

Host-microbe relationships and disease process

TERMS

- Parasitism** – relationship ; one organism benefits the other is harmed
- Mutualism** – relationship : both organisms benefit
- Commensalism** – relationship: one organism benefits, the other is unaffected
- Systemic** – body wide
- Pathogen** - microbe able to produce disease
- Disease** – host tissues affected
- Infection** – microbe overcomes host defense/barriers
- Virulence** – degree of potency
- Carrier:** host with microbe, but no symptoms
- Etiologic Agent:** microbe responsible for disease
- Opportunists** – low to moderately virulent pathogen: if able to gain access it will
Cause disease
- Saprophyte** – microbe that uses dead material (i.e. yeast)
- Communicable** – transmission between hosts occurs
- Disease reservoir-** natural source of the microbe: environment, carriers, infected,
Animals
- Antigen** – molecule capable of producing an immune response
- Host** - is an organism that harbors another organism.
- Symbiosis** - -means “living together”

Contamination, Infection, and disease

Contamination refers to the presence of microorganisms.

Infection, pathogens invade the body

Disease, pathogens or other factors disturb the state of health such that the body can not perform its normal functions.

Infestation refers to the presence of worms or arthropods in or on the body.

Pathogens, Pathogenicity, and Virulence

Pathogenicity is the capacity of a pathogen to produce disease.

The seven capabilities of a Pathogen

A successful pathogen must be able to do most or all of the following:

- a. Maintain a reservoir
- b. leave its reservoir and enter a host-transmission
- c. adhere to the surface of the host-attachment
- d. invade the body of the host
- e. evade the body's defenses
- f. multiply within the body.
- g. leave the body and return to its reservoir or enter a new host.

One: Maintaining a Reservoir

A disease reservoir is a place where pathogens are maintained between infections.

A human serving as a reservoir of infection is a carrier. An incubatory carrier is an apparently healthy individual who may be in the earliest, symptomless stages of the disease. A chronic carrier is someone who harbors a pathogen for months or years. Most animal reservoirs provide an environment similar to that of the human host. A human disease caused by a pathogen that maintains an animal reservoir is called a zoonosis.

Animal reservoirs can profoundly affect the pattern of human disease, leading in some cases to a pandemic.

Some pathogens survive in water, soil, and house dust.

Two: Getting to and entering a host

Disease transmission takes place when a pathogen leaves a reservoir and enters the body of a host.

The portal of entry for a pathogen is where it enters the host's body. The most common portals of entry are the same anatomical surfaces colonized by microbiota.

The ID₅₀ (infectious dose) is the number of microorganisms that must enter the body to establish infection in 50 percent of test animals.

The LD₅₀ (lethal dose) is the number of microorganisms that must enter the body to cause death in 50 percent of test animals.

Modes of transmission are categorized as contact between **humans (direct or indirect), vehicles (inanimate objects), and vectors (living transmitters, usually arthropods)**. Droplets of respiratory secretions are transmitted directly from one host to another through sneezing, coughing, or speaking. More human diseases are transmitted this way than by any other.

Fomites are inanimate **objects** such as eating utensils, towels, bedding, and handkerchiefs that transmit disease. Hand washing can break the transmission cycle. Direct body contact takes place by touching, kissing, or sexual intercourse. Sexually transmissible disease (STD) is spread by direct mucous membrane contact.

Vertical transmission is transmission of pathogens from mother to infant.

It can be prenatal or perinatal (occurring in the birth canal or immediately after birth). In the fecal-oral route, pathogens are transmitted from infected feces to the mouth of a new host. Fecal-oral transmission can be direct hand-to-hand or hand-to-mouth, by vehicles such as water, food, and fomites or by vectors.

Arthropods can be mechanical vectors, carrying pathogens on their bodies, or biological vectors, an essential link in the transmission of a disease because the microorganism spends part of its cycle in the arthropod host.

Airborne transmission occurs when microorganisms that can survive in air are inhaled. In parenteral transmission, pathogenic microorganisms are deposited directly into blood vessels or deep tissues. This occurs when a biological vector bites through the skin or when intravenous drug users share needles.

Deep wounds can allow anaerobic pathogens such as *Clostridium tetani* (which cause tetanus) to enter.

Air born: in mucus, dust. Can survive dry conditions
Oral: microbe on food, water, objects, insects, eg. Fecal-oral
Endogenous: from one part to another of same host, eg. Hand-mouth
i.e. Mouth, GI, respiratory tracts to open wounds
Intestinal bacteria into urethra → urinary infection
Oral microbes in eyes from licking contact lenses

Contact:

Direct: new host touches infected individual, blood, body fluids
i.e. sexual transmission, insect bites (vector living), nosocomial
(hospital), eg. Blood born

Indirect: new host touches infected inanimate object – Fomite (vehicle –
Non-living)
i.e. Tables, tools, equipments, tissues, play things

Three; Adhering to a body surface

Pathogens – like the body's normal biota – adhere to a body surface by means of adhesion on their pili or surface.

Attachment

Tissue Trophism: many bacterial and viral diseases are tissue specific
Receptor Mediated Endocytosis

Pilli:

Surface proteins that attach microbe to host tissues and cells

Four: Invading the body

Most pathogens are invasive. They enter host cells or tissues. A few are noninvasive. They remain on the surface.

Invasive pathogens that enter host cells to live are called intracellular pathogens. The cell provides a nutrient-rich environment safe from body defenses.

In the 1880s Robert Koch proved the germ theory of disease, that a particular microorganism causes a particular infection.

We still use **Koch's postulates** in certain cases today to prove the cause of an infectious disease.

KOCH'S POSTULATES

Koch's Postulates provide a way to link a pathogen with a disease.

1. A specific causative agent must be observed in every case of a disease.
2. the agent must be isolated from a host displaying the disease and grow in pure culture.
3. When the agent from the pure culture is inoculated into an experimental healthy, susceptible host, the agent must cause the disease.
4. The agent must be reisolated from the inoculated, diseased experimental host and identified as the original specific causative agent.

When Koch's Postulates are met, an organism has been proved to be the causative agent of an infectious disease.

We use **Rivers' postulates** to determine the etiology of viral infections.

1. The viral agent must be found either in the host's body fluids' at the time of disease or in infected cells.
2. The viral agent obtained by the host must produce the disease in a healthy animal or plant or must produce antibodies.
3. Viral agents from the newly infected animal or plant must in turn transmit disease to another host.

Five: Evading the body's defenses

Some pathogens have capsules that keep a phagocyte from establishing direct contact. Strains of *Streptococcus pneumoniae* without capsules are avirulent (harmless), Those with the thickest capsules are the most virulent.

Surface proteins on pathogens also keep phagocytes from establishing contact.

Streptococcus pyogenes, which causes strep throat, produces M protein.

Some pathogens, such as *Mycobacterium tuberculosis*, survive inside the phagocyte.

Phagocytes that evade nonspecific body defenses encounter the body's immune defenses. The immune system recognizes pathogens by means of markers on their surface called antigens.

Some pathogens change their surface antigens to avoid recognition (antigenic variation).

Some attack antibodies directly with enzymes called IgA proteases. Some use serum resistance, features on the bacteria surface that interfere with the host's defensive complement system.

Some pathogens obtain iron by producing iron-binding compounds called siderophores.

Six: Multiplying in the host.

The two most common forms of bacterial pathogenesis are production of toxins and damage caused by stimulation of the body's defense.

Exotoxins are highly destructive **soluble proteins** produced by both **Gram-positive and Gram-negative bacteria**. Most exotoxins are composed of two units, the A (active) unit and the B (binding) unit, and are highly specific.

Endotoxin is the lipopolysaccharide (LPS) component of the **outer membrane** of **Gram-negative** bacteria. It enters host tissue during division or after cell death.

It acts by stimulating human cells to secrete particular messenger proteins. For example, fever results when endotoxin stimulates white blood cells to secrete the protein interleukin.

Endotoxin is generally not very potent. Some pathogens produce extracellular enzymes. They are three types: cytolytins attack cell membranes; hemolysins lyse red blood cells; leukocidins lyse leukocytes.

The body defenses that fight off pathogens can disrupt body function in ways that cause disease. *Streptococcus pneumoniae*, for example, multiplies in the lungs and summons great numbers of phagocytes. As dead cells of both kinds accumulate, normal gas exchange is impaired and breathing becomes difficult.

Some pathogens stimulate hypersensitivity, an exaggerated immune response that causes damage.

Some viral infections are cytotoxic (they kill cells), whereas others are cytopathic (they damage but do not kill the cell).

Lytic infections kill the host cell by lysing it.

A persistent viral infection can last for years, producing new virus particles without killing the infected cells. In a latent viral infection, the virus lies dormant within the host cell, not producing new viral particles. Latent infections can last a lifetime and not be damaging unless the virus is reactivated.

Inclusion bodies are collections of viral components such as protein and nucleic acid.

Oncogenic viruses establish latent infections in human cells that transform the infected cells into cancer cells. Only a few virally caused cancers have been definitely established.

Seven: leaving the body

The anatomical route through which a pathogen leaves the body of its host is called its portal of exit.

For most respiratory pathogens, the portal of exit is the same as the portal entry, the nose. For most gastrointestinal pathogens, the portal of exit is the anus. Most sexually transmissible disease exit the same way they entered, through the genital mucous membranes. Pathogens transmitted parenterally by arthropod vectors exit the same way, in a small amount of blood.

Virulence is the intensity of a disease caused by a pathogen. It can increase by **animal passage**. Rapid transfer of the pathogen through animals of a species susceptible to infection. Each newly infected animal suffer more seriously after few passages due to the microbes becomes better able to damage the host.

Attenuation is **weakening** of a pathogen's disease-producing capacity.

Transposal of Virulence is a lab technique in which a pathogen is passed from its normal host to a new host species and then passed sequentially through many individuals of the new host species. Eventually, the pathogens is no longer virulent of the original host.

Normal (Indigenous) microflora

A baby begins to acquire its normal microbiota as it passes through the birth canal, but it can also be infected if pathogens are present, even though the mother shows no symptoms.

Normal microflora (normal flora) are microorganisms found in or on the body that do not normally cause disease. Normal biota inhabit only the surface of our bodies: the skin and the conjunctivae; the nasopharynx; and the mouth, intestinal tract, vagina ,and urethra.

Factors that determine the Normal Biota

Our microbiota survive because they are adapted to life on living tissue.

Structural, mechanical, and biochemical features of body surfaces constitute nonspecific surface defense, the body's first line of defense against infection. They are nonspecific because they are against all pathogens.

1).Structural defense are our epithelial surfaces, the skin and the conjunctivae, and the interior surfaces, which are mucous membranes. The normal sloughing of epithelium as it grows is another structural defense. When the dead cells are lost, the microbes on them are also lost

2).Mechanical defenses – movements – eliminate many transient microorganisms from body surfaces. Some surfaces move because of the action of underlying muscles. The mucociliary system protects by cilia moving a layer of mucus. Urine washes microorganisms out of urethra. Tears wash microorganisms off the conjunctivae.

3).Biochemicals that inhibit microbial growth include keratin, which keeps the skin surface dry; stomach acid and fatty acids, which lower the pH; and lysozyme and bile, which kill some microbes.

Site of Normal biota

The Skin

Skin Biota are mainly Staphylococcus spp., diphtheroids, or fungi.

Staphylococcus spp., which are facultative anaerobes, include the pathogen Staphylococcus aureus and the opportunist **Staphylococcus epidermis**.

Diphtheroids include the anaerobes Propionibacterium acnes, which cause acne.

Fungi on the skin include yeasts belonging to the genus pityrosporum, which use fats as a substrate for growth and grow on oily areas on the face, scalp, chest, and back.

The mite Demodex folliculorum lives on the face, within hair follicles and in the openings to oil glands.

The Conjunctivae

The conjunctivae are defended by their continuous and relatively impermeable surface and by tears.

Among the few species found at this site are Staphylococcus spp. And diphtheroids.

The Nasal cavity and Nasopharynx

Microbiota of the nasal cavity and nasopharynx are particularly well adapted to adhere because of the mucociliary system.

The same species that colonize the skin are found in these densely colonized sites. They include Staphylococcus epidermis, Staphylococcus aureus, diphtheroids, Lactobacillus spp., and Moraxella catarrhalis.

The Mouth

The mouth is a warm, moist environment with abundant nutrients. It is a densely populated with microorganisms. Streptococci predominate before teeth erupt and thereafter are present in smaller numbers.

This complex microbial population is stable and consists largely of commensals. One exception is Streptococcus mutans, which cause tooth decay.

The Intestinal Tract

The first intestinal tract evacuations in a newborn are germ-free.

The esophagus, stomach, and upper intestine are too inhospitable to sustain a normal biota. Peristalsis and stomach churning keep the region nearly germ-free.

In the lower intestine, intestinal movement is less vigorous. A complex microbial community develops there.

The majority of species in the lower intestine are strict anaerobes belonging to the genera Bacteroides, Bifidobacterium, Fusobacterium, and Clostridium.

Facultative anaerobes include the Enterobacteriaceae (such as Escherichia) and lactobacillus spp.

The Vagina

The vagina is a warm, moist, protected environment. When influenced by estrogen, it becomes acidic with the growth of lactobacilli. When estrogen is not being produced, it is alkaline and more prone to infections.

Aerobic anaerobic species colonize this site, including the fungus candida albicans, which can cause opportunistic infections.

The Urethra

Only the outermost part of the urethra, where the mucous membranes meet the skin, supports a microbiota.

The normal biota is scant, but usually enterococci and Staphylococcus epidermis are present on the outer part of the urethra.

Is Normal Biota helpful or harmful?

The benefits of normal biota probably outweigh possible harmful effects.

Research has yielded no proof of even subtle harm.

The most significant beneficial effect of microbiota derives from microbial antagonism.

Microbiota also stimulate our immune system in a nonspecific way. Some intestinal bacteria provide supplemental sources of vitamin K and B₁₂.

If our relationship with microorganisms is altered, pathogens can established themselves in underpopulated areas or normally harmless commensals can proliferate and cause opportunistic infections.

Categorizing microorganisms as harmful or harmless is not always clear-cut.

The host's state of health often determines whether disease occur.

Microorganisms exist along a continuous spectrum of disease-causing potential.

Today, because of advanced medical technology, more people die from infection by opportunists than by true pathogens.

Tissue	Normal flora	Common Pathogens
Skin	Staphylococcus epidermidis (colonize dead squamous cells)	Staphylococcus aureus Streptococcus Propionibacterium acnes (sebaceous glands)
Respiratory tract	S. epidermidis, S. aureus Branhamelia catarrhalis	Haemophilus influenzae Strep pyrogenes

		Strep pneumoniae Neisseria meningitidis
Mouth	Haemophilus, Lactobacillus Neisseria, Staph, Strep	Opportunists
Stomach	Non- pH 2 inhibits bacterial growth	Helicobacter pylori
Gastrointestinal Tract	Escherichia, Klebsiella, Enterobacter, Proteus, Candida albicans (yeast)	Opportunists
Genitourinary Tract	Bladder/Ureter/Kidney – none Lower urethra: Candida albicans, Staph, Ectero cocci	Opportunists

Resident microflora are those organisms that are always present on the body like **intestine**.

Transient microflora are those present temporarily and under certain conditions.

Opportunists are resident or transient microflora that can cause disease under certain conditions or in certain locations in the body.

KINDS OF DISEASES

Infectious and Noninfectious Diseases

Infectious disease are caused by infectious agents; **noninfectious diseases** are caused by other factors.

Classification of Diseases

Although many diseases are caused by noninfectious agents, some of these diseases may be associated with an infectious agent.

Communicable and Noncommunicable Diseases

A **communicable or contagious, infectious disease** can be spread from one host to another.

A **noncommunicable infectious disease** cannot be spread from host to host and may be acquired from soil, water, or contaminated foods.

How Bacterial Pathogen Penetrates Host Defense

1. **Capsule:** prevent them from phagocytized.
2. **Components of the Cell wall:** protein in the cell wall can facilitate adherence or preventing a pathogen from being phagocytized.
3. **Enzymes**
4. **Antigenic Variation:** can avoid the host's antibodies.
5. **penetration into host cytoskeleton**

THE DISEASE PROCESS

How Microbes cause disease

Many microbes have **virulent factors** that enable the establishment of infections. These factors include adhesion molecules, enzymes, and toxins.

Direct Actions of Bacteria

1). Bacteria cause disease by **adhering** to a host. **Adhesins** are proteins or glycoproteins found on attachment pili and capsules.

2). **Colonizing** and/or invading host tissues, and sometimes by invading cells. The ability of a pathogen to invade and grow in host tissues, called **invasiveness**, is related to particular virulence factors.

Hyaluronidase from Streptococci can digest hyaluronic acid that helps hold the cells and tissues together. It helps bacteria invade tissues.

3). **Release toxins** Bacteria release other substances, most of which damage host tissues.

Hemolysins lyse red blood cells in cultures and may or may not directly cause tissue damage in the host. Bacteria can use **Iron** from hemoglobin for their metabolism.

Leukocidins destroy neutrophils.

Coagulase accelerates blood clotting.

Streptokinase digests blood clots and helps pathogen spread to body tissues. It is used to dissolve blood clots in the arteries around heart.

Bacterial Toxins

Many bacteria also produce **toxins**.

Endotoxins are part of the cell wall of **Gram-negative** bacteria and are released when cells divided or are killed. Patient can die of severely reduced blood pressure – endotoxic shock.

Exotoxins are more powerful and produced by and releases from bacteria.

1). **Hemolysins** can lyse red blood cells, **Alpha-hemolysins** can partially break down hemoglobin and produce a greenish ring around colonies. **β-hemolysins** can completely break down hemoglobin and leave a clear ring around the colonies. Bacteria use the **iron** release from hemoglobin for their own metabolism.

2). **Leukocidins** can damage neutrophils and macrophages. **Leukostatin** interferes with the ability of leukocytes to engulf microorganism.

3) **Neurotoxins** if they effect the nervous system. Like **Botulinum toxin** release from Clostridium botulinum in food poisoning.

4). **Enterotoxins** if they affect the digestive system like in cholera.

5). **Toxoids** are inactivated exotoxins that retain antigenic properties and are used for immunization.

How Viruses Cause Disease

Viruses damage cells and produce a variety of observable changes called the **cytopathic effect (CPE)**.

A **productive infection**; leads to the release of virus progeny

Abortive infection does not produce infectious progeny.

Latent Viral Infection: are characteristics of herpes-virus, for example. Chickenpox occur during childhood, the virus may retreat into the nervous system and dormant for many years. Later in life, factors such as stress or other infections can reactivate the virus appears as shingles.

Persistent Viral Infection: involve a continued production of viruses over many years. The hepatitis B virus (HBV) infects the liver in a chronic way can lead to cirrhosis and liver cancer.

How Fungi, Protozoa, and Helminths cause disease

Pathogenic fungi can invade and progressively digest cells, and some produce toxins. Protozoa and helminthes damage tissues by ingesting cells and tissues fluids, releasing toxic wastes, and causing allergic reactions.

Sign, Symptoms, and Syndromes

A **sign** is an observable effect of a disease. A **symptom** is an effect of a disease felt by the infected person. A syndrome is a group of signs and **symptoms** that occur together.

Sequelae: even after recovery, some diseases leave after effects.

Portals of exit

Three common portals of exit are the respiratory tract via coughing, sneezing, the GI tract via saliva or feces, and the urogenital tract via secretion from the vagina or penis.

Arthropods and syringes provide a portal of exit for microbes in blood.

Types of Infection Disease

Acute disease: develops rapidly

Chronic disease: develops slowly

Subacute disease: between acute and chronic

Latent disease: periods of inactivity before symptoms

Local infection: confined to a specific area

Focal infection: confined to a specific area, but their toxins can spread to other areas.

Systemic infection: affects most of the body

Bacteremia – bacteria in blood but not multiply

Septicemia –bacteria in blood and multiply

Viremia: virus in blood but not multiply

Toxemia: toxins in blood

Primary infection: initial infection in a healthy person

Secondary infection: follows a primary infection

Superinfection: Secondary infection caused by an agent resistant to the treatment of the primary infection

Mixed infection: infection caused by two or more pathogens

Inapparent infection: fails to produce full set of signs and symptoms

Stages of Infectious disease

The incubation period is the time between infection and the appearance of signs and symptoms of a disease.

The prodromal phase is the stage during which pathogens begin to invade tissues; it is marked by early nonspecific symptoms.

The invasive phase is the period during which the individual experiences the typical signs and symptoms of the disease. During this phase the signs and symptoms reach their greatest intensity known as the **acme**. **Fulminating**: sudden and severe.

The **decline phase** is the stage during which host defenses overcome pathogens; signs and symptoms subside during this phase, and secondary infections may occur.

The **convalescence period** is the stage during which tissue damage is repaired and the patient regains strength. Recovering individuals may still transmit pathogens to others.