Microbial Mechanisms of Pathogenicity

Chapter 15
**Pathogenicity** - ability to cause disease

**Virulence** - degree of pathogenicity

- Many properties that determine a microbe’s pathogenicity or virulence are unclear or unknown

- But, when a microbe overpowers the host's defenses, disease results!
Portals of Entry

1. Mucus Membranes
2. Skin
3. Parenteral
1. Mucus Membranes

- A. Respiratory Tract
  - microbes inhaled into mouth or nose in droplets of moisture or dust particles
  - Easiest and most frequently traveled portal of entry
Common Diseases contracted via the Respiratory Tract

- Common cold
- Flu
- Tuberculosis
- Whooping cough
- Pneumonia
- Measles
- Strep Throat
- Diphtheria
**Mucus Membranes**

- **B. Gastrointestinal Tract**
  - microbes gain entrance thru contaminated food & water or fingers & hands
  - most microbes that enter the G.I. Tract are destroyed by HCL & enzymes of stomach or bile & enzymes of small intestine
Common diseases contracted via the G.I. Tract

- Salmonellosis
  - *Salmonella sp.*
- Shigellosis
  - *Shigella sp.*
- Cholera
  - *Vibrio cholorea*
- Ulcers
  - *Helicobacter pylori*
- Botulism
  - *Clostridium botulinum*
Fecal - Oral Diseases

- These pathogens enter the G.I. Tract at one end and exit at the other end.

- Spread by contaminated hands & fingers or contaminated food & water

- Poor personal hygiene.
Mucus Membranes of the Genitourinary System - STD’s

Gonorrhea

*Neisseria gonorrhoeae*

Syphilis

*Treponema pallidum*

Chlamydia

*Chlamydia trachomatis*

HIV

Herpes Simplex II
Mucus Membranes

- D. Conjunctiva –
  - mucus membranes that cover the eyeball and lines the eyelid

- Trachoma
  - *Chlamydia trachomatis*
2nd Portal of Entry: Skin

- Skin - the largest organ of the body. When unbroken is an effective barrier for most microorganisms.

- Some microbes can gain entrance thru openings in the skin: hair follicles and sweat glands
3rd Portal of Entry: Parenteral

- Microorganisms are deposited into the tissues below the skin or mucus membranes
- Punctures
- injections
- bites
- scratches
- surgery
- splitting of skin due to swelling or dryness
Preferred Portal of Entry

- Just because a pathogen enters your body it does not mean it’s going to cause disease.

- pathogens - preferred portal of entry
Preferred Portal of Entry

- *Streptococcus pneumoniae*
  - if inhaled can cause pneumonia
  - if enters the G.I. Tract, no disease

- *Salmonella typhi*
  - if enters the G.I. Tract can cause Typhoid Fever
  - if on skin, no disease
Number of Invading Microbes

- LD$_{50}$ - Lethal Dose of a microbes toxin that will kill 50% of experimentally inoculated test animal
- ID$_{50}$ - infectious dose required to cause disease in 50% of inoculated test animals
  - Example: ID$_{50}$ for Vibrio cholerae 10$^8$ cells (100,000,000 cells)
  - ID$_{50}$ for Inhalation Anthrax - 5,000 to 10,000 spores ?????
How do Bacterial Pathogens penetrate Host Defenses?

1. **Adherence** - almost all pathogens have a means to attach to host tissue

**Binding Sites**
- adhesins
- ligands
Adhesins and ligands are usually on Fimbriae

- *Neisseria gonorrhoeae*
- *ETEC* (Entertoxigenic E. coli)
- *Bordetello pertussis*
2. Capsules

- Prevent phagocytosis
- Attachment
- *Streptococcus pneumoniae*
- *Klebsiella pneumoniae*
- *Haemophilus influenzae*
- *Bacillus anthracis*
- *Streptococcus mutans*
- *Yersinia pestis*
3. Enzymes

- Many pathogens secrete enzymes that contribute to their pathogenicity
A. Leukocidins

- Attack certain types of WBC’s
- 1. Kills WBC’s which prevents phagocytosis
- 2. Releases & ruptures lysosomes
  - lysosomes - contain powerful hydrolytic enzymes which then cause more tissue damage
B. Hemolysins - cause the lysis of RBC’s

Streptococci
1. Alpha Hemolytic Streptococci
- secrete hemolysins that cause the incomplete lysis or RBC’s
2. Beta Hemolytic Streptococci

- secrete hemolysins that cause the complete lysis of RBC’s
3. Gamma Hemolytic Streptococci - do not secrete any hemolysins
C. Coagulase - cause blood to coagulate

- Blood clots protect bacteria from phagocytosis from WBC’s and other host defenses

- Staphylococci - are often coagulase positive
  - boils
  - abscesses
D. Kinases - enzymes that dissolve blood clots

- 1. Streptokinase - Streptococci
- 2. Staphylokinase - Staphylococci

- Helps to spread bacteria - Bacteremia

- Streptokinase - used to dissolve blood clots in the Heart (Heart Attacks due to obstructed coronary blood vessels)
E. Hyaluronidase

- Breaks down Hyaluronic acid (found in connective tissues)
- “Spreading Factor”
- mixed with a drug to help spread the drug thru a body tissue
F. Collagenase

- Breaks down collagen (found in many connective tissues)

- *Clostridium perfringens* - Gas Gangrene
  - uses this to spread thru muscle tissue
G. Necrotizing Factor

- causes death (necrosis) to tissue cells

“Flesh Eating Bacteria”

Necrotizing fasciitis
Summary of How Bacterial Pathogens Penetrate Host Defenses

- 1. Adherence
- 2. Capsule
- 3. Enzymes
  - A. leukocidins
  - B. Hemolysins
  - C. Coagulase
  - D. Kinases
  - E. Hyaluronidase
  - F. Collagenase
  - G. Necrotizing Factor
4. Toxins

- Poisonous substances produced by microorganisms
- Toxins - primary factor - pathogenicity
- 220 known bacterial toxins
  - 40% cause disease by damaging the Eukaryotic cell membrane
- Toxemia
  - Toxins in the bloodstream
2 Types of Toxins

- 1. Exotoxins
  - secreted outside the bacterial cell

- 2. Endotoxins
  - part of the outer cell wall of Gram (-) bacteria
Exotoxins

- Mostly seen in Gram (+) Bacteria

- Most gene that code for exotoxins are located on plasmids or phages
**3 Types of Exotoxins**

- **1. Cytotoxins**
  - kill cells

- **2. Neurotoxins**
  - interfere with normal nerve impulses

- **3. Enterotoxins**
  - effect cells lining the G.I. Tract
Response to Toxins

- If exposed to exotoxins: antibodies against the toxin (antitoxins)
- Exotoxins inactivated (heat, formalin or phenol) no longer cause disease, but stimulate the production of antitoxin
  - altered exotoxins - Toxoids
- Toxoids - injected to stimulate the production of antitoxins and provide immunity
Example: DPT Vaccine

- **D** - Diphtheria
  - *Corynebacterium diphtheriae*
- **P** - Pertussis
  - *Bordetella pertussis*
- **T** - Tetanus
  - *Clostridium tetani*

DPT - Diphtheria Toxoid

Pertussis Antigen

Tetanus Toxoid
Required Immunizations in Illinois

1. Diphtheria  - Corynebacterium diphtheriae
2. Pertussis  - Bordetello pertussis
3. Tetanus    - Clostridium tetani
4. Measles    - Measles virus
5. Mumps      - Mumps virus
6. Rubella    - Rubella virus
   - German Measles
7. Polio      - Polio virus
8. Hib        - Haemophilus influenzae
9. Hepatitis B - Hepatitis B Virus
10. Chicken Pox - Varicella-zoster virus
Type of Vaccines

- D
- P
- T
- M
- M
- R
- Polio
  - Salk
  - Sabin
- Hib
- HBV
- Chicken Pox
- Toxoid
- Antigen
- Toxoid
- Attenuated
- Attenuated
- Attenuated
- Attenuated
  - IPV — Inactivated Polio virus (Killed) 1953
  - OPV — Oral Polio vaccine (attenuated) 1964
- Conjugated vaccine
- Recombinant vaccine (antigen) yeast
  - Capsid produced by genetically engineered yeast
- Attenuated
Most genes that code for exotoxins - plasmids or phages

- Lysogenic convergence
- Diphtheria
- Cytotoxin inhibits protein synthesis - resulting in cell death
- Pseudomembrane
  - fibrin, dead tissue, bacterial cells
Lysogenic Convergence

- Scarlet Fever
- *Streptococcus pyogenes*
  - lysogenic convergence
- prophage
  - cytotoxin - damages blood capillaries and results in a skin rash
  - Strep Throat with a rash
Diseases caused by Neurotoxins

- **Botulism**
  - *Clostridium botulinum*
    - Gram (+), anaerobic, spore-forming rod, found in soil
    - works at the neuromuscular junction
    - prevents impulse from nerve cell to muscle cell
    - results in muscle paralysis
Newsweek

May 13, 2002: $3.95

Africa's Child Soldiers

The Real Barbara Bush

A Once-Feared Poison Could Become the Next Billion-Dollar Drug. Is It Safe? And Why Are We So Vain?

The Business of Botox
Tetanus (Lock Jaw)

- *Clostridium tetani*
- Gram (+), spore-forming, anaerobic rod
- Neurotoxin acts on nerves, resulting in the inhibition of muscle relaxation
- Tetanospasmin - “spasms” or “Lock Jaw”
Diseases caused by Enterotoxins

- Cholera
  - *Vibrio cholerae*
  - Gram (-) comma shaped rods
*Cholera toxin*

- Converts ATP into cAMP
- Causes cells to excrete Cl⁻ ions and inhibits absorption of Na⁺ ions
- Electrolyte imbalance
- H₂O leaves by osmosis
- H₂O Loss (Diarrhea)
Severe cases, 12 - 20 liters of liquid lost in a day

- Untreated cases - Mortality Rate about 50%
- Mortality may be reduced to about 1%
  - administering fluids and electrolytes
EHEC (Enterohemorrhagic E. coli)

- E. coli (0157:H7)
- enterotoxin causes a hemolytic inflammation of the intestines
- results in bloody diarrhea
- Toxin
  - alters the 60S ribosomal subunit
  - inhibits Protein Synthesis
  - Results in cell death
  - lining of intestine is “shed”
  - Bloody Diarrhea (Dysentary)
Endotoxins - part of the Gram (-) Bacterial cell wall

- LPS (Lipopolysaccharides)
  - O Antigen
  - Lipid A
- Lipid A - Toxin portion of the LPS
  - responsible for Fever that is associated with many Gram (-) Bacterial infections
  - Gram (-) cells are “digested” endotoxins are released - fever
  - Antibiotics