FUNDAMENTAL OF INFECTIOUS DISEASE

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Module Overview

This module fosters an understanding of the basic principles of infectious disease in the context of One Health. The module will use a One Health approach to examine various important zoonotic infectious diseases of humans and animals and help students to understand fundamentals of infectious disease spread and their impact on daily life.

Module Competencies

Competencies#1	Learning Objectives to Develop Competencies
Describe the fundamental concepts of infectious diseases.	a) Describe the etiology and epidemiology of important infectious diseases b) Compare the pathology, pathogenesis, clinical manifestations, and treatment of various infectious diseases c) Apply fundamental concepts to develop a One Health approach to control and prevention of an infectious disease d) 4) Design a One Health approach for health promotion related to infectious diseases at a community level
Competencies#2	**Learning Objectives to Develop Competencies**
Interpret the fundamentals of infectious diseases and the impact of daily life.	a) Identify and classify the types of infectious diseases influencing a given local area in humans and animals
Competencies#3	**Learning Objectives to Develop Competencies**
Integrate the respective elements of fundamental concepts of infectious disease	a) Understand all components of the “system” for an infectious disease with downstream effects b) 2) Describe how various stakeholders are involved in an infectious disease and how they may be impacted by the disease

A. CLASSIFICATION OF ORGANISMS THAT CAUSE INFECTIOUS DISEASE

The agents that cause disease fall into five groups: viruses, bacteria, fungi, protozoa, helminths (worms) and prions. Protozoa and worms are usually grouped together as parasites, and are the subject of the discipline of parasitology, whereas viruses, bacteria, and fungi are the subject of microbiology.

A.1. Bacteria

Bacteria are single-celled organisms that lack a nucleus. They are responsible for a wide range of human diseases, including:

a. Tuberculosis, a chronic lung disease that is a major cause of disability and death in many parts of the world.
b. Staphylococcal disease, which can affect almost every organ system. Severity ranges from a single pustule of impetigo, through pneumonia, arthritis, endocarditis, etc., to sepsis and death.
c. Chlamydia and gonorrhea, the most widespread sexually transmitted diseases. d. Tetanus and diphtheria, two diseases that were once major public health problems but are now well controlled through immunization.
d. Other vaccine-preventable diseases caused by bacteria are:
   - Pertussis
   - Hemophilic influenza type b (Hib)
   - Pneumococcal disease.

A.2. Virus

Viruses are very small, consisting of an RNA or DNA core and an outer coat of protein. They can reproduce and grow only inside of living cells. Many viral illnesses are significant to public health, including:

a. Influenza, a respiratory illness that contributes to development of pneumonia and occurs in annual epidemics during the winter months
b. HIV (human immunodeficiency virus), that causes Acquired Immunodeficiency Syndrome (AIDS). This severe, life-threatening pandemic disease has spread worldwide within the past 20-30 years.
c. Rabies that is spread to humans from animal bites or scratches. Rabies is almost always fatal in humans but is preventable by a vaccine.
d. Measles, mumps, rubella, and poliomyelitis are all well controlled in the US through immunization.

A.3. Protozoa

Protozoa are single-cell organisms with a well-defined nucleus. Some of these are human parasites. Examples of diseases cause by protozoa include:

a. Malaria, a mosquito-borne disease that is one of the top three infectious diseases in the world (along with tuberculosis and HIV).
b. Giardiasis, an infection of the upper small intestine that causes a diarrheal illness. Outbreaks can be difficult to control, especially in child care settings
c. Toxoplasmosis, transmitted to humans from cats and undercooked meat. When this systemic disease infects a pregnant woman, it can cause the death of the fetus.
d. Pneumocystis carinii pneumonia or PCP, which is often fatal, especially in people with compromised immune systems such as those infected with HIV.

A.4. Fungi

Fungi are nonmotile, filamentous organisms that cause diseases that can be very difficult to treat. Some examples important to public health are:

a. Histoplasmosis, transmitted by inhaling dust from soil that contains bird droppings. The severity varies widely, with the lungs the most common site of infection.
b. Candidiasis, transmitted by contact with human patients and carriers. This fungus causes lesions on the skin or mucous membranes, including "thrush" and vulvovaginitis. Symptoms can be severe in immuno compromised people.

A.5. Prions

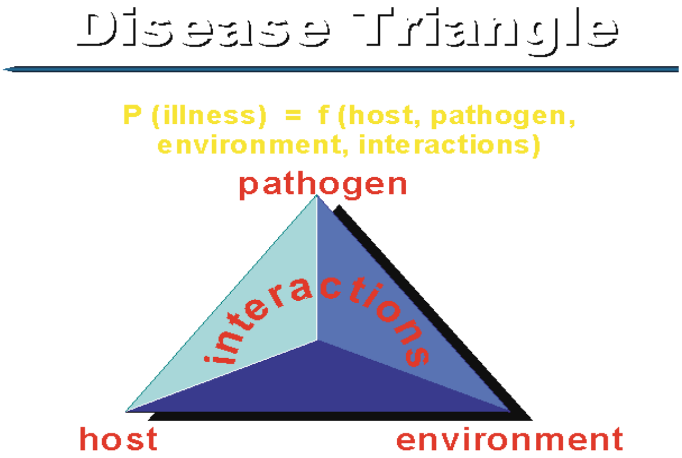
Prions are infectious agents that do not have any genes. They seem to consist of a protein with an aberrant structure, which somehow replicates in animal or human tissue. Prions cause severe damage to the brain. Diseases associated with prions include:

a. CWD, chronic wasting disease of mule, deer and elk;
b. BSE, bovine spongiform encephalopathy in cows; and
c. CJD, Creutzfeld-Jacob disease in humans.

B. HOST PATHOGEN RELATIONSHIP

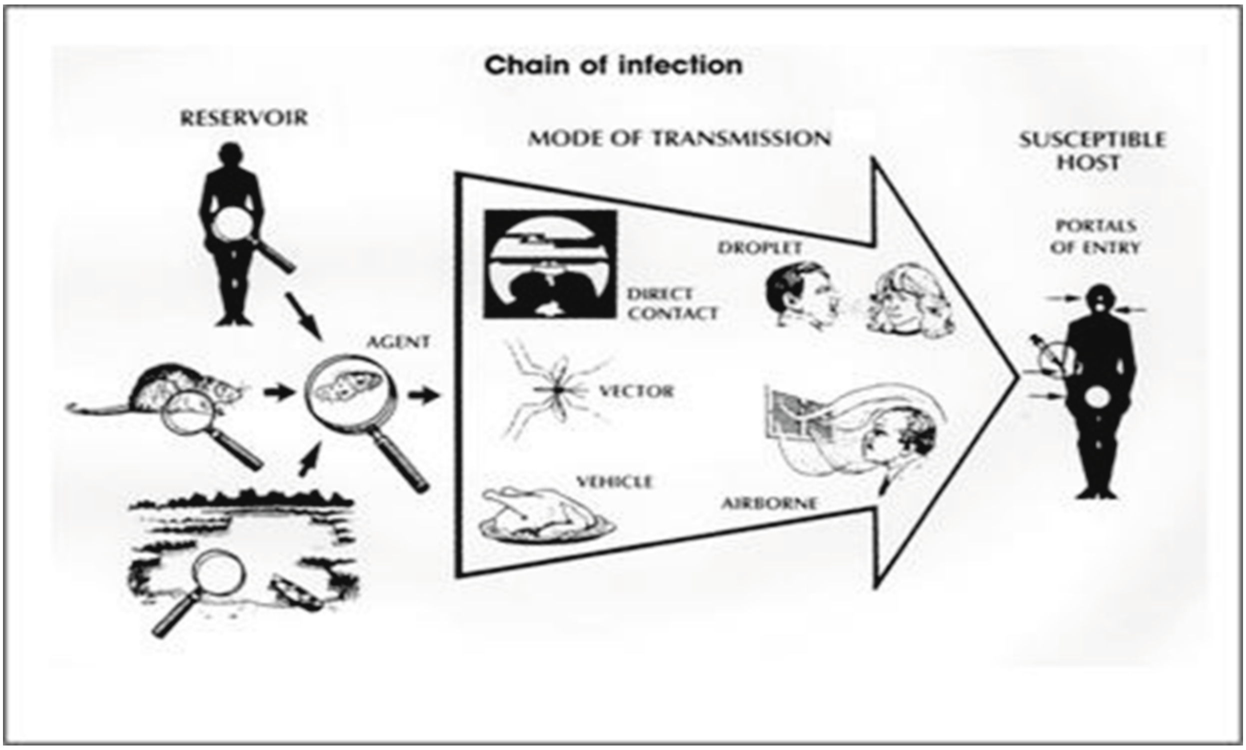
Over the years, pathologists have come to learn that disease development in a plant population is determined primarily by the interactions among three major factors. These are: the presence of a susceptible host plant, the presence of a virulent pathogen, and a favorable physical, chemical, and biological environment. Or conceptually, these interactions dictate that if either the host is less susceptible, the pathogen is less virulent, or the environment is less favorable, diseases will either occur at a reduced level, or they will not occur at all. The interactions among these factors have been traditionally conceptualized in the form of a disease triangle.

Disease transmission is a process that involved of environments, animals and people – is that for disease to occur, there must be the right mix of environmental conditions, a host that is susceptible and a pathogen capable of inciting disease. If any one of these is not present, disease will not occur.



The host must be susceptible to attack by the pathogen. The pathogen must be able to attack the host. The environment must favour the development of the pathogen.

As described above, the epidemiologic disease triangle model holds that infectious diseases result from the interaction of agent/pathogen, host, and environment. But more specifically, transmission occurs when the agent/pathogen leaves its reservoir or host through a portal of exit, is conveyed by some mode of transmission, and enters through an appropriate portal of entry to infect a susceptible host. This sequence is sometimes called the chain of infection.



B.1. Reservoir

The reservoir of an infectious agent is the habitat in which the agent normally lives, grows, and multiplies. Reservoirs include humans, animals, and the environment.

B.2. Portal of exit

Portal of exit is the path by which a pathogen leaves its host. The portal of exit usually corresponds to the site where the pathogen is localized. For example, influenza viruses and *Mycobacterium tuberculosis* exit the respiratory tract, schistosomes through urine, cholera vibrios in feces, *Sarcoptes scabiei* in scabies skin lesions, and enterovirus 70, a cause of hemorrhagic conjunctivitis, in conjunctival secretions. Some blood borne agents can exit by crossing the placenta from mother to fetus (rubella, syphilis, toxoplasmosis), while others exit through cuts or needles in the skin (hepatitis B) or blood-sucking arthropods (malaria).

B.3. Modes of transmission

An infectious agent may be transmitted from its natural reservoir to a susceptible host in different ways. There are different classifications for modes of transmission. Here is one classification:

- Direct
  - Direct contact
  - Droplet spread

In direct transmission, an infectious agent is transferred from a reservoir to a susceptible host by direct contact or droplet spread.

Direct contact occurs through skin-to-skin contact, kissing, and sexual intercourse. Direct contact also refers to contact with soil or vegetation harboring infectious organisms. Thus, infectious mononucleosis (“kissing disease”) and gonorrhea are spread from person to person by direct contact. Hookworm is spread by direct contact with contaminated soil.

Droplet spread refers to spray with relatively large, short-range aerosols produced by sneezing, coughing, or even talking. Droplet spread is classified as direct because transmission is by direct spray over a few feet, before the droplets fall to the ground. Pertussis and meningococcal infection are examples of diseases transmitted from an infectious patient to a susceptible host by droplet spread.

- Indirect
  - o Airborne
  - o Vehicleborne
  - o Vectorborne (mechanical or biologic)

Indirect transmission refers to the transfer of an infectious agent from a reservoir to a host by suspended air particles, inanimate objects (vehicles), or animate intermediaries (vectors).

Airborne transmission occurs when infectious agents are carried by dust or droplet nuclei suspended in air. Airborne dust includes material that has settled on surfaces and become resuspended by air currents as well as infectious particles blown from the soil by the wind. Droplet nuclei are dried residue of less than 5 microns in size. In contrast to droplets that fall to the ground within a few feet, droplet nuclei may remain suspended in the air for long periods of time and may be blown over great distances. Measles, for example, has occurred in children who came into a physician's office after a child with measles had left, because the measles virus remained suspended in the air.

Vehicles that may indirectly transmit an infectious agent include food, water, biologic products (blood), and fomites (inanimate objects such as handkerchiefs, bedding, or surgical scalpels). A vehicle may passively carry a pathogen — as food or water may carry hepatitis A virus. Alternatively, the vehicle may provide an environment in which the agent grows, multiplies, or produces toxin — as improperly canned foods provide an environment that supports production of botulinum toxin by *Clostridium botulinum*.

Vectors such as mosquitoes, fleas, and ticks may carry an infectious agent through purely mechanical means or may support growth or changes in the agent. Examples of mechanical transmission are flies carrying *Shigella* on their appendages and fleas carrying *Yersinia pestis*, the causative agent of plague, in their gut. In contrast, in biologic transmission, the causative agent of malaria or guinea worm disease undergoes maturation in an intermediate host before it can be transmitted to humans.

B.4. Portal of entry

The portal of entry refers to the manner in which a pathogen enters a susceptible host. The portal of entry must provide access to tissues in which the pathogen can multiply or a toxin can act. Often, infectious agents use the same portal to enter a new host that they used to exit the source host. For example, influenza virus exits the respiratory tract of the source host and enters the respiratory tract of the new host. In contrast, many pathogens that cause gastroenteritis follow a so-called "fecal-oral" route because they exit the source host in feces, are carried on inadequately washed hands to a vehicle such as food, water, or utensil, and enter a new host through the mouth. Other portals of entry include the skin (hookworm), mucous membranes (syphilis), and blood (hepatitis B, human immunodeficiency virus).

B.5. Susceptible Host

The final link in the chain of infection is a susceptible host. Individuals who are likely to develop a disease after exposure to the infectious agents are called susceptible hosts. However, susceptibility of a host depends on several risk factors, such as poor personal hygiene, or poor control of reservoirs of infection in the environment, genetic, and specific immunity. Some people in a community are more likely to develop the disease than others, even though they all have the same exposure to infectious agents. This is due to a low level of immunity within the more susceptible individuals. Low levels of immunity could be due to: diseases like HIV/AIDS which suppress immunity, poorly developed or immature immunity, as in very young children not being vaccinated, poor nutritional status (e.g. malnourished children) and pregnancy.

C. HOST DEFENSE MECHANISM

As mentioned above, susceptibility of a host depends on several factors includes host defences mechanism. Host defense that protect against infection includes:

The human body has several general mechanisms for preventing infectious diseases.

C.1. Nonspecific mechanisms

Nonspecific mechanisms are the body's primary defense against disease. These mechanisms include anatomical barriers to invading pathogens, physiological deterrents to pathogens, and the presence of normal flora. An example of an anatomical barrier is the nasal opening to the respiratory system. This natural opening is a long, convoluted passage covered by mucous membranes that trap airborne particles and prevent most of them from reaching the lungs. Other anatomical barriers are the skull and vertebral column, which protect the central nervous system- few pathogens are able to penetrate bone. The skin also is a major anatomical barrier to microorganisms. The surface layer of dead, hardened cells is relatively dry, and skin secretions make the surface somewhat acidic. When sweat evaporates, salt is left behind on the skin. All of these conditions (low moisture, low pH, and high salinity) prevent most microorganisms from growing and multiplying on the skin. The major medical challenge in treating burn patients is preventing and treating infections that result because of the absence of skin that ordinarily would prevent invasion of microorganisms.

Natural openings also are protected by a variety of physiological deterrents. For example, tears continually flush debris from the eyes. Vaginal secretions are acidic, a hostile environment that discourages the growth of many pathogens. The eye, mouth, and nasal openings are protected by tears, saliva, or nasal secretions that contain lysozyme, an enzyme that breaks down bacterial cell walls. Blood, sweat, and some tissue fluids contain lysozyme as well.

In addition to lysozyme, the blood has many elements that defend the body from disease-causing organisms. The white blood cells include several types of phagocytic cells that detect, track, engulf, and kill invading bacteria and viruses, as well as infected host cells and other debris. These phagocytic cells are part of the nonspecific immune system. Blood plasma also includes clotting factors that initiate a clot at the injury site, preventing pathogens from invading the body further. Finally, the complement proteins in the blood participate in a cascade of molecular events that result in inflammation, the release of molecules that stimulate phagocytic cells, and the formation of a complex of proteins that binds to the surface of bacterial or infected host cells and lyses those cells.

The inflammatory response is another nonspecific defense mechanism that helps prevent infectious agents from spreading in the body. Inflammation involves swelling, reddening, elevated temperature, and pain. Unfortunately, inflammation itself frequently causes tissue damage and, in severe cases, even death.

Finally, the protective role of the "normal flora" of microorganisms present on and in the body should not be overlooked. These organisms survive and grow on the skin and in the mouth, gastrointestinal tract, and other areas of the body, but do not cause disease because their growth is kept under control by the host's defense mechanisms and by the presence of other microorganisms. These organisms protect the host by successfully competing with disease-causing organisms, preventing the latter from invading host tissues. When the growth of the normal flora is suppressed (for example, due to antibiotic treatment), other "opportunistic" agents that normally do not grow in or on the body may be able to infect and cause disease.

C. 2. Specific mechanisms of host resistance

When these nonspecific mechanisms fail, the body initiates a second, specific line of defense. This specific immune response enables the body to target particular pathogens and pathogen-infected cells for destruction. It depends on specialized white blood cells called lymphocytes and includes T-cells (produced from lymphocytes that matured in the thymus gland) and B-cells (produced from lymphocytes that matured in the bone marrow).

The two complementary components of the specific immune response are the cell-mediated response and the antibody-mediated response (Figure 5). The cell-mediated response involves T-cells and is responsible for directly destroying body cells that are infected with a virus or have become cancerous, or for activating other immune cells to be more efficient microbe killers. The antibody-mediated response involves both T-cells and B-cells and is critical for the destruction of invading pathogens as well as the elimination of toxins.

Both the cell-mediated and antibody-mediated responses are initiated after a particular type of phagocytic cell, a macrophage, engulfs a pathogen. Macrophages digest the pathogen and then display antigens from the pathogen on their surface. Antigens are specific molecules, such as the proteins on the surface of pathogens that elicit an immune response. This display helps the macrophages stimulate specific helper T-cells to release signal molecules called lymphokines. The lymphokines, in turn, stimulate the cell-mediated and antibody-mediated responses.

The cell-mediated response occurs when the lymphokines released from the helper T-cells stimulate other cell types to participate in the immune response. Lymphokine-stimulated killer T-cells attach to the pathogen-infected cells and destroy them, whereas lymphokine-activated phagocytic cells produce more toxic molecules that can kill the pathogen directly.

The antibody-mediated response occurs when the lymphokines activate specific B-cells to produce antibodies (proteins that specifically recognize and bind to antigens). These antibodies attach to antigens on the surface of the pathogens and signal attack by phagocytic cells and complement system. Other B-cells go on to become memory B-cells, which respond quickly by producing more antibodies upon subsequent infection.

C. 3. Immunity

When a host encounters an antigen that triggers a specific immune response for the second or later time, the memory lymphocytes recognize it and quickly begin growing and dividing, as well as producing high levels of lymphokines and antibodies. Because memory cells are present, this response happens much more quickly than in the initial encounter with the antigen. This rapid response explains why hosts are immune to developing many diseases a second time: The immune response occurs so quickly in a second encounter with the pathogen that the pathogen does not have enough time to reproduce to levels that result in disease before the host's body has destroyed it. The memory response also explains the effectiveness of vaccination for preventing even the first occurrence of many diseases.

C. 4. Vaccination

A vaccine is either a killed or weakened (attenuated) strain of a particular pathogen, or a solution containing critical antigens from the pathogen. The body's immune system will respond to these vaccines as if they contain the actual pathogen, even though the vaccine is not capable of causing the disease. As a result of the specific immune response, memory lymphocytes will be present that respond rapidly when the actual pathogen is encountered. The resulting rapid activation of immune cells prevents disease.

Currently new types of vaccines, the DNA vaccines, are in early stage trials. These vaccines contain genes that encode proteins from pathogens. When these genes are inserted into host cells and are expressed in the form of pathogen proteins, an immune reaction may result.

> The ultimate effectiveness of vaccination-eradication of the infectious agent-has been achieved only for smallpox. The World Health Organization has identified the polio and measles viruses among the next targets for global eradication.

For a variety of reasons, many diseases are not easily prevented by vaccination. Antibody response is generally the simplest to induce by vaccination, but some pathogens have ways to evade the immune response. Intracellular pathogens (such as viruses and some bacterial and protozoan pathogens) are not directly affected by antibodies because antibodies cannot pass inside cells. Moreover, during the disease process, some pathogens acquire an external coat composed of host-derived material while others disguise themselves by making molecules that resemble host molecules. Thus, the host's immune system does not identify them as foreign invaders. Still other pathogens mutate quickly, producing variants of their antigens that are not recognized by the host's immune system, even though the host survived a previous encounter with that pathogen. Cold and influenza viruses are examples of rapidly mutating pathogens. Scientists are working to improve vaccines against these pathogens.

D. INFECTIOUS DISEASE AND DAILY LIFE

EXERCISE#1

Discussion

Daily activities for: ***Individual***: ▪ Food preparation ▪ Eating and serving food ▪ Care of pets ▪ Interaction with other animals ▪ Personal hygiene ▪ Interaction with other people	***Family***: ▪ Sharing meals and food preparation ▪ Care of children and elders ▪ Cleaning ▪ Celebration of events	***Community***: ▪ Food markets ▪ Restaurants and prepared food ▪ Gatherings – religious, celebrations

How do daily activities impact infectious disease transmission

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