Chapters 21-26: Selected Bacterial Pathogens

1. Gram⁺ Cocci
2. Gram⁺ Rods
3. Gram⁻ Pathogens
4. Spirochete Pathogens
Bacterial Sepsis to Septic Shock

1) Sepsis:
   • spread of bacteria or bacterial toxins from the point of infection via the blood

2) Septicemia:
   • proliferation of bacteria in the blood

3) Septic shock:
   • sepsis-triggered catastrophic (fatal) loss of blood pressure due systemic release of TNF
1. **Gram\(^+\) Cocci**
Genus *Staphylococcus*

*Staphylococcus aureus* (pp. 616-20, 751-2):

- various strains cause types of skin infections, pneumonia, food poisoning, toxic shock syndrome
  - depending on “extra” genes acquired by transformation, transduction…

- features that contribute to its virulence:
  - **protein A** – binds $F_C$ of IgG, prevents opsonization
  - produces **coagulase, hyaluronidase, staphylokinase**
  - **β-lactamase** (penicillinase)
Staphylococcal Food Poisoning

The most common cause of gastroenteritis is that caused by the exotoxin enterotoxin produced by certain strains of *Staphylococcus aureus*:

- enterotoxin gene acquired by phage transduction
- superantigen triggering massive immune response in gut resulting in vomiting & severe diarrhea
- suspect foods are meats that have been cooked and then not handled or stored properly
  - cooking kills all microbes initially
  - subsequent *S. aureus* contamination due to handling, poor storage conditions can lead to illness
Typical case of Food Poisoning

• S. aureus introduced to cooked food by handler

• extended storage at room temperature allows bacteria to proliferate & release enterotoxin

• ingested enterotoxin from food causes symptoms of food poisoning
Genus *Streptococcus*

*Streptococcus pyogenes* (pp. 714-5):

- cause of **scarlet fever**, **pharyngitis**, **rheumatic fever**
- have capsule made of **hyaluronic acid**
  - part of extracellular matrix, discourages IR
- produce **protein M** which interferes w/complement
- also produce **streptokinase**, **C5a peptidase**
- secrete **erythrogenic toxins** (cause fever, rash)

*Streptococcus mutans* (pp. 747-9):

- main culprit in **tooth decay**
Dental caries (tooth decay) is caused by the normal microbiota of the mouth that form a biofilm (containing *S. mutans*) we call plaque on the tooth enamel surface:

- due mainly to metabolism of the disaccharide sucrose (not glucose or fructose) which yields corrosive lactic acid

- avoidance of sucrose and mechanical removal of biofilm (brushing & flossing) minimizes tooth decay
2. Gram$^+$ Rods
Genus *Bacillus*

*Bacillus anthracis* (pp. 679-80):

- forms endospores, cause of *anthrax*
- produces 2 types of exotoxins:
  - *edema* toxin (swelling), *lethal* toxin (kills macrophages)
- unusual *glutamic acid* (an amino acid) based capsule
  - does NOT provoke IR, resists phagocytosis

*Bacillus cereus*:

- forms endospores, causes type of *food poisoning*
  - can survive pasteurization, cooking; psychrotophic
Anthrax

If *Bacillus anthracis* enters the bloodstream, the infection is usually fatal:

- once in blood they are ingested by macrophages, multiply, kill the macrophage and spread infection
- fatality rate is nearly 100% if untreated

Infection is due to exposure to endospores via:

- inhalation into lungs
- breaks in the skin
- ingestion into the digestive tract
Portals of entry for *B. anthracis* endospores:

- **cutaneous anthrax** (portal of entry = skin)
  - causes black scabs at point of infection
  - usually does NOT enter bloodstream
  - most common type of anthrax

- **gastrointestinal anthrax** (digestive tract)
  - stomach acid typically destroys the endospores
  - infection results in greater than 50% mortality

- **pulmonary anthrax** (lungs)
  - usually results in entry into the bloodstream
  - infection results in nearly 100% mortality
Signs of Anthrax:

- early signs are mild fever, coughing
- rapid proliferation results in septic shock & death within 3 to 4 days of infection

Treatment of Anthrax:

- the antibiotics ciprofloxacin & doxycycline are most effective if given early
- only available vaccine is not routinely given
  - is a toxoid (inactivated toxin) type of vaccine
  - main risk of infection is bioterrorism
Genus *Clostridium*

*Clostridium botulinum* (pp. 649-51):

- obligate anaerobe, produces endospores
- cause of the disease “botulism”
  - due to *botulinum* toxin, a potent A-B toxin

*Clostridium tetani* (pp. 647-9):

- obligate anaerobe, produces endospores
- cause of the disease “tetanus”
  - due to *tetanus* toxin, also a potent A-B toxin
Botulism

Botulinum toxin, inhibits neuromuscular junctions causing paralysis & frequently death:

• notorious in home canned goods

• symptoms include dry mouth, slurred speech, blurred vision, vomiting, diarrhea, respiratory failure

• illness is not due to bacterial infection but due to intoxication with botulinum toxin

• can be treated with antitoxins if caught early
Tetanus

Tetanus toxin impairs inhibitory nerve signals for the relaxation of muscles:

- transmitted via endospores in fecal matter that contaminate soil (typically via puncture wounds)
- causes muscle rigidity such as “lockjaw”
- spasms of respiratory muscles can be lethal
Genus *Mycobacterium*

*Mycobacterium tuberculosis* (pp. 719-23):

- cause of tuberculosis (kills ~2 million people/yr)
- typically transmitted via inhalation of droplets
- battle between host and pathogen takes place in the alveoli
  - phagocytosis by alveolar macrophages
  - in susceptible individuals, some bacilli can survive and proliferate within macrophages
  - inflammatory signals recruit more phagocytes to area resulting in formation of a tubercule, a “walled off” structure enclosing the infected cells
- tubercules can ultimately rupture leading to spread of the pathogen throughout the body:

- referred to as **miliary TB**

- such systemic infection can lead to the gradual “consumption” of infected tissues, hence TB’s more traditional name

- anti-mycobacterial drugs can be effective (rifampicin, isoniazid) though resistance is a problem
Mycobacterium leprae:

- cause of the disease leprosy (aka “Hansen’s disease)
  - chronic, non-lethal destruction, deformation of more peripheral body tissues
  - grows best at 30° C. (body extremities)
  - survive phagocytosis by macrophages
  - can infect and destroy myelin sheath of peripheral nerves compromising nerve function

- can be effectively treated with the drugs rifampicin and dapsone (a sulfone drug that inhibits folic acid synthesis)
Genus *Corynebacterium*

*Corynebacterium diphtheriae* (pp. 715-6):

- non-spore producing rod causing **diphtheria**, formerly the leading infectious killer of U.S. children
- spread mainly by droplet transmission
- virulence mainly due to diphtheria toxin
  - an A-B exotoxin encoded by a prophage that inhibits protein synthesis
- diphtheria toxoid vaccine provides protection
3. Gram- Pathogens
Genus *Salmonella* (pp. 753-55)

**Salmonella typhi:**
- Gram⁻ rod, cause of typhoid fever
- Effectively treated with cephalosporin derivatives

**Salmonella enterica:**
- Gram⁻ rod, cause of salmonellosis
Salmonellosis

A form of gastroenteritis called due to an actual infection, not intoxication:

• *Salmonella enterica* thrives in commercial poultry production, chicken & eggs are frequent sources

• tomatoes, alfalfa sprouts, pet reptiles and rodents are also sources of infection

• inadequate cooking (or raw food) or contamination of cooking surfaces, utensils can lead to infection

• incubation time is ~24 hr and symptoms include diarrhea, fever & vomiting which can last up to 1 wk
Salmonella Infection

- *Salmonella enterica* infects intestinal epithelial cells

- bacteria can pass through M cells in the mucosa (special gut immune cells) to spread to rest of body via lymph & blood

- can result in dangerous systemic infection
Genus *Bordetella*

*Bordetella pertussis* (pp. 715-6):

- Gram-negative rod & cause of “whooping cough”
  - formerly a very dangerous infectious childhood disease
- virulence due primarily to 2 exotoxins:
  - **Tracheal Cytotoxin**
    - inhibits cilia function in respiratory tract
  - **Pertussis Toxin**
    - A-B toxin that inhibits intracellular signaling

*Immunity due to vaccination tends to dissipate after ~10 yrs*
Genus *Vibrio*

*Vibrio cholerae* (pp. 755-8):

- curved rod that causes cholera
- transmitted via contaminated water or food
- massive fluid loss via diarrhea due to cholera toxin:
  - an A-B toxin acquired by phage transduction
  - inhibits regulation of salt ion balance in gut epithelium, leading to fluid loss via diffusion into gut lumen
*Helicobacter pylori* (pp. 760-1)

*H. pylori* is now known to be the cause of most peptic (stomach) ulcers:

- it has the unusual ability to grow in the acidic stomach environment
  - produces the enzyme *urease* which converts urea to ammonia thus raising the pH locally
- infection leads to localized destruction of mucus-secreting cells of the stomach
- loss of protective mucus layer leads to tissue damage due to stomach acid, ulcer formation
Ulcer formation due to *H. pylori*
Genus *Neisseria*

*Neisseria gonorrhoeae* (pp. 790-2):

- diplococcus that causes *gonorrhea* via infection of epithelial layer of urethra in males, cervix in females
- males exhibit pus-filled discharge from urethra
- females *may* experience abdominal discomfort
  - may go undetected, too
- dangerous systemic infection can result if untreated

Virulence factors: capsule, IgA protease, antigenic var.
• use of oral contraceptives, increased sexual partners caused spike of cases in 1970’s & 1980’s

• diagnosis is microscopic

• effectively treated with penicillin derivatives & several other antibiotics

(a) Incidence of gonorrhea in the United States from 1942 through the first 26 weeks of 2005

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Neisseria meningitis (pp. 645-6):

• diplococcus causing the extremely dangerous and lethal disease meningococcal meningitis

• infection begins with meningococcal pharyngitis
  • acquired via droplet transmission
  • polysaccharide capsule that resists degradation promotes survival, proliferation within phagocytes

• penetration of pharyngeal epithelium & invasion of bloodstream can transfer infection to the CNS
  • pilin proteins expressed on fimbriae allow adhesion to capillary endothelium, penetration of blood-brain barrier

**Lethal effects are primarily due to endotoxin**
• CNS phagocytes containing diplococci, & serological methods confirm diagnosis

• successfully treated with antibiotics if caught in time
4. Spirochete Pathogens
Spirochetes

*Borelia burgdorferi* (pp. 685-7):

- cause of **Lyme disease**
- biological transmission via tick vectors
- uses manganese (Mn) instead of iron (Fe) in electron transport chain
  - i.e., iron is NOT a limiting resource
- can be debilitating, difficult to diagnose & treat

*Treponema pallidum* (pp. 794-7):

- cause of **syphilis**
Syphilis

Syphilis is a STD caused by *Treponema pallidum* that progresses through 3 distinct phases:

**Primary (1°) stage**

- appearance of a painless, hard “sore” at site of infection

**2° stage**

- after spread throughout body, skin lesions appear on various parts of the body
3° stage syphilis

- after a latent period of up to several years, rubbery lesions called gummas appear on the skin and mucous membranes that lead to destruction of these tissues
- the nervous system can also become a target causing a variety of disabling symptoms

Diagnosis of syphilis:

- microscopic examination, serological testing for antibodies or the antigen (T. pallidum) itself

Treatment:

- a variety of antibiotics including penicillin derivatives are effective, so “full-blown” syphilis is relatively rare
The incidence of syphilis has dropped dramatically since antibiotics became readily available.

![Graph showing reported cases per 100,000 population from 1942 to 2005. The incidence of syphilis dropped dramatically after the availability of antibiotics.](image)

*First 26 weeks of 2005

(a) Incidence of syphilis in the United States from 1942 through the first 26 weeks of 2005

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Key Terms for Bacterial Pathogens
(Chapters 21-26)

- sepsis, septicemia, septic shock
- intoxication vs infection
- M cells
- protein A, protein M
- tubercule