

The viral pathogenesis refers to ability of viruses to cause diseases. The viral pathogenesis involves the following stages :

Stages of viral pathogenesis :

1. Transmission of virus from external source and entry into host.
2. Attachment of virus to host cell.
3. Replication of virus in target cell and damage to it.
4. Spread of the virus to other cells and organs.
5. Evasion of immune response.
6. Persistence and shedding of virus in some instances.

Sources of infection :

Main sources of infection are ;

1. Human : is common source of infection from patients or carriers. The carrier is person recovered from disease but harboring virus in his body. Fomites are inanimate objects of patients that may be contaminated and serves as source of infection. The infectious agent is transmitted from person to person by various ways such as direct contact, kissing, inhalation of aerosols, faecal-oral, venereal contact and arthropod-spread.
2. Animals :The animals can be serve either the source (reservoir)or made transmission (vector)of certain organism. The disease is called zoonosis. The virus can be transmitted from infected animals to human when direct contact with animals, and handling or consumption of their products ,or transmitted indirectly by bite of vectors.
3. Food: the foods are most important media for transporting the viruses to human during consumption of contaminated food, and therefore act as food-borne infection.
4. Water: many viruses may be found in water. The infectious agents are transmitted to human by consumption of water or when swimming in it , therefore act as water-borne infection.

Transmission and Portal of entry :

• Portals of entry(routes of infection) :

Major :

1. Respiratory tract(nose).
2. Elementary tract(mouth).
3. Skin, non-intact.
4. Genital tract(vagina).

Minor :

1. Eye.
2. Anus.
3. Ear canal.
4. Urethral canal.

• Mode of transmission :

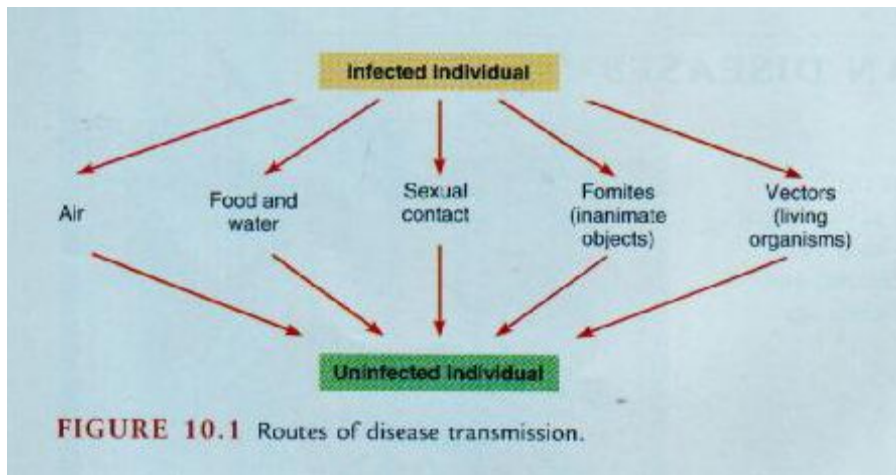
The intervening agents of transmission that bring viruses from source to human may be living entity, in which case they are called vectors(such as animals, insects, others) or they may be non-living entity referred to as vehicles(such as water, food, air, medical devices and various other inanimate objects) or fomites that harbor and transmit pathogen to host.

• Horizontal transmission :

1. Inhalation : the pathogenic agents may be transmitted by inhalation of respiratory secretions of patients, or by inhalation of contaminated dust (air-borne) .
2. Ingestion: the infectious agents can be transmitted by consumption (during eating or drinking) of contaminated water or food.
3. Skin : The transmission from person to person may occur through direct contact (such as handshaking, kissing)with infected person , or during handling of fomites of patients. The virus can be introduced into the skin through any small break, abrasion, and wound in skin that permit entry or during injection or blood transfusion. The transmission from infected animal to human also can take place either directly from bite of reservoir animal host, or indirectly through the bite of insect vectors.
4. Sexual intercourse: certain viruses can be transmitted by sexual contact in homosexual or heterosexual persons.

• Vertical transmission (from mother to her fetus):

The infection of fetus can occur between mother and offspring across the placenta (prenatal) ,or at time of delivery from birth canal (perinatal), or during breast feeding(postnatal) .



Attachment of virus :

The viruses tend to exhibit cell and organ specificities (cell tropism). The viral affinity for specific body tissue is dependent on :

1. Presence of specific cellular receptors on cell surface which interact with virus, and initial infection.
2. Ability of host cell to support viral replication . Factors affecting viral gene expression are important determinants of cell tropism.
3. Physical barriers ,local temperature , pH, oxygen tension are very important in tissue tropism. Another mechanism dictating tissue tropism involves proteolytic enzymes ,certain viruses (such as paramyxoviruses) are not infectious until an envelope glycoprotein undergoes proteolytic cleavage.

Viral replication and dissemination: The viruses replicate and produce diseases at site of entry or at site distant from their point of entry. In other word, the viral infections are either localized on the portal of entry or spread systemically through the body .The best example of localized infection is common cold , which involves only the upper respiratory tract. The influenza virus is localized primarily to upper and lower respiratory tracts. One of the best system viral infection is poliomyelitis (caused by poliovirus) . The poliovirus spread from small intestine to CNS and cause damage to anterior horn cells resulting in muscle paralysis.

After primary replicate at site of entry , then the virus spread within body of the host from local replication to target cells . Mechanism of viral spread vary , the most common route is via blood stream , lymphatics or nerves. The presence of virus in blood stream is called viremia.

Evasion of host defenses: The viruses have several ways by which they evade our host defenses:

1. Some viruses (such as: vaccinia virus and fibroma virus) encode some proteins act as receptors for immune mediators such as interferon (IFN) and tumor–necrosis factor (TNF). When the virus released from virus-infected cell , these proteins bind to immune mediators and block their ability to interact with receptor on their intended target . Because reducing host defense, the virulence of virus is enhanced. These virus-encoded proteins that block host immune mediators are called **cytokines decoys**.
2. Some viruses (such as HIV and CMV) can reduce the expression of class-1 MHC protein . Thereby reducing the ability of cytotoxic T-cell to kill virus-infected cell. Other viruses (e.g.: herpes virus) inhibit complement . Several viruses (HIV, Epstein-Barr virus=EBV , adenovirus) reduce the ability of IFN to block viral replication. These viral virulence factors are called **virokines**.
3. Some viruses (such as rhinovirus, influenza , HIV ,HCV) have **multiple antigenic types** (multiple serotypes). The patient can be infected with one serotype , recover , and have antibodies that protect from infection by that serotype in future , however , that person can be infected by other serotypes of virus.

Most viruses have one serotype , some have several serotypes such as rhinovirus which has more than 100 serotypes , this is the reason why the common cold by this virus is common.

Damage of host cell :

Multiplication of virus in host cell lead to disease. The time between exposure to virus and onset of disease is called incubation period .

The mechanisms of viral diseases are various:

1. Most viral diseases are result of cell death by shutoff macromolecules synthesis ,or by lysis of the cell membrane by lysozymes during viral replication.
2. Stimulate cellular cytokines .For example, diarrhea caused by rotavirus , the rotavirus-infected cells (enterocytes) produce cytokines that stimulate the enteric neuron , resulting in excess fluid and electrolytes secretion into the bowel lumen.
3. Immunological attack. Both the cytotoxic T-cell and antibodies play a role in immunopathogenesis. Example , the HAV, HBV, and HCV , they don't cause a cytopathic effect and the damage to hepatocytes is result of recognition of viral antigens on hepatocyte surface by cytotoxic T-cell.

Persistent viral infection: in most viral infection, the virus does not remain in the body for significant period after clinical recovery. In certain, the viruses persist for long periods either intact or in form of subviral component (eg: genome).

Three types of persistent viral infections:

1. Chronic infection: some patients who have infected with some viruses continue to produce significant symptoms of disease and significant amount of virus for long period.
2. Latent infection: some patients recover from initial infection and virus production stops. But the patients harboring the virus in their bodies (remain as carriers) without produce symptoms.
3. Slow virus infections: some infections require to long period between initial infection and onset of disease, which are usually measured in years (such as Kuru disease, and HIV).

The mechanisms that may play a role in persistence of viruses include:

1. Integration of provirus into chromosome of host cell without viral replication, as occur in retroviruses.
2. Spread from cell to cell without extracellular phase , so that is not exposed to immune response .
3. Occurrence of rapid antigenic variation in some viruses .
4. Location of virus within immunological sheltered e.g. : brain.
5. Immune tolerance may occur in some patients, because neutralizing antibodies are not formed.
6. Some patients suffer from immunosuppression , as in AIDS.

Virus shedding: The last stage in pathogenesis is the shedding of infectious virus into environment. The shedding usually occurs from the body surface involved in viral entry. The shedding occurs at different stages of disease dependent on particular agent involved.

In some infections such as rabies, human represent dead-end infection, and shedding does not occur.