19: Pathogenic Gram-Positive Cocci and Bacilli

1. Gram-positive pathogens
   - Color reaction ________________________________
     - Shapes __________________ and ___________________
     - Genera of cocci-shaped organisms:
       - ________________________________
       - ________________________________
     - Genera of bacilli-shaped organisms:
       - ________________________________
       - ________________________________
       - ________________________________
       - ________________________________

2. *Staphylococcus*
   - Normal members of every human’s microbiota
   - Can be opportunistic pathogens
   - Gram stain reaction
     - ________________________________
     - ________________________________
     - Cell division occurs along different planes and the daughter cells remain attached to one another
   - Salt-tolerant
     - Tolerates salt present on human skin
     - Culture considerations
   - Tolerant of desiccation
     - Survival on environmental surfaces (fomites)
     - Infection control
   - Species commonly associated with staphylococcal diseases in humans
     - *Staphylococcus aureus*:
       - More virulent strain
- Produces a variety of conditions depending on the site of infection
- Produces many extracellular enzymes/toxins

*Staphylococcus epidermidis:*
- Normal microbiota of human skin
- 

3. Pathogenicity
- “Staph’ infections result
- 
- Entry of only a few hundred bacteria can result in disease
- Pathogenicity results from three features
  - Structural defenses against phagocytosis
    - Protein A
      - Bound coagulase
        - Converts fibrinogen to fibrin to form blood clots
        - Fibrin clots hide the bacteria from phagocytic cells
    - Polysaccharide slime layers
      - Inhibit chemotaxis of and phagocytosis by leukocytes
      - Attachment of Staphylococcus to artificial surfaces
    - Enzymes
- Triggers blood clotting

- Dissolves fibrin threads in blood clots, allowing *S. aureus* to free itself from clots

- Breaks down penicillin

- Resistance to β-lactam antimicrobial drugs

- **Toxins**
  - *Staphylococcus aureus* produces toxins more frequently than *S. epidermidis*
  - Cytolytic toxins
    - Disrupts cytoplasmic membrane of a variety of cells
    - Leukocidin can lyse leukocytes specifically
  - Exfoliative toxins
    - Causes the patient’s skin cells to separate from each other and slough off the body
  - Toxic-shock-syndrome toxin
    - Causes toxic shock syndrome
  - Enterotoxins
    - Stimulate the intestinal muscle contractions, nausea, and intense vomiting associated with staphylococcal food poisoning

4. **Staphylococcal diseases**
   - Noninvasive disease
     - Food poisoning from the ingestion of enterotoxin-contaminated food
   - Cutaneous disease
     - Scalded Skin Syndrome (Fig. 19.2)
     - Impetigo (Fig. 19.3)
     - Folliculitis, furuncles, boils
   - Systemic diseases
     - Bacteremia – presence of bacteria in the blood
     - Endocarditis – occurs when bacteria attack the lining of the heart
Pneumonia – inflammation of the lungs in which the alveoli and bronchioles become filled with fluid

Osteomyelitis – inflammation of the bone marrow and the surrounding bone

Toxic shock syndrome – TSS toxin absorbed in blood, causing shock (Fig. 19.4)

5. Diagnosis, treatment, and prevention
   - Diagnosis: Detection of Gram-positive bacteria in grapelike arrangements isolated from pus, blood, or other fluids
   - Treatment: Methicillin is the drug of choice to treat staphylococcal infections
     - Semisynthetic form of penicillin not inactivated by β-lactamase
     - Caution: MRSA
   - Prevention
     - Hand antisepsis is the most important measure in preventing nosocomial infections
     - Also important is the proper cleansing of wounds and surgical openings, aseptic use of catheters or indwelling needles, an appropriate use of antiseptics

6. Streptococcus
   - Gram stain reaction
   - ____________________________________________
   - ____________________________________________
   - Often categorized based on the Lancefield classification
     - Rebecca Lancefield – Nobel prize
   - Serotype based on the bacteria’s antigens (surface polysaccharides)
   - Lancefield groups A and B include the significant streptococcal pathogens of humans

7. Group A Streptococcus: Streptococcus pyogenes
   - Colonial morphology: ____________________________________________
   - ____________________________________________
   - Pathogenic strains often form a capsule
   - Group A streptococci generally only cause disease in certain situations
   - ____________________________________________
   - ____________________________________________
   - ____________________________________________
8. Pathogenicity
   - Structural components
     - interferences with opsonization and lysis of the bacteria
     - Acts to camouflage the bacteria
   - Enzymes
   - Facilitate spread of organism through tissues
   - Pyrogenic toxins that stimulate macrophages and helper T cells to release cytokines
   - Streptolysins lyse __________, __________, __________

9. Group A streptococcal diseases
   - ____________________________ ("strep throat") – inflammation of pharynx (Fig. 19.6)
   - ____________________________ – rash begins on the chest, spreads across body
   - ____________________________ – inflammation leading to damage of heart valves
     muscle
   - ____________________________ – inflammation of the glomeruli and nephrons which
     obstruct blood flow through the kidneys
   - ____________________________ – confined, pus-producing lesion that usually occurs
     on the face, arms, or legs
   - Streptococcal toxic shock syndrome – bacteremia and severe multisystem infections
   - Necrotizing fasciitis – toxin production destroys tissues and eventually muscle and fat tissue
     (Fig. 19.8)

10. Diagnosis, treatment, and prevention
    - Diagnosis
      - Gram-positive bacteria in short chains or pairs
      - β-hemolytic colonies on blood agar
- Immunological tests for group A streptococcal antigens
- Streptococci normally in the pharynx – isolation of little diagnostic value
- Treatment: Penicillin
- Prevention
  - Strain-specific immunity

11. Group B Streptococcus: *Streptococcus agalactiae*
   - Gram-positive cocci that divide to form chains
   - Distinguished from group A streptococcus by its buttery colonies and smaller zone of beta-hemolysis on blood agar plates and its resistance to bacitracin
   - Normally colonizes the lower gastrointestinal, genital, and urinary tracts
   - Pathogenicity
     - Often infects newborns who have not yet formed type-specific antibodies and whose mothers are uninfected (and so do not provide passive immunity)
     - Produces various enzymes whose roles in virulence not understood
   - Diseases
     - Neonatal bacteremia, meningitis, pneumonia
     - Older people at risk from group B streptococcal infections

12. Alpha-hemolytic streptococci: Viridans group
   - Lack group-specific carbohydrates; not grouped by Lancefield system
   - Many produce green pigment on blood agar
     - Type of hemolysis ______________________________
     - Normally inhabit mouth, pharynx, GI tract, genital tract, and urinary tract
     - ______________________________: causes dental caries and dental plaques
     - ______________________________: meningitis and endocarditis

13. *Streptococcus pneumoniae* (Fig. 19.9)
   - Gram-positive cocci forms pairs and short chains
   - α-hemolytic colonies on blood agar when grown aerobically; β-hemolytic colonies when grown anaerobically
   - Normally colonizes mouth and pharynx but can cause disease if it travels to the lungs
   - Disease is highest in children and the elderly
   - Pathogenicity: ______________________________
     - Protects bacteria from digestion after endocytosis
   - Diseases
     - Pneumococcal pneumonia – bacteria multiply in the alveoli of the lower lung causing damage to alveolar lining and producing an inflammatory response
- Sinusitis and otitis media – bacteria invade sinuses or middle ear, often after viral infection
- Bacteremia and endocarditis – bacteria in bloodstream or lining of the heart
- Pneumococcal meningitis – bacteria that have spread to the meninges

14. Diagnosis, Treatment, and Prevention
- Diagnosis: Gram-strain of sputum smears
- Treatment: Penicillin
- Prevention: Vaccine made from purified capsular material
  - Provides long lasting immunity in normal adults
  - Not as effective in children, elderly, or AIDS patients

15. *Bacillus*
- Gram-positive bacilli, occurs singly, in pairs, or in chains
- ________________________________
  - _______________ is a strict pathogen of animals and humans
- Primarily a disease of herbivores, but humans can contract the disease from infected animals
- Humans contract the bacteria via one of three routes
  - Inhalation of spores
  - Inoculation of spores into the body through a break in the skin
  - Ingestion of spores

- Pathogenicity – Anthrax toxin

- Anthrax only disease caused by *Bacillus anthracis*
- Three clinical manifestations of Anthrax
  - Gastrointestinal anthrax - rare in humans
    - Intestinal hemorrhaging and eventually death
  - Cutaneous anthrax
    - Produces a ulcer called an eschar and toxemia (Fig. 19.12)
  - Inhalation anthrax - rare in humans
    - Spores germinate in lungs, secrete toxins absorbed into bloodstream
- High mortality rate

16. **Clostridium**
   - **Anaerobic** Gram-positive, endospore-forming bacillus
   - Compare and contrast with *Bacillus* species

   - Ubiquitous in soil, water, and the gastrointestinal tracts of animals and humans
   - The presence of endospores allows for survival in harsh conditions

17. **Clostridium perfringens**
   - Commonly grows in the digestive tracts of animals and humans
   - Produces 11 toxins that have various effects on the body and can result in irreversible damage

   **Diseases**
   - Food poisoning
     - Benign disease characterized by abdominal cramps and watery diarrhea
   - Gas gangrene (Fig 19.13)
     - Endospores enter body through traumatic event
     - Endospores germinate, cause necrosis accompanied by foul-smelling gaseous bacterial waste products

   **Diagnosis**
   - >10⁵ bacteria per gram of food or 10⁶ cells per gram feces indicates Clostridial food poisoning
   - Gas gangrene is usually diagnostic by itself

   **Treatment**
   - Food poisoning is self-limited
   - Gas gangrene is treated by removing the dead tissue and administering large doses of antitoxin and penicillin

18. **Clostridium difficile**
   - Anaerobic, endospore-forming, Gram-positive bacillus
   - Common member of the intestinal microbiota
   - Opportunistic pathogen in patients treated with broad-spectrum antimicrobial drugs

   - Minor infections can result in a self-limiting explosive diarrhea
   - Serious cases can cause ________________________
     - Perforation of the colon, leading to massive internal infection by fecal bacteria and eventual death

   **Diagnosed by isolating the organism from feces or by demonstrating the presence of toxins via immunoassay**
Minor infections usually resolved by discontinuing antimicrobial drug in use

Serious cases are treated with antibiotics

Proper hygiene is critical for limiting nosocomial infections

19. *Clostridium botulinum*

- Anaerobic, endospore-forming, Gram-positive bacillus
- Common in soil and water
- Botulism results when the endospores germinate and produce botulism toxin

The different botulism toxins are among the deadliest toxins known

**Botulism Toxin (Fig. 19.14)**

- Type of toxin __________________________
- Mechanism of action

**Reaction**

**Diseases**

- Botulism is not an infection, but an intoxication caused by the botulism toxin
- Three forms of botulism
  - **Food-borne botulism**
    - Usually occurs due to the consumption of toxin in home-canned foods or preserved fish
    - Can result in a progressive paralysis that results in death due to the inability to inhale
  - **Infant botulism**
    - Endospores ingested, germinate, and colonize the infant’s gastrointestinal tract
      - Lack of sufficient numbers of normal microbiota
      - Symptoms include constipation and “failure to thrive”;
      - Paralysis and death are rare
  - **Wound botulism**
    - Wound contaminated with endospores
    - Symptoms same as with food-borne botulism

**Diagnosis**

- Symptoms are diagnostic – flaccid paralysis
- Confirm by culturing the organism from food, feces, or the patient’s wound

**Treatment – three approaches**

- Repeated washing of the intestinal tract to remove *Clostridium*
- Administer antibodies to neutralize toxin in the blood before it binds to neurons
- Administer antimicrobial drugs to kill clostridia in infant botulism cases

- Prevention
  - ______________________________________________________
  - ______________________________________________________

20. *Clostridium tetani*
- Obligate anaerobic, endospore-forming, Gram-positive bacillus
- Ubiquitous in soil, dust, and the GI tract of animals and humans
- Endospores germinate, produce tetanus toxin
- Tetanus results in spasms and contractions that can result in death because patients can’t exhale

- Tetanus Toxin (Fig. 19.16, Fig. 19.17)
  - Type of toxin_____________________________________
  - Mechanism of action

- Reaction

- Diagnosis
  - Characteristic muscular contraction – spastic paralysis
  - Bacterium rarely isolated from clinical samples because it grows slowly and is sensitive to oxygen

- Treatment
  - Thorough cleaning of wounds to remove endospores
  - Passive immunization with immunoglobulin directed against the toxin
  - Administration of antimicrobials
  - Active immunization with tetanus toxoid
    - Define toxoid

- Prevention
  - Immunization with tetanus toxoid

  - Vaccine____________________________________________________
  - Administration timeline________________________________________

21. *Listeria*
- Gram-positive non-spore-forming, coccobacillus
- Temperature requirement__________________________
Listeria produces no toxins or enzymes
Virulence is directly related to bacteria’s ability to live within cells (Fig. 19.18)

Diagnosis
- Presence of the bacteria in the cerebrospinal fluid
- Rarely seen by Gram-staining because so few Listeria cells are required to produce disease
- Culture considerations

Treatment
- Most antimicrobial drugs inhibit Listeria

Prevention
- Difficult because the organism is ubiquitous
- Avoid undercooked vegetables, unpasteurized milk, undercooked meat, soft cheeses

22. Corynebacterium
- Ubiquitous on plants and in animals and humans
- Colonizes skin, respiratory system, and gastrointestinal, urinary, & genital tracts
- Corynebacterium diphtheriae, cause of diphtheria, is the most widely known
  - Transmitted from person to person via respiratory droplets or skin contact
  - Endemic in poor parts of the world that lack adequate immunization
  - Diphtheria toxin is responsible for the signs and symptoms of diphtheria

Disease
- Diphtheria toxin: ___________________________________________________________________
  - Infections are asymptomatic or produce mild respiratory disease in immune or partially immune individuals
  - Severe respiratory infections of non-immune patients produce the signs and symptoms of diphtheria
    - Pseudomembrane results from fluid that has thickened and adheres throughout the respiratory tract (fig. 19.20)
    - The pseudomembrane can completely occlude the respiratory passages and cause suffocation
- Cutaneous diphtheria causes cell death and formation of a pseudomembrane on the skin

- **Diagnosis**
  - Initial diagnosis is based on the presence of pseudomembrane

- **Treatment**
  - Administration of antitoxin to neutralize toxin before it binds to cells
  - Penicillin and erythromycin kills the bacteria

- **Prevention**
  - Immunization with ______________________________________________________
  - Vaccine____________________________________________________
  - Administration timeline___________

23. *Mycobacterium*

- Stain reaction ______________________________________________________________
- Cell wall contains a waxy lipid called __________________________________________
- The unusual cell wall results in a number of unique characteristics
  - Slow growth
  - Protection from lysis once the bacteria are phagocytized
  - Capacity for intracellular growth
  - Resistance to Gram-staining, detergents, many antimicrobial drugs, and dessication

- Three main mycobacterial diseases
  - Tuberculosis
  - Leprosy
  - Opportunistic infections in AIDS patients

- **Tuberculosis (TB)**
  - Respiratory disease caused by *Mycobacterium tuberculosis*
  - Cases are declining in the United States but it is pandemic in other parts of the world
  - Virulence factor________________________________________

  - Three types of tuberculosis (Fig 19.22)
    - Primary TB
      - Results from the initial infection with *M. tuberculosis*

    - Secondary TB
      - Reestablishment of an active infection after a period of dormancy

- Disseminated TB
  - Results when the infection spreads throughout the body

- Diagnosis
  - Tuberculin skin test identifies individuals with previous exposure to *M. tuberculosis* by the presence of a hard, red swelling at the test site
  - Chest x-rays are used to identify individuals with active disease

- Treatment
  - Treatment with common antimicrobials is difficult because the bacteria grow slowly and can live within macrophages
  - Combination therapy must be used for a number of months to treat the disease

- Prevention
  - Prophylactic use of antibacterial drugs is used to treat patients who have shown a conversion from a negative to a positive skin test or were exposed to active cases of tuberculosis
  - Immunization with BCG vaccine is used in countries where TB is common

24. Leprosy
- Caused by *Mycobacterium leprae*
- Bacteria have never been grown in cell-free culture
  - Culture
  - Cases of leprosy are becoming relatively rare
  - Transmission is via person-to-person contact or through a break in the skin

- Diagnosis
  - Based on the signs and symptoms of the disease
    - Loss of sensation in skin lesions in the case of tuberculoid leprosy
    - Disfigurement in the case of lepromatous leprosy

- Treatment
  - Treatment with a combination of antimicrobial drugs
  - Lifelong treatment is sometimes needed

- Prevention
  - Primarily prevented by limiting exposure to the pathogen
  - BCG vaccine provides some protection
25. Mycobacterial Infections in AIDS Patients
   - *Mycobacterium avium-intracellulare* is the most common mycobacterial infection among AIDS patients in the United States
     - Infections are a result of ingestion of contaminated food or water
     - Infections can simultaneously affect almost every organ and result in massive organ failure
     - Treatment is difficult due to the disseminated nature of the infection

26. *Propionibacterium*
   - Small, Gram-positive rods
   - Location: _________________________________________________________
   - *Propionibacterium acnes* species most commonly involved in human infections
     - Causes __________________________________________________________
     - May also be an opportunistic pathogen
     - Treatment often involves the use of antimicrobial drugs though many cases require no treatment
     - Development of acne (Fig. 19.25)