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

Principles of Disease

THE RELATIONSHIP BETWEEN THE HUMAN HOST AND MICROORGANISMS
THE ETIOLOGY OF DISEASE
DEVELOPMENT OF DISEASE
THE SCOPE OF INFECTIONS

USEFUL DEFINITIONS

- A disease is any damage to the host (patient)
- Etiology is the cause of a disease
- Normal microbial flora (the microbiota of humans) are the useful microorganisms found in the body

COMMON TERMS FOR DESCRIBING INFECTION
THE HUMAN MICROBIOME

- Humans are ecosystems, called a superorganism
- In a healthy adult microbial cells can make up as much as five pounds of adult body weight
- The human microbiome:
  - Includes the microbes inhabiting us, their genetic information (called metagenome), and the environment in which they interact
  - Affects our development, physiology, immunity, and nutrition

NORMAL MICROBIAL FLORA

HOST-MICROORGANISM RELATIONSHIPS
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

HOST RELATIONSHIPS

- The microbiome composition
  - Varies from person to person
  - Naturally depends on the site of the body
  - Fluctuates due to dietary change, seasonal change, hormonal change, and exposure to antibiotics
  - Possibly imparts susceptibility to certain infectious diseases
  - Could contribute to obesity, diabetes, atherosclerosis, autism, allergies, and asthma, chronic gastrointestinal diseases, can affect response to drug treatment, and even choice of partner
  - The delivery mode and the mother’s microbiome may affect the child’s microbiota and health
MICROBIOME OF VARIOUS ANATOMICAL SITES

MICROBIOME IN NEWBORNS

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

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, we need to adapt the tests when using Koch’s postulates in our modern times, 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 – first mild symptoms appear.

FIVE PERIODS OF DISEASE

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

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

COMMUNICABLE & CONTAGIOUS DISEASES: Three Methods of Control

- 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
COMMUNICABLE & CONTAGIOUS DISEASES: Three Methods of Control

◆ 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 6–12 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
PERSISTENT BACTERIAL INFECTIONS

- Examples of persistent bacterial infections include:
  - *Mycobacterium tuberculosis* (causes tuberculosis)
  - *Salmonella enterica* serovar Typhi (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
**TUBERCULOSIS (TB)**

- 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

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**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

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 nitric oxide as it is produced by the host
  - Form megasomes inside host cells which prevent the host enzymes from reaching the pathogens
  - Block the adaptive immune response of the host
  - Use genetic diversity to confuse the host defenses

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

THE SCOPE OF INFECTIONS

- 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 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 bacterial surface proteins such as 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

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

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