Microbial Mechanisms of Pathogenicity

- Pathogenicity - the ability of a pathogen to cause a disease by overcoming the defenses of the host.
- Virulence - the degree or extent of pathogenicity.

- A pathogenic organism is able to cause a disease.
- A pathogen that is highly *virulent* causes damaging disease.
Portals of entry

Portals of entry – avenues that pathogens can use to gain entry into the human body

1. Mucous membranes
   - Respiratory tract, gastrointestinal (GI) tract, genitourinary (GU) tract, conjunctiva (eyes)

Most common portals are respiratory, GI tracts
   - Inhaled through mouth, nose
   - Eaten
Portals of Entry

2. Skin
   - Largest organ, first line of defense
     - Unbroken skin is impenetrable to most microbes
   - Some gain access through openings in skin
   - Some fungi can infect skin directly

3. Parenteral route – access through breaks in skin
   - From cuts, bites, drying

All microbes have preferred portal of entry
- Some microbes have multiple portals of entry
Numbers of Invading Microbes

- Too few pathogens can be overwhelmed by immune system
- Likelihood of disease increases as number of pathogens increase
Virulence of a disease expressed as ID$_{50}$ - infectious dose for 50% of a test population

Expression of relative virulence under experimental conditions – can be different for different portals

*Bacillus anthracis* has 3 portals of entry

<table>
<thead>
<tr>
<th>Portal of Entry</th>
<th>ID$_{50}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>10-50 endospores</td>
</tr>
<tr>
<td>Inhalation</td>
<td>10,000-20,000 endospores</td>
</tr>
<tr>
<td>Ingestion</td>
<td>250,000-1,000,000 endospores</td>
</tr>
</tbody>
</table>
Numbers of Invading Microbes

- Potency of toxin expressed as \( \text{LD}_{50} \) – lethal dose for 50% of a test population

<table>
<thead>
<tr>
<th>Toxin</th>
<th>( \text{LD}_{50} ) in mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botulinum toxin</td>
<td>0.03 ng/kg</td>
</tr>
<tr>
<td>Shiga toxin</td>
<td>250 ng/kg</td>
</tr>
<tr>
<td>Staphylococcal enterotoxin</td>
<td>1350 ng/kg</td>
</tr>
</tbody>
</table>
So you think you are an epidemiologist?

Giardiasis is a disease that is commonly contracted by drinking fecal contaminated water. The pathogen, *Giardia lamblia*, affects the intestines, causing diarrhea, vomiting, and flatulence.

1. What is the reservoir of infection?
2. What is the mode of transmission?
3. What is the portal of entry?
1. What is the reservoir of infection?
   - Water

2. What is the mode of transmission?
   - Vehicle waterborne

3. What is the portal of entry?
   - Mucous membranes (of the GI tract)
The most frequently used portal of entry for pathogens is the _______.

1. mucous membranes of respiratory tract
2. conjunctiva
3. skin
4. mucous membranes of the genitourinary tract
A sexually transmitted disease is an example of which portal of entry?

1. **Mucous membranes**
2. The skin
3. Parenteral route

![Bar chart showing percentages: 64% for Mucous membranes, 36% for The skin, and 0% for Parenteral route]
Which of these is not considered entry via the parenteral route?

1. Injection
2. Bite
3. Hair follicle
4. Surgery

![Bar chart showing percentages]

- Injection: 18%
- Bite: 9%
- Hair follicle: 64%
- Surgery: 9%
Virulence factors

- Molecules or structures that a pathogen uses to cause disease
- Many virulence factors exist
Virulence factors

1. Adhesins
   - Adherence, adhesion – means of attachment
     - Necessary for pathogenicity in most pathogens
     - Interfere with binding, interfere with infection
   - “Adhesins” bind to “receptors” on host cell
   - Adhesins may be located on glycocalyx, surface structures (ie, fimbriae)
   - Binding is specific for certain host tissues, receptors
Virulence factors

2. Capsules

- Capsules impair phagocytosis (being eaten)
  - Prevents binding to pathogen
  - Capsules do not mean a bacterium is virulent
Virulence factors

3. Cell wall components

- Some cell walls contain chemicals that contribute to virulence
  - *Streptococcus pyogenes* produces “M protein” that helps cells attach, resist phagocytosis
  - Waxy lipid coating of *Mycobacterium* increase virulence by resisting phagocytosis
Virulence factors

4. Enzymes
   - Many have enzymes that aid in pathogenesis
     - Some allow invasion of pathogen
     - Some allow evasion of host defenses
     - Some damage host cells
How Bacterial Pathogens Damage Host Cells

- Bacteria can damage host by:
  - Using host’s nutrients
  - Direct damage
  - The production of toxins
How Bacterial Pathogens Damage Host Cells

1. Using host’s nutrients: Siderophores
   - Iron is required for growth
     - Iron in human body is tightly bound, unavailable to pathogens
   - Siderophores – proteins that tightly bind iron
     - Used to take away iron from host
How Bacterial Pathogens Damage Host Cells

2. Direct Damage

- A number of ways that microbes can damage cells
  - Grow within cells, multiply and rupture cell
  - Attach to host cell and cause damage as pathogen uses host for nutrients
  - “Swim” into host cells – damages membranes
3. Production of Toxins

- Toxins – poisonous substances that are produced by some microbes
- Toxigenicity – ability of microbes to produce toxins
- Two types of toxins
  - Endotoxins
  - Exotoxins
Exotoxins

- Exotoxins – protein toxins made inside bacterium and secreted to its surroundings
- Many are enzymes, so small amounts harmful
  - Why?
Exotoxins

- Soluble in body fluids, can be transported all over body
- Diseases caused by bacteria that produce toxins are a direct result of toxin
  - Staphylococcal food poisoning is an “intoxication”
- Antitoxins – antibodies produced by the body that neutralize toxins
Types of exotoxins

- A-B toxins – consist of two parts, “A” and “B”
- A part is active (enzyme) component
- B part is the binding component
- Diptheria toxin is A-B toxin
Endotoxins

- Part of cell wall of gram-negative bacteria
  - LPS portion of outer membrane
  - Endotoxin is the lipid portion, called Lipid A

*Exotoxins are proteins, Endotoxins are lipids*
Endotoxin

- All endotoxins produce the same signs and symptoms
  - Chills, fever, weakness, aches, shock, death
  - “Disseminated intravascular clotting”
- Shock – life threatening drop in blood pressure
- Endotoxic shock – shock produced by gram-negative bacterial endotoxin
Endotoxins

- Endotoxins are released when gram-negative bacteria die and cells lyse
  - Liberates endotoxins
  - Antibiotics can cause lysis $\rightarrow$ release LPS

$S. typhi$, $N. meningitidis$
E. coli and its virulence factors
Which of these toxins is the most deadly given their LD$_{50}$ values?

1. Sarin - 17 mg/kg
2. VX nerve gas - .14 mg/kg
3. E. coli O157:H7 - 27 mg/kg
4. Tetanus toxin - .000002 mg/kg
If an A-B toxin is missing its B component it cannot cause an intoxication because _____.

1. the toxin does not have enzymatic activity
2. the toxin will get degraded in the cell
3. the toxin cannot enter the cell
4. the toxin cannot be produced
Which of these microbes contain endotoxins?

1. A gram-positive bacterium
2. A gram-negative bacterium
3. A protozoa
4. A fungus

100%
An encapsulated bacteria can be virulent because the capsule _____.

1. **resists phagocytosis**
2. is an endotoxin
3. is an exotoxin
4. destroys host tissues
Pathogenic Properties of Viruses

- Viruses have a number of mechanisms to evade immune system
  - Can grow inside of host cells
  - Some can “hide” attachment sites
    - HIV has attachment sites too small for antibodies to bind
  - Some attack immune cells
    - HIV
Cytopathic Effects of Viruses

- Cytopathic effects (CPE) – visible effects of viral infection
  - Cytocidal effects – CPE that result in death
  - Noncytocidal effects – CPE that cause cell damage without causing cell death
- CPE used to diagnose many viral infections
Cytopathic effects of Viruses

1. Inhibition of macromolecular synthesis of host cell
2. Release of enzymes from host’s lysosomes
3. Formation of inclusion bodies – granules in cytoplasm
4. Formation of syncytium – fusion of adjacent cells
Cytopathic effects of Viruses

5. Change in host cell’s function without visible changes
   - Measles virus reduces production of cytokines

6. Production of “interferons” by virus infected cells
   - Protect uninfected cells from viral infection

7. Produce antigenic changes on host cell surface
   - Host cell targeted for destruction

8. Changes to host cell chromosomes

9. “Transformation” of host cell
   - Contact Inhibition - inhibition of growth by close contact
Portals of Exit

- Specific route that microbes use to leave the body
  - In secretions, excretions, discharges, tissue that’s been shed
- In general, portals of exit are related to infected tissue
- Respiratory tract
  - Coughing and sneezing
- Gastrointestinal tract
  - Feces and saliva
- Genitourinary tract
  - Urine and vaginal secretions
Summary of Microbial Pathogenicity

- **Portals of Entry**
  - Mucous membranes
  - Respiratory tract
  - Gastrointestinal tract
  - Genitourinary tract
  - Conjunctiva
  - Skin
  - Parenteral route

- **Number of Invading Microbes**

- **Penetration or Evasion of Host Defenses**
  - Capsules
  - Cell wall components
  - Enzymes
  - Antigenic variation
  - Invasins
  - Intracellular growth

- **Damage to Host Cells**
  - Siderophores
  - Direct damage
  - Toxins
  - Exotoxins
  - Endotoxins
  - Lysogenic conversion
  - Cytopathic effects

- **Portals of Exit**
  - Generally the same as the portals of entry for a given microbe