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 Fc 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

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**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

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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; psychrotrophic

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**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

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**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

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**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*

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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

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**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
**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

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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 (1st) stage**
- appearance of a painless, hard “sore” at site of infection

**2nd stage**
- after spread throughout body, skin lesions appear on various parts of the body

**3rd 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.

Key Terms for Bacterial Pathogens (Chapters 21-26)

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