Chapter 15
Microbial Mechanisms of Pathogenicity

Identify the principal portals of entry.
- Mucous membranes (respiratory, gastrointestinal, genitourinary, conjunctiva)
- Skin (follicles, sweat gland ducts)
- Parenteral route (punctures, injections, bites, cuts, wounds, surgery, splitting of skin)
- Respiratory tract – most common portal of entry
- Many organisms only cause infections when access their specific portal of entry

**Table 15.1** Portals of Entry for the Pathogens of Some Common Diseases (continued)

<table>
<thead>
<tr>
<th>Portal of Entry</th>
<th>Pathogen</th>
<th>Disease</th>
<th>Incubation Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucous Membranes</td>
<td><em>Haemophilus influenzae</em></td>
<td>Respiratory tract</td>
<td>0-10 days</td>
</tr>
<tr>
<td>Skin or Parenteral</td>
<td><em>Staphylococcus aureus</em></td>
<td>Skin infections</td>
<td>2-3 days</td>
</tr>
<tr>
<td>Skin or Parenteral</td>
<td><em>Escherichia coli</em></td>
<td>Urinary tract infections</td>
<td>1-5 days</td>
</tr>
</tbody>
</table>

*All pathogens are bacteria, unless indicated otherwise. For viruses, the host species and/or genus name is given.

**Numbers of Invading Microbes**

Define LD50 and ID50.

- **Virulence:**
  - ID50: Infectious dose for 50% of the test population
  - LD50: Lethal dose (of a toxin) for 50% of the test population
**Bacillus anthracis**

<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>

**Adherence**

Using examples, explain how microbes adhere to host cells.

- Adhesions/ligands (surface projections) bind to receptors on host cells
  - Glycocalyx (protective casing) *Streptococcus mutans*
  - Fimbriae *E. coli*
  - M protein (virulence) *Streptococcus pyogenes*
  - Opa protein *Neisseria gonorrhoeae*
  - Tapered end *Treponema pallidum*
- Biofilms – masses of microbes that can attach to living and nonliving surfaces (dental plaque, shower door scum)

**Enzymes**

**Adherence**

- Coagulase
  - Coagulate blood (protect local infection in clot)
- Kinases
  - Digest fibrin clots (spread from focal infection)
- Hyaluronidase
  - Hydrolyses hyaluronic acid that holds cells together
- Collagenase
  - Hydrolyzes collagen (connective tissue)
- IgA proteases
  - Destroy IgA antibodies
- Siderophores
  - Take iron from host iron-binding proteins
- Antigenic variation
  - Alter surface proteins, avoiding antibodies

**Antigenic variation**

Define and give an example of antigenic variation.

- Some pathogens can alter their surface antigens to avoid attack from host’s antibodies
  - Influenza
  - Gonorrhea
  - African sleeping sickness

Describe how bacteria use the host cell’s cytoplasm to enter the cell.

- Microbes produce surface proteins (invasins) that rearrange nearby actin filaments of the cytoskeleton of the host cell (microfilaments, microtubules)
- *Salmonella* (next slide)
Siderophores

Describe the function of siderophores.

- To obtain free iron, which is normally tightly bound, some pathogens secrete proteins called siderophores which remove iron from iron-transport proteins.

Toxins

Provide an example of direct damages, and compare this to toxin production.

- Direct damage – as pathogens metabolize and multiply in a cell, the cells often rupture (lyse)
- Toxin Poisonous substances that contribute to pathogenicity
- Toxigenicity Ability to produce a toxin
- Toxemia Presence of toxin in the host's blood
- Toxoid Inactivated toxin used in a vaccine
- Antitoxin Antibodies against a specific toxin

Endotoxin

Contrast the nature and effects of exotoxins and endotoxins.

Exotoxins

- Small
- Yes
- Neutradized by antitoxin
- No
- LD50: Relatively large

Endotoxins

- Large
- No
- Neutradized by antitoxin
- Yes
- LD50: Relatively large
Exotoxins

- A-B toxins or type III toxins (diphtheria)

- Membrane-disrupting toxins or type II toxins
  - Lyse host’s cells by:
    - Making protein channels in the plasma membrane (e.g., leukocidins, hemolysins)
    - Disrupting phospholipid bilayer
  - Plasmids may carry genes for antibiotic resistance, toxins, capsules, and fimbriae
  - Lysogenic conversion (new properties due to lysogenic phage) can result in bacteria with virulence factors, such as toxins or capsules

- Superantigens or type I toxins
  - Cause an intense immune response due to release of cytokines from host cells
  - Fever, nausea, vomiting, diarrhea, shock, death

<table>
<thead>
<tr>
<th>Exotoxin</th>
<th>Lysogenic conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corynebacterium diphtheriae</td>
<td>A-B toxin. Inhibits protein synthesis. +</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>Membrane-disrupting. Erythrogenic. +</td>
</tr>
<tr>
<td>Clostridium botulinum</td>
<td>A-B toxin. Neurotoxin +</td>
</tr>
<tr>
<td>C. tetani</td>
<td>A-B toxin. Neurotoxin +</td>
</tr>
<tr>
<td>Vibrio cholerae</td>
<td>A-B toxin. Enterotoxin +</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Superantigen. Enterotoxin +</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 15.2: Diseases Caused by Exotoxins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exotoxin</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Botulism</td>
</tr>
<tr>
<td>Staphylococci aureus</td>
</tr>
<tr>
<td>Staphylococci carriers</td>
</tr>
</tbody>
</table>

Bacteria | Enterotoxin |
---|---|
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Bacterial source | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Chemistry | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Microscopic effect on body | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Neurotoxin | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Toxicity to cause death | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Immunity | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Infectious disease | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Susceptible host | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Diagnosis | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

Treatment | Enterotoxin |
---|---|
Staphylococci aureus | Enterotoxin |
C. tetani | Enterotoxin |
V. cholerae | Enterotoxin |
C. botulinum | Neurotoxin |
C. diphtheriae | A-B toxin |
S. pyogenes | A-B toxin |

<table>
<thead>
<tr>
<th>Exotoxin and Endotoxin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Property</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Bacterial source</td>
</tr>
<tr>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Neurological effect</td>
</tr>
<tr>
<td>Toxicity to cause death</td>
</tr>
<tr>
<td>Immunity</td>
</tr>
<tr>
<td>Infectious disease</td>
</tr>
<tr>
<td>Susceptible host</td>
</tr>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>Treatment</td>
</tr>
</tbody>
</table>

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Endotoxins and pyrogenic (fever) response

- Endotoxins released by bacterial cell death, antibiotics, and antibodies
- Allow bacteria to cross blood-brain barrier
- LAL (Limulus ameobocyte lysate) assay used to detect endotoxins in drugs and on medical devices

Pathogenic Properties of Viruses

- Viruses avoid host’s immune system by growing inside cells
- Viruses gain access due to attachment sites for receptors on the host cell
- CPE – cytopathic effects that are visible
- Cytopathic effects include:
  - stopping mitosis
  - lysis
  - inclusion bodies
  - cell fusion
  - antigenic changes
  - chromosomal changes
  - transformations

Cytopathic Effects of Viruses

<table>
<thead>
<tr>
<th>Virus (Genus)</th>
<th>Cytopathic Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poliovirus</td>
<td>Cytopathic (cell death)</td>
</tr>
<tr>
<td>Poxovirus</td>
<td>Acidophilic inclusion bodies in nucleus</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Basophilic inclusion bodies in nucleus</td>
</tr>
<tr>
<td>Hsvirus (family Herpesviridae)</td>
<td>Acidophilic inclusion bodies in cytoplasm</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Acidophilic inclusion bodies in nucleus and cytoplasm</td>
</tr>
<tr>
<td>Measles virus (Morbillivirus)</td>
<td>Cell fusion</td>
</tr>
<tr>
<td>Polyomavirus</td>
<td>Transformation</td>
</tr>
<tr>
<td>HIV (Lentivirus)</td>
<td>Destruction of T cells</td>
</tr>
</tbody>
</table>

Pathogenic Properties of Fungi

Discuss the causes of symptoms in fungal, protozoan, helminthic, and algal diseases.

- Fungal symptoms caused by capsules, toxins, and allergic responses
- Fungal waste products may cause symptoms
- Chronic infections provoke an allergic response
- Tichothecene toxins inhibit protein synthesis
  - Fusarium
  - Proteases
  - Candida, Trichophyton
Pathogenic Properties of Fungi

- Capsule prevents phagocytosis
  - Cryptococcus
- Ergot toxin
  - Claviceps
- Aflatoxin
  - Aspergillus
- Mycotoxins
  - Neurotoxins: Phalloidin, amanitin
    - Amanita

Pathogenic Properties of Protozoa

- Presence of protozoa
- Protozoan waste products may cause symptoms
- Avoid host defenses by
  - Growing in phagocytes
  - Antigenic variation (changing antigens)

Pathogenic Properties of Helminths

- Use host tissue
- Presence of parasite interferes with host function
- Parasite's metabolic waste can cause symptoms

Pathogenic Properties of Algae

- Neurotoxins produced by dinoflagellates
  - Saxitoxin
    - Paralytic shellfish poisoning
    - Can cause paralysis

Portals of Exit

Compare and contrast portal of entry and portal of exit.

- Respiratory tract
  - Coughing, sneezing
- Gastrointestinal tract
  - Feces, saliva
- Genitourinary tract
  - Urine, vaginal secretions
- Skin
- Blood
- Biting arthropods, needles/syringes

Mechanisms of Pathogenicity