CHAPTER 7
PRINCIPLES OF DISEASE

WHY IS THIS IMPORTANT?

- How diseases are caused (etiology), how they can be characterized, and the concepts of sepsis and shock are important for developing an in-depth understanding of infections.
- It is important to understand the differences between normal microbial flora and abnormal or infectious microbial organisms.

WHY IS THIS IMPORTANT?

- Understanding how diseases develop will help you to understand the communicability and contagiousness of microorganisms.
- Understanding the etiology of a disease is critical to understanding the progression of disease into systemic circulation.
OVERVIEW

USEFUL DEFINITIONS

- A disease is any negative change in a person’s health.
- Etiology is the cause of a disease.
- Normal microbial flora are the useful microorganisms found in the body.

COMMON TERMS FOR DESCRIBING INFECTION
NORMAL MICROBIAL FLORA

<table>
<thead>
<tr>
<th>Region of the Body</th>
<th>Representative Microorganisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Staphylococcus aureus, Streptococcus spp., Propionibacterium acnes, Candida spp., and Corynebacterium species</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>Staphylococcus aureus, Staphylococcus epidermidis, and Corynebacterium species</td>
</tr>
<tr>
<td>Nose and throat</td>
<td>Staphylococcus aureus and Staphylococcus epidermidis in the nose; Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus, Corynebacterium, and Nocardia species in the throat</td>
</tr>
<tr>
<td>Mouth</td>
<td>Streptococcus species, Lactobacillus, and Corynebacterium</td>
</tr>
<tr>
<td>Large intestine</td>
<td>Lactobacillus, Enterococcus, Escherichia coli, Enterobacter, Proteus, Klebsiella, and Corynebacterium species</td>
</tr>
<tr>
<td>Urogenital tract</td>
<td>Staphylococcus epidermidis, Enterococcus, Lactobacillus, Paracolonella, Klebsiella, and Proteus in the urethra; Lactobacillus, Streptococcus, and Staphylococcus in the vagina</td>
</tr>
</tbody>
</table>

HOST-MICROORGANISM RELATIONSHIPS

<table>
<thead>
<tr>
<th>Type of Relationship</th>
<th>Microorganism</th>
<th>Host</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commensalism</td>
<td>Benefits</td>
<td>Neither benefits nor is harmed</td>
<td>Saprophytic bacteria that live off sloughed-off cells in the ear and external genitalia</td>
</tr>
<tr>
<td>Mutualism</td>
<td>Benefits</td>
<td>Benefits</td>
<td>Bacteria in colon</td>
</tr>
<tr>
<td>Parasitism</td>
<td>Benefits</td>
<td>is harmed</td>
<td>Tuberculosis in lungs</td>
</tr>
</tbody>
</table>

HOST RELATIONSHIPS

- Microbial flora can protect us through microbial antagonism.
- Many bacteria produce bacteriocins which are localized bacterial antibiotics.
- Bacteriocins can kill invading organisms but do not affect the bacteria that produce them.
HOST RELATIONSHIPS

- Opportunistic pathogenicity occurs when normal flora become pathogenic.
  - *E. coli* is part of the normal flora of the digestive tract but can cause infection if it enters the urinary tract.

THE ETIOLOGY OF DISEASE

- Etiology is the cause of disease.
- Proof of etiology can be found using Koch’s postulates.
  - Allow us to identify the cause of a disease.

THE ETIOLOGY OF DISEASE

- In some cases, Koch’s postulates cannot be used because some organisms cannot be grown in pure culture:
  - *Treponema pallidum* (syphilis)
  - *Mycobacterium leprae* (leprosy)
  - Viruses and rickettsial organisms
FIVE PERIODS OF DISEASE

- Incubation period – the time between the initial infection and the first symptoms. The more virulent the pathogen, the shorter the incubation time.
- Prodromal period – when the first mild symptoms appear.
FIVE PERIODS OF DISEASE

- Period of illness – when the majority of symptoms manifest and when the immune response is at its highest level.
- Period of decline – when symptoms subside. During the period, secondary nosocomial infections can occur of a nature more serious than the original infection.
- Period of convalescence – when the patient actively regains strength and returns to health.

DEVELOPMENT OF DISEASE

COMMUNICABLE AND CONTAGIOUS DISEASES

- Some diseases are communicable.
  - They can spread from one person to another.
- Some diseases are not communicable.
  - They cannot spread from one person to another and simply remain within the infected host.
- Some communicable diseases are easily spread from person to person and these are referred to as being contagious.
  - They spread very easily through contact with an infected person.
COMMUNICABLE & CONTAGIOUS DISEASES: Three Methods of Control

First method – Isolation:
- It prevents an infected individual from having contact with the general population
- There are seven categories of isolation
- Patients are usually isolated in hospital
- Can be difficult to achieve as it cannot be imposed until firm diagnosis

Second method – Quarantine:
- Exposed humans or animals are separated from the general population
- Lasts as long as the incubation period for the disease in question
- If there are no longer any symptoms, the quarantine is lifted
- Rarely used today because it is difficult to enforce

Third method – Vector Control:
- It is used to control the population of vectors, such as mosquitoes, that carry pathogens.
DURATION OF DISEASE

- Disease duration can vary depending on the overall health of the host.
- There are four categories of disease duration:
  - Acute diseases develop quickly and last only a short time e.g. measles.
  - Chronic diseases develop slowly but last for a long time e.g. tuberculosis.
  - Sub-acute diseases have an insidious onset (usually 6 to 12 months) and are almost always fatal e.g. sclerosing panencephalitis.
  - Latent diseases remain in the host after the symptoms disappear and can become reactivated years later e.g. chicken pox/shingles.

PERSISTENT BACTERIAL INFECTIONS

- Some pathogenic bacteria are capable of maintaining infections in hosts, even in the presence of inflammatory and specific antimicrobial mechanisms as well as a perfectly good immune response.
- Persistent bacterial infections are treated with specific antimicrobial therapy.

Examples of persistent bacterial infections include:
- *Mycobacterium tuberculosis* (causes tuberculosis)
- *Salmonella enterica* (causes typhoid fever)
- *Helicobacter pylori* (causes stomach and duodenal ulcers)
- *Neisseria gonorrhoeae* (causes gonorrhea).
TUBERCULOSIS (TB)

- TB is one of the oldest known diseases and affects one-third of the world's population.
- The infection starts at a site in a lung and can move throughout the lung, possibly via host defense cells.
- Most people resolve the infection after the onset of the adaptive immune response.

Some hosts become persistently infected and harbor the pathogen for life.
- It can then be reactivated later in life, with reactivation usually associated with a diminished immune response.
- In persistent TB, the pathogen is found inside granulomas.

Granulomas are composed of host defensive cells including:
- Macrophages, T cells, B cells, dendritic cells, neutrophils, and fibroblasts.
- Granulomas form as activated macrophages and aggregate into gigantic cells similar to the syncytia seen in viral infections.
TUBERCULOSIS (TB)

- How pathogens survive in a macrophage is not completely understood.
  - They may “remodel” the phagocytic vesicle.
  - They do prevent formation of phagolysosomes.

TYPHOID FEVER

- Typhoid fever is caused by *Salmonella enterica* serovar Typhi and can cause a variety of problems in the intestinal tract.
  - It begins as a localized infection that eventually becomes systemic.
  - The localized infection elicits an inflammatory reaction.
**TYPHOID FEVER**

- The pathogen infects macrophages in the lamina propria of the intestine and can then gain access to the blood and the lymph.
- Once the infection is the blood and lymph, it can spread to the liver and spleen and can become persistent in the gall bladder and bone marrow.
- Typhoid fever is difficult to treat because the level of antibiotic resistance is rising.

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**TYPHOID FEVER**

- One in six people who contract typhoid fever will become carriers and shed off large numbers of the pathogens in their stool and urine.
- *Salmonella* organisms are phagocytozed by the host cell defenses but are not destroyed.
PATHOGENS USE SPECIFIC MECHANISMS TO SURVIVE HOST DEFENSES

- *Mycobacterium* and *Salmonella* prevent formation of the phagolysosome.
- Some pathogens:
  - produce enzymes that destroy antimicrobial toxins produced by the host to prevent infection.
  - form megasomes inside host cells which prevent the host enzymes from reaching the pathogens.
  - block the adaptive immune response of the host.
  - use genetic changes to confuse the host defenses.

HERD IMMUNITY

- Herd immunity is an important concept in limiting the spread of infection.
- It is conferred to people through vaccination or if they are naturally exposed to the infection and prevents re-infection by the same pathogen.
- When a majority of a population (herd) is immune to an infection there are very few potential hosts and the disease essentially disappears.
- Good examples of herd immunity are polio and smallpox.

HERD IMMUNITY

- Herd immunity for polio is high.
  - The polio vaccine is routinely administered to children so there are few targets available for infection.
- Herd immunity for smallpox is low.
  - Smallpox has been putatively wiped out worldwide.
  - As a result, no one is vaccinated for this infection anymore except for the military.
  - Since vaccinations have ceased, the number of people immune to smallpox is low and there are many potential targets available for infection.
HERD IMMUNITY

THE SCOPE OF INFECTIONS

- Infections can be localized.
  - A local infection is contained (walled off) such as a boil or an abscess.
  - Local infections are the easiest to deal with medically.

- Infections can be systemic.
  - Systemic infections occur when pathogens move away from the initial infection location (also known as the focus of infection).
  - This movement is usually associated with the blood or the lymphatic system.
**TERMS RELATED TO SYSTEMIC INFECTIONS**

- Bacteremia – bacteria in the blood
- Septicemia – bacteria growing in the blood
- Toxemia – toxins in the blood
- Viremia – viruses in the blood

**THREE TYPES OF SYSTEMIC INFECTION**

- Primary – the initial infection which has acute onset of symptoms.
- Subclinical – no symptoms are visible even though the person is infected
  - These people are carriers of the disease and can infect others.
- Secondary – seen in people that are already weakened from a primary infection and can be more dangerous.

**TOXIC SHOCK AND SEPSIS**

- Toxic shock and sepsis are two different clinical situations that can result from infection.
- Toxic shock is a massive leakage of plasma from the circulatory system.
  - This causes a dramatic drop in blood pressure (hypotension)
  - It is fatal for 30–70% of patients
  - It is caused when neutrophils come in contact with M proteins.
TOXIC SHOCK AND SEPSIS

- Sepsis is a general term referring to the presence of the pathogen or toxin in the blood.
- There are two forms of sepsis:
  - Severe sepsis
  - Acute septic shock

TOXIC SHOCK AND SEPSIS

- Severe sepsis is characterized by systemic inflammation and organ dysfunction.
  - It is accompanied by abnormal temperature, heart rate, respiratory rate, and white blood cell count.
  - It induces elevated numbers of liver enzymes and altered cerebral function.
  - Severe sepsis kills slowly over a period of weeks with minimal tissue inflammation or damage.

TOXIC SHOCK AND SEPSIS

- Acute septic shock has a sudden onset and death occurs in 24 to 48 hours.
  - It causes widespread tissue inflammation and cell damage.