Pathogenesis and Transmission

Lec 4

Introduction

- **Pathogenesis is the process by which virus infection leads to disease**
- **Pathogenic mechanisms include implantation of the virus at a body site**
  - **the portal of entry**
  - **replication at that site**
  - **and then, spread to and multiplication within sites (target organs) where disease or shedding of virus into the environment occurs**
- **Most viral infections are subclinical, suggesting that body defenses against viruses arrest most infections before disease symptoms become manifest**
- **Knowledge of subclinical infections comes from serologic studies showing that sizeable portions of the population have specific antibodies to viruses even though the individuals have no history of disease**

Pathogenic Properties of Viruses

The viral pathogenesis refers to ability of viruses to cause diseases

1. **Viruses avoid the host's immune response by growing inside cells**
2. **Viruses gain access to host cells because they have attachment sites for receptors on the host cell**
3. **Visible signs of viral infections are called cytopathic effects (CPE)**
4. **Some viruses cause cytocidal effects (cell death), and others cause noncytocidal effects (damage but not death)**
5. **Cytopathic effects include the stopping of mitosis, lysis, and the formation of inclusion bodies, cell fusion, antigenic changes, chromosomal changes, and transformation.**

Cytopathic effects [CPE]

1. **Cytocidal effects: are cytopathic effects that lead to host cell death**

   Noncytocidal effects are cytopathic effects that do not lead to cell death. Basically, viral infection can lead to cell abnormalities (biochemical and morphological)

   Syncytia [giant cells] or Big cells: Syncytia are multi-nucleated, giant cells formed through the fusion of host cells

2. **Inclusion bodies: Inclusion bodies are intracellular granules whose presence is a result of viral infection. The characterization of inclusion bodies is useful for the identification of some viral infections**

Stages of viral pathogenesis

The viral pathogenesis involves the following stages

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**

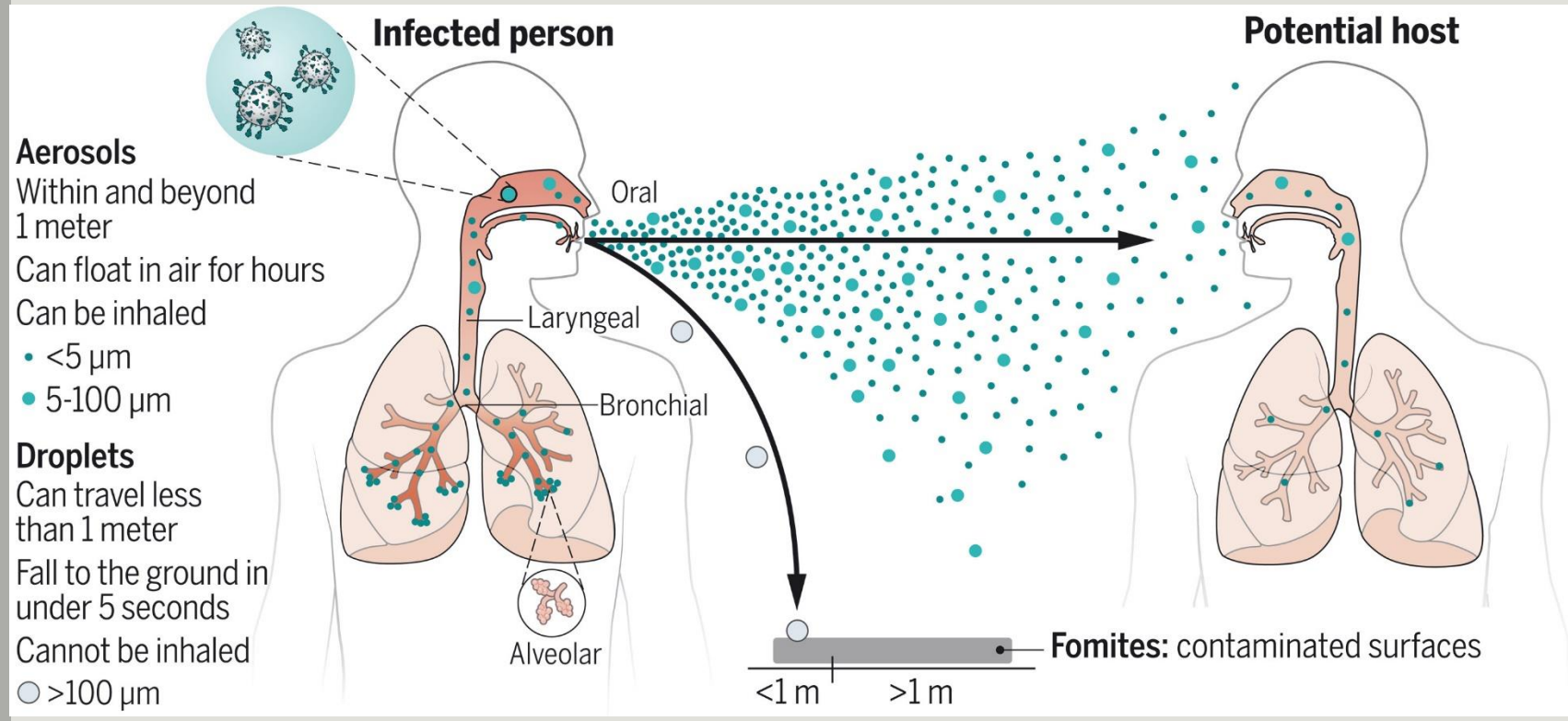
Sources of infection

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 serve as a source of infection

The infectious agent is transmitted from person to person by various ways such as direct contact, kissing, inhalation of aerosols, fecal-oral, venereal contact and arthropod spread

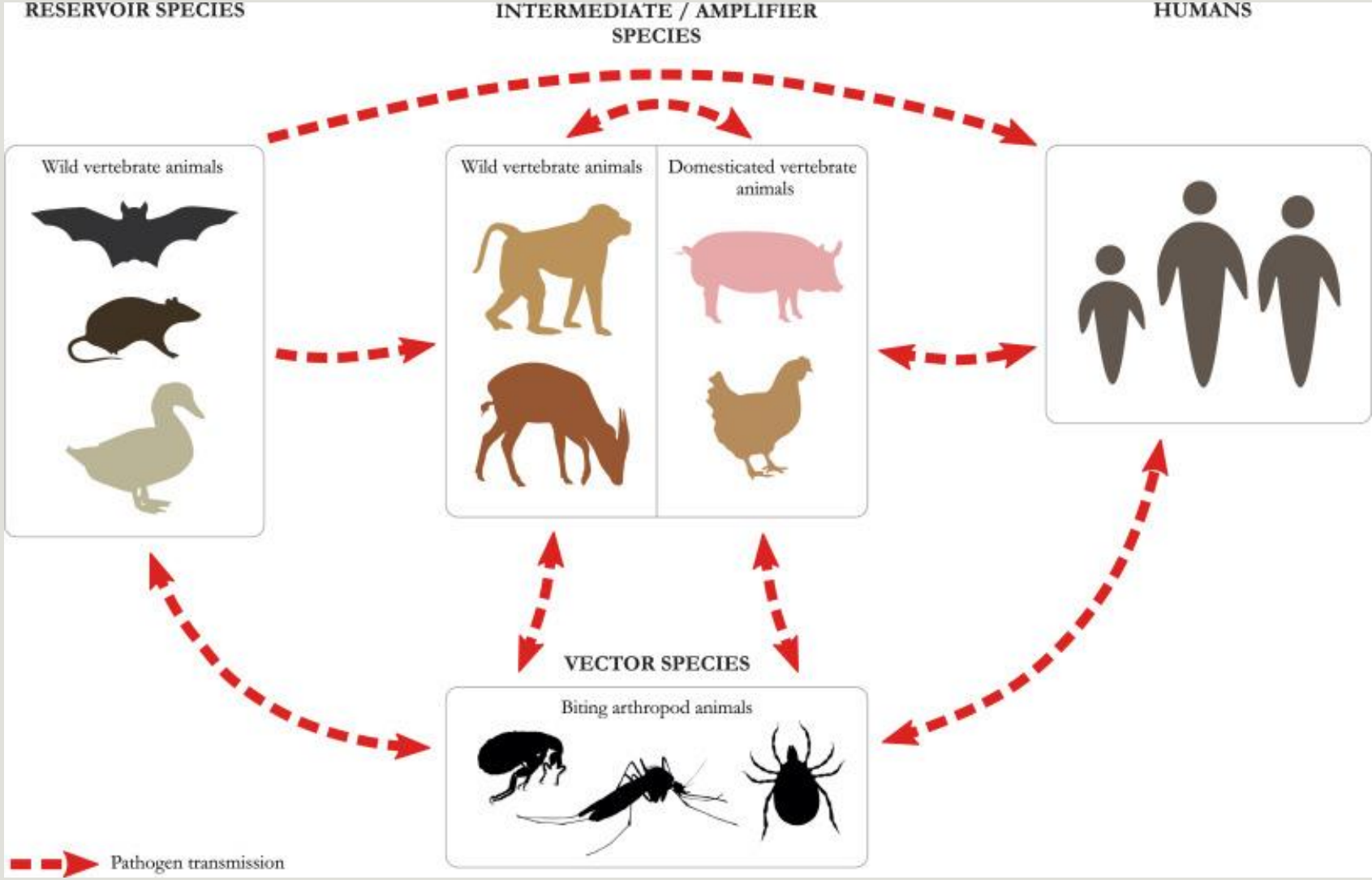


Sources of infection

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

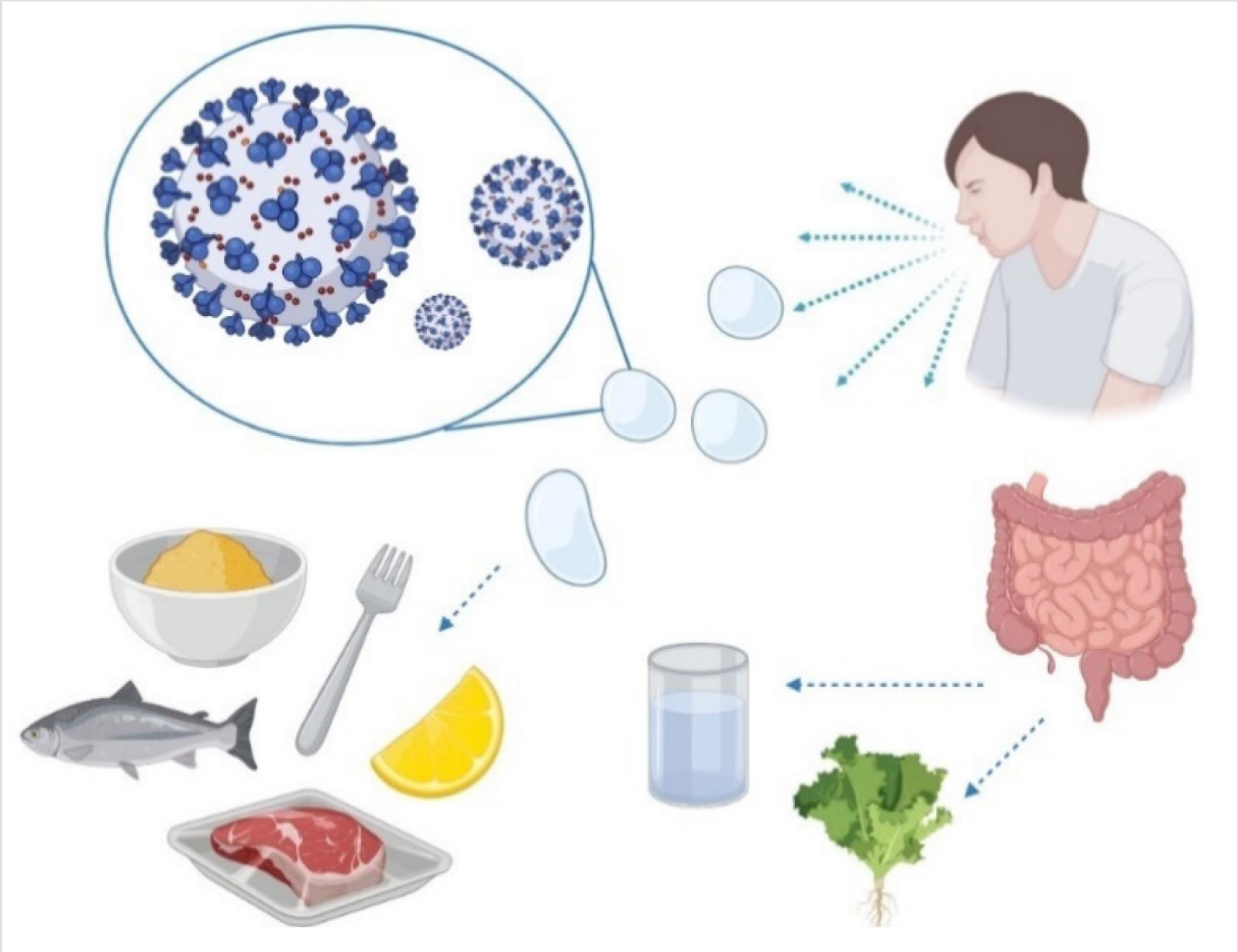


Sources of infection

3. Food: the foods are most important media for transporting

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 :

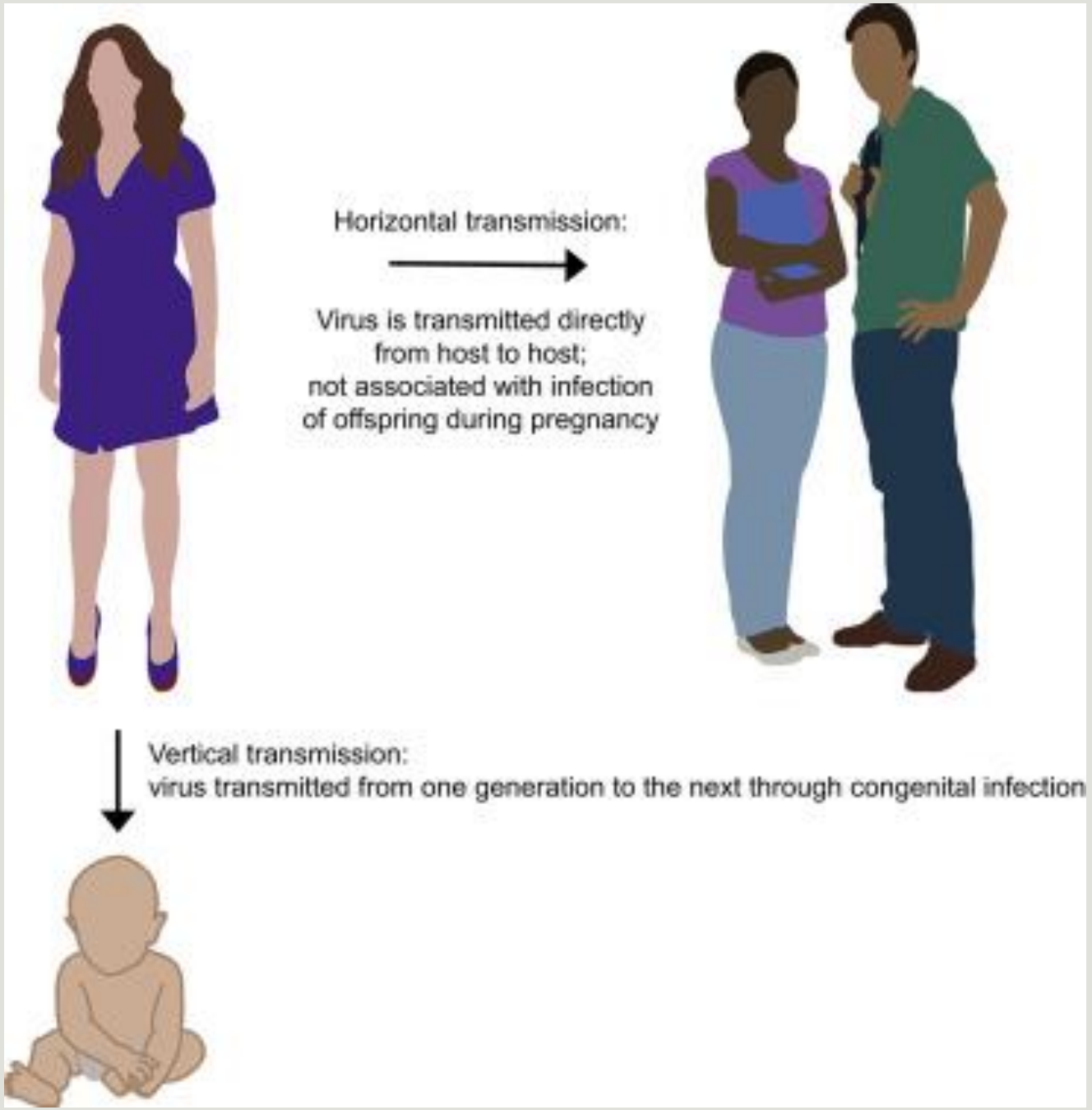
1. **Respiratory tract (nose)**
2. **Elementary tract (mouth)**
3. **Skin, non-intact**
4. **Genital tract(vagina)**

Minor :

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

viral transmitted pathways

1. **Horizontal Transmission**
2. **Vertical Transmission**

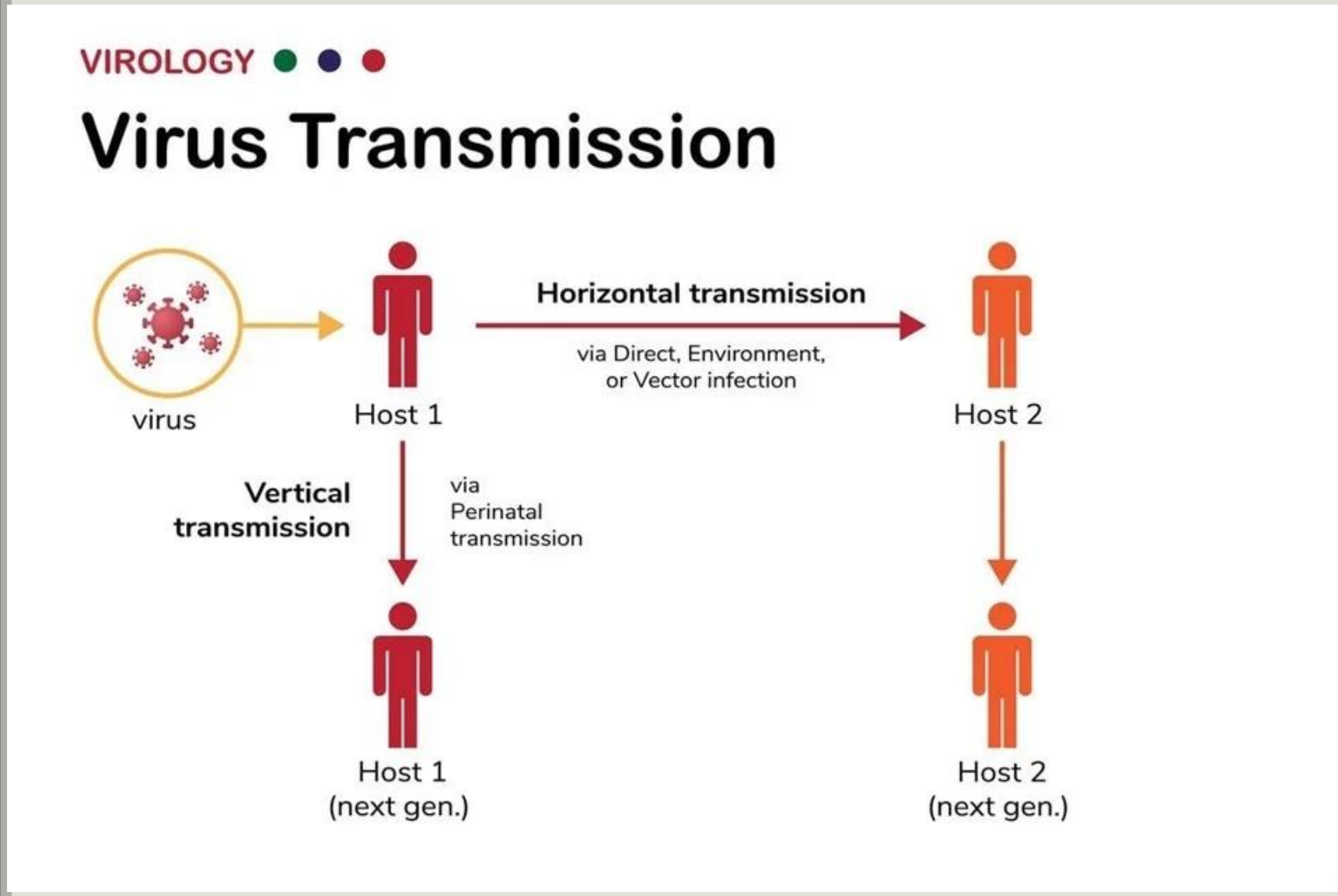


Horizontal Transmission

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 introduces 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**
3. **Physical barriers ,local temperature , pH, oxygen tension are very important in tissue tropism**

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 central neural system (CNS) and cause damage to anterior horn cells resulting in muscle paralysis**

Evasion of host defenses

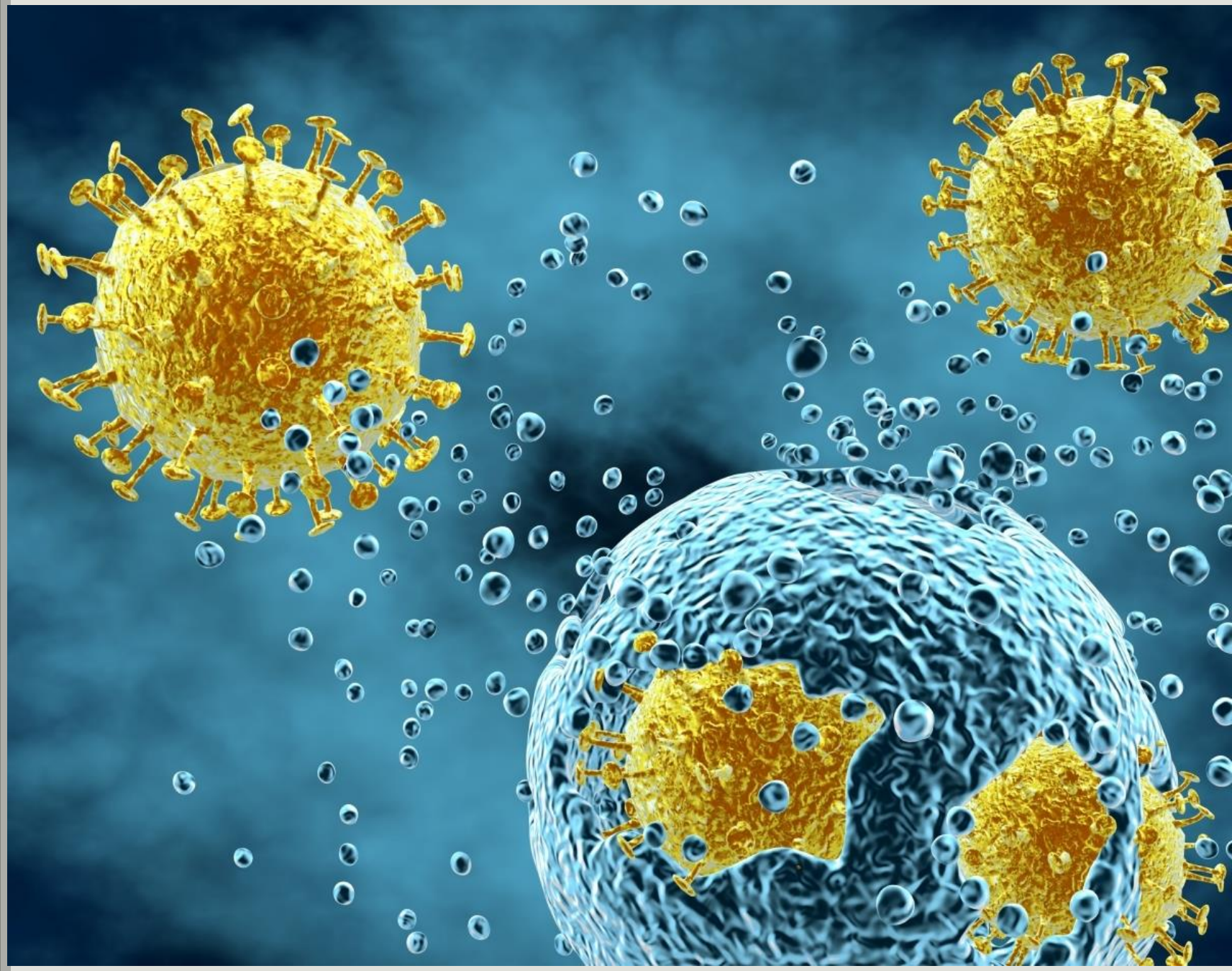
The viruses have several ways by which they evade host defenses

1. **Some viruses (such as vaccinia virus) encode some proteins that act as receptors for immune mediators such as interferon (IFN) and tumor–necrosis factor (TNF). these proteins bind to immune mediators and block their ability to interact with receptors on their intended target**
2. **Some viruses (such as HIV and CMV) can reduce the expression of class-1 MHC protein. Thereby reducing the ability of cytotoxic T cells to kill virus-infected cells. Other viruses (e.g.: herpes virus) inhibit complement. Several viruses (HIV, 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)**

Damage of host cell

Multiplication of virus in host cell lead to disease.

The time between exposure to virus and onset of disease or appearance disease symptoms is called incubation period



The mechanisms of viral diseases are various

1. **Most viral diseases are result of cell death by shut off 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 such as HBV, HCV**
2. **Latent infection such as herpes viruses**
3. **Slow virus infections such as 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