Infectious Diseases

Chapter 16, 19, 20, 21
Gram-Positive Pathogens

- Stain purple when gram-stained
- Can be categorized into two major groups based on their DNA
  - Low G + C organisms
    - Genera of cocci-shaped organisms – *Staphylococcus, Streptococcus, and Enterococcus*
    - Genera of bacilli-shaped organisms – *Bacillus, Clostridium*
  - High G + C organisms
    - Genera of bacilli-shaped organisms – *Corynebacterium, Mycobacterium*
Staphylococcus

- Normal members of every human’s microbiota
- Can be opportunistic pathogens
- Gram-positive cocci, nonmotile, facultative anaerobes
- Cells occur in grapelike clusters because cells division occurs along different planes and the daughter cells remain attached to one another
- Salt-tolerant – allows them to tolerate the salt present on human skin
- Tolerant of desiccation – allows survival on environmental surfaces (fomites)
Two species are commonly associated with staphylococcal diseases in humans

- *Staphylococcus aureus* – the more virulent strain that can produce a variety of conditions depending on the site of infection

- *Staphylococcus epidermidis* – normal microbiota of human skin that can cause opportunistic infections in immunocompromised patients or when introduced into the body
Pathogenicity

“Staph’ infections result when staphylococci breach the body’s physical barriers

Entry of only a few hundred bacteria can result in disease

Pathogenicity results from three features
  - Structures that enable it to evade phagocytosis
  - Production of enzymes
  - Production of toxins
Structural Defenses Against Phagocytosis

- Protein A coats the cell surface
  - Inhibits the complement cascade

- Bound coagulase
  - Converts the soluble blood protein fibrinogen in insoluble fibrin molecules that form blood clots
  - Fibrin clots hide the bacteria from phagocytic cells

- Synthesize loosely organized polysaccharide slime layers (often called capsules)
  - Inhibit chemotaxis of and phagocytosis by leukocytes
  - Facilitates attachment of Staphylococcus to artificial surfaces
Enzymes

- Cell-free coagulase
  - Triggers blood clotting
- Hyaluronidase
  - Breaks down hyaluronic acid, enabling the bacteria to spread between cells
- Staphylokinase
  - Dissolves fibrin threads in blood clots, allowing *S. aureus* to free itself from clots
Toxins

- *Staphylococcus aureus* produces toxins more frequently than *S. epidermidis*

- Cytolytic toxins
  - Disrupts the 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
Toxins

- Toxic-shock-syndrome toxin
  - Causes toxic shock syndrome
- Enterotoxins
  - Stimulate the intestinal muscle contractions, nausea, and intense vomiting associated with staphylococcal food poisoning
Enzymes

- **Lipases**
  - Digest lipids, allowing staphylococcus to grow on the skin’s surface and in cutaneous oil glands
- **β-lactamase**
  - Breaks down penicillin
  - Allows the bacteria to survive treatment with β-lactam antimicrobial drugs
Staphylococcal Diseases

- Three categories
  - Noninvasive disease
    - Food poisoning from the ingestion of enterotoxin-contaminated food
  - Cutaneous disease
    - Various skin conditions including scalded skin syndrome, impetigo, folliculitis, and furuncles
Staphylococcal Diseases

- Systemic disease
  - Toxic shock syndrome – TSS toxin is absorbed into the blood and causes shock
  - 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
Staphylococcal Diseases

Toxic shock syndrome

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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
  - Is a semisynthetic form of penicillin and is not inactivated by β-lactamase

[Chemical structure image]
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
Streptococcus

- Gram-positive cocci, arranged in pairs or chains, that are facultative anaerobes
- Often categorized based on the Lancefield classification
  - Divides the streptococci into serotype groups based on the bacteria’s antigens
  - Lancefield groups A and B include the significant streptococcal pathogens of humans
Group A Streptococcus: 
*Streptococcus Pyogenes*

- *S. pyogenes* forms white colonies surrounded by zone of beta-hemolysis on blood agar plates
- Pathogenic strains often form a capsule
- Group A streptococci generally only cause disease in certain situations
  - Normal microbiota are depleted
  - Large inoculum enable the streptococci to establish themselves before antibodies are formed against them
  - Specific immunity is impaired
Pathogenicity

- **Structural components**
  - Protein M, which interferes with opsonization and lysis of the bacteria and a hyaluronic acid capsule, which acts to camouflage the bacteria

- **Enzymes**
  - Streptokinases, deoxynucleases, and C5a peptidase all facilitate the spread of streptococci through tissues

- **Pyrogenic toxins** that stimulate macrophages and helper T cells to release cytokines

- **Streptolysins** lyse red blood cells, white blood cells, and platelets
Group A Streptococcal Diseases

- Pharyngitis ("strep throat") – inflammation of the pharynx
- Scarlet fever – rash that begins on the chest and spreads across the body
- Pyoderma – confined, pus-producing lesion that usually occurs on the face, arms, or legs
- Streptococcal toxic shock syndrome – bacteremia and severe multisystem infections
Group A Streptococcal Diseases

Pharyngitis

Erysipelas

Necrotizing Fasciitis
Group A Streptococcal Diseases

- Necrotizing fasciitis – toxin production destroys tissues and eventually muscle and fat tissue
- Rheumatic fever – inflammation that leads to damage of heart valves muscle
- Glomerulonephritis – inflammation of the glomeruli and nephrons which obstruct blood flow through the kidneys
Diagnosis

- Observation of Gram-positive bacteria in short chains or pairs or immunological tests that identify the presence of group A streptococcal antigens
- Streptococci are normally in the pharynx so their presence in a respiratory sample is of little diagnostic value
Diagnosis, Treatment, and Prevention

- **Treatment**
  - Penicillin is very effective

- **Prevention**
  - Antibodies against M protein provide long-term protection against future infection of *S. pyogenes*, but only if it is the same strain
Alpha-Hemolytic Streptococci: The Viridans Group

- Lack group-specific carbohydrates and cannot be grouped by the Lancefield system
- Many produce a green pigment when grown on blood media
- Normally inhabit the mouth, pharynx, GI tract, genital tract, and urinary tract
- One of the causes of dental caries and dental plaques
- If enter the blood can cause meningitis and endocarditis
Streptococcus pneumoniae

- Gram-positive cocci that most commonly forms pairs but may also form chains
- Forms unpigmented, alpha-hemolytic colonies when grown on blood agar (anaerobic incubation produces beta-hemolytic colonies)
- Normally colonizes the mouths and pharynx but can cause disease if travels to the lungs
- Disease is highest in children and the elderly
Streptococcus pneumoniae

Figure 19.9
Pathogenicity

- Phosphorylcholine – stimulates cells to phagocytize the bacteria
- Polysaccharide capsule – protects the bacteria from digestion after endocytosis
- Protein adhesin – mediates binding of the cells to epithelial cells of the pharynx
- Secretory IgA protease – destroys IgA
- Pneumolysin – lyses epithelial cells and suppresses the digestion of the endocytized bacteria
Diseases

- Pneumococcal pneumonia – bacteria multiply in the alveoli of the lower lung causing damage to the alveolar lining and producing an inflammatory response
- Sinusitis and otitis media – bacteria invade the sinuses or middle ear, often following a viral infection
- Bacteremia and endocarditis – bacteria in the bloodstream or in the lining of the heart
- Pneumococcal meningitis – bacteria that have spread to the meninges
Diagnosis, Treatment, and Prevention

- **Diagnosis**
  - Gram-strain of sputum smears
  - Quellung reaction – anti-capsular antibodies cause the capsule to swell, confirming the presence of bacteria

- **Treatment**
  - Penicillin

- **Prevention**
  - Vaccine made from purified capsular material
    - Provides long lasting immunity in normal adults but is not as effective in children, the elderly, or AIDS patients
Enterococcus

- Previously classified as group D streptococci but differed enough to be reclassified as a separate genus
- Form short chains and pairs and lack a capsule
- Found in the human colon but are rarely pathogenic at this site
- Can cause disease if they are introduced into other parts of the body, such as the urinary tract or bloodstream
Enterococcus

- Important cause of nosocomial infections
- Treatment is difficult because enterococci are often resistant to antimicrobials
- Prevention is difficult, especially in a health care setting, where patients’ often have weakened immune systems
Enterococcus faecalis

Figure 19.10
Diseases

- Skin infections
- Urinary tract infections
- Bacteremia and endocarditis – bacteria in the bloodstream or in the lining of the heart
- VRE infections in ICU will increase mortality by 50%
Diagnosis

- Gram-strain of smears
- Quellung reaction – anti-capsular antibodies cause the capsule to swell, confirming the presence of bacteria

Treatment

- Vancomycin, linezolid, Daptomycin

Prevention

- Difficult due to high numbers in body and certain environments.
Bacillus

- Gram-positive bacilli, that occurs singly, in pairs, or in chains
- Forms endospores
- *Bacillus anthracis* 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 by three routes
    - Inhalation of spores
    - Inoculation of spores into the body through a break in the skin
    - Ingestion of spores
Bacillus anthracis

Figure 19.11
Pathogenicity and Diseases

- Pathogenicity
  - Anthrax toxin

- Diseases
  - Anthrax is the only disease caused by *Bacillus anthracis*
  - Anthrax can have three clinical manifestations
    - Gastrointestinal anthrax
      - Rare in humans
    - Intestinal hemorrhaging and eventually death
Pathogenicity and Diseases

- Cutaneous anthrax
  - Produces a ulcer called an eschar and toxemia
- Inhalation anthrax
  - Rare in humans
  - Spores germinate in the lungs and secrete toxins that are absorbed into the bloodstream
  - High mortality rate
Diagnosis, Treatment, and Prevention

- **Diagnosis**
  - Presence of large, nonmotile, Gram-positive bacilli in clinical samples of the lungs or skin

- **Treatment**
  - Ciproflaxacin and many other antimicrobials are effective against *B. anthracis*

- **Prevention**
  - Control the disease in animals
  - An anthrax vaccine is available but requires multiple doses and boosters
Clostridium

- Gram-positive, anaerobic, endospore-forming bacillus
- Ubiquitous in soil, water, and the gastrointestinal tracts of animals and humans
- The presence of endospores allows for survival in harsh conditions
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
Clostridium perfringens

- Diseases
  - Food poisoning
    - Benign disease characterized by abdominal cramps and watery diarrhea
  - Gas gangrene
    - Endospores are introduced into the body through some traumatic event
    - The endospores germinate and cause necrosis that is often accompanied by foul-smelling gaseous bacterial waste products
Clostridium perfringens
Diagnosis

- The presence of more than $10^5$ bacteria in a gram of food or $10^6$ cells per gram of feces indicates the involvement of *Clostridium* in 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.
Diagnosis, Treatment, and Prevention

- Prevention
  - Difficult to prevent because it is so common
  - Proper cleaning of wounds can often prevent gas gangrene
Clostridium difficile

- 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 pseudomonas colitis
    - Can result in perforation of the colon, leading to massive internal infection by fecal bacteria and eventual death
**Clostridium difficile**

- Diagnosed by isolating the organism from feces or by demonstrating the presence of toxins via immunoassay.
- Minor infections are usually resolved by discontinuing use of the antimicrobial drug in use.
- Serious cases are treated with antibiotics.
- Proper hygiene is critical for limiting nosocomial infections.
**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

Figure 19.14

(a) Normal neuromuscular junction

1. Vesicles with acetylcholine
2. Cytoplasmic membrane of neuron
Cytoplasmic membrane of muscle cell
Acetylcholine

(b) Neuromuscular junction with botulism toxin present

Vesicles with acetylcholine
Botulism toxin
Diseases

- Botulism is not an infection, but an intoxicification 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
Diseases

- Infant botulism
  - Results from the ingestion of endospores, which germinate, and colonize the infant’s gastrointestinal tract due to the lack of sufficient numbers of normal microbiota
  - Symptoms include constipation and “failure to thrive”; paralysis and death are rare

- Wound botulism
  - Wound becomes contaminated with endospores
  - Symptoms are the same as with food-borne botulism
Diagnosis, Treatment, and Prevention

- **Diagnosis**
  - Symptoms of botulism are diagnostic
  - Confirm diagnosis by culturing the organism from food, feces, or the patient’s wound

- **Treatment**
  - Can involve three approaches
    - Repeated washing of the intestinal tract to remove *Clostridium*
    - Administer antibodies against botulism toxin to neutralize toxin in the blood before it can bind to neurons
    - Administer antimicrobials drugs to kill clostridia in infant botulism cases
- Prevention
  - Proper canning of food to prevent contamination
  - Infants should not consume honey under the age of 1
Clostridium tetani

- Endospore-forming, obligately anaerobic, Gram-positive bacilli
- Ubiquitous in soil, dust, and the GI tract of animals and humans
- Tetanus results when the bacterial endospores germinate and produce tetanus toxin
- Tetanus results in spasms and contractions that can result in death because patients can’t exhale
Tetanus Toxin

Figure 19.16a

- **Excitatory neuron**
- **Inhibitory neuron**
- **Inhibitory neurotransmitter blocks nerve impulse**
- **No nerve impulse**
- **Motor neurons**
- **Nerve impulse**
- **Excitatory neurotransmitter**

- **Biceps brachii muscle relaxed**
- **Triceps brachii muscle contracted**
Small polypeptide of tetanus toxin blocks release of inhibitory neurotransmitter

Both muscles fully contract. The arm flexes because biceps brachii is larger and stronger.
Patient with Tetanus

Figure 19.17
Diagnosis, Treatment, and Prevention

- **Diagnosis**
  - Characteristic muscular contraction
  - The bacteria is 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
Diagnosis, Treatment, and Prevention

- Prevention
  - Immunization with tetanus toxoid
Listeria

- Gram-positive non-spore-forming, coccobacillus
- Found in soil, water, mammals, birds, fish, and insects
- Enters body in contaminated food and drink
- *Listeria* produces no toxins or enzymes
- Virulence is directly related to the bacteria’s ability to live within cells
**Listeria**

Figure 19.18

(a) Diagram showing the process of endocytosis involving Listeria. The stages include:

1. **Endocytosis**
2. Listeria enters the cell
3. Originally infected cell (1)
4. Actin "tail"
5. Newly infected cell (2)
6. Endocytosis

(b) TEM image of Listeria in a cell. Labeled parts include:

- Listeria
- Pseudopod of cell 1
- Pseudopod of cell 2

Scale: 2 μm
Diagnosis

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

Treatment

- Most antimicrobial drugs inhibit *Listeria*

Prevention

- Difficult because the organism is ubiquitous
- At risk individuals should avoid undercooked vegetables, unpasteurized milk, undercooked meat, and all soft cheeses
A listeria outbreak linked to cantaloupes from Colorado has infected 72 people in the United States and killed 13, U.S. health officials said Tuesday.

The outbreak in melons is the deadliest in the United States since a 1998 multistage Listeria outbreak involving contaminated hotdogs and deli meats that killed 32 people and sickened 101.
**Corynebacterium**

- Ubiquitous on plants and in animals and humans
- Colonizes the skin and the respiratory, gastrointestinal, urinary, and genital tract
- *Corynebacterium diphtheriae*, the 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 inhibits polypeptide synthesis which results in cell death
- Infections are asymptomatic or produce mild respiratory disease in immune or partially immune individuals
Disease

- Severe respiratory infections of nonimmune patients produce the signs and symptoms of diphtheria
  - Pseudomembrane results from fluid that has thickened and adheres throughout the respiratory tract
  - 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
- Absolute identification is based on the Elek test
  - Antibodies against the toxin react with toxin in a sample of fluid from the patient

Treatment

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

Immunization with the DPT vaccine
Mycobacterium

- Cell wall contains a waxy lipid called mycolic acid
- 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 cause by *Mycobacterium tuberculosis*
- Cases are declining in the United States but it is pandemic in other parts of the world
- Virulent strains of *M. tuberculosis* contain the cell wall component, cord factor, that is necessary to cause disease
Tuberculosis (TB)

- Three types of tuberculosis
  - 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
Primary Tuberculosis

Figure 19.22a
Secondary Tuberculosis

(b) Secondary or reactivated tuberculosis

Figure 19.22b
Diagnosis, Treatment, and Prevention

- 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.
Leprosy

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

Leprosy

- Two different forms of disease
  - Tuberculoid leprosy
    - Nonprogressive disease that is characterized by loss of sensation in regions of the skin
  - Lepromatous leprosy
    - Produces gradual tissue destruction that results in the loss of facial features, digits, and other body structures


Leprosy is India's secret epidemic, says report

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

http://www.hrsa.gov/hansensdisease/dataandstatistics.html
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.
Miscellaneous Bacterial Pathogens

- Stain pink in a Gram stain but differ from typical Gram-negative organisms
- Have different morphology, growth habits, or reproductive strategies
- Traditionally discussed separately due to their unique features
Chlamydiae

- Do not have cell walls
  - Have two membranes but without any peptidoglycan between them
- Grow and multiply only within the vesicles of host cells
- Have a unique developmental cycle involving two forms
  - Both forms can occur within the phagosome of a host cell
Life Cycle of *Chlamydia*

1. EB attaches to receptor on host cell (0 hour)
2. EB enters host cell via endocytosis
3. EB converts into RB in food vesicle (10 hours)
4. RB divides rapidly resulting in multiple RBs in an inclusion body
5. Most RBs convert back into EBs (21 hours)
6. EBs are released from host cell (40 hours)

*Figure 21.8b*
Chlamydia trachomatis

- Has a limited host range
  - One strain infects mice, all others infect humans
- Infect the conjunctiva and various mucous membranes
- Enters the body through abrasions and lacerations
- Clinical manifestations result from the destruction of infected cells at the infection site and from the resulting inflammatory response
Chlamydia trachomatis

- Causes two main types of disease
  - Sexually transmitted diseases
    - Causes the most common sexually transmitted disease in the United States
  - Ocular disease called trachoma
    - Occurs particularly in children
    - Endemic in crowded, poor communities with poor hygiene, inadequate sanitation, and inferior medical care
Sexually Transmitted Diseases

- Lymphogranuloma veneruem
- Characterized by a transient genital lesion and swollen, painfully inflamed, inguinal lymph nodes
- Occurs in three stages
  - Initial stage
    - Produces a lesion at the infection site that is small, painless, and heals rapidly
  - Second stage
    - Buboes develop at the infection site
Sexually Transmitted Diseases

- Third stage
  - Only some cases progress to this stage
  - Characterized by genital sores, constriction of the urethra, and genital elephantiasis
- Most infections in women are asymptomatic but men often have symptoms
- Women can develop pelvic inflammatory disease if reinfected with *C. trachomatis*
Chlamydia trachomatis
Trachoma

- Disease of the eye
- Leading cause of nontraumatic blindness in humans
- Bacteria multiply in the conjunctival cells resulting in scarring
- The scarring causes the eyelashes to turn inwards and abrade the eye; may eventually result in blindness
- Typically a disease of children who have been infected during birth
- Infection of the eye with bacteria from the genitalia can also result in disease
Chlamydia trachomatis
Diagnosis, Treatment, and Prevention

- Diagnosis
  - Demonstration of the bacteria inside cells from the site of infection

- Treatment
  - Antibiotics can be administered for genital and ocular infections
  - Surgical correction of eyelid deformities from trachoma may prevent blindness
Diagnosis, Treatment, and Prevention

- Prevention
  - Abstinence and safe sex can prevent sexually transmitted chlamydial infection
  - Blindness can only be prevented by prompt treatment with antibacterial agents and preventing reinfections
Chlamydia pneumoniae

- Causes bronchitis, pneumonia, and sinusitis
- Most infections are mild and don’t require hospitalization
- Some more severe cases can resemble primary atypical pneumonia caused by Mycoplasma pneumoniae
- Prevention is difficult because C. pneumoniae is ubiquitous and spreads via respiratory droplets
Chlamydia psittaci

- Causes ornithosis, a disease of birds, that can be transmitted to humans
- Usually causes flulike symptoms
- Rarely nonrespiratory conditions are observed
- Individuals that handle animals are at greatest risk of infection
- Transmission occurs via inhalation of aerosols or through contact with infected material or a pet bird
- Diagnosis is difficult because symptoms are similar to those of many other respiratory infections
Spirochetes

- Thin, tightly coiled, helically shaped bacteria
- Moves in a corkscrew fashion through its environment
  - This movement is thought to enable pathogenic spirochetes to burrow through their hosts’ tissues
- Three genera cause human disease
  - *Treponema, Borrelia, and Leptospira*
Treponema pallidum pallidum

- Cannot survive in the environment
- Lives naturally only in humans as an obligate parasite
- Causative agent of syphilis
- Syphilis occurs worldwide
- Transmission is almost solely via sexual contact
- Endemic among sex workers, men who have sex with men, and users of illegal drugs
- Can also be spread from an infected mother to her fetus
  - Often results in the death of the fetus or in mental retardation and malformation
- Treponema pallidum pallidum

- Syphilis can proceed through four stages
  - Primary, secondary, latent, and tertiary syphilis
Chancre

Figure 21.15a
Rash

Figure 21.15b
Gumma

Figure 21.15c
Diagnosis, Treatment, and Prevention

- **Diagnosis**
  - Primary, secondary, and congenital can be readily diagnosed with antibody tests against bacterial antigens
  - Tertiary syphilis is difficult to diagnose

- **Treatment**
  - Penicillin is the drug of choice except with tertiary syphilis which is a hyperimmune response and not an active infection

- **Prevention**
  - Abstinence and safe sex are the primary ways to avoid contracting syphilis
Treponema species cause three nonvenereal diseases that occur primarily in impoverished children who live in unsanitary conditions

- **Bejel**
  - *T. pallidum endemicum* is the causative agent
  - Results in the formation of lesions around the lips and inside the mouth
  - The bacteria are spread by contaminated eating utensils
Nonvenereal Treponemal Diseases

- **Pinta**
  - *T. carateum* is the causative agent
  - Causes a skin disease that can result in scarring and disfigurement
  - Spread by skin-to-skin contact
- **Yaws**
  - *T. pallidum pertenue* is the causative agent
  - Characterized initially by skin lesions that can develop into large draining lesions
  - Spread via contact with the bacteria in the fluid draining from the lesions
*Treponema pallidum* Infection in the Wild Baboons of East Africa: Distribution and Genetic Characterization of the Strains Responsible

Figure 1. Gross pathology of olive baboons (*P. anubis*) with genital and circum-anal ulceration caused by *T. pallidum* at Lake Manyara National Park, Tanzania (2007).


[http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0050882](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0050882)
FIGURE 207e-1  Geographic distribution of endemic treponematoses.  
(Courtesy of the World Health Organization; updated from www.who.int/yaws/epidemiology/Map_yaws_90s.jpg.)  

http://clinicalgate.com/lyme-borreliosis-2/
Gram-Negative Bacteria

- Constitute the largest group of human bacterial 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 if evades 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 often arranged as diplococci
- Distinguished from many other Gram-negative pathogens by being oxidase positive
- Two species are pathogenic to humans
  - The gonococcus, *N. gonorrhoeae*
  - The meningococcus, *N. meningitides*
Neisseria gonorrhoeae

- Causes gonorrhea, a sexually transmitted disease
- Gonococci adhere to epithelial cells of the mucous membranes lining the genital, urinary, and digestive tracts of humans spreading to deeper tissue as they multiply
- Gonorrhea in men
  - Usually symptomatic producing inflammation that causes painful urination and pus-filled discharge
Neisseria gonorrhoeae

Figure 20.1
Neisseria gonorrhoeae

- 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 or blindness
Diagnosis

- Gonorrhea in men can be identified by the presence of Gram-negative diplococci in pus from an inflamed penis
- Asymptomatic cases can be identified with commercially available genetic probes

Treatment

- Complicated due to resistant gonococcal strains
- Broad-spectrum antimicrobial drugs are often used

Prevention

- Most effective prevention is sexual abstinence
Neisseria meningitidis

- Humans are the only natural carrier of *N. meningitides*
- Can be member of the 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 the bacteria among people living in close contact, especially students living in dormitories
Neisseria meningitidis

- Meningococcal meningitis can result in death as early as 6 hours after initial symptoms
- 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**
  - 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
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
Antigens and Virulence Factors

Antigens
- Outer membrane: (common antigen, O antigen, Lipid A)
- Type III secretion system
- Capsular antigens (K; Vi in Salmonella)
- Flagellar antigens (H)

Virulence Factors
- Pilus
- Exotoxin
- Adhesin
- Plasmid (virulence genes)
- Iron-binding protein
- Hemolysin

Nucleoid

Figure 20.8
Diagnosis

- Enterobacteriaceae are cultured using selective and differential media
- Commercially available biochemical tests can rapidly identify enteric bacteria

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

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.
Enterobacteriaceae Classification

- Pathogenic Enterobacteriaceae are often classified into three groups
  - Coliforms, which rapidly ferment lactose, are part of the normal microbiota, and may be opportunistic pathogens
  - Noncoliform opportunists, which do not ferment lactose
  - True pathogens
Coliform Opportunistic Enterobacteriaceae

- Aerobic or facultatively anaerobic, Gram-negative, rod-shaped bacteria that ferment lactose to form gas on lactose broth
- 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
Escherichia coli

- The most common and important of the coliforms
- Virulent strains have genes located on virulence plasmids that 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
Klebsiella

- Found in the digestive and respiratory systems of humans and animals
- Can cause opportunistic infections
- Produce a capsule that protect the bacteria from phagocytosis
- *K. pneumoniae* is the most commonly isolated pathogenic species
  - Causes pneumonia
  - May be involved in bacteremia, meningitis, wound infections, UTIs
Figure 20.10

Klebsiella pneumoniae

Capsules

LM

25 μm
Detection of the KPC Gene in *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* during a PCR-Based Nosocomial Surveillance Study in Puerto Rico

Iraida E. Robledo, Edna E. Aquino and Guillermo J. Vázquez*
Serratia

- Produce a red pigment when grown at room temperature
- Can grow on catheters, in saline solutions, and other hospital supplies
- Can cause life-threatening opportunistic infections in the urinary and respiratory tracts of immunocompromised patients
- Difficult to treat due to resistance to various antimicrobial drugs
Serratia marcescens

Figure 20.11
Enterobacter, Hafnia, and Citrobacter

- Found in soil, water, decaying vegetation, and sewage
- Reside in the digestive tracts of animals and humans
- All can be opportunistic pathogens
- Frequently involved in nosocomial infections of immunocompromised patients
- Difficult to treat due to resistance to various antimicrobial drugs
Noncoliform Opportunistic Enterobacteriaceae

- Include a number of opportunistic pathogens
- *Proteus*
  - Gram-negative, facultative anaerobe
  - *Proteus mirabilis* is the most common species associated with human disease
    - Can cause urinary tract infections in patients with long-term urinary catheters
    - Infection-induced kidney stones can develop
    - Resistant to many antimicrobial drugs
Noncoliform Opportunistic Enterobacteriaceae

- *Morganella, Providencia, and 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
- Most salmonella infections in humans are the result of consumption of food contaminated with animal feces
- Poultry and eggs are also common sources of *Salmonella*
- Two important pathogens
  - *S. typhimurium*-causes salmonellosis
  - *S. typhi*-causes typhoid fever
The Events of Salmonellosis

1. *Salmonella* attaches to epithelial cells lining small intestine
2. *Salmonella* triggers endocytosis
3. *Salmonella* multiplies within food vesicle
4. *Salmonella* kills host cell, inducing fever, cramps, and diarrhea
5. Bacteremia: *Salmonella* moves into bloodstream

*Figure 20.13*
Salmonella typhi

- Humans are the only host
- Causes typhoid fever
- Infection occurs via ingestion of food or water contaminated with sewage containing bacteria from carriers
- Bacteria can pass through the intestines into the bloodstream and into the liver, spleen, bone marrow, and gall bladder
- Bacteria from the gall bladder can reinfect the intestines, producing gastroenteritis and a recurrence of bacteremia
Salmonella typhi

- In some patients the bacteria ulcerate and perforate the intestinal wall causing peritonitis
- Treatment is through the replacement of fluids and electrolytes and the use of antimicrobial drugs
- Vaccines are available to provide temporary protection to individuals traveling to areas where typhoid fever is endemic
Shigella

- Gram-negative, nonmotile bacteria
- Primarily a parasite of the digestive tract of humans
- Produce a diarrhea-inducing enterotoxin
- Cause a severe form of dysentery called shigellosis
The Events of Shigellosis

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

Figure 20.15
Yersinia

- Normal pathogens of animals
- Three 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
**Yersinia pestis Life Cycle**

(a) Natural endemic reservoir hosts (rodents)

(b) Amplifying hosts (most mammals)

(c) Bubonic plague

(d) Pneumonic plague

- Direct contact
- Flea bite
- Airborne transmission

*Figure 20.16*
Diagnosis, Treatment, and Prevention

- 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*
Enterobacteriaceae: Sites of Infection

- **Central nervous system**
  - *Escherichia*

- **Lower respiratory tract**
  - *Klebsiella*
  - *Enterobacter*
  - *Escherichia*

- **Bloodstream**
  - *Escherichia*
  - *Klebsiella*
  - *Enterobacter*

- **Gastrointestinal tract**
  - *Salmonella*
  - *Shigella*
  - *Escherichia*
  - *Yersinia*

- **Urinary tract**
  - *Escherichia*
  - *Proteus*
  - *Klebsiella*
  - *Morganella*
Haemophilus

- Small, pleomorphic bacilli
- Obligate parasites due to their requirement of heme and NAD\(^+\) for growth
- Colonize the mucous membranes of humans and some animals
Haemophilus influenzae

- Most strains have a polysaccharide capsule that resists phagocytosis and is used in classification of the bacteria

- *H. influenzae* type b is the most significant
  - Was the most common form of meningitis in infants prior to the use of an effective vaccine
  - Can cause a number of other diseases in young children
  - Use of the Hib vaccine has eliminated much of the disease caused by *H. influenzae* b

- Other strains still cause a variety of diseases
Haemophilus influenzae

Pleomorphism

Figure 20.19
Other Species of *Haemophilus*

- **H. ducreyi**
  - Causes a sexually transmitted disease
  - Results in the formation of a genital ulcer called a chancroid
  - Often asymptomatic in women but in men the chancroid is often painful
- **H. aphrophilus** causes a rare type of endocarditis
- Other species primarily cause opportunistic infections
Bartonella

- Aerobic bacilli
- Found in animals but only cause disease in humans
- Three species are pathogenic
  - *Bartonella bacilliformis*
    - Bartonellosis
    - Transmitted by blood-sucking sand flies
Bartonella

- *Bartonella quintana*
  - Trench fever
  - Spread person to person by human body lice
  - Also causes disease in immunocompromised patients
- *Bartonella henselae*
  - Cat scratch fever
  - Introduced into humans through cat scratches or bites
Brucella

- Small, nonmotile, aerobic coccobacilli
- Can infect animals or humans
- Causes brucellosis
  - Often an asymptomatic or mild disease
  - Illness is characterized by a fluctuating fever
  - Humans become infected by coming in contact with contaminated dairy products or from infected animal parts
Bordetella

- Small, aerobic, nonmotile coccobacillus
- *B. pertussis* is the most important
  - Causes pertussis, also called whooping cough
  - Most cases of disease are in children
  - Produce various adhesins and toxins, including pertussis toxin, that mediate the disease
  - Bacteria are first inhaled in aerosols and multiply in epithelial cells
  - Then progress through four stages of disease
Progression of Pertussis

1. Incubation
   No symptoms

2. Catarrhal
   Rhinorrhea, sneezing, malaise, fever

3. Paroxysmal
   Repetitive cough with whoops, vomiting, exhaustion

4. Convalescent
   Diminishing cough, possible secondary complications

Time in weeks
Relative number of bacteria involved in interaction
Diagnosis, Treatment, and Prevention

- **Diagnosis**
  - Symptoms of pertussis are usually diagnostic

- **Treatment**
  - Primarily supportive
  - Antibacterial drugs have little effect on the course of the disease

- **Prevention**
  - Immunization with the DPT vaccine
  - Cases in the United States have increased due to a refusal by some parents to have their children immunized
Diagnosis, Treatment, and Prevention

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  - Symptoms of pertussis are usually diagnostic

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Pseudomonads

- Gram-negative, aerobic bacilli
- Ubiquitous in soil, decaying organic matter, and almost every moist environment
- Problematic in hospitals because they can be found in numerous locations
- Opportunistic pathogens
Pseudomonas aeruginosa

- Rarely part of the normal microbiota
- Opportunistic pathogen of immunocompromised patients
- Can colonize almost every organ and system and result in various diseases
- Often infects the lungs of cystic fibrosis patients
  - The bacteria form a biofilm that protects them from phagocytosis
  - Increases the likelihood of death in these patients
Diagnosis can be difficult as the presence of bacteria may represent contamination of the sample.

Treatment is difficult because *P. aeruginosa* is resistant to many antibacterial drugs.
Pathogenic, Gram-Negative, Anaerobic Bacilli

- Anaerobic bacteria are the predominant microbiota of the gastrointestinal, urinary, reproductive, and lower respiratory tracts

- Important for human health
  - Inhibit the growth of most pathogens, synthesize vitamins and vitamin precursors, and aid in digestion of food

- Cause disease only when they are introduced into other parts of the body by trauma or surgery
Bacteroides

- Normal microbiota of the intestinal tract and the upper respiratory tract
- *Bacteroides fragilis* is the most important
- Can be involved in abdominal infections, genital infections in women, and wound infections of the skin
- Metronidazole is used for infections
Vibrio

- Members of this genus share many characteristics with enteric bacteria such as *Escherichia* and *Salmonella*
- Found in water environments worldwide
- *Vibrio cholerae* is the most common species to infect humans
  - Causes cholera
  - Humans become infected with *V. cholerae* by ingesting contaminated food and water
  - Found most often in communities with poor sewage and water treatment
Vibrio

- A large inoculum is required to cause disease because the bacteria are susceptible to the acidic stomach environment
- Cholera toxin is the most important virulence factor of *V. cholerae*
Action of Cholera Toxin

1. Cholera toxin binds to membrane of epithelial cell
2. Portion of toxin (part of A) enters cell
3. A1 stimulates adenylate cyclase (AC)
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 21.25
Cholera Pathology

- Some infections are asymptomatic or cause mild diarrhea
- Can cause severe disease resulting in abrupt watery diarrhea and vomiting
  - “Rice-water stool” is characteristic
  - Results in severe fluid and electrolyte loss
  - Can progress to coma and death
Health officials have said there are signs that the cholera outbreak in central Haiti may be stabilising. More than 250 people have died and more than 3,000 have been infected, but the rate of increase has slowed. The UN and aid agencies are aiming to educate Haitians about how to prevent the spread of cholera, as well as setting up dedicated treatment centres. The disease is seen as a serious threat to 1.3 million earthquake survivors living in tent camps near the capital.
The death toll in Haiti's cholera epidemic has risen to 303, the World Health Organisation has said as the number of cases creeps towards the 5000 mark. "As of 27 October, the Ministry of Health in Haiti reported 4722 cholera cases including 303 deaths," the WHO said in an update on the cholera epidemic.

The data included 11 new deaths and 575 more infections since figures given by Haiti's health department on Wednesday. The WHO said four departments (administrative areas) had reported confirmed cases, with the overwhelming majority (99.4 percent) in the Artibonite and Central Plateau.

It warned on Wednesday that the outbreak was far from over and Haiti should prepare for the disease to hit its capital Port-au-Prince, which is teeming with tent cities after January's catastrophic earthquake.

The acute intestinal bacteria is is thought to have infected the Artibonite River, a major waterway that runs through Haiti to the coast near Saint Marc - the outbreak's epicentre, located some 100 kilometres north of Port-au-Prince.

- AFP
Diagnosis, Treatment, and Prevention

- Diagnosis
  - Usually based on the characteristic diarrhea

- Treatment
  - Fluid and electrolyte replacement
  - Antimicrobial drugs are not as important because they are lost in the watery stool

- Prevention
  - Adequate sewage and water treatment can limit the spread of *V. cholerae*
Other Diseases of *Vibrio*

- **Vibrio parahaemolyticus**
  - Results from ingestion of shellfish
  - Causes cholera-like gastroenteritis

- **Vibrio vulnificus**
  - Causes septicemia following consumption of contaminated shellfish
  - Infections can result from washing wounds with contaminated seawater
Helicobacter pylori

- Slightly helical, highly motile bacterium that colonizes the stomach of its hosts
- Causes gastritis and most (if not all) peptic ulcers
- *H. pylori* produces numerous virulence factors that enable it to colonize the stomach
1 Bacteria invade mucus and attach to gastric epithelial cells.
H. pylori and Peptic Ulcers

2 Helicobacter, its toxins, and inflammation, cause the layer of mucus to become thin.

Figure 21.27.2
H. pylori and Peptic Ulcers

Gastric acid destroys epithelial cells and underlying tissue.
Diagnosis, Treatment, and Prevention

- **Diagnosis**
  - Presence of *H. pylori* can be demonstrated by a positive urease test
  - Biochemical tests provide a definitive identification

- **Treatment**
  - Antimicrobial drugs are used in combination with drugs that inhibit acid production

- **Prevention**
  - Prevention involves good hygiene, adequate sewage treatment, water purification, and proper food handling