**Microbial Mechanisms of Pathogenicity**

- **A**: An infectious dose of microorganisms penetrates the host's defensive barrier.
- **B**: Microorganisms enter the sterile environment of the host's tissues.
- **C**: They move into a specific target tissue, such as an organ.
- **D**: Here they cause tissue damage, leading to disease.
- **E**: Microorganisms leave the host through a portal of exit to infect another host.
Portals of Entry

Mucous membranes

- Conjunctiva
- **Respiratory tract**: Droplet inhalation of moisture and dust particles. Most common portal of entry.
- **GI tract**: food, water, contaminated fingers
- Genitourinary tract

Skin

- Impenetrable for most microorganisms; can enter through hair follicles and sweat ducts.

Parenteral Route

- **Trauma** (*S. aureus, C. tetani*)
- **Arthropods** (*Y. pestis*)
- Injections
Adhesins: surface projections on pathogen, mostly made of glycoproteins or lipoproteins. Adhere to complementary receptors on the host cells. Adhesins can be part of:

- Glycocalyx: *e.g.* *Streptococcus mutans*
- Fimbriae (also pili and flagella): *e.g.* *E. coli*

**Host cell receptors are most commonly sugars (e.g. mannose for *E. coli*)**

**Biofilms** provide attachment and resistance to antimicrobial agents.
Overcoming Host Defenses

- **Capsules:** inhibition or prevention of __________________
- **Cell Wall Proteins:** *e.g.* M protein of *S. pyogenes*
- **Antigenic Variation:** Avoidance of Immune system. *e.g.* *Neisseria*
- **Penetration into the Host Cell Cytoskeleton:** *Salmonella* and *E. coli* produce **invasins**, proteins that cause the actin of the host cell’s cytoskeleton to form a basket that carries the bacteria into the cell.
  - Use actin to move from one cell to the next
    - *Listeria*
    - *Shigella*
Enzymes

Coagulase: Blood clot formation. Protection from phagocytosis (virulent S. aureus)

Kinase: blood clot dissolve (e.g.: streptokinase)

Hyaluronidase: (Spreading factor) Digestion of “intercellular cement” \( \Rightarrow \) tissue penetration

Collagenase: Collagen hydrolysis

IgA protease: IgA destruction
Enzymes Used for Penetration

- coagulase: dissolves clot and releases pathogens
- streptokinase: blood clot around pathogen
- hyaluronidase: dissolves intracellular cement, allows pathogen to spread to deeper tissues
How Pathogens Damage Host Cells

1. Use **host’s nutrients**; *e.g.*: Iron
2. Cause **direct damage**
3. Produce **toxins**
4. Induce **hypersensitivity** reaction
Toxins

**Exotoxins:** proteins (Gram- and + bacteria can produce)

**Endotoxins:** Gram- bacteria only. LPS, Lipid A part ⇒ released upon cell death. Symptoms due to vigorous inflammation. Massive release ⇒ endotoxic shock
Membrane-Disrupting Toxins

Lyse host’s cells by

1. Making protein channels into the plasma membrane, *e.g.* *S. aureus*
2. Disrupting phospholipid bilayer, *e.g.* *C. perfringens*

*Examples:*

**Leukocidin:** PMN and MΦ destruction

**Hemolysin** (*e.g.:* Streptolysin) : RBCs lysis
Superantigens

Special type of Exotoxin
Nonspecifically stimulate T-cells.
Cause intense immune response due to release of cytokines from host cells.
Fever, nausea, vomiting, diarrhea, shock, and death.
## Representative Examples of Exotoxins

<table>
<thead>
<tr>
<th>Bacterial Species</th>
<th>Exotoxin</th>
<th>Lysogeny</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C. diphtheriae</em></td>
<td>A-B toxin</td>
<td>+</td>
</tr>
<tr>
<td><em>S. pyogenes</em></td>
<td>Membrane-disrupting erythrogenic toxin</td>
<td>+</td>
</tr>
<tr>
<td><em>C. botulinum</em></td>
<td>A-B toxin; neurotoxin</td>
<td>+</td>
</tr>
<tr>
<td><em>C. tetani</em></td>
<td>A-B toxin; neurotoxin</td>
<td></td>
</tr>
<tr>
<td><em>V. cholerae</em></td>
<td>A-B toxin; enterotoxin</td>
<td>+</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>Superantigen</td>
<td>+</td>
</tr>
</tbody>
</table>
Endotoxins

- Bacterial cell death, antibiotics, and antibodies may cause the release of endotoxins.
- Endotoxins cause **fever** (by inducing the release of interleukin-1) and **shock** (because of a TNF-induced decrease in blood pressure).
- TNF release also allows bacteria to cross BBB.
## Endotoxin Summary

<table>
<thead>
<tr>
<th>Source:</th>
<th>Gram –</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relation to microbe:</td>
<td>Present in LPS of outer membrane</td>
</tr>
<tr>
<td>Chemistry:</td>
<td>Lipid A component of LPS</td>
</tr>
<tr>
<td>Fever?</td>
<td>Yes</td>
</tr>
<tr>
<td>Neutralized by antitoxin?</td>
<td>No</td>
</tr>
<tr>
<td>$LD_{50}$:</td>
<td>Relatively large</td>
</tr>
</tbody>
</table>
Microbial Mechanisms of Pathogenicity - Overview

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

Adherence

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