Chapter 19
The **Gram-Positive Bacilli of Medical Importance**
Can be subdivided into three general groups, based on presence or absence of endospores and acid-fastness.

Three general groups:
1. Endospore-formers
2. Non-endospore-formers
3. Irregular shaped and staining properties
Gram-Positive Bacilli

**TABLE 19.1 Scheme for Differentiating Gram-Positive Bacilli**

- **Gram-positive rods**
  - Sporeformers
    - Aerobic or facultative anaerobes
      - *Bacillus*
    - Obligate anaerobes
      - *Clostridium*
  - Non-sporeformers
    - Regular shape and staining properties
      - *Listeria, Erysipelothrix*
    - Irregular shape and staining properties
      - Non-acid-fast
        - *Corynebacterium Propionibacterium*
      - Acid-fast
        - *Mycobacterium*
      - Filamentous, branching cells
        - *Actinomyces, Nocardia*
19.2 Gram-Positive Spore-Forming Bacilli

Genus Bacillus

a. Bacillus anthracis

Genus Clostridium

b. Clostridium perfringens

Genus Sporolactobacillus

c. C. tetani
General Characteristics of the Genus *Bacillus*

- Gram-positive, endospore-forming, motile rods
- Mostly saprobic – decompose material
- Aerobic and catalase positive
- Versatile in degrading complex macromolecules
- Source of antibiotics
- Primary habitat is soil
- 2 species of medical importance:
  - *Bacillus anthracis*
  - *Bacillus cereus*
**Bacillus anthracis and Anthrax**

- Large, block-shaped rods
- Central spores that develop under all conditions except in the living body
- Virulence factors – polypeptide capsule and exotoxins
Bacillus anthracis

• 3 types of anthrax:
  – **Cutaneous**: spores enter through skin, black sore- eschar; least dangerous
  – **Pulmonary**: inhalation of spores, can cause rapid death if untreated
  – **Gastrointestinal**: ingested spores

Figure 19.2 Cutaneous anthrax

a. Early stage
b. Later stage
Control and Treatment

• Treated with penicillin, tetracycline, or ciprofloxacin

• Vaccines
  – Live spores from a special strain and toxoid to protect livestock
  – Purified toxoid; for high risk occupations and military personnel; toxoid 6 inoculations over 1.5 years; annual boosters
**Bacillus cereus** – Other *Bacillus* species

- Common airborne and dustborne; usual methods of disinfection and antisepsis are ineffective
- Grows in foods, spores survive cooking and reheating
- Ingestion of toxin-containing food causes nausea, vomiting, abdominal cramps, and diarrhea; 24-hour duration
- No treatment
- Increasingly reported in immunosuppressed
The Genus *Clostridium*

- Gram-positive, spore-forming rods
- Anaerobic and catalase negative
- 120 species
- Oval or spherical spores produced only under anaerobic conditions
- Synthesize organic acids, alcohols, useful in biotech; and exotoxins
- Cause wound infections, tissue infections, and food intoxications
Gas Gangrene / Myonecrosis

- **Clostridium perfringens** most frequent clostridia involved in soft tissue and wound infections – **myonecrosis**
- Spores found in soil, human skin, intestine, and vagina
- Predisposing factors – surgical incisions, compound fractures, diabetic ulcers, septic abortions, puncture wounds, gunshot wounds (anaerobic environment)

![Image of Spore and Vegetative cell](Image)

Figure 19.1 b.
Virulence Factors – *Clostridium*

- Virulence factors
  - Toxins
    - **Alpha toxin** – causes RBC rupture, edema, and tissue destruction
  - Collagenase
  - Hyaluronidase
  - DNase

Figure 19.3 *C. perfringens* causing gas gangrene
Pathology – *Clostridium*

- Not highly invasive; requires damaged and dead tissue and anaerobic conditions
- Conditions stimulate spore germination, vegetative growth and release of exotoxins, and other virulence factors
- Fermentation of muscle carbohydrates results in the formation of gas and further tissue destruction

Figure 19.4 myonecrosis
Treatment and Prevention of gas gangrene

- Immediate cleansing of dirty wounds, deep wounds, compound fractures, and infected incisions
- Debridement of disease tissue
- Large doses of cephalosporin or penicillin
- Hyperbaric oxygen therapy
- No vaccines available

Figure 19.5 treatment for wound infection

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Tetanus, or Lockjaw

• *Clostridium tetani*

• Common resident of soil and GI tracts of animals

• Causes tetanus or lockjaw, a neuromuscular disease

• Most commonly among geriatric patients and IV drug abusers; neonates in developing countries
The Course of Infection and Disease

- Spores usually enter through accidental puncture wounds, burns, umbilical stumps, frostbite, and crushed body parts
- Anaerobic environment is required for vegetative cells to grow and release toxin

Figure 19.6 a. The events in tetanus – bacilli infecting local tissue secrete tetanospasmin, toxins are carried to the spinal column
The Course of Infection and Disease

- **Tetanospasmin** – neurotoxin causes paralysis by binding to motor nerve endings; blocking the release of neurotransmitter for muscular contraction inhibition; muscles contract uncontrollably
- Death most often due to paralysis of respiratory muscles

![Figure 19.6 The events in tetanus – the toxin causes the muscles to contract uncontrollably](image)
Figure 19.7 Neonatal tetanus

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Courtesy of Dr. T.F. Sellers
Treatment and Prevention of Tetanus

- Treatment aimed at deterring degree of toxemia and infection and maintaining homeostasis

- Antitoxin therapy with human tetanus immune globulin; inactivates circulating toxin but does not counteract that which is already bound

- Control infection with penicillin or tetracycline; and muscle relaxants

- Vaccine available; booster needed every 10 years
Clostridium difficile-Associated Disease (CDAD)

- Normal resident of colon, in low numbers
- Causes **antibiotic-associated colitis**
  - Relatively non-invasive; treatment with broad-spectrum antibiotics kills the other bacteria, allowing *C. difficile* to overgrow
- Produces enterotoxins that damage intestines
- Major cause of diarrhea in hospitals
- Increasingly common in community-acquired diarrhea
Figure 19.8 Antibiotic-associated colitis

- Mild uncomplicated cases respond to fluid and electrolyte replacement and withdrawal of antimicrobials
- Severe infections treated with oral vancomycin or metronidazole and replacement cultures
- Increased precautions to prevent spread, spores in stool
**Clostridial Food Poisoning**

- *Clostridium botulinum* – rare but severe intoxication usually from home canned food

- *Clostridium perfringens* – mild intestinal illness; second most common form of food poisoning worldwide
Botulinum Food Poisoning

- **Botulism** – intoxication associated with inadequate food preservation, home preparations

- **Clostridium botulinum** – spore-forming anaerobe; commonly inhabits soil and water
Pathogenesis of Botulism

• Spores are present on food when gathered and processed

• If reliable temperature and pressure are not achieved air will be evacuated but spores will remain

• Anaerobic conditions favor spore germination and vegetative growth

• Potent toxin, botulin, is released
Pathogenesis of Botulism

- **Botulin toxin** is carried to neuromuscular junctions and blocks the release of acetylcholine, necessary for muscle contraction to occur.

- Double or blurred vision, difficulty swallowing, neuromuscular symptoms

Figure 19.9 the pathophysiological effects of botulin
Infant and Wound Botulism

- **Infant botulism** – caused by ingested spores that germinate and release toxin; flaccid paralysis; contracted by home made baby food, raw honey

- **Wound botulism** – spores enter wound and cause food poisoning symptoms, seen most often in IV drug users
Treatment and Prevention of Botulism

- Determine presence of toxin in food, intestinal contents or feces
- Administer antitoxin; cardiac and respiratory support
- Infectious botulism treated with penicillin
- Practice proper methods of preserving and handling canned foods; addition of preservatives
Clostridial Gastroenteritis

- *Clostrium perfringens*

- Spores contaminate food that has not been cooked thoroughly enough to destroy spores.

- Spores germinate and multiply (especially if unrefrigerated).

- When consumed, toxin is produced in the intestine; acts on epithelial cells, acute abdominal pain, diarrhea, and nausea.

- Rapid recovery.
# Spore-Forming Pathogens

<table>
<thead>
<tr>
<th>Species</th>
<th>Oxygen Requirements</th>
<th>Motility</th>
<th>Disease in Humans</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bacillus anthracis</em></td>
<td>Aerobe</td>
<td>−</td>
<td>Cutaneous anthrax, Pulmonary anthrax, Gastrointestinal anthrax</td>
<td>Antibiotics, Vaccines for high risk, Antibiotics</td>
</tr>
<tr>
<td><em>Bacillus cereus</em></td>
<td>Facultative anaerobe</td>
<td>+</td>
<td>Food poisoning</td>
<td>None; disease self-limiting</td>
</tr>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>Strict anaerobe</td>
<td>−</td>
<td>Gas gangrene, Food poisoning (mild)</td>
<td>Debridement; antibiotics; oxygen therapy, None; disease self-limiting</td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
<td>Strict anaerobe</td>
<td>+/−</td>
<td>Antibiotic-associated colitis</td>
<td>Withdrawal of antibiotics; administration of probiotics</td>
</tr>
<tr>
<td><em>Clostridium tetani</em></td>
<td>Strict anaerobe</td>
<td>+</td>
<td>Tetanus</td>
<td>Vaccination; passive immunization</td>
</tr>
<tr>
<td><em>Clostridium botulinum</em></td>
<td>Strict anaerobe</td>
<td>+/−</td>
<td>Botulism</td>
<td>Antitoxin</td>
</tr>
</tbody>
</table>
19.3 Gram-Positive Regular Non-Spore-Forming Bacilli

Regular: stain uniformly and do not assume pleomorphic shapes

Medically important:

- *Listeria monocytogenes*
- *Erysipelothrix rhusiopathiae*
An Emerging Food-Borne Pathogen: *Listeria monocytogenes*

- Non-spore-forming gram-positive
- Ranging from coccobacilli to long filaments
- 1-4 flagella and lack capsules
- Resistant to cold, heat, salt, pH extremes, and bile
- Virulence attributed to ability to replicate in the cytoplasm of cells after inducing phagocytosis; avoids humoral immune system

Figure 19.10
Multiplication cycle of *Listeria monocytogenes*
Epidemiology and Pathology of Listeriosis

- Primary reservoir is soil and water; animal intestines
- Can contaminate foods and grow during refrigeration
- **Listeriosis** – most cases associated with dairy products, poultry, and meat
- Often mild or subclinical in normal adults
- Immunocompromised patients, fetuses, and neonates; affects brain and meninges
  - 20% death rate
Diagnosis and Control and of Listeriosis

• Culture requires lengthy cold enrichment process – 4 weeks

• Rapid diagnostic tests using ELISA, immunofluorescence, and DNA analysis

• Ampicillin and trimethoprim/ sulfamethoxazole

• Prevention – pasteurization and cooking
Erysipelothrix rhusiopathiae: A Zoonotic Pathogen

- Gram-positive rod widely distributed in animals and the environment
- Primary reservoir – tonsils of healthy pigs
- Enters through skin abrasion, multiplies to produce erysipeloid, dark red lesions
- Penicillin or erythromycin and vaccine for pigs

Figure 19.11 Erysipeloid on the hand of an animal handler
19.4 Gram-Positive Irregular Non-Spore-Forming Bacilli

Irregular: pleomorphic, stain unevenly

Medically important genera:

- *Corynebacterium*
- *Propionibacterium*
- *Mycobacterium*
- *Actinomyces*
- *Nocardia*
Corynebacterium diptheriae

- Gram-positive irregular bacilli

Figure 19.12 C. diptheriae

Pleomorphism  Palisades arrangement  Granules

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Epidemiology of Diphtheria

• Reservoir of healthy carriers; potential for diphtheria is always present

• Most cases occur in non-immunized children living in crowded, unsanitary conditions

• Acquired via respiratory droplets from carriers or actively infected individuals
Pathology of Diphtheria

2 stages of disease:

1. Local infection – upper respiratory tract inflammation
   – Sore throat, nausea, vomiting, swollen lymph nodes;
     **pseudomembrane** formation can cause asphyxiation

2. Diptherotoxin production and toxemia
   – Target organs: primarily heart and nerves
Diagnostic Methods for Corynebacterium

- Pseudomembrane and swelling indicative
- Stains – pleomorphic, granulated cells
- Conditions, history – living conditions, travel
- Serological assay to detect antibodies
Treatment and Prevention of Diphtheria

- Antitoxin to diphtheria toxin
- Penicillin or erythromycin
- Prevented by toxoid vaccine series and boosters
The Genus *Propionibacterium*

- *Propionibacterium acnes* most common
- Gram-positive rods
- Aerotolerant or anaerobic
- Nontoxigenic
- Common resident of pilosebaceous glands
- Causes acne
19.5 Mycobacteria: Acid-Fast Bacilli

- Gram-positive irregular bacilli
- Acid-fast staining
- Strict aerobes
- Produce catalase
- Possess mycolic acids and a unique type of peptidoglycan
- Do not form capsules, flagella, or spores
- Grow slowly

Figure 19.14 Microscopic morphology of mycobacteria

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# Mycobacterium Species

**TABLE 19.3 Differentiation of Important *Mycobacterium* Species**

<table>
<thead>
<tr>
<th>Species</th>
<th>Primary Habitat</th>
<th>Disease in Humans</th>
<th>Treatment</th>
<th>Rate of Growth*</th>
<th>Pigmentation**</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. tuberculosis</em></td>
<td>Humans</td>
<td>Tuberculosis (TB)</td>
<td>Combined drugs</td>
<td>S</td>
<td>NP</td>
</tr>
<tr>
<td><em>M. bovis</em></td>
<td>Cattle</td>
<td>Tuberculosis</td>
<td>Same as TB</td>
<td>S</td>
<td>NP</td>
</tr>
<tr>
<td><em>M. ulcerans</em></td>
<td>Humans</td>
<td>Skin ulcers</td>
<td>Surgery, grafts</td>
<td>S</td>
<td>NP</td>
</tr>
<tr>
<td><em>M. kansasii</em></td>
<td>Not clear</td>
<td>Opportunistic lung infection</td>
<td>Difficult, similar to TB</td>
<td>S</td>
<td>PP</td>
</tr>
<tr>
<td><em>M. marinum</em></td>
<td>Water, fish</td>
<td>Swimming pool granuloma</td>
<td>Tetracycline, rifampin</td>
<td>S</td>
<td>PP</td>
</tr>
<tr>
<td><em>M. scrofulaceum</em></td>
<td>Soil, water</td>
<td>Scrofula</td>
<td>Removal of lymph nodes</td>
<td>S</td>
<td>PS</td>
</tr>
<tr>
<td><em>M. avium—M. intracellulare complex</em></td>
<td>Birds</td>
<td>Opportunistic AIDS infection; lung infection like TB</td>
<td>Combined drugs</td>
<td>S</td>
<td>NP</td>
</tr>
<tr>
<td><em>M. fortuitum—M. chelonea complex</em></td>
<td>Soil, water, animals</td>
<td>Wound abscess; postsurgical infection</td>
<td>4–6-drug regimen; surgery</td>
<td>R</td>
<td>NP</td>
</tr>
<tr>
<td><em>M. phlei</em></td>
<td>Sputum, soil</td>
<td>Not pathogenic</td>
<td>None</td>
<td>R</td>
<td>PS</td>
</tr>
<tr>
<td><em>M. smegmatis</em></td>
<td>Smegma, soil</td>
<td>Not pathogenic</td>
<td>None</td>
<td>R</td>
<td>Usually NP</td>
</tr>
<tr>
<td><em>M. leprae</em></td>
<td>Strict parasite of humans</td>
<td>Leprosy</td>
<td>See text</td>
<td>S</td>
<td>Cannot be grown in artificial media</td>
</tr>
</tbody>
</table>
Mycobacterium tuberculosis: The Tubercle Bacillus

• **Tubercle bacillus**

• Produces no exotoxins or enzymes that contribute to infectiousness

• **Virulence factors** – contain complex waxes and cord factor that prevent destruction by lysosomes or macrophages

Figure 19.15 Diagnosing tuberculosis

From Gillies and Dodds, Bacteriology Illustrated, 5th ed., fig. 45, p. 58. Reprinted by permission of Churchill Livingstone
Epidemiology and Transmission of Tuberculosis

- Predisposing factors include: inadequate nutrition, debilitation of the immune system, poor access to medical care, lung damage, and genetics

- Estimate 1/3rd of world population and 15 million in U.S. carry tubercle bacillus; highest rate in U.S. occurring in recent immigrants

- Bacillus very resistant; transmitted by airborne respiratory droplets
The Course of Infection and Disease

• 5% to 10% of infected people develop clinical disease

• Untreated, the disease progresses slowly; majority of TB cases contained in lungs

• Clinical tuberculosis divided into:
  – Primary tuberculosis
  – Secondary tuberculosis (reactivation or reinfection)
  – Disseminated (extrapulmonary) tuberculosis
Primary TB

- Infectious dose 10 cells
- Phagocytosed by alveolar macrophages and multiply intracellularly
- After 3-4 weeks immune system attacks, forming tubercles, granulomas consisting of a central core containing bacilli surrounded by WBCs – **tubercle**
- If center of tubercle breaks down into necrotic **caseous** lesions, they gradually heal by calcification

Figure 19.16 b. section of a tubercle
Secondary TB

- If patient doesn’t recover from primary tuberculosis, reactivation of bacilli can occur
- Tubercles expand and drain into the bronchial tubes and upper respiratory tract
- Gradually the patient experiences more severe symptoms
  - Violent coughing, greenish or bloody sputum, fever, anorexia, weight loss, fatigue
- Untreated, 60% mortality rate

Figure 19.16 stages of tuberculosis infection

1. Exposure to TB droplets
2. Inhaled into lungs
   - No infection in 10220% of cases
   - Inhale into lungs
   - Lung macrophages engulf bacilli, infection occurs in 80–90% of cases; TB test +
   - Infection cleared by immune system in 90–95% of cases; TB test –
   - Primary TB disease with tubercles, symptoms occur in 5–10% of cases within 2 years; TB test +
   - Latency; bacilli go dormant in lungs; carrier state without symptoms may last for many years; TB test +
   - Recurrent disease; tubercles break down; bacilli are released into lung cavities and circulation; TB test +
   - Infection and disease can clear with long-term treatment; TB test + or –
   - Disease spreads to extrapulmonary sites such as kidney, bones, brain with severe morbidity; TB test +

(a) Infection □ Disease □ Infection free
Extrapulmonary TB

- During secondary TB, bacilli disseminate to regional lymph nodes, kidneys, long bones, genital tract, brain, and meninges.

- These complications are grave.

Figure 19.16 Stages of tuberculosis infection
1. *In vivo* or tuberculin testing

**Mantoux test** – local intradermal injection of purified protein derivative (PPD); look for red wheal to form in 48-72 hours – *induration*; established guidelines to indicate interpretation of result based on size of wheal and specific population factors.
Figure 19.18 X-ray of a secondary tubercular infection

1. *In vivo* or tuberculin testing
2. X-rays

3. Direct identification of acid-fast bacilli in specimen
4. Cultural isolation and biochemical testing
Management and Prevention of TB

• 6-24 months of at least 2 drugs from a list of 11

• One pill regimen called *Rifater* (isoniazid, rifampin, pyrazinamide)

• Vaccine based on attenuated bacilli Calmet-Guerin strain of *M. bovis* used in other countries
Mycobacterium leprae: The Leprosy Bacillus

- **Hansen’s bacillus/Hansen’s Disease**
- **Strict parasite** – has not been grown on artificial media or tissue culture
- **Slowest growing of all species**
- **Multiplies within host cells in large packets called globi**
- **Causes leprosy**, a chronic disease that begins in the skin and mucous membranes and progresses into nerves
Epidemiology and Transmission of Leprosy

- Endemic regions throughout the world
- Mechanism of transmission is not fully verified
- Not highly virulent; appears that health and living conditions influence susceptibility and the course of the disease
- May be associated with specific genetic marker
The Course of Infection and Disease

- Macrophages phagocytize the bacilli, but a weakened macrophage or slow T cell response may not kill bacillus

- Incubation from 2-5 years; if untreated, bacilli grow slowly in the skin macrophages and Schwann cells of peripheral nerves

- 2 forms possible:
  1. Tuberculoid
  2. Lepromatous
Course of Infection and Disease

• 2 forms possible:
  1. **Tuberculoid**: asymmetrical, shallow lesions, damage nerves – results in local loss of pain reception.

Figure 19.20 leprosy lesions

(a) Dark skinned people

(b) Light skinned people
The Course of Infection and Disease

• 2 forms possible:

  2. **Lepromatous** – a deeply nodular infection that causes severe disfigurement of the face and extremities, widespread dissemination

Figure 19.21 a clinical picture of lepromatous leprosy

Figure 19.22 Deformation of hands
Diagnosing Leprosy

- Combination of symptomology, microscopic examination of lesions, and patient history
- Numbness in hands and feet, loss of heat and cold sensitivity, muscle weakness, thickened earlobes, chronic stuffy nose
- Detection of acid-fast bacilli in skin lesions, nasal discharges, and tissue samples
Treatment and Prevention of Leprosy

- Treatment by long-term combined therapy
- Prevention requires constant surveillance of high-risk populations
- WHO sponsoring a trial vaccine
Infections by Non-Tuberculosis Mycobacteria (NTM)

- *M. avium* complex – third most common cause of death in AIDS patients
- *M. kansaii* – pulmonary infections in adult white males with emphysema or bronchitis
- *M. marinum* – water inhabitant; lesions develop after scraping on swimming pool concrete
- *M. scrofulaceum* – infects cervical lymph nodes
- *M. paratuberculosis* – raw cow’s milk; recovered from 65% of individuals diagnosed with Crohn’s disease
Figure 19.23 Chronic Swimming Pool Granuloma
19.6 Actinomycetes: Filamentous Bacilli

- Genera *Actinomyces* & *Nocardia* are nonmotile filamentous bacteria related to mycobacteria that may cause a chronic infection of skin and soft tissues.

- *Actinomyces israelii* responsible for diseases of the oral cavity, thoracic or intestines – *actinomycoses*

- *Nocardia brasiliensis* causes pulmonary disease similar to TB.