CH 11

Interaction between Microbes and Humans
SLOs

1. Differentiate among the terms colonization, infection, and disease.
2. Enumerate the sites where normal biota is found in humans.
3. Discuss how the Human Microbiome Project is changing our understanding of normal biota.
4. Differentiate between a microbe’s pathogenicity and its virulence.
5. Define opportunism and list examples of common opportunistic pathogens.
6. List the steps a microbe has to take to get to the point where it can cause disease.
7. List several portals of entry and exit.
8. Define infectious dose, and explain its role in establishing infection.
9. Describe three ways microbes cause tissue damage.
10. Compare and contrast major characteristics of endotoxins and exotoxins.
11. Provide a definition of virulence factors.
13. Differentiate among various types of reservoirs, providing examples of each.
14. List several different modes of transmission of infectious agents.
15. Define healthcare-associated infection, and list the three most common types.
16. List Koch’s postulates, and discuss when they might not be appropriate in establishing causation.
17. Summarize the goals of epidemiology, and differentiate it from traditional medical practice.
18. Explain what is meant by a diseases being “notifiable” or “reportable,” and provide examples.
19. Define incidence and prevalence, and explain the difference between them.
20. Discuss the three major types of epidemics, and identify the epidemic curve associated with each.
11.1 The Human Host - HMP

• In health: Dynamic equilibrium with microbes
• Launched by NIH in 2007
• Mission: Generate resources and expertise needed to characterize the human microbiome and analyze its role in health and disease.
• Microbiome has much broader impact on our health than previously realized.

• Bioinformed Design
A map of diversity in the human microbiome

Streptococcus dominates the oral cavity with S. mitis > 75% in the cheek.

Propionibacterium acnes lives on the skin and nose of most people.

Many Corynebacterium species characterize different body sites:
  - C. matruchoti the plaque
  - C. accolens the nose
  - C. croppenstedtii the skin

Lactobacillus species (L. gasseri, L. jensenii, L. crispatus, L. iners) are predominant but mutually exclusive in the vagina.

Staphylococcus epidermidis colonizes external body sites.

Several Prevotella species are present in the gastrointestinal tract. P. copri is present in 19% of the subjects and dominates the intestinal flora when present.

Bacteroides is the most abundant genus in the gut of almost all healthy subjects.

Campylobacter includes opportunistic pathogens, but members live in the oral cavities of most healthy people in the cohort.

E. coli is present in the gut of the majority of healthy subjects but at very low abundance.

The four most abundant phyla:
- Actinobacteria
- Bacteroidetes
- Firmicutes
- Proteobacteria

Low abundance phyla:
- Chloroflexi
- Cyanobacteria
- Euryarchaeota
- Fusobacteria
- Lentisphaerae
- Spirochaetes
- Synergistetes
- Tenericutes
- Verrucomicrobia

Bar lengths indicate microbial abundance (colored by body site of greatest prevalence).

National Institutes of Health
Human Microbiome Project

Research funded by the National Institutes of Health (NIH) (U54 AI130194 and U01 AI133735) and the Massachusetts Institute of Technology (MIT), the Broad Institute, and the New York Genome Center.
• Human cells: How many protein-encoding genes?

• Microbiota: 8 million protein encoding genes

• Microbes found in locations previously thought to be sterile.

• All healthy people harbor potentially dangerous pathogen in low numbers.

• The makeup of one’s intestinal biota can influence overall health.

**Table 11.1 Sites Previously Known to Harbor Normal Microbiota**

<table>
<thead>
<tr>
<th>Skin and adjacent mucous membranes</th>
<th>External genitalia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract</td>
<td>Vagina</td>
</tr>
<tr>
<td>Gastrointestinal tract, including mouth</td>
<td>External ear canal</td>
</tr>
<tr>
<td>Outer portion of urethra</td>
<td>External eye (lids, conjunctiva)</td>
</tr>
</tbody>
</table>

**Additional Sites Now Thought to Harbor At Least Some Normal Microbiota (or Their DNA)**

<table>
<thead>
<tr>
<th>Lungs (lower respiratory tract)</th>
<th>Breast milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder (and urine)</td>
<td>Amniotic fluid and fetus</td>
</tr>
</tbody>
</table>

**Sites in Which DNA from Microbiota Has Been Detected**

<table>
<thead>
<tr>
<th>Brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloodstream</td>
</tr>
</tbody>
</table>
The Normal Microbiota (Flora)

= resident flora. Acquisition was thought to start during passage through birth canal. Current thinking?

Establishes permanent colonies on & inside body without producing disease. Protection of host via Microbial antagonism or ____________________________

• Limited number of attachment sites
• Chemical or physiological environment created by resident biota is hostile to other microbes.
Factors that weaken host defenses and increase susceptibility to infection?

_Name at least 5:_

1.
2.
3.
4.
5.
Pathogens cause infectious diseases

Steps of Infection:

1. Using a portal of entry – endogenous vs. exogenous pathogens
2. Attaching
3. Surviving host defenses
4. Causing disease
5. Exiting host through a portal of exit
Vocabulary

• Pathogenicity: ____________________________

• Virulence: ____________________________

• Virulence factors: ____________________________

• True or 1° pathogens vs. ____________________________ pathogens

• Infection: invasion and growth of pathogens in the body

• Disease: Abnormal state in which the body is not functioning normally.

• Etiology: ____________________________
Step One: Portals of Entry

Mucous membranes

• Conjunctiva
• **Respiratory tract**: Droplet vs. airborne
• **GI tract**: food, water, contaminated fingers
• **Genitourinary tract**

Skin

• Mostly impenetrable; possible to enter through hair follicles and sweat ducts.

Parenteral Route

➤ **Trauma** (*S. aureus, C. tetani*)
➤ **Arthropods** (*Y. pestis*)
➤ Injections
**Bacillus anthracis** has more than one portal of entry

<table>
<thead>
<tr>
<th>Portal of Entry</th>
<th>ID&lt;sub&gt;50&lt;/sub&gt;</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>

-ID for rickettsia: a single cell.
-ID for tuberculosis, giardiasis, and coccidioidomycosis: about 10 cells.
-ID for gonorrhea: 1,000 cells.
-ID for cholera is 1,000,000,000 cells.
Step Two: Attachment

**Adhesins:** surface projections on pathogen, mostly made of glycoproteins or lipoproteins. Adhere to complementary receptors on host cell. They can be part of:

- **Fimbriae**, also pili and flagella
- **Capsules**: *e.g.* *S. mutans*
- **Biofilms**
- **Spikes**
- **Mechanical devices** on worms
Step Three: Surviving Host Defenses

• Phagocytes = ?

• Antiphagocytic Factors:
  • Capsules (and slime layers) avoid phagocytosis
  • Leukocidins: kill phagocytes
  • Some bacteria survive inside the phagocyte.

Step Four: Causing Disease

Bacteria, fungi, protozoa, worms cause damage to their hosts via

1. Enzyme action
2. Toxins (endotoxins and exotoxins)
3. Excessive or inappropriate host defense
Enzymes

- **Coagulase**
  - Pathogens in blood vessel
  - Blood clot around pathogen

- **Streptokinase**
  - Dissolves clot and releases pathogens

- **Hyaluronidase**
  - Pathogens and epithelial cells
  - Basement membrane
  - Dissolves intracellular cement, allows pathogen to spread to deeper tissues
Toxins

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

**Endotoxins:** Gram- bacteria only. LPS, Lipid A part \Rightarrow released upon cell death. Symptoms due to vigorous inflammation. Massive release \Rightarrow endotoxic shock
Vocabulary related to Toxin Production

• **Toxin**: Substances that contribute to pathogenicity.

• **Toxigenicity**: Ability to produce a toxin.

• **Toxemia**: 

• **Toxoid**: 

• **Antitoxin**: 
### Exotoxins Summary

<table>
<thead>
<tr>
<th>Source:</th>
<th>Gram + and Gram -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relation to microbe:</td>
<td>By-products of growing cell</td>
</tr>
<tr>
<td>Chemistry:</td>
<td>_________</td>
</tr>
<tr>
<td>Fever?</td>
<td>No</td>
</tr>
<tr>
<td>Neutralized by antitoxin?</td>
<td>_________</td>
</tr>
<tr>
<td>LD&lt;sub&gt;50&lt;/sub&gt;:</td>
<td>Small</td>
</tr>
</tbody>
</table>

Circulate to site of activity. Affect body before immune response possible. Exotoxins with special action sites: **Neuro-**, **entero-**, and **nephrotoxins**, **hemolysins** ....
### Representative Examples of Exotoxins

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

- Bacterial cell death, antibiotics, and antibodies may cause the release of endotoxins.

- **Pyrogen**: Endotoxins cause **fever** by inducing the release of **interleukin-1**. Dramatic fall in blood pressure can lead to **shock** and death.
# Endotoxin Summary

Compare to Table 11.3

<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>____________________________</td>
</tr>
<tr>
<td>Fever?</td>
<td>Yes</td>
</tr>
<tr>
<td>Neutralized by antitoxin?</td>
<td>________</td>
</tr>
<tr>
<td>$\text{LD}_{50}$:</td>
<td>Relatively large</td>
</tr>
</tbody>
</table>
Warning Signals of Disease

**Symptoms** are subjective. Change in body function felt by patient as result of disease.

**Signs** are objective. Change that can be measured or observed. E.g.: ?

**Syndrome**: Group of signs and/or symptoms that accompany a disease.

**Signs & Symptoms of Inflammation:**

4 (5) cardinal signs:?
Signs of Blood Infections

- Leukocytosis

- Leukopenia

- Difference between septicemia and Bacteremia?

- Asymptomatic = subclinical = inapparent infections
Types of Infections

• Systemic vs. localized
• Focal
• Polymicrobial
• Primary vs. secondary
• Acute vs. chronic

Compare to Table 11.4
Step Five: Portals of Exit

Usually same as portal of entry, but some pathogens use different route.
Persistence of Microbes and Pathologic Conditions

• **Latency**: dormant state
  - Viruses: _________________________________
  - Bacteria/protozoa : Syphilis, typhoid fever, TB

• **Sequelae**: long-term or permanent damage to tissues or organs
  - Meningitis: deafness
  - Strep throat: rheumatic heart disease
  - Lyme disease: arthritis
  - Polio: paralysis
Disease Stages

Incubation period: Time interval between ......

Compare to Fig 11.7
Reservoirs: Where Pathogens Persist

Continual source of infectious agents

**Transmitters:** Individuals or objects from which infection is acquired

- Syphilis: reservoir and transmitter are the same
- Hepatitis A: reservoir is a human, transmitter is food

- **Zoonoses** make up 70% of new emerging diseases worldwide

*Compare to Table 11.5*
Aquisition and Transmission of Disease

How does disease behave in population?

• Contagious
• Communicable
• Non-communicable

Transmission Patterns:

• Horizontal vs. vertical

• Direct: Close association between infected and susceptible host. Touch, droplet, parenteral

• Indirect: Spread via fomites and vehicle transmission.

• Vector transmission
Vectors

Vector Transmission: **Arthropods** carry pathogens from one host to another. **Mechanical** vector vs. **biological** vector.
Healthcare-Associated Infections

- **Urinary tract**: 40%
- **Surgical sites**: 19%
- **Respiratory**: 15%
- **Other (meningitis, gastroenteritis)**: 12%
- **Skin**: 8%
- **Septicemia**: 6%

*Fig 11.8*: Use UPs
# Common Causes of HAIs

<table>
<thead>
<tr>
<th></th>
<th>Percentage of Total Infections</th>
<th>Percentage Resistant to Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>15%</td>
<td>89%</td>
</tr>
<tr>
<td>S. aureus</td>
<td>15%</td>
<td>80%</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>10%</td>
<td>4–71%</td>
</tr>
<tr>
<td>Gram-negative rods</td>
<td>15–25%</td>
<td>3–32%</td>
</tr>
<tr>
<td>C. difficile</td>
<td>13%</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Koch’s Postulates: Proof of Etiology of Infectious Diseases

1. The same pathogen must be present in every case of the disease

2. The pathogen must be isolated from the diseased host and grown in pure culture

3. The pathogen from the pure culture must cause the disease when it is inoculated into a healthy, susceptible lab animal

4. The pathogen must be isolated from the inoculated animal and must be shown to be the original microbe
**Table 11.9 Koch’s Postulates**

**Postulate #1**
Find evidence of a particular microbe in every case of a disease.

**Postulate #2**
Isolate that microbe from an infected subject and cultivate it in pure culture in the laboratory; perform full microscopic and biological characterization.

**Postulate #3**
Inoculate a susceptible healthy subject with the laboratory isolate and observe the same resultant disease.

**Postulate #4**
Reisolate the same agent from this subject.
Exceptions to Koch’s Postulates

Modification of Koch’s postulates were necessary

1. to establish disease etiology for viruses and bacteria, which cannot be grown on artificial media

2. Certain pathogens, such as HIV, cause disease in humans only or have a very narrow host range

3. Some diseases, e.g.: pneumonia and nephritis, may be caused by polymicrobial infections.

4. Some pathogens, such as S. pyogenes, cause different diseases in different hosts.
For each of the descriptions below, determine if it pertains to an exotoxin or an endotoxin.

- Toxic in minute amounts
- Causes systemic effects such as fever and inflammation
- Released by a cell via shedding or during lysis
- Composed of small proteins
- Composed of lipopolysaccharide
- Can be converted into a toxoid

Click A for Exotoxin and B for Endotoxin
11.3: Epidemiology: The Study of Disease in Populations

Tracking Disease in the Population: Reportable or notifiable diseases

- Certain diseases must be reported to authorities.
- Other diseases are reported on a voluntary basis.

• **Nationally notifiable diseases**: Physicians are required to report occurrence. *(also Table 11.10)*

• Morbidity vs. mortality rates
Frequency of Cases

**Prevalence**: How much of a disease is in population

\[
\text{Prevalence} = \frac{\text{Total # of cases in population}}{\text{Total # of persons in population}} \times 100 = \%
\]

**Incidence**: Rate of occurrence of new cases

\[
\text{Incidence} = \frac{\text{# of new cases in a designated time period}}{\text{Total # of susceptible persons}}
\]

(Usually reported per 100,000 persons)
More Key Epidemiological Terms

• **Index case:** 1\(^{st}\) found in epidemiological investigation.
  – May not be 1\(^{st}\) case of disease
  – first case of the disease = _____________________________

• **Sporadic:** _____________________________

• **Endemic:** Constantly present at _________________

• **Epidemic:** Widespread at given time and in given area

• **Pandemic:** _____________________________

*Look at Fig 11.11*
Inside the Clinic: **Fecal Transplants**

The End