Bacterial infection

SCBM 341 General Pathology

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Bacteria

- Bacteria cells are prokaryotes
- There are two forms of cell wall structures
  - **Thick wall** → retains crystal-violet stain (Gram-positive bacteria)
  - **Thin wall** → Gram-negative bacteria
# Bacteria

## Microscopic Appearance of Cell

<table>
<thead>
<tr>
<th>Step</th>
<th>Gram (+)</th>
<th>Gram (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Crystal violet (primary dye)</td>
<td>![Image of Gram (+) cell]</td>
<td>![Image of Gram (-) cell]</td>
</tr>
<tr>
<td>2. Gram’s iodine (mordant)</td>
<td>![Image of Gram (+) cell with dye crystals]</td>
<td>![Image of Gram (-) cell with no dye]</td>
</tr>
<tr>
<td>3. Alcohol (decolorizer)</td>
<td>![Image of Gram (+) cell with dye crystals remaining]</td>
<td>![Image of Gram (-) cell with outer membrane weakened]</td>
</tr>
<tr>
<td>4. Safranin (red dye counterstain)</td>
<td>![Image of Gram (+) cell with dye]</td>
<td>![Image of Gram (-) cell with dye not stained]</td>
</tr>
</tbody>
</table>

## Chemical Reaction in Cell Wall (very magnified view)

<table>
<thead>
<tr>
<th>Gram (+)</th>
<th>Gram (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both cell walls stain with the dye</td>
<td>![Image of Gram (-) cell with no effect]</td>
</tr>
<tr>
<td>Dye crystals trapped in cell</td>
<td>![Image of Gram (-) cell with no effect]</td>
</tr>
<tr>
<td>Crystals remain in cell</td>
<td>![Image of Gram (-) cell with dye not stained]</td>
</tr>
<tr>
<td>Outer membrane weakened; cell loses dye</td>
<td>![Image of Gram (-) cell with dye not stained]</td>
</tr>
<tr>
<td>Red dye has no effect</td>
<td>![Image of Gram (-) cell with dye not stained]</td>
</tr>
</tbody>
</table>
Bacteria

- Bacteria are classified by:
  - **Gram staining** (positive or negative)
  - **Shape** (e.g., cocci, rod-shaped, bacilli)
  - **Form of respiration** (aerobic, anaerobic)
  - **Their survive and replication**
    - Facultative intracellular bacteria $\rightarrow$ both
    - Obligate intracellular bacteria $\rightarrow$ grow only inside host cells
Bacteria

- **Gram-positive cocci in cluster**
- **Gram-positive cocci in pairs**
- **Gram-positive and Gram-negative rods**
- **Gram-negative intracellular rods**
- **Gram-negative diplococci**
- **Helical spirochetes**
Mechanism of bacterial injury

- Bacterial virulence
- Bacterial adherence to host cells
- Virulence of intracellular bacteria
- Bacterial toxin
  - Endotoxin (lipopolysaccharide)
  - Exotoxins
    - Enzymes (proteases, hyaluronidases, coagulases, fibrinolysin)
    - Toxin (alter intracellular signaling or regulatory pathway)
    - Neurotoxins (*Clostridium botulinum* and *Clostridium tetani*)
    - Superantigens (stimulate large number of T cells → toxic shock syndrome)
Pathology from bacterial infection

- **Suppurative (Purulent) Inflammation**
  - characterized by increased vascular permeability and leukocytic infiltration, predominantly of **neutrophils**
  - mostly extracellular **gram-positive cocci** and **gram-negative rods**

- **Granulomatous Inflammation**
  - intracellular bacteria (resist eradication)
  - *M. tuberculosis*
Pathology from bacterial infection

- **Gangrenous necrosis**
  - *Clostridium perfringens* and other organisms that secrete powerful toxins can cause such rapid and severe necrosis
  - Dry gangrene = infarction
  - Wet gangrene = infarction + bacterial infection

![Dry gangrene](image1.jpg) ![Wet gangrene](image2.jpg)
Gram-Positive Bacterial infection
Gram-Positive Bacterial infections

- Staphylococcal infections
- Streptococcal infections
- Diphtheria
- Anthrax
Staphylococcal infection

**Staphylococcus aureus**
- + cocci that form grapelike clusters
- cause a myriad of skin lesions (boils, carbuncles, impetigo and scalded skin)

**Staphylococcus epidermidis**
- causes opportunistic infections in catheterized patients, patients with prosthetic cardiac valves

**Staphylococcus saprophyticus**
- common cause of urinary tract infections
Pathogenesis of Staphylococcal infection

**Lipase**
- degrades lipids on the skin surface

**Hemolytic toxin**
- α-toxin, pore forming protein

The pore-forming mechanism for the *S. aureus*
Pathogenesis of Staphylococcal infection

Exfoliative toxin
epidermis split away from deeper skin

Superantigens
food poisoning, toxic shock syndrome
S. aureus causes pyogenic inflammation

- Impetigo, which is streptococcal infection restricted to the superficial epidermis
- Boil
- Carbuncle
- Paronychia
- Staphylococcal scalded skin syndrome (Ritter disease)
Pathology

Impetigo

Boil

Carbuncle

Paronychia

Staphylococcal scalded skin syndrome (SSSS)
Facultative or obligate anaerobic Gram-positive cocci in pairs or chains

- *Streptococcus pyogenes* (group A) causes pharyngitis
- *Streptococcus agalactiae* (group B) causes sepsis and meningitis in neonates
- *Streptococcus pneumoniae* causes community-acquired pneumonia
Pathology of Streptococcal infections

- Resemble with staphylococci
- **Erysipelas** is erythematous cutaneous swelling like “butterfly” (caused by exotoxins from *S. pyogenes*)
- Streptococcal pharyngitis
- Scarlet fever
Diphtheria

- Result from blocking the airway and create a barking cough as in croup
  - *Corynebacterium diphtheriae*
- Aerosols or skin shedding
- Pseudomembrane in the posterior pharynx
Anthrax

- **Bacillus anthracis**
- Potent biologic weapon
- Pathology
  - **Cutaneous anthrax**, vesicle with black eschar
  - **Inhalation anthrax**, shock and death
  - **Gastrointestinal anthrax**, severe bloody diarrhea

Spore-forming Gram-positive rod-shaped bacterium

eschar
Gram-Negative Bacterial infection
Gram-Negative Bacterial infections

- Neisseria infections
- Pseudomonas infection
- Chancroid
Neisserial infection

Gram-negative diplococci, shape of coffee bean

**Neisseria meningitidis**
- Cause of *meningitis* in young people
- Invade respiratory epithelial cells → enter the blood

**Neisseria gonorrhoeae**
- Important cause of *sexually transmitted disease*
- Men → *urethritis*
- Woman → asymptomatic → pelvic inflammatory disease → infertility, neonatal *N. gonorrhoeae*
  *N. gonorrhoeae* infection causes *blindness*
Pseudomonas infection

- *Pseudomonas aeruginosa*
- Opportunistic aerobic Gram-negative bacillus
- Deadly pathogen of patient with severe burns
- Complex bacteria, very resistant to antibiotics
- Hospital-acquired infections
- Corneal keratitis in wearers of contact lenses
Pseudomonas aeruginosa: Corneal keratitis

Common in immunocompromised patients, contact lens wearers with faulty hygiene.

Typical Gram-negative corneal ulcer: Rapid evolution, marked tendency to spread.

Can perforate in 48 hours.

Treatment: Topical tobramycin, ciprofloxacin, moxifloxacin, gatifloxacin
Pseudomonas infection

• Pathogenesis
  • **Alginate**, which is mucoid exopolysaccharide → protected from host antibodies, complement, phagocytes and antibiotic
  • **Exotoxin** that inhibits protein synthesis
  • **Elastase** degrades IgGs and extracellular matrix proteins (keratitis)
Pseudomonas infection

• Pathology
  • Necrotizing inflammation
  • Well-demarcated necrotic and hemorrhagic skin lesions of oval shape often arise during these bacteremias, called *ecthyma gangrenosum*
Chancroid

- Caused by *Hemophilus ducreyi*
- Sexually transmitted
- Chancroid is a tender, erythematous papule and multiple lesions may be present
Mycobacteria infection
Mycobacteria

- Mycobacteria cannot be demonstrated by Gram stain
- Possess a capsule containing long chain fatty acid (mycolic acid) that makes them hydrophobic
- Can be stained by a strong stain like carbol fuchsin
Mycobacteria

- Tuberculosis
- *Mycobacterium Avium-Intracellularure Complex (MAC)*
- Leprosy
Tuberculosis

- *Mycobacterium tuberculosis* is responsible for most cases
- Delayed hypersensitivity to *M. tuberculosis* antigens
- Enters macrophage by endocytosis
- Blocking fusion of the phagosome and lysosome to inhibit phagocytosis
Pathogenesis of tuberculosis

A. PRIMARY PULMONARY TUBERCULOSIS (0–3 weeks)

- Mycobacteria
- Alveolar macrophage
- Mannose-capped glycolipid
- Macrophage mannose receptor
- "Endosomal manipulation"
  - Maturation arrest
  - Lack of acid pH
  - Ineffective phagolysosome formation
- Bacteremia with seeding of multiple sites
- Unchecked bacillary proliferation
- NRAMP1 polymorphism

B. PRIMARY PULMONARY TUBERCULOSIS (>3 weeks)

- Alveolar macrophage
- IL-12
- Class II MHC
- MTb antigen
- T-cell receptor
- T-cell
- T\(_{H1}\)
- γ-IFN
- TNF, chemokines
- Monocyte recruitment
- Epithelioid granuloma ("hypersensitivity")
- Production of nitric oxide and reactive oxygen species
- Tuberculosis positivity ("hypersensitivity")
- Bactericidal activity ("immunity")
- Caseous necrosis
- Sensitized T-cell
Pathology of tuberculosis

Primary pulmonary tuberculosis

Miliary tuberculosis

Granulomatous inflammation
Mycobacterium Avium-Intracellulare Complex (MAC)

- MAC is common in soil, water, dust and domestic animals
- Infection in HIV patient
- Causes widely disseminated infections in lung and gastrointestinal system
- Pathology
  - Enlargement of involved lymph nodes, liver and spleen

*Mycobacterium avium* with acid-fast organism
Leprosy

- Caused by *Mycobacterium leprae*
- Affected the skin and peripheral nerves and resulting in disabling deformities
- Transmitted from person to person through aerosols from lesions in the respiratory tract
- It grows more slowly than other mycobacteria and grows best at 32°C to 43°C

Acid-fast bacilli (“red snappers”) within macrophages
Pathology

- **Tuberculoid leprosy**: scaly skin lesions that lack sensation
- **Lepromatous leprosy**: symmetric skin thickening and nodules (mycobacteria invade to Schwann cells)
Spirochetes bacterial infection
Spirochetes

- Spirochetes are **Gram-negative**, slender corkscrew-shaped bacteria
- Periplasmic flagella
- Morphology is too slender to be seen in Gram stain, but it can be visualized by silver stains, **dark-field examination**
Syphilis

- A chronic venereal disease
- Caused by *Treponema pallidum*
- Sexual intercourse is the usual mode of spread
- Transplacental transmission during pregnancy results in congenital syphilis
Pathology of syphilis

Primary syphilis

- 3 weeks after contact
- Chancre, a single firm, nontender, raised, red lesion

Secondary syphilis

- 2-10 weeks after primary chancre
- The skin lesions, which frequently occur on the palms or soles of the feet, may be maculopapular, scaly or pustular
Pathology of syphilis

Tertiary syphilis
- Cardiovascular syphilis
- Neurosyphilis

Congenital syphilis
- Nasal discharge
- Hepatomegaly and skeletal abnormalities
- Interstitial keratitis with blindness
Anaerobic bacterial infection
Clostridial infections

**Clostridium perfringens**
- Cellulitis and myonecrosis of traumatic and surgical wounds (**gas gangrene**)
- Uterin myonecrosis often associated with illegal **abortions**

**Clostridium tetani**
- Convulsive contractions of skeletal muscles (**lockjaw**)
**Clostridium botulinum**
- Grows in inadequately sterilized canned foods
- Severe **paralysis** of respiratory and skeletal muscles (botulism)

**Clostridium difficile**
- Overgrows other intestinal flora in antibiotic-treated patients, releases toxins, and causes **pseudomembranous colitis**
Clostridial infections

Gangrenous cellulitis

- Differentiated from infection caused by pyogenic cocci by its foul odor, its thin, discolored exudate
- Quick and wide tissue destruction

Gangrenous cellulitis

Pyogenic abscess
Gas gangrene

- Characterized by marked edema and enzymatic necrosis
- Large bullous vesicles, gas bubbles caused by bacterial fermentation
- Severe myonecrosis is the result of massive proteolytic bacterial enzymes
Obligate intracellular bacterial infection
Chlamydial infections

- Obligate intracellular bacteria proliferate only within host cells
- *Chlamydia trachomatis*
  - Causes genital infection *(Urethritis)*
  - Is the most common bacterial sexually transmitted disease in the world
  - Is the cause of about half the cases of nongonococcal urethritis *(NGU)*
Reference

- Jawetz, Melnick & Adelberg’s. Medical Microbiology. 26th Edition. LANGE®