

Pathogenic Bacteria Lecture Notes

Bacteria are often characterized first by their cell wall (gram positive and negative) and morphology. Metabolism and other characteristics can also be used in classification.

Newer DNA based genetic studies can also help us understand how bacteria are related. However, because of horizontal gene transfer this can be complicated! Remember from Unit 2, horizontal gene transfer involves the exchange of genes through transformation, transduction, and conjugation

Gram Positive Cocci

Staphylococcus – all species in this genus have these traits: G+ cocci in clusters, facultative anaerobe, Catalase +, Lipase +, Halophile

- *S. epidermidis* – Opportunist, ubiquitous on skin, primarily infectious in immune compromised
- *S. aureus* – main pathogen, MANY virulence factors (VF)
 - Virulence Factors:
 - Coagulase +, Kinase, Hyaluronidase, β hemolytic
 - Protein A – binds stem of IgG preventing opsonization and complement
 - Slime layer (sometimes capsule) – inhibits phagocytes, allows attachment to artificial surfaces (catheters, shunts, heart valves, artificial joints, loves plastic!)
 - Beta lactamase: breaks β lactam ring of penicillin = resistant to penicillin and other antibiotics, 90% of strains are resistant
 - Typical diseases:
 - Pyogenic (pus forming) infections and abscesses of many organs (subcutaneous tissue, bone marrow, endocardium), septicemia (blood poisoning from bacteria)
 - Toxic Shock Syndrome (TSS): toxin absorbed in blood results in fever rash, $\downarrow\downarrow$ blood pressure (bp), linked to high absorbency tampons
 - Food intoxication: heat stable toxin results in nausea, vomiting, diarrhea, pain, 4 to 24hrs
 - Scalded Skin Syndrome (SSS): toxin breaks adhesion of keratinocytes so skin peels off in sheets within 2 days, risk of secondary infections

Streptococcus – G+ cocci in pairs or chains, Facultative anaerobe with peroxidase (so this bacterium is Catalase Negative), classified into groups by Rebecca Lancefield (1938) based on Ag, hemolysis patterns, arrangement, Groups A-H and K-V

- *Streptococcus pyogenes* = Group A Strep
 - VFs:
 - β hemolytic, hyaluronic acid capsule, streptokinase
 - M protein: binds Ab which destabilizes complement and opsonization, *S. pyo* are classified by their M
 - DNase – break down DNA from dead cells and spread further
 - Streptolysin – lyses RBCs and phagocytes from inside out!
 - Pyrogenic toxin – “pyro” = fire = fever, stimulates release of chemical signals to induce fever – gene acquired from lysogenic phage!
 - Typical diseases:
 - Pharyngitis (“Strep throat”): in kids more than adults because adults are immune to most M proteins
 - Scarlet Fever – lysogenic toxin gene leads to fever and rash

- Untreated Pharyngitis and Scarlet fever causes Ab to be produced → Ab bind to *Strep* → *Strep* are lysed but fragments of dead cell's Ag+Ab may stick in heart tissue or kidneys → leads over long term to Rheumatic Fever and Glomerulonephritis → Type III Hypersensitivity
- STSS – Strep Toxic Shock Syndrome, increase in significance, 40% mortality
- Necrotizing Fasciitis – “Flesh eating Strep”, secrete enzymes and toxins that destroy tissues, muscles, fat; spreads through connective tissue (fascia); then toxemia, organ failure, 50% mortality, amputate before it spreads!
- Treatment: Penicillin in most cases, bacitracin for external infections, antitoxins for more serious disease

Gram Positive Rods

Bacillus – G+ rod often in chains, endospores, aerobes and facultative anaerobes, common in environment (soil)

- *Bacillus anthracis* - causative agent of Anthrax, main human pathogen
 - VFs:
 - *B. anthracis* has two main virulence factors: a capsule and the anthrax toxin (which destroys WBCs)
 - Mainly a pathogen of animals, humans contract by accident
 - Three forms of disease:
 - Cutaneous Anthrax: spores enter through break in skin and form an obvious sign of infection, a black lesion called an eschar, 25% mortality
 - Inhalation (also known as pulmonary): spores are inhaled into lungs, no obvious signs/symptoms, direct access to bloodstream = 99% mortality without treatment in 24-48hrs
 - Gastrointestinal: Spores enter through ingestion of contaminated meat, no obvious signs/symptoms, direct access to bloodstream = HIGH mortality
 - Treatment: Most antibiotics are effective, including penicillin, vaccine for prevention in high risk groups

Clostridium - G+ rod often in chains, endospores, obligate anaerobes (fermentation), common in environment, many species produce toxins

- *C. tetani* = Causative agent of Tetanus
 - VF's: main virulence factor is Tetanus toxin, a neurotoxin that prevents nerves from signaling muscle relaxation (muscles contract uncontrollably), “Lock jaw”, prevent with vaccine to toxin
 - Disease: Tetanus or “Lock jaw”, prevent with vaccine to form Ab against toxin
- *C. botulinum* = Causative agent of Botulism
 - VF's: main virulence factor is Botulism toxin, one of the strongest known toxins, a neurotoxin that prevents nerves from signaling muscle contraction (muscles stay relaxed)
 - Botulism found in 3 forms:
 - Food-borne: food contaminated with Botulism toxin, linked with home canning, heating foods should destroy toxin (heat labile), can lead to death from inability to inhale, treat with antitoxin from CDC, an intoxication not an infection
 - Infant: “Floppy baby syndrome”, Infant is colonized by *C.bot*, constipation and “failure to thrive” are signs, no honey under age of 1
 - Wound: wound contaminated with endospores, similar to food-borne
- *C. difficile*= Opportunist
 - Common member of intestinal normal flora, opportunist in patients treated with broad spectrum antibiotics (other normal flora is killed resulting in *C.dif* superinfection)

- Minor infections have self limiting explosive diarrhea
- Serious infections lead to pseudomembranous colitis which may result in perforation of the colon, a massive internal infection by fecal bacteria, and death
- Some *C.dif* strains are drug resistant and survive better in patients on acid inhibitors (Pepcid, Prilosec). New treatment option involves transplanting fecal material (with normal microbiota) to replenish lost normal microbiota in patient.

Mycobacterium – G+ rod, aerobe, ACID FAST (mycolic acid in cell wall), s l o w growth. Most of the virulence of *Mycobacterium* comes from the waxy mycolic acid which protects the cells from lysis and makes them resistant to detergents, antibiotics, and desiccation. Also, many *Mycobacterium* can be intracellular and their slow growth means that an infection may exist for a long time before obvious signs/symptoms.

- *M. tuberculosis* = Causative agent of Tuberculosis (TB), a respiratory infection with infectious dose of 10 cells
 - VF's: Mycolic acid and cord factor (part of the cell wall that attaches cells to each other, inhibits chemotaxis of neutrophils, is toxic to cells .
 - Disease:
 - Primary TB results when *M. tuberculosis* cells are ingested by macrophages and grow within the macrophages, some escape and stimulate the immune system. The immune system tries to destroy the TB with Cytotoxic T cells and more macrophages. TB kills the immune cells and the host deposits collagen to trap the TB. This forms tubercles. See video on Blackboard.
 - If TB cells escape the tubercles this leads to secondary TB
 - If TB spreads throughout body known as disseminated TB: "Consumption", body wastes away
 - Detection/Prevention/Treatment:
 - Detect with skin test, chest x-ray
 - Link with low protein diet: with sufficient protein in diet most are not susceptible to disease – prevent
 - BCG vaccine: effective in disseminated TB, vaccine used in countries with high TB
 - Treatment with combination of antibiotics over 6-9 months. DOTS: Directly Observed Treatment Shortcourse) monitors patients over treatment to make sure there are no missed doses. TB already resistant but significant resistance is increasing: MDRTB (multi drug resistant, resistant to 2 drugs). XDRTB (extensive drug resistant TB, resistant to 5 drugs.)

Gram Negative Cocci

Neisseria – main pathogenic G (-) diplococci, aerobic, oxidase positive, difficult to grow in lab

- *N. gonorrhoeae* – the Gonococcus - Causative agent of gonorrhea
 - VF's: fimbriae that aid in attachment and slow phagocytosis, endotoxin, IgA protease
 - Disease:
 - STD, attaches to mucous membranes of genital, urinary, and digestive tracts
 - Symptomatic in men with painful urination and pus-filled discharge from penis
 - Often asymptomatic in women, can infect cervix and fallopian tubes leading to scarring and sterility, can infect eyes/cornea of children during birth and lead to blindness
 - Prevention/Treatment: Prevent with abstinence and "safe" sex practices, Treat with antibiotics but there is high resistance
- *N. meningitidis* – the Meningococcus - Causative agent of bacterial meningitis
 - VF's: capsule, fimbriae, IgA protease, endotoxin
 - Disease:

- Humans are the only carrier for *N. men*, can be part of normal flora of upper respiratory
- If bacteria invade blood or cerebrospinal fluid causes life-threatening meningitis
- Respiratory droplet transmission among people living in close contact (day care, college dorms, military barracks)
- VERY FAST progression – death can result in 6 hrs after symptoms appear, small blood lesions, petechiae, are common
- Treat with penicillin. Prevent with Meningococcal vaccine.

Facultative Anaerobic Gram Negative Rods

Family Enterobacteriaceae - This family contains gram negative, oxidase negative, facultative anaerobes that are significant as normal microbiota in the gastrointestinal tract of humans. This family can be divided into three groups:

- a. The coliforms – those that ferment lactose. Example: *Escherichia*
 - b. The non coliform opportunists - No disease to study. *Serratia marcescens* fits into this category.
 - c. The true pathogens –not opportunists. Examples: *Salmonella* and *Yersinia*
- These bacteria have similar VF's:
 - Flagella (called the H Ag)
 - Capsules (called the K Ag)
 - Fimbriae with adhesins
 - Type III Secretion System: a way to inject their own receptor into a host cell
 - In addition many times these VFs are on plasmids that can be exchanged (potentially across species)
 - Exotoxins: especially enterotoxins (stimulate loss of Na, Cl, K, H₂O = watery diarrhea, cramps, nausea = allows microbe to exit host and spread)
 - Not always useful to treat with antibiotics because risk of Lipid A from dead cells, if possible treat loss of fluids and electrolytes and allow disease to run its course

Escherichia coli: Coliform

- Most common coliform, most strains are normal flora or opportunists, a few are pathogenic
- Most common disease is gastroenteritis, also #1 cause of non-nosocomial UTI's
- Some severe forms like *E. coli O157:H7* has extra toxins, can lead to Hemolytic Uremic Syndrome and death in immune compromised

Yersinia pestis: True Pathogen = Causative agent of Plague

- VFs: capsule and adhesins, Type III system that triggers apoptosis of phagocytes, see video on Blackboard.
- Disease:
 - Bubonic Plague – transmission by flea vector, results in obvious sign, bubo (inflamed lymph node), also high fever, possible septicemia if bacteria spreads to blood, fast progression.
 - Pneumonic Plague – if *Y.pestis* spreads to lungs can turn into Pneumonic plague and be transmitted airborne, very rapid progression and death within days
- Treat with antibiotics ASAP, mortality in untreated 50% for bubonic, 100% for pneumonic

Salmonella: True pathogen, motile, normal flora in birds and reptiles

- *S. typhimurium* = Causative agent of Salmonellosis
 - Most often from food contaminated by animal feces, raw eggs, raw/undercooked poultry

- *S.typhimurium* triggers endocytosis into intestinal cells, multiplies within vesicle, kills host cell inducing fever, cramps, diarrhea, and potentially spreading to blood then heart, bones, joints
- *S. typhi* = Causative agent of Typhoid Fever
 - Humans are only host, infection from food/water contaminated by feces from asymptomatic carriers
 - Disease:
 - Cells enter intestinal cells and continue to blood, then phagocytes ingest but don't destroy and carry cells to liver, spleen, bone marrow, and gall bladder (patients with pathogen in gall bladder become carriers) – leads to fever, headache, muscle pain, malaise, loss of appetite
 - When pathogen is in gall bladder can re-infect gastrointestinal tract or spread to new host
 - Treatment/prevention: replace fluids and electrolytes, antibiotics, vaccine, removal of gallbladder in carriers
- **Note:** *Salmonella* has a complex naming system that involves classification into serogroups. You may find information about *S.enterica* with a subspecies listed last. For example: *Salmonella enterica typhimurium*

Pathogenic Gram (-) Aerobic Rods

Bordatella -- Small aerobic, nonmotile, gram (-) coccobacillus of family *Betaproteobacteria*

- *B. pertussis* = Causative agent of Pertussis, "Whooping Cough"
 - VFs:
 - Adhesins
 - Toxins – Pertussis toxin (an adhesin and toxin that increases mucus production in ciliated epithelial cells of trachea), Adenylate cyclase (triggers increased mucus and inhibits WBCs), Dermonecrotic toxin (constricts and hemorrhage of blood, resulting in cell death), and Tracheal cytotoxin (inhibits and kills tracheal cilia)
 - Disease:
 - Bacteria enter and multiply without symptoms, 1 week
 - Catarrhal phase: common cold symptoms, 1-2 wks
 - Paroxysmal phase: ciliated epithelial cells are inhibited and killed, patient tries to clear dead cells and mucus with 40-50 SEVERE coughing spells followed by "whoop" intake of air, coughing exhausts the patient and leads to low oxygen so some patients may turn blue or their ribs may break from the coughing spells, see video on Blackboard.
 - Convalescent phase: bacteria disappear, coughing slows, tracheal cells grow back, risk of secondary infections from *Staph* and *Strep*, 3-4 wks
 - Treatment/prevention:
 - Immune system can fight off disease but must monitor during regrowth of tracheal cells for secondary infections. Good vaccine (DPT or DaPT) but cases increasing from lack of vaccination, mostly disease in age 5 and under

Other Gram Negatives

Vibrio cholera = Causative agent of Cholera

- Slightly curved G(-) rods, similar VFs as *Enterobacteriaceae* (O polysaccharides), facultative anaerobe, oxidase positive, polar flagella, water borne
- VFs:

- Main VF is cholera toxin which stimulates intestinal cells to release fluid and electrolytes resulting in watery diarrhea. Toxin gene from lysogenic phage.
 - In order to pick up toxin gene another lysogenic phage must infect *V. cholera* and form a special pilus. Once *V. cholera* has the pilus a 2nd phage enters through pilus with gene for cholera toxin.
- Disease/Treatment:
 - Infection requires approx. 10^8 cells (from contaminated H₂O) because most are destroyed by stomach acid
 - Prolific “rice-water” diarrhea rapidly leads to dehydration and eventually death. Replace fluids and electrolytes. Antibiotics are not useful.

Treponema pallidum = Causative agent of Syphilis

- G(-) thin spirochete, obligate human pathogen, does not survive long outside of humans (destroyed by heat, air, drying, soap, disinfectants, pH changes)
- Sexually transmitted disease; also may be transmitted from mother to child, and rarely through blood transfusion with contaminated blood, not transmitted by fomites.
- VFs: Adhesins, glycocalyx, hyaluronidase, corkscrew motility. It is difficult to grow *T. pallidum* outside of a human so many factors are unknown.
- Disease/Treatment:
 - 4 stages of disease:
 - Stage 1: Primary Syphilis: Highly infectious. A small, painless, reddened lesion called a chancre forms at the site of infection 10-21 days after exposure. Chancres remain for 3 – 6 wks then disappear.
 - Stage 2: Secondary Syphilis: Pathogen invades the bloodstream and spreads throughout the body leading to sore throat, headache, fever, malaise, muscle pain, diseased lymph nodes, and widespread rash. Lesions of rash are highly contagious. May last for several months.
 - Stage 3: Latent phase: inactive phase of the disease that may last 30 years or more. Most cases do not progress past this stage.
 - Stage 4: Tertiary Syphilis: This stage does not result from the pathogen directly but from inflammation and a hyperimmune response against the pathogen. Results in dementia, blindness, paralysis, heart failure, gummas.
 - Congenital Syphilis: If pathogen crosses placenta to fetus. If the mother is in primary or secondary stage the result is usually death to the fetus. If the mother is in latent phase this results in a latent infection in the fetus with mental retardation, and malformation of fetal organs.
 - Diagnose with antibody test (MHA-TP) or observation of spirochetes from lesions. Treat with Penicillin in primary, secondary, or congenital cases, no effect in tertiary syphilis because it relates from hyperimmune response. Prevent with safe sexual practices.