53. Coronavirus** (family *Coronaviridae*)
Characteristics: enveloped, helical nucleocapsid symmetry; 1 segment pos pol RNA genome; E2 protein (attachment), E1 protein (matrix for assembly), E3 protein (hemagglutinin on some strains), L protein (RNA-dependent-RNA polymerase (synthesizes neg pol template RNA; early protein during replication), N protein (nucleocapsid)
Replication: replication and assembly in cytoplasm; neg pol template strand made from which several mRNAs and progeny genomes are made; bud into ER for assembly; released through golgi
Pathogenesis: peak late winter through early spring; transmitted by aerosols, hand to hand, object to hand; infects mostly URT epithelial cells; inflammation and cytokines contribute to pathogenesis. Reinfections possible
Infections: cold (with pharyngitis), pneumonia, gastroenteritis
Control/prevention: none
**SARS-associated Coronavius** causes a spectrum of symptoms from mild to severe lower respiratory tract infections; severe form associated with pneumonia or acute respiratory distress syndrome.
Control/prevention: none

**54. *Flaviviridae*** (genus *Flavivirus*; St. Louis Encephalitis virus, Dengue virus, Yellow Fever virus, Japanese encephalitis virus, West Nile virus)
Characteristics: similar to *Togaviridae* except envelope derived from intracytoplasmic membranes
Replication: similar to *Togaviridae* except all of genome translated into one protein that is processed into structural and non-structural proteins (protease, RNA-dep-RNA-pol)
Pathogenesis:

1. **St. Louis Encephalitis**: transmitted by mosquito; bird reservoir; infects reticuloendothelial tissue, then viremia and dissemination to CNS
2. **Dengue virus:** transmitted by mosquito and vertically to neonate; primate and mosquito reservoir; infects reticuloendothelial tissue, then viremia (virus circulates in blood cells) with dissemination to many tissues; inflammatory cytokines associated with pathogenesis and symptoms.
3. **Yellow Fever virus:** transmitted by mosquito; primate reservoir; pathogenesis similar to Dengue except hepatitis, nephritis and circulatory failure more prominent.
4. **Japanese encephalitis virus**: transmitted by mosquito; pigs and aquatic birds main reservoir
5. **West Nile virus**: transmitted by mosquito; crows and aquatic birds main reservoir

Infections:

1. **St. Louis encephalitis virus**: fever & headache, meningitis, encephalitis
2. **Dengue virus**: Dengue fever (self-limited disease), Dengue hemorrhagic fever, Dengue shock syndrome
3. **Yellow fever virus**: self-limited disease, hemorrhagic form
4. **Japanese encephalitis virus**: asymptomatic or encephalitis
5. **West Nile virus**: same as St. Louis encephalitis virus

Control/prevention: control vector; vaccine for Yellow fever virus and Japanese encephalitis virus

**55. Hepatitis viruses**: A, B, C, D, E, F, G (infect hepatocytes)
**Hepatitis A virus** (~ 20 strains) (family *Picornaviridae*)
Characteristics: like Enterovirus but more resistant
Replication: like Enterovirus but infects hepatocytes
Pathogenesis: fecal/oral and common-source transmission; humans only significant reservoir; incubation 2-6 wks; portal inflammation and periportal necrosis (mediated by virus and CMI); no carriers or chronic disease

Infections: Hepatitis (acute)
Control/prevention: block transmission; passive or active immunizations; single vaccine for both HAV and HBV now on market (Twinrix)

**Hepatitis B virus** (family *Hepadnaviridae*)
Characteristics: enveloped; circular partially dsDNA genome; Major antigens: HBsAg (envelope protein), HBcAg (core/capsid protein), HBeAg (truncated core protein); core has reverstranscriptase
Replication: replicates in hepatocytes; dsDNA synthesis completed in core, DNA to nucleus; following transcription and translation, RNA pregenome enclosed in progeny core; RNA pregenome serves as template for synthesis of neg pol DNA strand, then partial synthesis of pos DNA strand; buds into golgi and released by exocytosis
Pathogenesis: blood, sex, direct contact, transplacental or during birth transmission; portal and periportal necrosis (mediated mostly by inflammatory infiltrate) that may lead to fibrosis and cirrhosis; estimated that 1 million are carriers; humans most significant reservoir; incubation 1 to 4 months (avg 8 wks)
Infections: Hepatitis (subclinical; acute, self-limited; chronic persistent; chronic active; cirrhosis; hepatocellular carcinoma)
Control/prevention:
block transmission; passive or active immunizations; single vaccine for HAV and HBV (Twinrix); a IFN plus reverse transcriptase inhibitor (adefovir, lamivudine) for chronic infection

**Hepatitis D virus** (genus *Deltavirus*)
Characteristics: satellite virus that co-infects with HBV; enveloped; circular ssRNA genome; HDVAg is core protein; requires HBsAg for replication
Replication: replication in hepatocytes completed only in presence of HBV
Pathogenesis: exacerbation of HBV infection
Infections: coinfection with HBV yielding fulminant hepatitis with death (~4%) or recovery with immunity (~90%); superinfection of HBV carriers yielding fulminant hepatitis with death (~10%), acute hepatitis with recovery (~10%), or chronic HBV/HDV hepatitis with cirrhosis (~80%)
Control/prevention: block transmission; a IFN + lamivudine for chronic infection

**Hepatitis C virus** (family *Flaviviridae*)
Characteristics: enveloped; pos pol RNA genome; E1 and E2 envelope proteins; genome codes for 2 proteases and a RNA-dep-RNA-pol
Replication: similar to other Flaviviruses; genome encodes for a polyprotein that is cotranslationally processed into at least 10 proteins; may replicate in cells other than hepatocytes; multiple genetic variants recovered from single individual
Pathogenesis: transmitted predominantly by blood (transfusions, iv drug use); high percentage (~80%) of infections become chronic; incubation 2-26 wks (avg 6-12 wks); characterized by inflammation with fibrosis
Infections: Hepatitis (acute with resolution [~15%], chronic [~85%] that is stable [~80%] or results in cirrhosis [~20%][stable, progressive with death, or hepatocellular carcinoma])
Control/prevention: block transmission; chronic treated with a IFN or a IFN + ribavirin (Rebetron)

**Hepatitis E virus** (genus *Hepevirus*, family *Hepeviridae*)
Characteristics: non-enveloped; pos pol ssRNA genome
Pathogenesis: pathogenesis and transmission like HAV; incubation 4-8 wks; infects a number of mammals but humans probably main reservoir for human strain-associated infection
Infections: Hepatitis (acute) with a high mortality in pregnant women (~20%)

Control/prevention: block transmission

Other Hepatitis viruses
Hepatitis F virus (unknown family affiliation)
Hepatitis G virus (family *Flaviviridae*)

**56.** ***Herpesviridae*** (enveloped [from nucleus], icosahedral capsid, dsDNA genome, no core enzymes, replication in host nucleus, three phases of protein synthesis: immediate early [alpha proteins], early [beta proteins], late [gamma proteins]; viral-encoded DNA polymerase [a beta protein] replicates the genome; viruses released by budding or cell lysis; human reservoir; envelope proteins for attachment, fusion, and cell trophism)

**Herpes simplex virus 1 and 2** (Human Herpes virus -1 & -2; *Alphaherpesvirinae*)
Pathogenesis: lytic and latent (in neurons) infections; transmission by saliva, sex, and vesicle fluid; syncytia and intranuclear inclusions occur
Infections: gingivostomatitis, pharygotonsillitis, vulvovaginitis, skin infections (whitlow, gladiatorum), eye infections, genital herpes, meningitis, encephalitis, neonatal infection, infection in the immunocompromised, recurrent infections
Control/prevention: acyclovir, famciclovir, valacyclovir; topical preparations; cesarean section for overt disease in genital tract

**Varicella-zoster virus** (Human Herpes virus -3)
Pathogenesis: lytic and latent (in neurons) infections; transmission by aerosols (RT droplets) and vesicle fluid; rarely transplacental; syncytia and intranuclear inclusions occur; infects reticuloendothelial tissue then mucous membranes and skin following viremia
Infections: chickenpox (varicella), shingles (zoster)
Control/prevention: vaccine for varicella, VZIG; acyclovir for varicella; famciclovir or valacyclovir for zoster (experimental vacine for zoster)

**Epstein Barr Virus** (Human Herpes virus-4)
Pathogenesis: cellular receptor is CD21 (CR2), MHCII are coreceptors; productive (EBNA, VCA), transforming and latent infections (EBNA, LMPs); transmission by intimate contact (saliva); B cell activation and proliferation (heterophile Abs), 2 phases of lymphocytosis (B cells and Downey cells); IL-10-like protein inhibits Th1 response
Infections: heterophile positive mononucleosis (complications), lymphoproliferative disease, neoplastic diseases (Burkitt's lymphoma, Hodgkin's lymphoma, nasopharyngeal carcinoma)
Control/prevention: none

**Cytomegalovirus** (Human Herpes virus-5)
Replication: large nuclear inclusions occur (Owl's eye inclusion bodies); human CMV grows only in human cells
Pathogenesis: inhibits expression of MHCI proteins; productive and latent (in many cell types) infections; congenital, perinatal, oral, sexual, blood, and transplants route of transmission
Infections: congenital infection (cytomegalic inclusion disease), perinatal infection, heterophile-negative mononucleosis, hepatitis, infection in immunocompromised (pneumonia, chorioretinitis, colitis/esophagitis, CNS)
Control/prevention: ganciclovir, valganciclovir, foscarnet, cidofovir

**Human Herpes Virus -6 (& 7)** (Roseolovirus)
Pathogenesis: transmitted by saliva; productive and latent infections; infects mononuclear cells; downregulates

MHCI and CD3 expression
Infections: Roseola (6th disease, exanthem subitum) in children; adult infection (lymphadenopathy, hepatitis, mono-like syndrome); in immunocompromised (pneumonitis, encephalitis, hepatitis); HHV-7 may cause second cases of roseola
Control/prevention: none

**Human Herpes Virus -8** (Rhadinovirus)
Pathogenesis: latent and lytic infections; latency-associated nuclear antigen important in neoplasia and during latent genome replication
Infections: Kaposi's sarcoma
Control/prevention: none

**57. Influenza virus** (family *Orthomyxovirus;* species *Influenza A, B, C*)
Characteristics: helical symmetry, enveloped, 7-8 negative polarity ssRNA genome; NA (N) and HA (H) envelope proteins (antigenic drifts and shifts)
Replication: replicates in nucleus, assembles in cytoplasm; viral RNA-dependent RNA Pol synthesizes pos pol RNA for translation and templates for genome replication
Pathogenesis: birds and other animals reservoirs for Inf A; human reservoir for B and C; aerosol transmission; NS1 inhibits antiviral effects of interferons; replication in RT induces desquamation with loss of ciliated epithelium; cytokines and T cells responses contribute to pathogenesis
Infections: influenza (complications: influenza pneumonia, bacterial pneumonia, myositis, meningitis, aspirin-associated Reye syndrome), common cold
Control/prevention: vaccines; amantadine, rimantadine, zanamivir, oseltamivir

**58. Marburg and Ebola viruses** (family *Filoviridae*)
Characteristics: enveloped, helical nucleocapsid symmetry; 1 segment neg pol RNA genome; filamentous and pleomorphic
Replication: similar to Rabies; genome codes for 7 proteins
Pathogenesis: reservoirs and routes of spread uncertain; probably spread by direct contact or vectors; massive tissue necrosis and hemorrhage; cytokines contribute to pathogenesis
Infections: hemorrhagic fever
Control/prevention: Possible use of hyperimmune serum

**59. Miscellaneous Viruses**: Areanaviruses, prions, Human Astrovirus

**Arenaviruses** (helical symmetry, enveloped, 2 cirular ssRNA segments as genome; rodent reservoir, rodent urine transmission)
**Lymphocytic Choriomeningitis virus:** self-limited febrile disease to meningitis/encephalitis
**Lassa virus**: hemorrhagic fever

**Prions:** spongiform encephalopathies associated with the accumulation of insoluble prion proteins leading to progressive dementia and death (Kuru, Crueutzfeldt-Jakob disease variants, Mad cow disease)

**Human Astrovirus** (8 serogroups) (family *Astroviridae*)
Characteristics: non-enveloped, icosahedral nucleocapsid symmetry; 1 segment neg pol ssRNA genome filamentous and pleomorphic

Replication: similar to Noroviruses
Pathogenesis: fecal/oral transmission; peak in winter; mostly infects children under 3yr but all can be infected; estimated 4 million cases per yr
Infections: gastroenteritis (nausea and diarrhea)
Control/prevention: block transmission

**60. Norovirus** (5 serogroups) (family *Caliciviridae*)
Characteristics: non-enveloped, icosahedral symmetry; genome pos pol ssRNA
Replication: replicates and assembles in cytoplasm
Pathogenesis: transmitted by fecal/oral, aerosol, common source, human to human; many animal reservoirs; estimated 20 million cases per year; infects epithelial cells in jejunum and prevents absorption; peaks in fall and winter; all ages infected
Infections: gastroenteritis (vomiting and diarrhea)
Control/prevention: control transmission

**61a. Human Papillomavirus** (Family *Papillomaviridae*)
Characteristics: non-enveloped, icosahedral symmetry; circular dsDNA genome
Replication: in nucleus utilizing host enzymes
Pathogenesis: the most common viral STD; transmission by direct contact (lesions or inanimate objects); long incubation; latent and productive infections occur; infection induces epithelial acanthosis, parakeratosis, and hyperkeratosis (inhibits apoptosis); the koilocyte is diagnostic
Infections: Papillomas: cutaneous, head and neck, anogenital; cervical cancer
Control/prevention: chemicals, surgery, imiquimod

**61b. Polyomavirus** (family *Polyomaviridae*; JC and BK viruses)
Characteristics: similar to the Papillomaviruses
Replication: similar to Papilloma viruses except prefer to replicate in the respiratory and urinary tracts (JC and BK) and CNS (JC)
Pathogenesis: multiply in respiratory tract then kidney after viremia; latent infection in kidney
Infections: JC: progressive multifocal leukoencephalopathy; BK & JC: UTI in immunosuppressed
Control/prevention: none

**62. *Paramyxoviridae*: Parainfluenza, Mumps, Measles, Respiratory Syncytial, Metapneumovirus**
(enveloped [have fusion protein],helical nucleocapsid [NP] symmetry, 1 segment neg pol RNA genome, RNA polymerase in core, matrix protein, replicate in cytoplasm)

**Parainfluenza (Human Parainfluenza viruses, HPIV 1, 2, 3, 4A, 4B)**
Characteristics: HN protein (hemagglutinin/neuraminidase for attachment)
Pathogenesis: transmitted by aerosols or direct contact; humans only reservoir; replicates in mucosal epithelium of URT; immunity short-lived so re-infections common; Th1 response contributes to path; HPIV-1 and 2 peaks in fall and winter; HPIV-3 all year with peak in spring; HPIV-4 all year
Infections: HPIV-1-3: croup, pneumonia, bronchiolitis/bronchitis; HPIV-1-4: cold, otitis media, conjunctivitis
Control/prevention: upper airway support

**Mumps virus** (genus *Rubulavirus*)
Characteristics: like Parainfluenza
Pathogenesis: transmitted by aerosols; humans only reservoir; replicates in mucosal epithelium of URT yielding

viremia; infects parotids and submandibular glands; also may infect pancreas, testes, ovaries, peripheral nerves, eye, inner ear, and CNS; virus occurs in oral secretions and urine
Infections: mumps (parotitis); complications (orchitis, oophoritis, meningitis, encephalitis)
Control/prevention: vaccine

**Measles virus** (genus *Morbillivirus*)
Characteristics: H protein for attachment
Pathogenesis: transmitted by aerosols; humans only reservoir; replicates in URT, then reticuloendothelial tissue yielding viremia; infects conjunctivae, UT, CNS, RT; infection of endothelial cells results in vasculitis; virus occurs in RT secretions, urine
Infections: Rubeola (measles); complications (encephalitis, pneumonia, giant cell pneumonia in immunocompromised, subacute sclerosing panencephalitis)
Control/prevention: vaccine

**Respiratory Syncytial virus** (genus *Pneumovirus*)
Pathogenesis: transmitted by aerosols and direct contact (hands); humans only reservoir; replicates in mucosal epithelium of URT then spreads to LRT; incomplete immunity from infection; pathologic change associated with syncytia and inflammation-mediated necrosis
Infections: infants and young children: bronchiolitis, pneumonia, tracheobronchitis, croup, otitis media; older children and adults: cold, pharyngitis, tracheobronchitis, pneumonia
Control/prevention: Ribavirin, RSV Ig

**Metapneumovirus**
Characteristics and pathogenesis: like RSV
Infections: bronchiolitis and pneumonia in young children; cough, congestion in older children and adults
Control/prevention: none

**63. *Parvoviridae***
**Human Parvovirus (B19)** (genus *Erythrovirus*)
Characteristics: non-enveloped, icosahedral symmetry; ssDNA genome
Replication: in nucleus
Pathogenesis: aerosol or transplacental routes of infection; infects erythroid precursors; requires mitotically active cells; humans only reservoir
Infections: Erythema infectiosum (5th disease) in children; mild disease in adults (polyarthritis); fetal infections and complications (hydrops fetalis); aplastic crisis in those with hemolytic anemias
Control/prevention: none

**64. *Picornaviridae*:** Enteroviruses, Rhinovirus **(**positive polarity ssRNA genome; non-enveloped, icosahedral symmetry; capsid proteins mediate adherence; replication in the cytoplasm, one large protein processed to structural proteins, polymerase, and protease; release by cell lysis; human reservoir)
**Enteroviruses** (C*oxsackie* A & B, *Echovirus*, *Enterovirus*, *Poliovirus*)
Pathogenesis: transmitted by fecal oral, direct contact, or aerosols; initial replication in GIT; humans only reservoir; resistant to low pH, salt, detergents; final target tissue varies with virus (e.g. skin, heart, CNS)
Infections: Poliovirus (Poliomyelitis), Coxsackie A (acute febrile disease, meningitis, encephalitis, cold w/ fever, febrile rash {hand, foot and mouth disease, pericarditis, hemorrhagic conjunctivitis, herpangina), Coxsackie B (acute febrile disease, meningitis, encephalitis, cold w/ fever, myocarditis, pericarditis, pleurodynia, transplacental infection), Echovirus A (acute febrile disease, meningitis, encephalitis, cold w/ fever, febrile

rashes, diarrhea w/ fever), Enterovirus (hemorrhagic conjunctivitis)
Control/prevention: no treatment; vaccine for *Poliovirus* (IPV)

**Rhinovirus**
Pathogenesis: most infections in early fall & late spring; transmitted by direct contact (hand to hand, object to hand) or aerosols; replication in URT; ICAM-1 host cell receptor; cytokines contribute to pathogenesis
Infections: cold, lower RT infection, exacerbation of chronic lung and bronchial diseases (e.g. asthma); recurrent infections
Control/prevention: none

**65. *Poxviridae*: Smallpox, Molluscum contagiosum, Orf, Monkeypox** (complex envelope and symmetry; genome is linear dsDNA; core contains DNA-dependent-RNA pol; replicates and assembles in cytoplasm; release by cell lysis)
**Smallpox** (genus *Orthopoxvirus*, species Variola virus)
Pathogenesis: humans only reservoir; transmission by aerosols or direct contact; replicates in reticuloendothelial tissue then disseminates to skin and mucous membranes
Infections: variola major and minor
Control/prevention: no treatment; vaccine (Vaccinia virus; not available to public)

**Molluscum contagiosum virus** (genus *Molluscipoxvirus*)
Pathogenesis: transmitted by direct contact including sexual transmission; self-limiting cutaneous lesions occur (umbilicated nodule with caseous plug)
Infections: Molluscum contagiosum
Control/prevention: no treatment

**Orf virus** (genus *Parapoxvirus*)
Pathogenesis: zoonosis; transmitted by direct contact
Infections: Orf (Ecthyma contagiosum)
Control/prevention: no treatment

**Monkeypox virus** (genus *Orthopoxvirus*)
Pathogenesis: zoonosis; transmitted by direct contact
Infections: monkeypox (fever with smallpox-like rash)
Control/prevention: smallpox vaccine; cidofovir

**66. Rabies Virus** (family *Rhabdoviridae*)
Characteristics: enveloped, helical nucleocapsid symmetry; 1 segment neg pol RNA genome
Replication: replication and assembly in cytoplasm; pos pol template strand made from which progeny genomes are made; several mRNAs made from neg pol strand
Pathogenesis: zoonotic disease (common reservoirs are bats, foxes, raccons, and skunks); transmission by bite or scratch or aerosols; virus travels by retrograde axonal transport to CNS then via afferent neurons to eye, skin, salivary glands
Infections: Rabies encephalitis
Control/prevention: vaccine

**67. *Reoviridae*:** Rotavirus, Colorado tick fever virus (non-enveloped, dsRNA genome)

**Rotavirus** (genus *Rotavirus*, serogroups A-E)

Characteristics: 2 capsid layers and inner core; outer capsid composed of VP4 (host attachment); core contains complete transcription system; genome composed of 11 segments of dsRNA

Replication: transcription occurs in inner core, translation in cytoplasm; genome replicated in progeny core using pos pol RNA template; buds into ER, release by cell lysis

Pathogenesis: estimated 4 million cases/yr; fecal/oral or human to human transmission (virus survives in environment); humans probably only reservoir; peak age 6mo-2yr but all ages can be infected; infects villus cells in small intestine preventing absorption

Infections: gastroenteritis (fever, vomiting, watery diarrhea)

Control/prevention: none

**Colorado tick fever virus** (genus *Coltivirus*)

Characteristics: like Rotavirus but outer capsid not as organized; genome 12 dsRNA segments

Replication: like Rotavirus

Pathogenesis: transmitted by wood ticks; small mammals are reservoirs; infects erythroid precursors

Infections: Colorado tick fever (relapsing fever, headache, myalgia)

Control/prevention: control vector and reservoirs

**68. *Retroviridae*:** Human immunodeficiency virus 1 & 2, Human T-cell lymphotrophic 1 (enveloped, 2 identical pos pol RNA stands as genome; proviral DNA integrates into host chromosome; core contains reverse transcriptase, protease, integrase; genome encodes regulator proteins; humans only significant reservoir; transmitted by sex, blood, perinatal [in utero, at delivery, breast-feeding])

**Human immunodeficiency virus 1 & 2** (genus *Lentivirus*)

Characteristics: envelope proteins gp 120, gp 41 for attachment/entry; inner core (Gag protein p24)

Replication: attaches via CD4 and chemokine receptor; envelope fuses, core enters cytoplasm, reverse transcriptase synthesizes DNA; transcripts and progeny genomes synthesized; assembly and buds through plasma membrane; core maturation occurs after release

Pathogenesis: chronic infection that induces profound immunosuppression resulting in life-threatening secondary infections; lymphopenia, reduced T-cell activity, and reduced macrophage activity; incubation 1-6 wks before onset of acute retroviral syndrome; routes of transmission like HBV; Infections: AIDS; CDC classification: acute (acute retroviral syndrome ["mononucleosis-like"]), chronic (asymptomatic with persistent generalized lymphadenopathy), final crisis (secondary infections, neurologic disease, secondary neoplastic disease, unexplained constitutional diseases); presentations peculiar to women or children

Control/prevention: block transmission; nucleoside RT inhibitors, non-nucleoside RT inhibitors (only for HIV-1), protease inhibitors (see antiviral section)

**Human T-cell lymphotrophic virus 1** (genus *Deltaretrovirus*)

Replication: similar to HIV except genome encodes a variety of transregulatory proteins associated with transformation and oncogenesis

Pathogenesis: HTLV-1 transforms T cells; induces IL-2R expression

Infections: adult T-cell leukemia (HTLV-1)

Control/prevention: block transmission; cytotoxic chemotherapy

**69. *Togaviridae*: Rubella virus, Alphaviruses** (enveloped [from cytoplasm], icosahedral symmetry, 1 segment pos pol RNA genome; 2/3 of genome translated into early proteins (protease, RNA-dep-RNA pol); neg pol strand made for genome template and 26S transcript; 26S translated into precursor protein that is

cleaved by protease into structural proteins

**Rubella Virus** (genus *Rubivirus*)

Pathogenesis: aerosol transmission; humans only reservoir; infects URT, then 1st viremia, infection of reticuloendothelial tissue then second viremia (fetal infection possible) and immune complex-mediated vascultis (rash)

Infections: Rubella (German measles), congenital rubella syndrome

Control/prevention: vaccine

***Alphavirus*** (Eastern Equine, Western Equine, Venezuelan Equine Encephalitis viruses)

Pathogenesis: transmitted by mosquito; birds (WEE & EEE), rodents reservoirs (VEE) and possibly also amphibians and reptiles; infection of reticuloendothelial tissue then viremia and CNS infection; inflammatory neuronal necrosis

Infections: encephalitis

Control/prevention: control vector; veterinary vaccines

# **V.** Fungi

## 71. General mycology

A. General Mycology

1. Morphology & Structure
   a. Yeasts (single cells that reproduce by budding)
      (1) Pseudohyphae (Yeasts like *Candida albicans* can, under special conditions, form elongated cells that stick together and look like hyphae.)
   b. Molds (grow as filaments or hyphae [septate or non-septate] and reproduce with specialized structures that bear the conidia or produce conidia within the filament.)
      (1) Dimorphism is an important trait in many pathogenic fungi. It means that at one temperature (usually 25C), the fungus grows as a mold, and at another temperature (usually 37C) the fungus grows as a yeast.
   c. Cell wall composition (Usually composed of a mixture of chitin, glucan, and mannan. Yeasts usually only have chitin at the bud scar. The cell wall is a potent immunogen, however the role of Abs in protection is limited.)
   d. Plasma membrane (Fungal plasma membranes contain the sterols ergosterol & zymosterol. Ergosterol and enzymes that synthesize it are the major targets of antifungal drugs.)
2. Asexual Reproduction
   Examples of conidia and conidiophore structures
3. Physiology
   (heterotrophic; utilize a variety of carbohydrates [specific for the species] some are strict aerobes, some facultative anaerobes)
4. Pathogenesis
   a. Portals of entry (skin, inhalation, GIT, UT, normal flora)
   b. Virulence determinants (predisposing condition [reduced CMI, underlying

disease]; filament vs. yeasts; components immunosuppress and/or evade immune system; extracellular enzymes; induction of proinflammatory cytokines; tissue trophism and adherence; allergic reactions)

c. Disease Classification
   (1) superficial (Pityriasis versicolor, Tinea nigra)
   (2) cutaneous (Dermatophytosis)
   (3) subcutaneous (Sporotrichosis)
   (4) systemic
      (a) primary (Coccidioidomycosis, Histoplasmosis, Blastomycosis, Cryptococcosis)
      (b) opportunistic (Candidiasis, Aspergillosis, Mucormycosis)

5. Lab Diagnosis
   a. Microscopy (cotton blue, KOH, methenamine silver stain, periodic acid-Schiff stain)
   b. Culture (slide culture, birdseed agar for *Cryptococcus,* dermatophyte test medium, Sabouraud dextrose agar, biochemical tests)
   c. Serology
      (1) *Cryptococcus neoformans* (EIA for capsular Ag in serum and CSF, latex agglutination for Ag, tube agglutination for low Ag conc.)
      (2) *Coccidioides immitis* (latex agglutination for Ab, immunodiffusion for Ab, complement fixation [CF] for Ab to mycelial Ag)
      (3) *Histoplasma capsulatum* (latex agglutination for Ab, immunodiffusion for Ab, CF for Ab to mycelial and yeast Ag)
      (4) *Sporothrix schenckii* (latex agglutination for Ab)
      (5) *Candida albicans* (immunodiffusion for Ab, EIA for Abs to cytoplasmic Ag)
      (6) *Blastomyces dermatitidis* (immunodiffusion for Ab, CF for Ab)
      (7) *Aspergillus* (immunodiffusion for Ab, CF for Ab)

6. Antifungal drugs
   a. Polyenes (Nystatin, Amphotericin B [AmB]; bind ergosterol and cause an increase in membrane permeability; nystatin used topically for oral and vaginal candidiasis; AmB used topically and systemically [colloidal complex in desoxycholate or as a lipid complex]; AmB drug of choice for most disseminated fungal infections)
   b. Azoles (Miconazole, Ketoconazole, Clotrimazole, Itraconazole, Fluconazole, Voriconazole; inhibit cytochrome P-450 and thus block ergosterol synthesis that results in increased membrane permeability; miconazole used topically for superficial infections; ketoconazole & clotrimazole used topically for superficial infections; itraconazole, voriconazole & fluconazole used to treat certain systemic infections [non-life threatening candidiasis, cryptococcosis, histoplasmosis, blastomycosis])
   c. Flucytosine (inhibits DNA synthesis; used systemically in combination

with AmB)

d. Griseofulvin (disrupts microtubules; used for dermatophyte infections)

e. Terbinafine (inhibits squalene epoxidase and thus ergosterol synthesis; used for dermatophyte infections)

f. Caspofungin (an echinocandin; inhibits glucan synthesis; used to treat aspergillosis)

**72. <u>Dermatophytes and agents causing superficial infections</u>** (anthropophilic, zoophilic, & geophilic varieties; routes of transmission usually direct contact with spores or spore-laden hair or skin scales; pathogenesis: spores adhere to keratinized tissue, germinate, secrete keratinases, and invade and grow; hair infection may be endothrix or ectothrix pattern; extent of inflammation varies; Th1 response needed to control)

**A. <u>Dermatophytoses</u>**

(1) Tinea pedis (infection of foot and toes; etiology usually *Trichophyton mentagrophytes, T. rubrum,* or less frequently *Epidermophyton floccosum*; treat topical, itraconazole, terbinafine, fluconazole)

(2) Tinea manus (infection of hands; etiology usually *T. rubrum*; treatment as for T. pedis)

(3) Onychomycosis (Tinea unguium; infection of nails; etiology like T. pedis; treat with terbinafine, fluconazole, griseofulvin)

(4) Tinea corporis and Tinea faciei (infection of the skin and face, respectively; etiology: *Microsporum audouinii, M. canis, M. gypseum, T. rubrum, T. verrucosum*; treat topical, terbinafine, fluconazole, itraconazole)

(5) Tinea barbae (infection of the beard; etiology: *T. verrucosum, T. mentagrophytes*; treat topical, terbinafine, fluconazole, itraconazole)

(6) Tinea cruris (infection of the groin; etiology: *T. rubrum, E. floccosum*; treat topical, terbinafine, fluconazole, itraconazole)

(7) Tinea capitis (infection of the scalp; etiology: *T. tonsurans* (most common in this country), *M. canis, M. audouinii, T. verrucosum*; treat griseofulvin, terbinafine, itraconazole)

**B. <u>Superficial infections</u>**

(1) Tinea nigra (infection of the epidermis, usually hands; etiology: *Exophiala werneckii*; treat topical, ketoconazole, itraconazole)

(2) Tinea versicolor (infection of the skin, trunk common; etiology: *Malassezia furfur*; treat topical selenium sulfide, ketoconazole, fluconazole, itraconazole

**73. <u>Fungi causing subcutaneous and systemic infections</u>**

**A. *Sporothrix schenckii*** (Sporotrichosis)

<u>Characteristics</u>: ubiquitous (especially soil and vegetation) dimorphic fungus; at ambient temps grows as branching septate hyphae with single or clusters of microconidia; at 37C grows as elongated yeasts

<u>Pathogenesis</u>: traumatic inoculation of skin with conidia or hyphae; inflammation, induration at site; asending lymphangitis may occur; pulmonary infection initiated by inhaling conidia

<u>Infections</u>: lymphocutaneous sporotrichosis, pulmonary sporotrichosis, osteoarticular sporotrichosis, disseminated in AIDS

<u>Control</u>: cutaneous with itraconazole or fluconazole, disseminated with amphotericin B

**B.** ***Coccidioides immitis*** (Coccidioidomycosis)
Characteristics: found in desert soil (endemic in southern Texas, New Mexico, Arizona, and California); at ambient temps grows as branching, septate, hyphae that forms arthrospores; at 37C forms spherules containing endospores
Pathogenesis: ~60% of the infections are asymptomatic; infection initiated by inhalation of arthrospores; pulmonary symptoms generally mild and are associated with inflammatory reaction to spherules; may form cavity or nodular granuloma; may disseminate to skin, bone and joints, and CNS
Infections: primary pulmonary coccidioidomycosis, disseminated coccidioidomycosis, primary cutaneous coccidioidomycosis
Control: fluconazole, itraconazole, amphotericin B

**C.** ***Histoplasma capsulatum*** (var *capsulatum* and var *duboisii*) (Histoplasmosis)
Characteristics: grows in rich, acidic soil enriched by bird and bat feces (endemic in the Ohio-Mississippi valleys); at ambient temps grows as branching, septate hyphae that form microconidia and tuberculate macroconidia; at 37C grows as small, oval yeasts
Pathogenesis: ~90% of cases asymptomatic or mild influenza-like; inhale microconidia, ingested by macrophages, undergoes dimorphic transition; disseminates to reticuloendothelial tissue; a facultative intracellular parasite (in macrophages)
Infections: acute primary pulmonary histoplasmosis, chronic (cavitary) pulmonary histoplasmosis, progressive disseminated histoplasmosis (acute and chronic), cutaneous histoplasmosis (African histoplasmosis caused by *H. capsulatum* var *duboisii*)
Control: itraconazole, amphotericin B

**D.** ***Blastomyces dermatitidis*** (Blastomycosis)
Characteristics: epidemiology similar to *H. capsulatum* except endemic area larger; grows in rich soil contaminated with bird feces or decaying vegetation; at ambient temps grows as branching, septate hyphae that produce microconidia; at 37C grows as a thick-walled yeast with large-pore buds
Pathogenesis: ~50% of infections are asymptomatic; inhale microconidia, dimorphic transition, WI-1 cell wall protein mediates adherence to host cells; yeast cell wall may be antiphagocytic; tissue damage mediated by inflammatory infiltrate; lesions may become granulomatous
Infections: primary pulmonary blastomycosis (course may invole complete recovery or become progressive with or without dissemination), chronic pulmonary blastomycosis, disseminated blastomycosis, cutaneous blastomycosis
Control: itraconazole, amphotericin B

**E.** ***Cryptococcus neoformans*** (serotypes D and A) and ***C. bacillospora*** (formery *C. neoformans* var *gattii*, sero B and C) (Cryptococcosis)
Characteristics: sero A has worldwide distribution, found in areas contaminated with dried bird feces, infects the immunocompromised; *C. bacillospora* restricted to regions with eucalyptus trees, infects the immunocompetent; grows as a yeast at all temps; prominent polysaccharide capsule; deposits melanin in cell wall when grown on catecols
Pathogenesis: capsule is antiphagocytic and immunosuppressive; melanin protects from oxidative damage; small-capsule yeasts inhaled, primary infection established in lung,

disseminates to CNS
Infections: pulmonary cryptococcosis (acute and chronic), disseminated cryptococcosis (skin, CNS)
Control: itraconazole, fluconazole, amphotericin B

**F.** ***Candida albicans*** (*C. tropicalis, parapsilosis, glabrata*) (Candidiasis)
Characteristics (C. alb): grows as yeasts at all temps; at 37C in the presence of inducers forms germ tubes and eventually hyphae (dimorphic transition); on special media forms pseudohyphae and chlamydospores; C. albicans causes ~70% of the candidiasis cases; normal inhabitant of the GIT
Pathogenesis: usually requires predisposing condition to cause infection; attachment followed by release of proteases and tissue invasion associated with acute infection; chronic infection often involves formation of granulomas
Infections: oral and vaginal candidiasis, intertriginous candidiasis, paronychia, onychia, generalized cutaneous, chronic mucocutaneous, esophagitis, gastrointestinal candidiasis, bronchopulmonary candidiasis, UTI, fungemia, endocarditis, hepatosplenic candidiasis
Control: topical (nystatin, miconazole), itraconazole, fluconazole, amphotericin B

**G.** ***Aspergillus sp.*** (*A. fumigatus* and *A. flavus*) (Aspergillosis)
Characteristics: *A. fumigatus* causes ~90% of the infections; common soil fungus, worldwide distribution; thin septate hyphae that typically branch at 45 degree angles; asexual cycle involves formation of conidia on complex conidiophore
Pathogenesis: inhale conidia, germinate, hyphae adhere to extracellular matrix proteins, secrete enzymes and toxic secondary metabolites, hyphae invade tissue or grow in cavities; Th1 response induced; immunocompromised at greatest risk
Infections: allergic bronchopulmonary aspergillosis, aspergilloma (fungus ball), invasive sinusitis, invasive pulmonary aspergillosis, disseminated aspergillosis
Control: amphotericin B, itraconazole, caspofungin, voricinazole

**H.** **Mucormycosis** (*Rhizopus, Absidia, Mucor, Rhizomucor*)
Characteristics: ubiquitous soil fungi; grow as irregularly shaped, non-septate hyphae with right-angle branches; sporangiospores contained in sporangia
Pathogenesis: infections limited to the immunocompromised, diabetics, and trauma; inhale spores, germinate, invade tissue and blood; results in tissue necrosis, thrombosis
Infections: rhinocerebral mucomycosis (most in poorly managed diabetics), pulmonary mucormycosis (neutropenia), cutaneous mucomycosis (trauma)
Control: amphotericin B

**I.** ***Pneumocystis jirovecii*** (formerly P. *carinii*) (Pneumocystosis)
Characteristics: complex sexual cycle, simple asexual cycle involving yeast-like trophic form
Pathogenesis: transmitted by aerosols; trophozoite or sporozoite infectious form inhaled, adheres to type I epithelial cells, proliferates, and induces inflammatory exudate resulting in hypoxemia; immunosuppression required for infection
Infections: pneumonia (disseminates to reticuloendothelial tissue in advance AIDS patients)
Control: trimethoprim+sulfamethoxazole

# VI. Eucaryotic Parasites

**81. <u>General parasitology</u>**

1. Morphology, physiology, and reproduction
   a. Protozoa (size 2-100 $\mu$m, cytoplasm often composed of inner endoplasm [nutrition] and outer ectoplasm[organelles of locomotion])
      (1) Rhizopods (amebas; reproduce by binary fission)
      (2) Ciliates (reproduce by binary fission)
      (3) Flagellates (reproduce by binary fission)
      (4) Sporozoans (reproduce sexually [sporogony] and asexually [shizogony])
      (5) Physiology (most fac. anaerobes; heterotrophic; engulf food by pinocytosis or phagocytosis; some have specific site for ingestion [the peristome or cytostome]; many can form resistant cysts)
   b. Helminths (elongated, bilaterally symmetric, length varies from <1mm to >1m; body wall covered with cuticle; anterior end may possess suckers, hooks, teeth, etc. for attachment; all have differentiated organs [primitive nervous and excretory systems and well developed reproductive systems
      (1) Roundworms (nematodes; have cylindrical bodies, tubular alimentary track, and the sexes are separate)
      (2) Tapeworms (cestodes; have flattened bodies; the anterior end [scolex] has suckers and or hooklets for attachment; reproductive segments are called proglottids and each contains both male and female gonads; no digestive tract)
      (3) Flukes (trematodes; flat with branching alimentary tracts; particulate wastes are regurgitated through the mouth; have two suckers for attachment; most are hermaphroditic [except *S. mansoni*])
      (4) Physiology (ingest or absorb body fluids, etc.; usually anaerobic respiration)
2. Immunity (all aspects of the immune system important; eosinophils directed at worms; IgE made to many; acquired resistance often absent or incomplete; effector mechanisms usually directed at surface antigens of the parasite)
3. Diagnosis (direct examination of specimens [microscopy], serology [ELISA, IF, CF], molecular probes)
4. Major chemotherapeutic agents
   a. Heavy Metals (arsenicals and antimonial agents)
   b. Antimalarial Quinolines
      (1) Chloroquine phosphate
      (2) Primaquine phosphate
      (3) Quinine
      (4) Mefloquine
   c. Folate Antagonists

(1) Trimethoprim
(2) Pyrimethamine

d. Nitroimidazoles
(1) Metronidazole

e. Benzimidazoles
(1) Thiabendazole
(2) Mebendazole
(3) Albendazole

f. Avermectins
(1) Ivermectin

g. Praziquantel

## 82. Pathogenic parasites

### 82a. Protozoans

**A.** ***Plasmodium*** (*P. vivax, P. ovale, P. malariae, P. falciparum*)
Characteristics/life cycle: sporogeny in mosquito (gametocytes, ookinete, oocyst, sporozoites), schizogony in human (sporozoite, merozoite [liver & RBC], trophozoite, schizont, gametocyte
Pathogenesis: transmitted by female *Anopheles*; symptoms associated with RBC rupture and proinflammatory cytokines; anemia associated with depression of marrow function; RBCs sequestered in spleen
Infections: malaria: *P. vivax* most prevalent worldwide, invades immature RBC, may cause chronic infection; *P. falciparum* invades any RBC, associated with microvascular disease as a result of mature trophozoite-infected RBC adhering to microvascular endothelium
Control: chloroquine, mefloquine, primaquine, doxycline, quinine

**B.** ***Toxoplasma gondii***
Characteristics/life cycle: schizogony and sporogeny in cat GIT (trophozoites, merozoites, gametocytes), oocyst released in feces that mature to contain sporozoites; oocyst ingested by intermediate host (humans), intracellular schizogony occurs yielding tachyzoites that encyst; cyst produces sporozoites and bradyzoites that are passed in feces and infect definitive host
Pathogenesis: transmitted by fecal-oral route or from ingesting undercooked infected meat; various sizes cysts occur in tissue with varying degrees of inflammation
Infections: acute and chronic toxoplasmosis, congenital toxoplasmosis, toxoplasmosis in the immunocompromised
Control: pyrimethamine + sulfadiazine

**C.** ***Cryptosporidia parvum***
Characteristics/life cycle: acid fast oocysts containing 4 sporozoites ingested, sporozoites released and attach to microvilli in GIT; become schizonts that release merozoites that become gametes that mate and become oocyst that is released in the feces

Pathogenesis: many animals serve as reservoirs; transmitted by fecal/oral and person to person; oocyst resistant to chlorination
Infections: Cryptosporidiosis (noninflammatory, watery diarrhea); may be prolonged in immunocompromised
Control: avoid contaminated water; Nitazoxanide (Alina)

**D.** ***Cyclospora cayetanensis***
Characteristics/life cycle: like *C. parvum* but oocyts (fluoresce under UV light) contain 2 sporocysts that each contain 2 sporozoites
Pathogenesis: like *C. parvum* except oocyts mature in the environment
Infections: like *C. parvum*
Control: trimeth-sulfameth

**E.** ***Entamoeba histolytica***
Characteristics/life cycle: trophozoite with ameboid morphology; forms cyst with chromatoidal body
Pathogenesis: transmitted by anal sex, fecal/oral, fomites; ingest cyst, gastric acid induces release of trophozoites, adhere to epithelial cells in colon via galactose-specific lectin, release pore-forming protein, invade, and multiply; kill epithelial cells resulting in a loss of fluid uptake and inflammatory diarrhea
Infections: amebiasis (inflammatory diarrhea), may be asymptomatic (carriers), may disseminate in immunocompromised
Control: metronidazole, diloxanide

**F.** ***Trichomonas vaginalis***
Characteristics/life cycle: flagellate morphology (flagella, axostyle, undulating membrane); exists only as trophozoite that divides by binary fission
Pathogenesis: transmitted by sexual contact; infects urethra, vagina, prostate; serious infections involve necrosis and inflammation; men mostly asymtomatic and the predominant reservoirs
Infections: women: asymptomatic, vaginitis; men: asymtomatic, urethritis, prostatitis
Control: safe sex; metronidazole

**G.** ***Giardia lamblia***
Characteristics/life cycle: flagellate morphology (flagella, sucker [adhesive disk], 2 nuclei); trophozoite and cysts occur; trophozoites multiply by longitudinal binary fission
Pathogenesis: transmitted by fecal/oral or contaminated food or water; ingest cyst, trophozoites released and attach to epithelial cells in duodenum; attachment induces inflammation, tissue damage, and reduce absorption
Infections: acute or chronic noninflammatory diarrhea; may be asymptomatic
Control: metronidazole

**H.** ***Leishmania*** (*L. tropica, L. mexicana, L. braziliensis, L. major, L. donovani*)
Characteristics/life cycle: hemoflagellate morphology of free-living promastigote, intracellular amastigote
Pathogenesis: numerous animal reservoirs; transmitted by the bite of female sandfly; promastigote invades reticuloendothelial tissue and becomes the intracellular amastigote;

replicates and invades other tissue, resulting in inflammation and necrosis
Infections: cutaneous, mucocutaneous, and disseminated (visceral) leishmaniasis
Control: amphotericin B

**I.** ***Trypanosoma cruzi***
Characteristics/life cycle: epimastigote in insect gut, trypomastigote free-living in host (hemoflagellate morphology), amastigote intracellular
Pathogenesis: numerous animal reservoirs; transmitted by feces of reduviid (kissing) bug; trypomastigote invades tissue, becomes intracellular amastigote that replicates and lyses cell; trypomastigote released into blood; tissue inflammation and necrosis
Infections: American trypanosomiasis (Chagas' disease)
Control: nifurtimox, benznidazole

**82b. Helminths**

**A.** ***Enterobius vermicularis*** (Pinworm)
Characteristics: nematode morphology (cylindrical body, tubular alimentary tract, separate sexes)
Pathogenesis: humans only reservoir; hand to mouth or fecal/oral transmission; ingest eggs, hatch, larvae penetrate mucosa of large intestine, mature into different sexes, mate, female lays eggs in perianal area; eggs induce allergic reaction
Infections: Pinworm disease (Enterobiasis)
Control: pyrantel pamoate, mebendazole, albendazole

**B.** ***Trichuris trichuria*** (Whipworm)
Characteristics: nematode morphology (cylindrical body, tubular alimentary tract, separate sexes)
Pathogenesis: humans only reservoir; fecal/oral transmission; ingest embyonated egg, larvae penetrate mucosa of large intestine, sexes mature, mate, female releases eggs in feces; larvae develop in moist, dark environment; whip penetrates and damages mucosa; symptoms related to worm burden
Infections: Whipworm disease (Tricuriasis)
Control: mebendazole, albendazole

**C.** ***Ascaris lumbricoides***
Characteristics: nematode morphology; worms may reach 1 m in length
Pathogenesis: humans main reservoir; fecal/oral, hand to mouth transmission; ingest embyonated egg, larvae penetrate duodenal wall, enter blood then lung, grow in alveoli, coughed up and swallowed, mature in small intestine, mate, female produces eggs that are passed in feces; larvae in fertilized eggs mature in moist dark environments; symptoms related to worm burden
Infections: Ascariasis
Control: albendazole, mebendazole, pyrantel pamoate

**D.** ***Necator americanus*** *(Ancylostoma duodenale)* (Hookworm)
Characteristics: nematode morphology; 2 larval morphologies (rhabditiform [free-living], filariform [infective])

Pathogenesis: transmitted by contact with contaminated soil; filariform larvae penetrate skin, enter blood, then lungs, coughed up, swallowed, attach to mucosa of small intestine, induces inflammation and necrosis; mate, eggs pass in feces, mature in soil, rhabditiform larvae released, free-lining, develop into infective filariform larvae
Infections: Hookworm disease (hypersensitive pneumonitis, GIT symptoms); cutaneous larval migrans caused by non-human hookworms
Control: albendazole, mebendazole, pyrantel pamoate

**E.** ***Strongyloides stercoralis***
Characteristics: like *Necator*
Pathogenesis: transmitted by contact with contaminated soil; filariform larvae penetrate skin, enter blood, then lungs, coughed up, swallowed, mate in small intestine, males ejected, female burrow into mucosa and produce eggs; hatch liberating rhabditiform larvae, some pass in feces, some develop into filariform and continue the infection; pathogenesis dependent on worm burden
Infections: Strongyloidiasis (acute [hypersensitive pneumonitis, GIT asyptomatic to inflammatory diarrhea], hyperinfection syndrome in immunocompromised)
Control: ivermectin, albendazole

**F.** ***Toxocara canis*** (and ***T. cati***)
Characteristics: eggs of non-human ascarid hatch in GIT and undergo limited development
Pathogenesis: ascarids migrate into tissue; symptoms and pathogenesis related to migration (eosinophilia and hepatomegaly common)
Infections: Toxocariasis (Visceral larva migrans); Ocular larval migrans associated with infection by larvae
Control: no effective therapy

**G.** ***Trichinella spiralis*** (*T. murrelli*)
Characteristics: nematode morphology
Pathogenesis: many reservoirs (*T. spiralis* worldwide, *T. murrelli* in North American bears); transmitted by eating undercooked meat; ingest cyst, larvae released, develop in intestinal mucosa of small intestine (intracellular parasites), mature, mate, females produce larvae that enter the blood, then muscle where the coil and encyst; pathogenesis depends on worm burden; myositis and vasculitis occur
Infections: Trichinosis (symptoms depend on worm burden and location of cysts)
Control: mebendazole or albendazole stops development of new larvae

**H.** ***Taenia*** (*T. saginata, T. solium*)
Characteristics: cestode morphology and life cycle (proglottids, scolex, resistant cuticle)
Pathogenesis: pig ingests embryophores, cattle ingest gravid proglottids and embyonated eggs, larvae liberated in intestine, enter blood then muscle; humans eat undercooked meat containing cysticerci, scolex attaches to mucosa of small intestine, worms mature, eggs and gravid proglottids released in feces; dead end when human ingests *T. solium* embryophore (Cysticercosis)
Infections: tapeworm disease (GIT symptoms depend on worm burden); Cysticercosis

when *T. solium* embryophore is ingested
Control: avoid undercooked meat; niclosamide, praziquantel

**I.** ***Diphyllobothrium latum*** (freshwater fish tapeworm)
Characteristics: cestode morphology; crustaceans and fish intermediate hosts; prevalent in cool lake water
Pathogenesis: humans ingest undercooked fish infected with sparganum larvae, attach to mucosa of small intestine, mature, eggs in feces, eggs released into freshwater develop into coracidium that infects crustaceans
Infections: Fish tapeworm disease (GIT symptoms depend on worm burden)
Control: niclosamide, praziquantel

**J.** ***Schistosoma mansoni*** (blood fluke)
Characteristics: trematode morphology; unlike most trematodes sexes are separate; eggs have characteristic lateral spine; adults are obligate intravascular parasites; aquatic snail intermediate host
Pathogenesis: cercaria penetrate skin, enter blood, develop in portal circulation (inferior mesenteric vein near lower colon), coat themselves with host proteins, mate, eggs produced; eggs pass into GIT and released in feces
Infections: Schistosomiasis (blood fluke infection; hypersensitive skin reaction at sites of skin penetration; hepatic and GIT symptoms depend on worm and egg burden)
Control: praziquantel

**82c. Miscellaneous parasites**

**A.** ***Echinococcus*** (dog tapeworm; human infection results in cysts in lung and liver)

**B.** ***Babesia*** (intraerythrocytic protozoan transmitted by same tick that transmits Lyme disease; malaria-like syndrome)

**C.** ***Naegleria fowleri*** (amebic meningoencephalitis)

**D.** ***Baylisascaris procyonis*** (raccoon roundworm; causes visceral, ocular, and neural larval migrans in humans)

**83. Ectoparasites**

**A.** ***Sarcotes scabiei*** (itch mite; scabies in humans, mange in animals)

**B.** ***Pediculus humanus*** (body or head louse)

**C.** ***Phthirus pubis*** (crab louse)

**D.** ***Xenopsylla cheopis*** (rodent flea; vector of plague and murine typhus)

**E.** ***Cimex hemipterus*** (bed bugs)