Chapter 20

Pathogenic Gram-Negative Cocci and Bacilli
Gram-Negative Bacteria

• Largest group of human pathogens
  – Due in part to the presence of lipid A in the bacterial cell wall
    • Triggers fever, vasodilation, inflammation, shock, and disseminated intravascular coagulation (blood clots within blood vessels)

• Almost every Gram-negative bacterium that can breach the skin or mucous membranes, grow at 37°C, and evade the immune system can cause disease and death in humans
Neisseria

• Only genus of Gram-negative cocci that regularly causes diseases in humans
• Nonmotile, aerobic bacteria - Microaerophilic
• Need enriched media
• Capsules = pathogenic
• oxidase positive
• Fragile – strict parasites
• 2 species are pathogenic to humans
  – The gonococcus, *N. gonorrhoeae*
  – The meningococcus, *N. meningitides*
Neisseria gonorrhoeae

• Gonorrhea - sexually transmitted disease
  – Ancient disease
  – Named for Dr. Neisser

• Virulence
  – Fimbriae
    • Adhere to epithelial cells of the mucous membranes
    • genital, urinary, and digestive tracts
    • spread to deeper tissue as they multiply
  – 2-6 days inflammatory response
Neisseria gonorrhoeae

• Subclinical infections – carriers (main reservoir)
  – Transmit to others

• Gonorrhea in men
  – Usually symptomatic
  – inflammation that causes painful urination and pus-filled discharge

• Gonorrhea in women
  – Often asymptomatic
  – Can infect the cervix and other parts of the uterus, including the Fallopian tubes
  – Can result in pelvic inflammatory disease (PID)
    • Can result in ectopic pregnancy or sterility
  – Gonococcal infection of children can occur during childbirth producing inflammation of the cornea and sometimes blindness
    • Silver nitrate solution → antibodies
Diagnosis, Treatment, and Prevention

• Diagnosis
  – Men – Gram stain of pus from an inflamed penis
  – Females – Gram stain of vaginal discharge
  – Asymptomatic cases can be identified with commercially available genetic probes

• Treatment
  – Complicated due to resistant gonococcal strains
  – Broad-spectrum antimicrobial drugs

• Prevention
  – Most effective prevention is sexual abstinence
Neisseria meningitidis

- Humans - only natural carrier
- Can be normal microbiota of the upper respiratory tract
- Causes life-threatening disease when the bacteria invade the blood or cerebrospinal fluid
- Most common cause of meningitis in individuals under 20
- Respiratory droplets transmit
  - At risk people living in close contact, especially students living in dormitories
Neisseria meningitidis

- Virulence Factors
  - Capsule
  - Pili
  - IgA protease
  - Lipopolysaccharide
- Death as early as 6 hours after initial symp.
- Meningococcal septicemia, blood poisoning, can also be life threatening
  - Can produce blood coagulation and the formation of minute hemorrhagic lesions
Diagnosis, Treatment, and Prevention

• Diagnosis - rapid
  – Presence of Gram-negative diplococci in phagocytes of the central nervous system

• Treatment
  – Penicillin, administered intravenously, is the drug of choice

• Prevention
  – Eradication is unlikely due to the presence of asymptomatic carriers
  – High risk vaccine
Enterobacteriaceae

- Members of the intestinal microbiota of most animals and humans
- Ubiquitous in water, soil, and decaying vegetation
- Enteric bacteria are the most common Gram-negative pathogens of humans
- Coccobacilli or bacilli
Dichotomous Key for Enterics

1. Rapid lactose fermentation
   - (+) Motility
     - (+) Citrate utilization
       - (+) Gelatin hydrolysis
         - (+) Serratia
         - (-) Enterobacter
       - (-) Voges-Proskauer
     - (-) Motility
       - (+) H₂S production
         - (+) Urea utilization
           - (+) Yersinia
           - (-) Shigella
         - (-) Urea utilization
           - (+) Morganella
           - (-) Citrate utilization
             - (+) Voges-Proskauer
               - (+) Serratia
               - (-) Providencia
             - (-) Voges-Proskauer
               - (+) Hafnia
               - (-) Edwardsiella
Diagnosis and Treatment

• Diagnosis
  – Enterobacteriaceae are cultured using selective and differential media
  – Rapid ID biochemical tests - Enterotube

• Treatment
  – Treatment of diarrhea involves treating the symptoms with fluid and electrolyte replacement
  – Antimicrobial drugs are not usually needed since diarrhea is self-limited
Prevention

• Prevention
  – Preventing enteric infections is almost impossible since they are a major component of the normal microbiota
  – Good personal hygiene and proper sewage control are important in limiting the risk of infection
  – Cook food thoroughly
Pathogenic Enterobacteriaceae are often classified into three groups

- Coliforms
  - rapidly ferment lactose
  - part of the normal microbiota
  - may be opportunistic pathogens

- Noncoliform opportunists
  - do not ferment lactose

- True pathogens
Coliform Opportunistic Enteriobacteriaceae

- Serratia
- Klebsiella
- Escherichia
- Enterobacter
- Citrobacter

- Aerobic or facultatively anaerobic, Gram-negative, rod-shaped
- Commonly found in soil, on plants, and on decaying vegetation
- Colonize the intestinal tracts of animals and humans
- Presence of coliforms in water is indicative of impure water and of poor sewage treatment
Coliform Opportunistic Enteriobacteriaceae

• Routes of entry
  – sponges
  – washclothes
  – humidifiers
  – IV resuscitation equipment
  – contaminated water
  – contact lens
Escherichia coli

• Most common and important of the coliforms
• Virulent strains
  – have genes located on virulence plasmids
  – allow the bacteria to colonize human tissue
• Gastroenteritis is the most common disease associated with *E. coli*
  – Often mediated by exotoxins that produce the symptoms associated with gastroenteritis
• Most common cause of non-nosocomial urinary tract infections
Escherichia coli

- E. coli O157:H7 is the most prevalent strain of pathogenic E. coli in developed countries
  - Causes diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome, a severe kidney disorder
  - Most epidemics associated with undercooked ground beef or unpasteurized milk or juice
  - Produces a type III secretion system and Shiga-like toxin that aid in the virulence of the bacteria
Noncoliform Opportunistic Enterobacteriaceae

- *Proteus*
- *Morganella*
- *Providencia*
- *Edwardsiella*

- Cause nosocomial infections in immunocompromised patients
- Primarily involved in urinary tract infections
Important members of this group almost always pathogenic due to numerous virulence factors

- Type III secretion system allows entry of proteins that inhibit phagocytosis, rearrange the cytoskeletons of eukaryotic cells, or induce apoptosis
Salmonella

• Gram-negative, motile, bacilli

• Found in the intestines and feces of most birds, reptiles, and mammals

• In humans - result of consumption of food contaminated with animal feces

• Poultry and eggs are particularly common sources of Salmonella

• 2 important pathogens
  – S. typhimurium-causes salmonellosis
  – S. typhi-causes typhoid fever
The events of salmonellosis

1. Epithelial cells lining small intestine
2. Salmonella trigger phagocytosis
3. Salmonella multiply within phagocytic vacuole
4. Salmonella kills host cell, inducing diarrhea.
5. Bacteremia: Salmonella moves into bloodstream
Salmonella typhi

• Humans only host – asymptomatic carriers
• Causes typhoid fever
• Infection occurs via ingestion
  – food or water contaminated with sewage
  – Need a large inoculum 200,000 cfu
• Bacteria can pass through the intestines into the bloodstream
  – into liver, spleen, bone marrow, & gall bladder
• Infected gall bladder can reinfect
  – intestines - gastroenteritis
  – blood - bacteremia
Salmonella typhi

• Bacteria can ulcerate and perforate the intestinal wall - peritonitis
• Symptoms – fever, diarrhea, abdominal pain
• Treatment - antimicrobial drugs (chloramphenical, ampicillin)
• Vaccines – whole cell killed vaccine
  – 6 months protection
  – Travelers to typhoid fever endemic areas
Shigella

- Gram-negative, nonmotile bacteria
- Primarily a parasite of the digestive tract of humans
- Produce a diarrhea-inducing enterotoxin – Shiga toxin
- Cause a severe form of dysentery called shigellosis
  - Crippling abdominal pains
  - Watery stools
Shigella

- 4 well-defined species
  - S. boydii
  - S. sonnei - most commonly isolated in industrialized nations
  - S. flexneri - most commonly isolated in developing countries
  - S. dysenteriae - produces a more serious disease than the other species

- Shigellosis treatment - fluid & electrolyte replacement, sometimes ampicillin
The events of shigellosis

1. Shigella attaches to epithelial cell of colon.
2. Shigella triggers phagocytosis.
3. Shigella multiplies in cytosol.
4. Shigella invades neighboring epithelial cells, thus avoiding immune defenses.
5. A mucosal abscess forms as epithelial cells are killed by the infection.
6. Shigella that enters the blood is quickly phagocytized.
Yersinia

• Normal pathogens of animals
• 3 important species
  – *Y. enterocolitica*
    • Acquired via consumption of food or water contaminated with animal feces
    • Causes inflammation of the intestinal tract
  – *Y. pseudotuberculosis*
    • Similar to *Y. enterocolitica* but produces a less severe intestinal inflammation
Yersinia

– Y.pestis
  • Bubonic plague-characterized by high fever and swollen, painful lymph nodes called buboes
  • Pneumonic plague-rapidly developing infection of the lungs
– 100 million died in 6th – 8th centuries – Justinian Plague
– 25% of pop. Black Plague
  • 40% of the population died in 1300 – 1400s
– Late 1855 epidemic began in
  • China
  • spread on rat infested ships (SF)
Mice no disease

Very few microbes needed

Incubation 2-4 days

Brown rat gets the disease

Untreated
50-70% fatal

Untreated 100% fatal
Diagnosis and Treatment

• Diagnosis and treatment must be rapid due to the fast progression and deadliness of the plague

• Diagnosis
  – Characteristic symptoms are usually sufficient for diagnosis

• Treatment
  – Many antibacterial drugs are effective against Yersinia

• Prevention
Pathogenic Gram-Negative Vibrios

• *Vibrios*
  – Share many characteristics with enteric bacteria
  – Found in water environments worldwide
  – *Vibrio cholerae*
    • Most common species to infect humans
    • Causes cholera
    • Humans infected by ingesting contaminated food and water
    • “Rice-water stool” is characteristic
    • Most important virulence factor is cholera toxin
Vibrio cholerae
The spread of cholera

Figure 21.20

- Initial epidemics January 1991
- August 1991
- February 1992
- November 1994
The action of cholera toxin in intestinal epithelial cells

1. Cholera toxin binds to membrane of epithelial cell.
2. Portion of toxin (part of A) enters cell.
4. Cyclic AMP (cAMP) is synthesized.
5. Cyclic AMP stimulates cell to secrete Cl⁻, Na⁺, and other electrolytes.
6. Water follows electrolytes into lumen.

Intestinal lumen

Epithelial cell

Figure 21.21
Pathogenic Gram-Negative Vibrios

- **Vibrios**
  - Diagnosis usually based on characteristic diarrhea
  - Treatment
    - Fluid and electrolyte replacement
    - Antimicrobial drugs are lost in the watery stool
  - Adequate sewage and water treatment can limit spread of *V. cholerae*