

Viral pathogenesis : The study of the Capability & manner of viruses to infect and cause disease.

Virulence : The degree to which a virus causes disease. Strains of virus differ greatly in their ability to cause disease

How do Viruses Cause Diseases

Viruses are capable of infecting all types of living organism from bacteria to humans.

Factors in viral pathogenesis

1- Cell tropism a major factor that controls which cells a virus can infect is the presence on the cell surface of the appropriate receptor, to which the virus must attach in order to gain entry into the cell.

2- Viruses enter the body (Routs of infection)

Inhalation, ingestion, sexual intercourse or inoculation through the skin or mucous membranes. Infection may also sometimes be passed from a mother to her fetus transplacentally (**Vertical transmission**).

3- Type of infection

Once a virus has gained entry into the body, it may either remain **localized** and replicate only in the tissues adjacent to the site of entry (an example of this is influenza where the virus remains confined to the respiratory tract) or it may cause a **disseminated** infection. Here, the virus replicates initially at the site of entry, but then enters the blood (viraemia) or lymphatic system and spreads throughout the body (e.g. Measles). Other viruses such as Rabies and Herpes Simplex may replicate locally initially, then enter nerve endings and travel up the axon to infect the central nervous system.

4- Incubation period

defines the time from exposure to an organism to the onset of clinical disease. In general, viruses that cause localized infections have short incubation periods (<7 days), while in disseminated infections, the incubation period tends to be longer.

5- Immune response

Viruses replicate intra-cellular, recovery from a viral infection requires the action of specific **cytotoxic T lymphocytes** which recognize and lyses the infected cells. Antibody plays only a limited role in recovery from an established infection, but is very important in preventing infection.

Mechanisms Of Viral Pathogenicity

Generally, the virulence of pathogenic bacteria is directly related to the ability of the organism to produce one or more toxins. However, the virulence of viruses is not well defined . **A number of factors contribute to the virulence (pathogenicity) of a particular strain of virus.**

- a. Ability to enter the cell
- b. Ability to grow within the cell
- c. Ability to combat host defense mechanisms
- d. Ability to produce temporary or permanent damage in the host via:
 - 1) Cell lyses
 - 2) Production of toxic substances
 - 3) Cell transformation
 - 4) Induction of formation of substances which apparently are cellular products normally not produced by the cell.
 - 5) Induction of structural alterations in the host cell :

(a) Nuclear (including chromosomal).

(b) Cytoplasmic

The host anti-viral defense mechanisms include:

A. Non-specific host defense mechanisms

1. Humoral factors
 - (a) Low pH of inflammatory exudates
 - (b) Enzymes
 - (c) Mucous
2. Cellular factors
 - (a) Nucleases
 - (b) Proteases
 - (c) Interferon

B. Specific host defense mechanisms

1. T-Cytotoxic
2. Antibody .
3. Activated phagocyte.

Host Damage

A- Cell lyses

This may occur due to a physical internal pressure exerted by the multiplying virus. The cell becomes filled with virus and merely bursts.

B- Production of toxic substances

During the course of virus replication, many viral components as well as by-products of viral replication accumulate in the cell. These are often cytotoxic. The molecular mechanism of these toxins is not known in most cases. Only gross morphological defects can be observed generally. Some examples are:

1. Herpesvirus components produce syncytia (multi-nucleated protoplasmic mass, seemingly an aggregation of numerous cells without a regular cell outline).
2. The antigen of the adenovirus capsid inhibits RNA, DNA and protein synthesis.

3- Large quantities of some viruses, such as influenza virus and poxviruses, cause rapid toxic effects in some animals.

C. Cell transformation

Certain viruses have the ability to enter a cell and follow one of two alternative courses. They either multiply in a normal manner and are eventually released from the cell, or they may be dormant in the cell and eventually transform the cell into a malignant cell.

D.Suppression of the immune mechanism

Since many viruses are known to replicate in cells of the **lymphoreticular system**, it is possible that these viruses can affect the immune system. Viruses have been found in the thymus, lymph nodes, spleen, bone marrow, stem cells, plasma cells, lymphocytes, macrophages, monocytes, polymorphonuclear leukocytes and Kupffer cells. The nature and extent of the immunologic alteration depends on the organ or cell type infected and the species of virus causing the infection. These effects have been demonstrated in each of the following systems.

Humoral Immunity : Many theories have been proposed to explain how viruses depress immune function.

- (a) Viruses alter the processing of antigens.
- (b) Viruses destroy antibody-producing cells.
- (d) Viruses increase immunoglobulin catabolism

Cellular immunity: Infection with measles virus, influenza virus, chickenpox virus, polio virus or rubella virus causes delayed hypersensitivity .

E. Structural alterations in the host cell

Viruses can induce structural alterations in the host cell's cytoplasm and nucleus. These are often of diagnostic importance.

1- Cytoplasmic change

Small non-enveloped RNA viruses produce a large eosinophilic mass which displaces the nucleus. Other Viruses cause cytoplasmic vacuolization, contraction and degeneration. "Buds" appear on cell surface. Cytoplasmic inclusion (inclusion bodies in the cytoplasmic).

2- Nuclear changes

(a) Pyknosis (nucleus pushed to eccentric position in cell); e.g., influenza virus, mumps virus.

(b) Nuclear inclusion (bodies in the nucleus); e.g., herpesvirus, adenovirus.

(c) Polykaryocytosis (many nuclei in the same cytoplasmic field); e.g., herpesvirus and measles virus.

(f) Formation of chromosomal breaks.

Patterns of diseases

1. Acute non persistent disease.
2. Persistent viral infection.

Mechanism of Persistent viral infection.

- 1- Integration of proviral DNA to host DNA.
- 2- Immune tolerance & neutralization not formed.
- 3- Formation of viral –Antibody –Complement complexes.
- 4- Location of the virus in immunological sheltered (brain).
- 5- Raped antigenic variation.
- 6- Spread from cell to cell.
- 7- Infection of immune suppressed patients.

Types of persistent viral infection

- 1- Chronic carrier infection (asymptomatic infection).
- 2- Latent infection-Herpes virus group
- 3- slow virus infection-Prions disease .