Host-Microbe Relationships

There are four biologic interrelationships of living organisms:

1. **independence** - Two different organisms living independently of each other.

   The other three involve two or more different organisms living together and they are collectively referred to as *symbiosis* ("living together").

2. **mutualism** - Both organisms benefit from the relationship. *E. coli* live in the large intestines which provides them nutrients. The *E. coli* synthesizes vitamin K which is used to make some blood-clotting factors. Other bacteria synthesize B-complex vitamins.

3. **commensalism** - One organism is benefitted and the other is neither benefitted nor harmed. Many organisms live on the skin and use secretions for metabolic activities.

4. **parasitism** - One organism, which is the parasite, is benefitted, and the other, which is the host, is harmed. Parasites living in tissues or cells are referred to as endoparasites. Many helminths are endoparasites. *Ectoparasites* live on the surface and receive nutrients from blood or tissues. Mites and lice are ectoparasites.

Normal Flora or Microbiota

Bacteria and other microorganisms that live on or in the body, but do not cause disease are known as *normal flora* or *normal microbiota*.

There are two types of normal flora:

1. **resident flora or indigenous microbiota** - They grow and reproduce and persist throughout life because they are adapted to life in or on the human body. They are found on the skin, outer covering of the eye or conjunctiva, and on the mucosal membranes of the mouth, nose, throat, large intestine, urinary tract, and reproductive tract.

2. **transient flora or microbiota** - They are not permanent residents and are not well enough adapted to live in or on the human body to persist indefinitely. They are often found on exposed areas of the skin or taken in with air or food. They may survive for days, weeks, or months, and are eliminated by washing the skin, secretions from the skin or mucosal membranes, or by resident flora.
Among the resident and transient flora are some species that do not usually cause disease, but can do so under certain circumstances such as a weakened immune system, stress, injury, surgery, malnutrition, or the use of broad-spectrum antibiotics (act against a wide variety of bacteria). These microorganisms are called opportunists because they take advantage of particular opportunities to cause disease. Nosocomial infections acquired during hospitalization are caused by opportunistic pathogens.

Development of Disease

The invasion or colonization of the body by a disease-causing organism, called a pathogen, is known as an infection. When an infection results in any change from the normal state of good health and interrupts the normal functioning of the body it is known as a disease. An infection may exist in the absence of detectable disease. Changes in body functions (pain, malaise) which are subjective and not apparent to an observer are known as symptoms. Signs are objective changes that a physician can observe and measure. A specific group of signs and symptoms that always accompany a particular disease is a syndrome. A disease caused by pathogens that can be transmitted and produce infection is an infectious disease.

The manner in which a disease originates and develops is called pathogenesis ("disease origin"). The ability of an organism to produce an infectious disease is pathogenicity. The degree of pathogenicity of an organism is called virulence (full of poison).

Virulence differs between organisms and has two properties:

1. invasiveness - The ability to invade host tissues, survive the host’s defense mechanisms, multiply, and spread.

2. toxigenicity - The ability to produce substances that are toxic to host cells and tissues.

The severity of an infectious disease and the resulting damage indicates the virulence of the pathogen as well as the ability of the host to defend against invasion and toxicity.

Pathogens gain access to the body through portals of entry such as the skin and mucous membranes, sexual transmission (genitourinary tract), ingestion with food or water (gastrointestinal tract), inhalation of air (respiratory tract), direct deposit beneath the skin (parenteral), or insect bites (blood). Portals of exit are usually the same as the portals of entry.

If only a few microorganisms enter the body, they will probably be overcome by the host’s defense mechanisms. The probability of infection is expressed as the ID₅₀ (infectious dose), or the number of microorganisms that must enter the body to establish infection in 50% of test or experimental animals.
The virulence of a microorganism or the potency of its toxin is expressed as the LD₅₀ (lethal dose), or the number of microorganisms that must enter the body and cause death in 50% of test or experimental animals.

Once pathogens gain entry to a host, they must have a means of attaching themselves to host tissues and it is known as adherence. The attachment occurs between surface molecules on the pathogen called adhesins and surface receptors on the cells of the host tissues. Adhesins may be found on the capsule or fimbriae of bacteria and consist of glycoproteins or lipoproteins.

Many factors may be involved in invasiveness of pathogens. Some pathogens can cause damage on the surface of tissues, but most must penetrate tissues to cause disease. The presence of a capsule or surface proteins on the cell wall or fimbriae resist phagocytic activity of the host’s leukocytes. Capsules and surface proteins interfere with the cell-to-cell contact that is necessary for phagocytosis.

As bacteria grow and reproduce they may produce extracellular substances, many of which are enzymes, that aid in invasiveness.

The substances include:

1. **leukocidins** - They can destroy leukocytes that are active in phagocytosis.

2. **hemolysins** - They cause lysis of erythrocytes and the iron released is used by the bacteria to grow and reproduce.

3. **hyaluronidase or spreading factor** - It is produced by streptococci and digests hyaluronic acid which is a polysaccharide that holds cells together in certain tissues. The streptococci can then pass between cells of connective tissues and invade deeper tissues.

4. **collagenase** - It is produced by bacteria such as Clostridium. It destroys collagen which is a major structural protein in connective tissue such as bone, skin, and cartilage. It allows the spread of microorganisms from the initial site of infection.

5. **streptokinase** and **staphylokinase** - They are produced by streptococci and staphylococci respectively. They dissolve fibrin in blood clots which were formed as a defense mechanism of the body to prevent the spread of the bacteria.

6. **coagulase** - It is produced by bacteria such as Staphylococcus aureus and it causes coagulation of plasma which produces a fibrin clot. It walls off the organism from host defense mechanisms such as that found in abscesses.
Bacteria also produce toxins which are involved in their toxigenicity.

There are two types of toxins:

1. **endotoxins** - They are part of the cell wall in gram-negative bacteria and are released when they die and the cell walls lyse. Endotoxins consist of the Lipid A portion of the lipopolysaccharides of the cell wall. Endotoxins cause chills, fever, blood vessel damage, which may cause hemorrhaging, body aches, weakness, general malaise, and in some cases, shock (severe drop in blood pressure) and death.

2. **exotoxins** - They are proteins which are released by many gram-positive and a few gram-negative bacteria during growth and metabolism. Exotoxins are among the most lethal substances known and they act by destroying parts of cells or by inhibiting certain metabolic functions.

There are three major types of exotoxins:

a. **cytotoxins** - They kill host cells or affect their functions (scarlet fever).

b. **neurotoxins** - They interfere with normal nerve impulse conduction of the nervous system (Clostridium which causes botulism or tetanus).

c. **enterotoxins** - They affect cells lining the intestinal tract (E. coli, S. aureus, and Shigella which cause diarrhea, dysentery, or vomiting).

Toxoids, which are altered forms of the exotoxins that can no longer produce disease, may be injected into the body. The body then produces antibodies, called antitoxins, which provide immunity to the exotoxin.