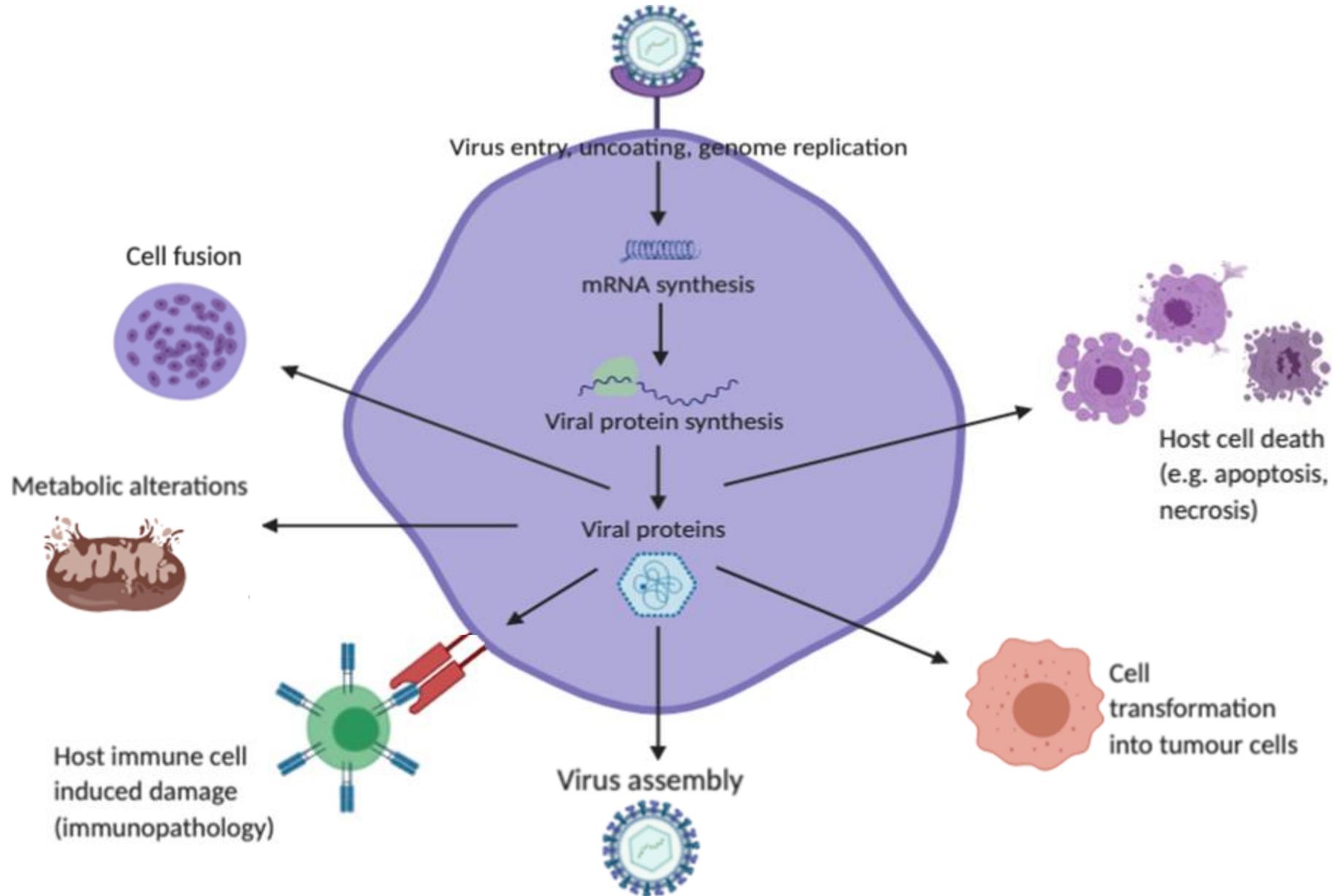


**General Microbiology**  
**Lecture 15**  
**2022-2023**

**Pathogenesis of viral infection**

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# Possible outcomes of viral infection



# Definitions

## Viral Pathogenesis

- It is the process by which a viral infection leads to disease.
- The consequences of viral infections depend on the interplay between a number of viral and host factors.

### Why study viral pathogenesis?

The study of viral pathogenesis is have a knowledge on the molecular mechanisms by which viruses cause disease to treat and prevent viral disease

# Definitions

## Viral Virulence

- The ability of a virus to cause disease in an infected host
- A virulent strain causes significant disease
- An avirulent or attenuated strain causes no or reduced disease
- Virulence depends on
  - Dose
  - Virus strain (genetics)
  - Inoculation route - portal of entry
  - Host factors

# Factors affecting Viral Pathogenic Mechanisms

The accessibility of tissues to the virus.

virulence factors of the infecting virus

Accessibility is influenced by:

1. physical barriers (such as mucus and tissue barriers)
2. The distance to be traversed within the body
3. The natural defense mechanisms

Virulence factors are important to

- overcome the inhibitory effects of physical barriers and
- host defenses

Virulence factors enable the virus to

- initiate infection,
- spread in the body,
- replicate to large enough numbers to impair the target organ.

# Factors Involved in Viral Pathogenesis

- Transmission of the viruses
- Routes of entry.
- Viral adhesions
- Mode of viral spreading
- Viral pathogenesis at the cellular level
- Viral pathogenesis at the host level
- Mechanisms of Viral Persistence
- Cell/Tissue Tropism
- Virus Shedding
- Damage caused by the virus

# Pathogenesis of Viral Infection

## Transmission of the viruses:

- Person to person
- Animal to person

### Horizontal

- Skin contact.
- Blood routes
- Respiratory routes.
- Fecal - oral routes.
- Genital contact.

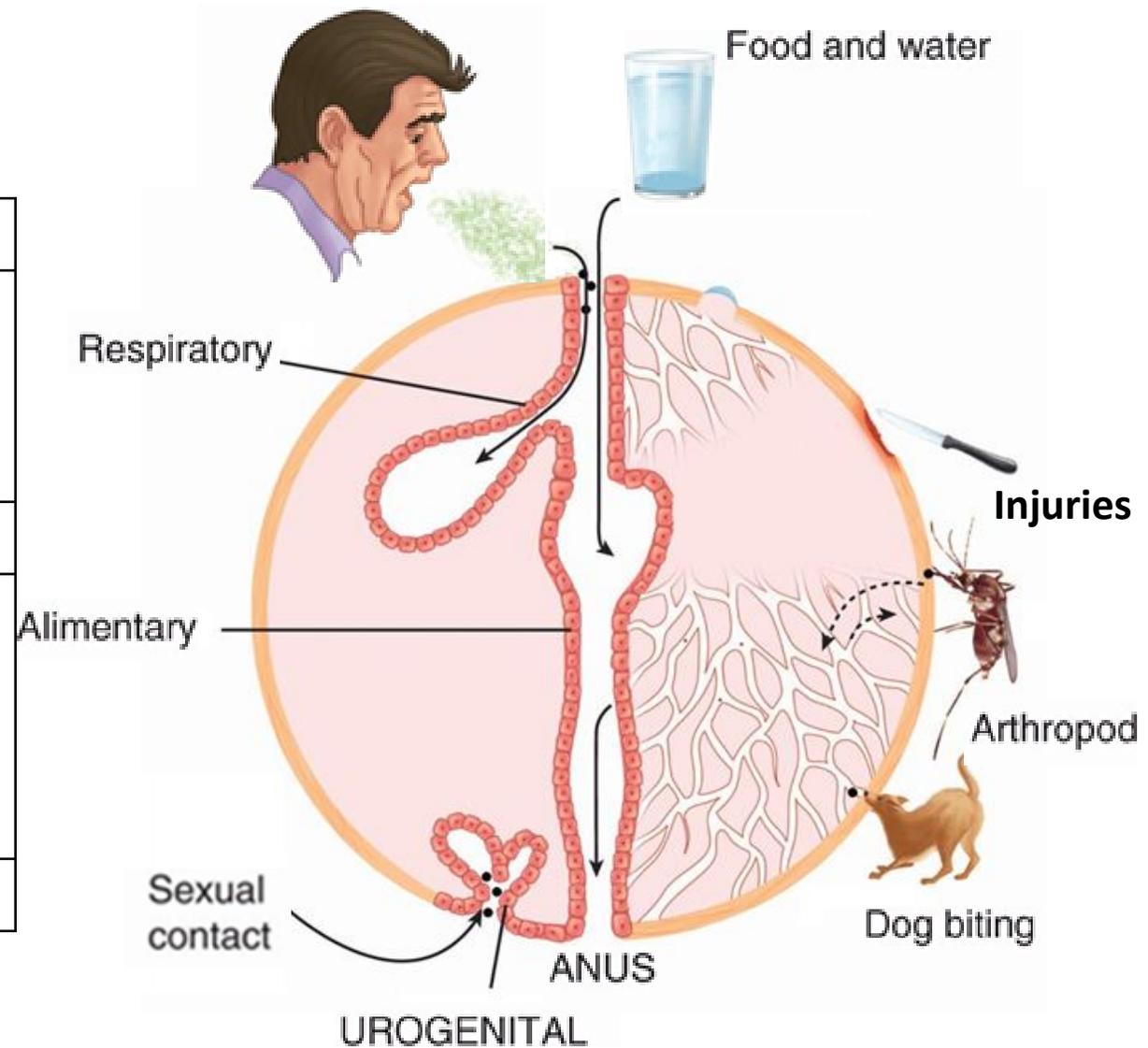
### Vertical

- From the mother to her baby.
- During delivery through an infected birth canal

# Pathogenesis of Viral Infection

## Routes of Entry

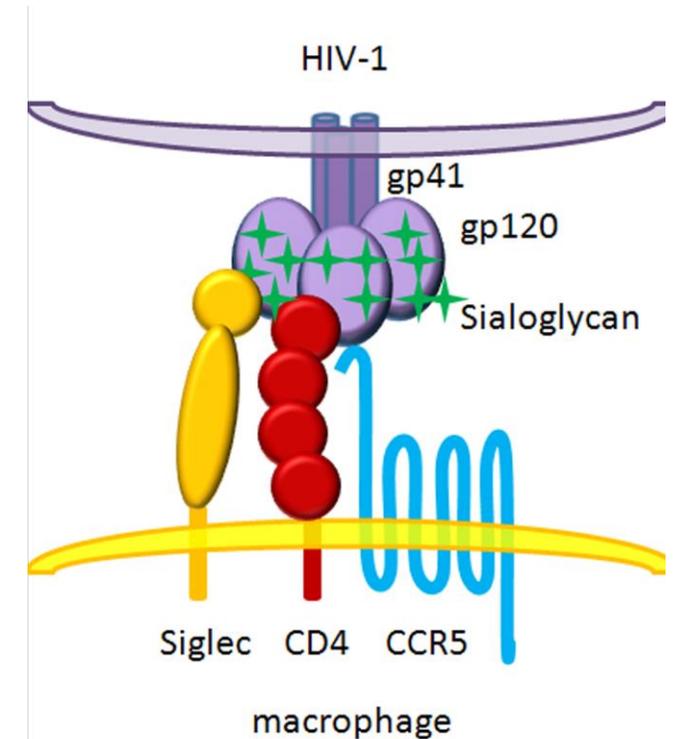
<b>Respiratory Tract</b>	adenoviruses, influenza
<b>Ingestion</b>	Rotaviruses, Caliciviruses, and Enteroviruses (acid and bile resistant)
<b>Skin</b>	Rabies, Papillomaviruses
<b>Genitourinary Tract</b>	papillomaviruses, Herpes simplex virus 2) -HIV-1 and 2, human T-lymphotropic viruses 1 and 2 and hepatitis B and C viruses,
<b>Eyes</b>	some adenoviruses, influenza viruses



# Pathogenesis of Viral Infection

## Viral adhesions

- All viral pathogens must bind to host cells, enter them, and replicate within them.
- Viral coat proteins serve as the ligands for cellular entry
- More than one ligand receptor interaction may be needed, for example
  - HIV glycoprotein (gp) 120 to enter host cells by binding to both CD4 and one of two receptors for chemokines (designated CCR5 and CXCR4).
  - Similarly, the measles virus H glycoprotein binds to both CD46 and the membrane-organizing protein moesin on host cells.



# Pathogenesis of Viral Infection

## Mode of viral spreading

### A. Extracellularly:

Occurs by release of virus into the extracellular fluid and subsequent infection of the adjacent cell.

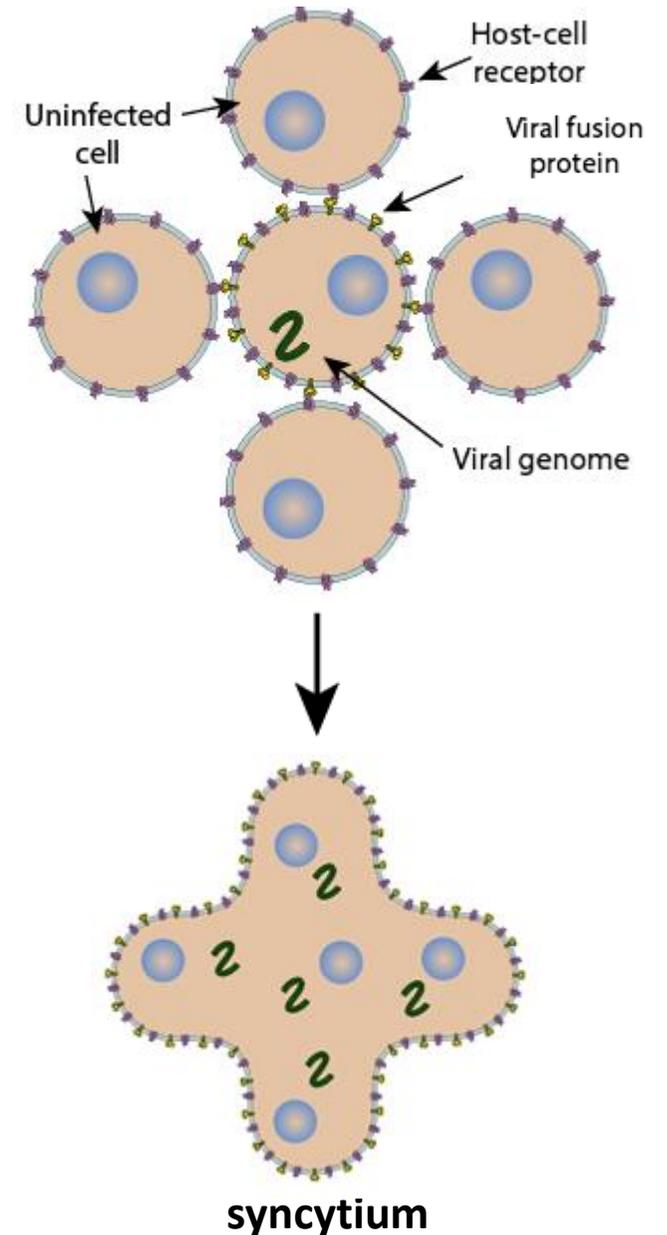
### B. Intracellularly (syncytium):

- occurs by fusion of infected cells with adjacent, uninfected cells or by way of cytoplasmic bridges between cells.

- Intracellular spread provides virus with a partially protected environment because the antibody defense does not penetrate cell membranes

### C. Spread to cells beyond adjacent cells:

- Occur through the lymphatics.
- Diffusion through surface fluids such as the mucous layer of the respiratory tract.
- Through infected migratory cells such as lymphocytes and macrophages may spread the virus within local tissue.



# Levels of viral Infections

Viral disease at the cellular  
Level (cytopathogenesis):

Abortive  
"virus not produced"

Productive  
"Virus produced"

Non-productive  
"Virus not produced but viral NA Present"

Viral disease at the host level:

Asymptomatic infection  
"most common"

Acute infection

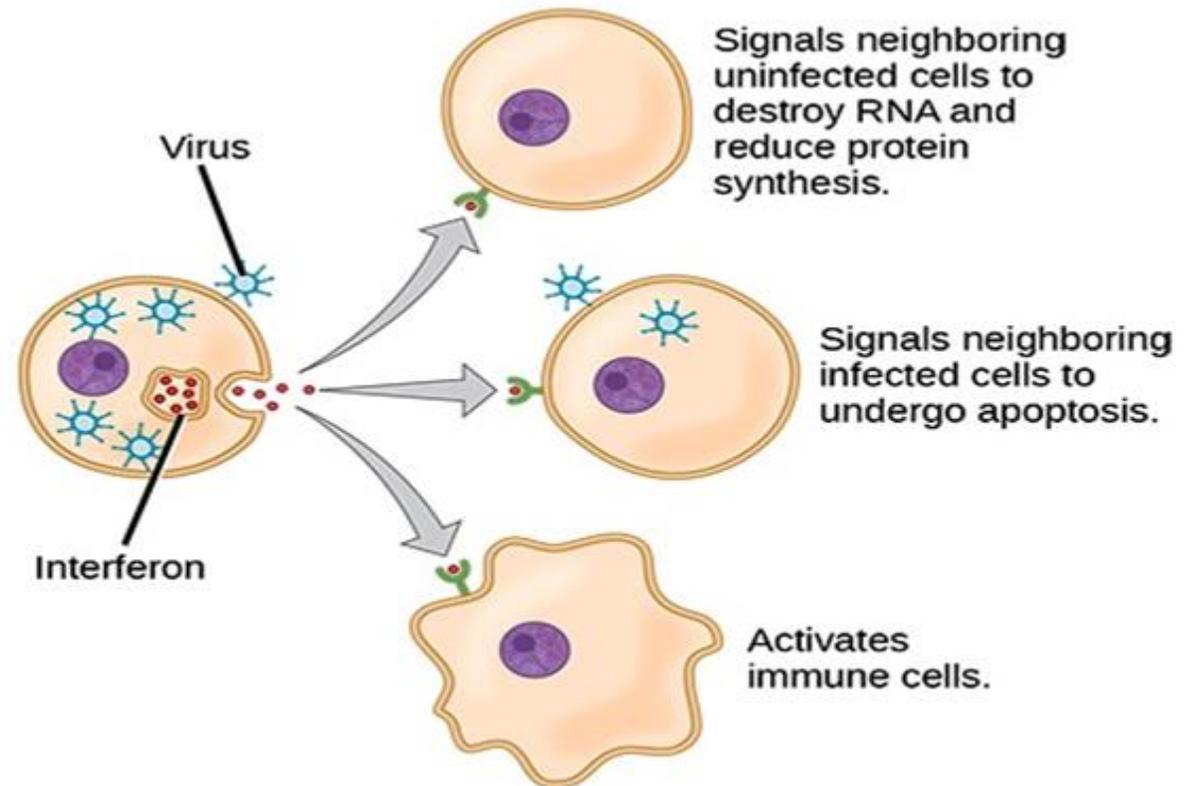
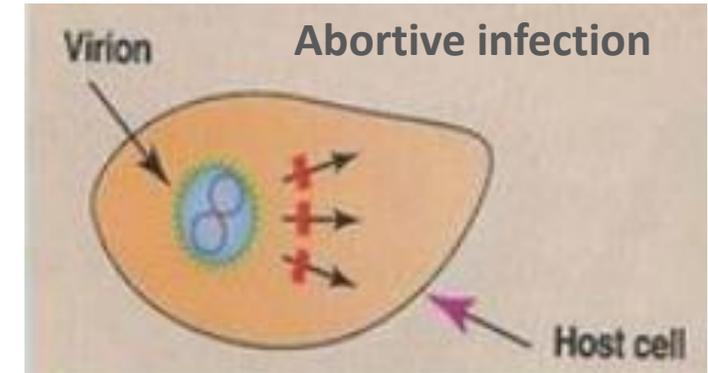
Persistent infection

# Pathogenesis Of Viral Infection

## Viral disease at the cellular level (cytopathogenesis):

### 1- Abortive infection:

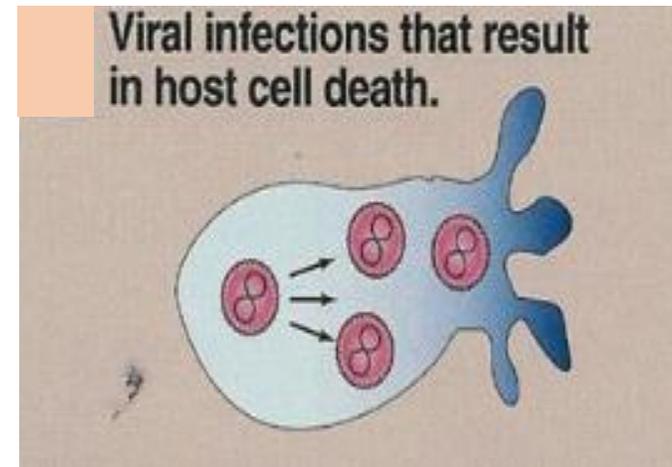
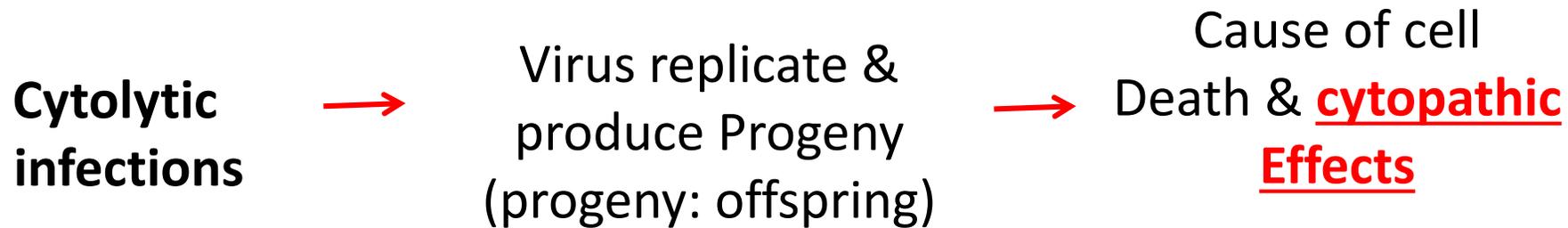
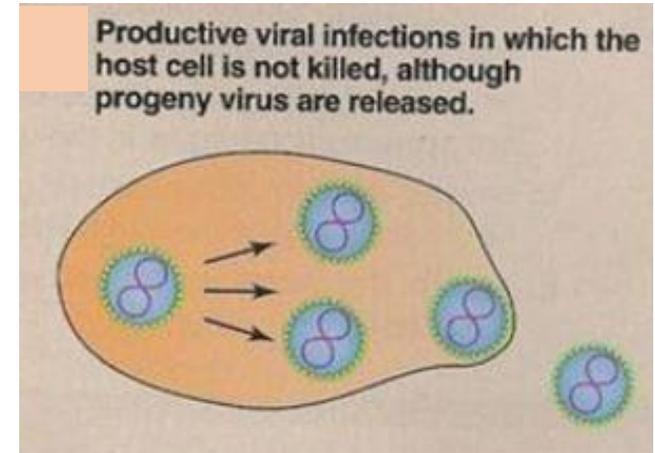
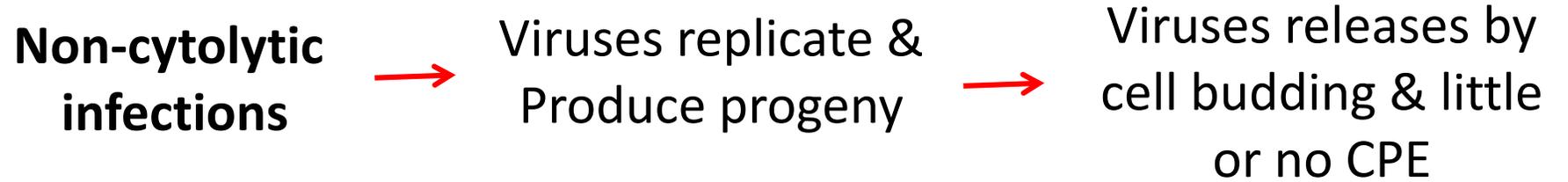
- Viruses don't complete the replication cycle.
- Due to: mutation and interfering factors.
- (Ex: interferons are proteins released by animal cells, usually in response to the entry of a virus, which has the property of inhibiting virus replication.)



# Pathogenesis Of Viral Infection

## Viral disease at the cellular level (cytopathogenesis):

### 2- Productive infection:



# Pathogenesis of Viral Infection

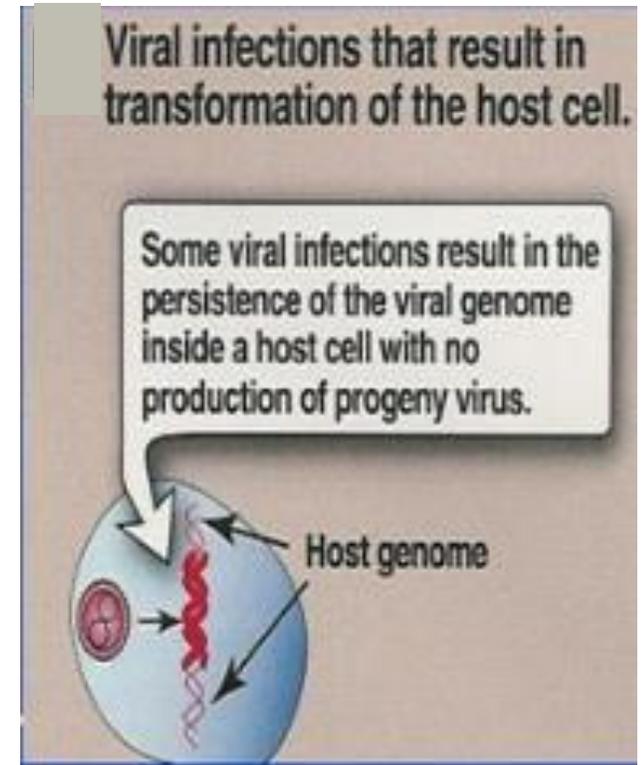
## Viral disease at the cellular level (cytopathogenesis):

### 2- Non-productive infection:

- Viruses infect cells that restrict or lack the machinery for transcribing viral genes.
- Viral genome is found either integrated into cell DNA or as a circular episome or both.
- Two types:

**A. Latent infection** → The cell retains its normal properties → There is limited expression of viral genes  
e.g. HSV

**B. Transformation** → Cause tumor in animals & human and it can transform cell culture e.g. EBV, HPV & HTLV

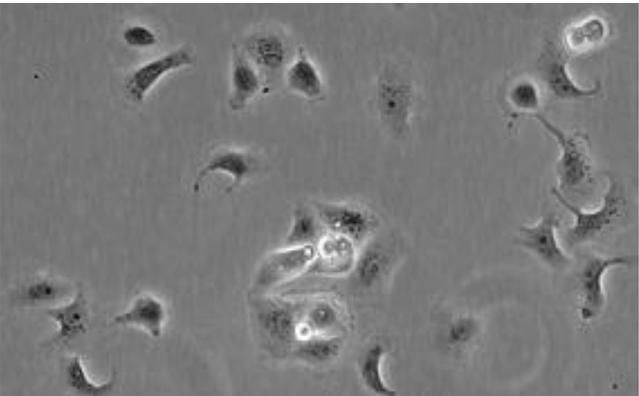
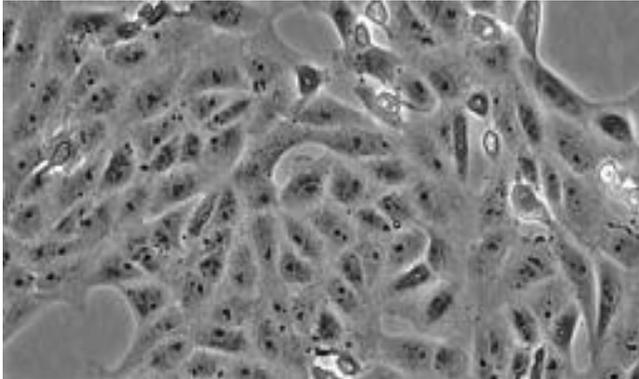


# Pathogenesis of Viral Infection

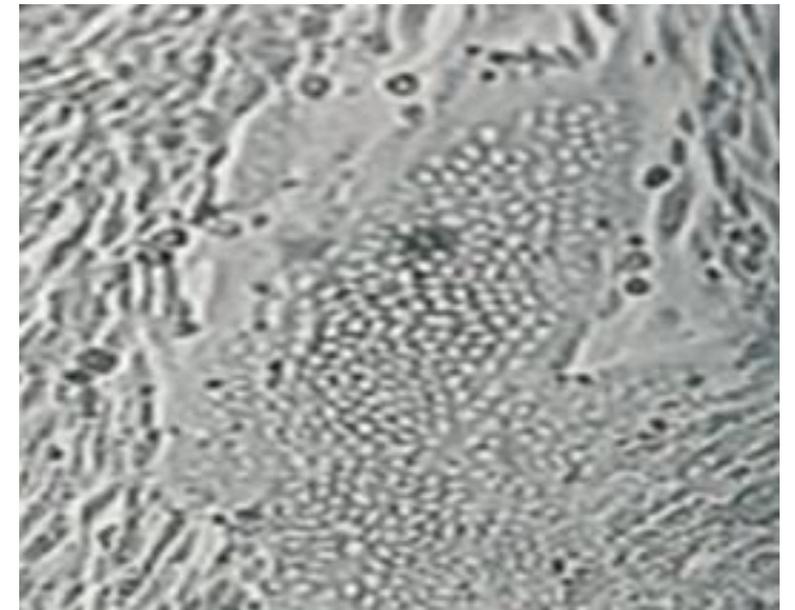
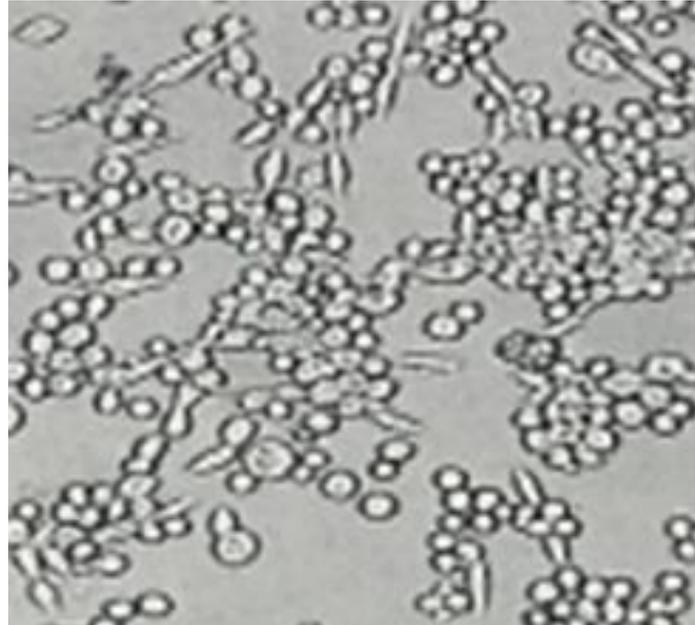
## Cytopathic effects

### Seen in several forms:

Cell lysis "cell disintegration"  
(non-enveloped viruses)



Cell rounding (enveloped)



Syncytium formation "Cell fusion"  
Ex: Herpes Paramyxo Viruses,  
Respiratory Syncytial virus (RSV)

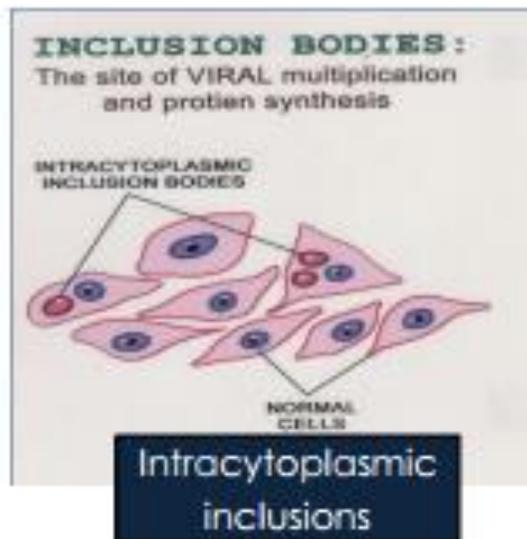
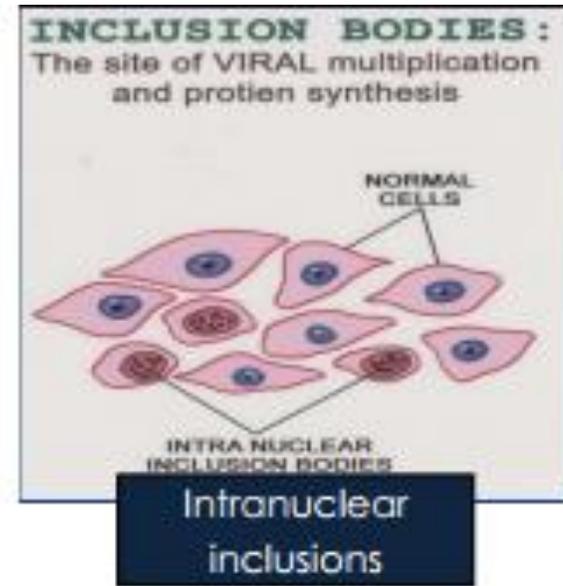
# Pathogenesis of Viral Infection

## Cytopathic effects

### Seen in several forms:

Takes a Place in:

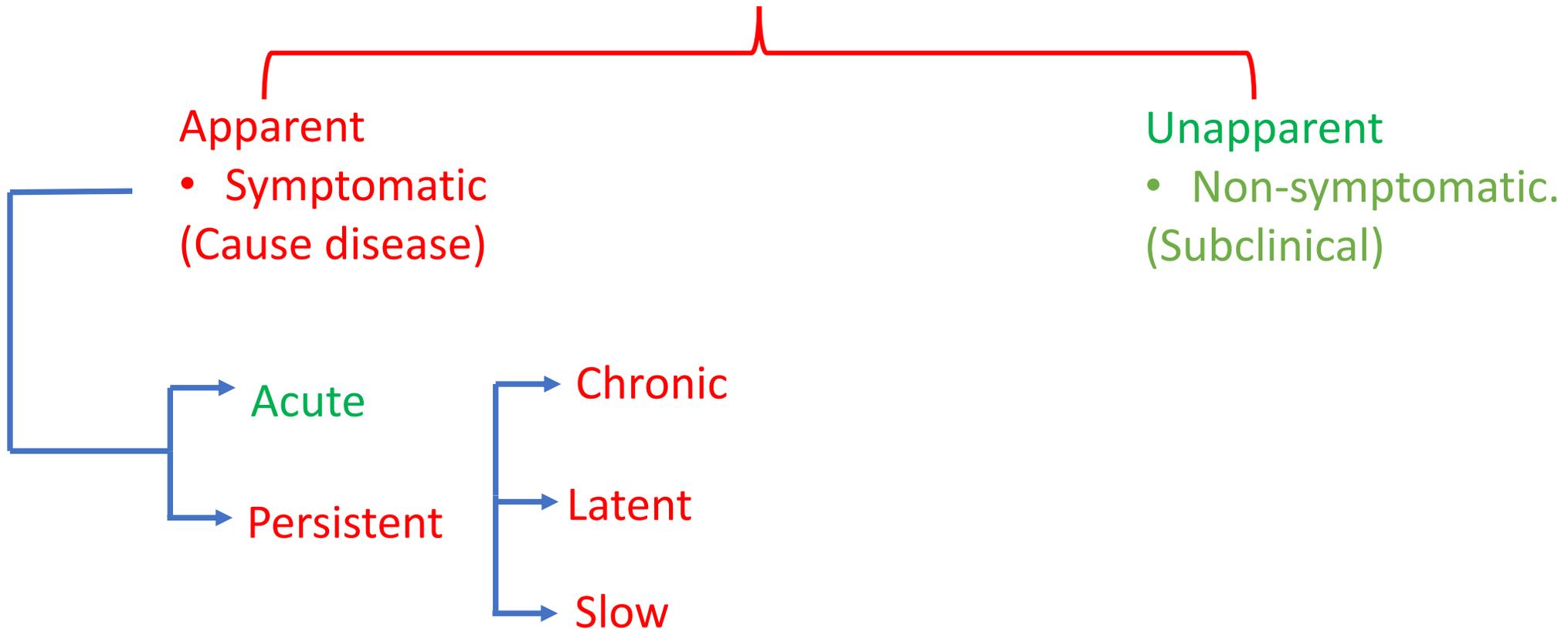
- Intranuclear (DNA Vs):
  - Protein synthesis and multiplication
  - accrue in the nucleus. Ex: Herpes Vs.
- Intracytoplasmic (RNA Vs):
  - Protein synthesis and multiplication accrue in the cytoplasm.
  - Ex: Rabies Vs. it causes Negri bodies



# Pathogenesis of Viral Infection

## Viral disease at the host level

### Patterns of viral infections

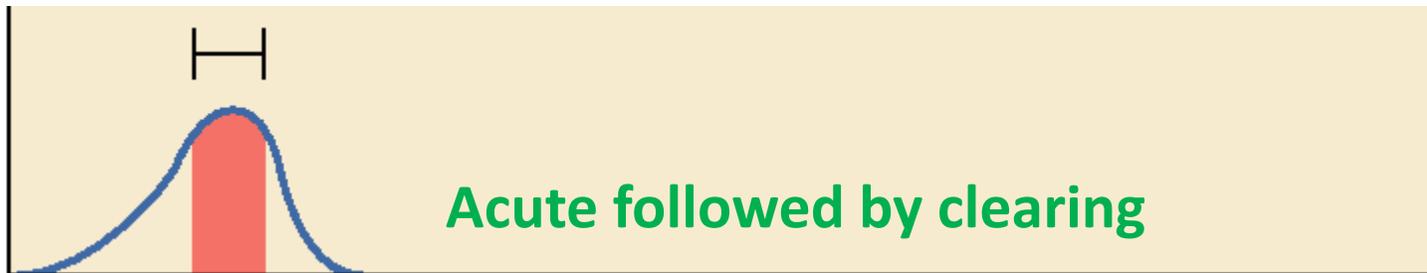


# Pathogenesis of Viral Infection

## Patterns of viral infections

### 1. Acute infection:

- In acute infections, lytic viruses are shed at high titers for rapid infection
- Generally develop suddenly and last a short time, often only a few days or weeks.
- The patients become symptomatic.
- The virus completely cleared from the body with 5-7 days.
- This type of infection is cytotoxic (Is it good or bad?).



#### Acute infection

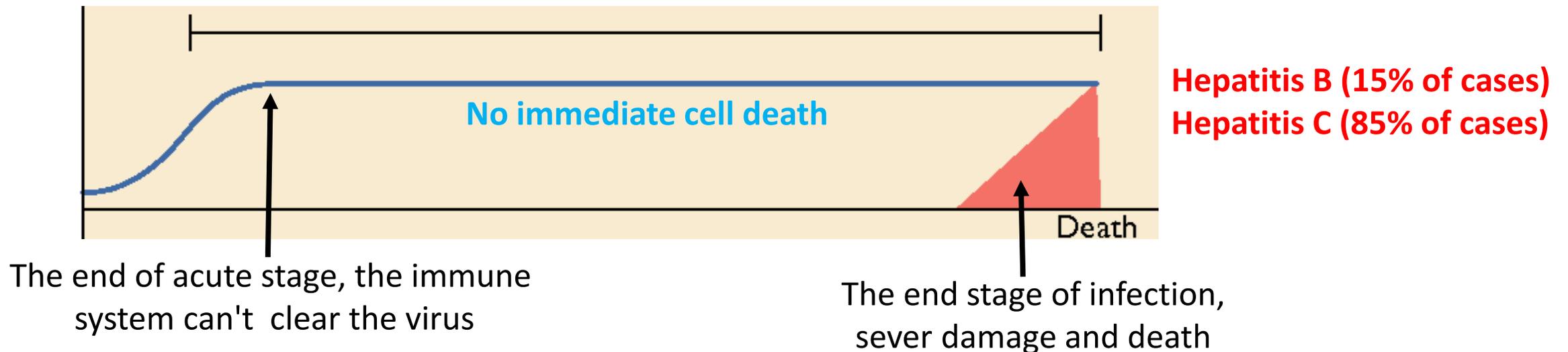
- Rhinovirus
- Rotavirus
- Influenza virus
- **Small pox**
- **SARS**

**Acute** : virus rapidly kills cells; rapid, self-limiting or fatal disease.

# Pathogenesis of Viral Infection

## 2. Persistent chronic infections

- They usually develop from acute infection.
- Cells continue to survive despite a viral infection
- Then persists with no clearance (replication at slow rates with positive serological tests)
- Mild or no clinical symptoms may be evident.
- People may be able to transmit the germ to others.
- serious signs may not appear until as long as 20 years after the infection began.
- For example: hepatitis B & C, which affects the liver is a chronic viral infection.



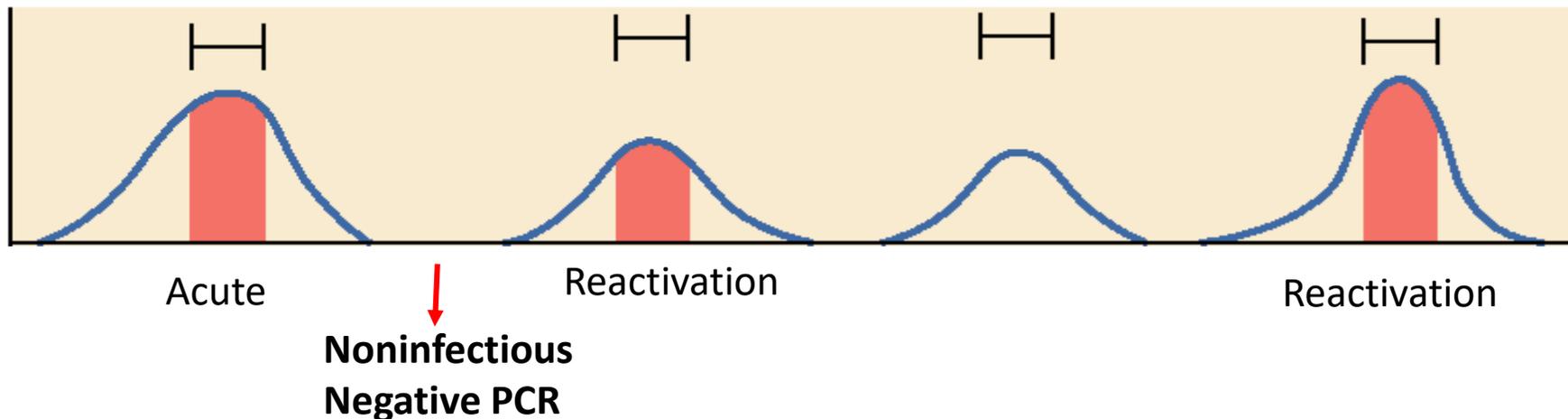
# Pathogenesis of Viral Infection

## 3. Latent persistent infections:

- Characterized by having acute periods between the latent periods.
- During the infection the viral titer peaks several times but in between the virus is in the latent phase.

### Latency conditions

- The virus never cleared out of the body
- The virus lays dormant in the form of episome (extrachromosomal circular DNA)
- virus is present in the body, but it remains dormant, not causing any overt symptoms.
- People can pass the virus on to others.
- Eg: **HSV1 (Oral infections)** **HSV2 (genital infections)**, which periodically flares up to cause cold sores before going dormant again.



### What causes reactivation

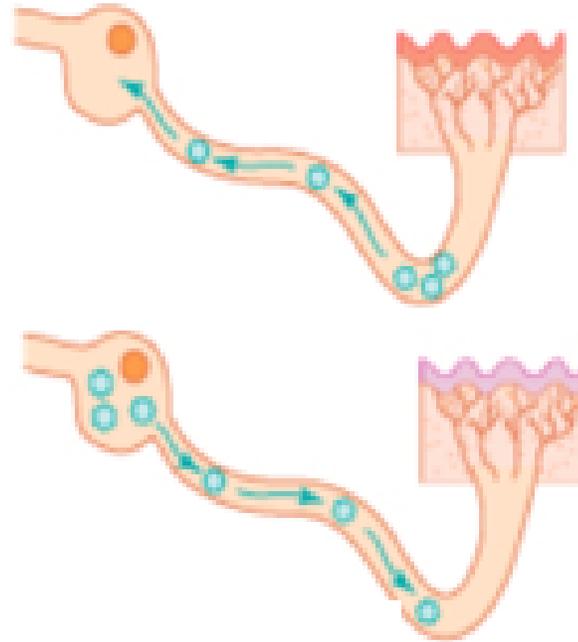
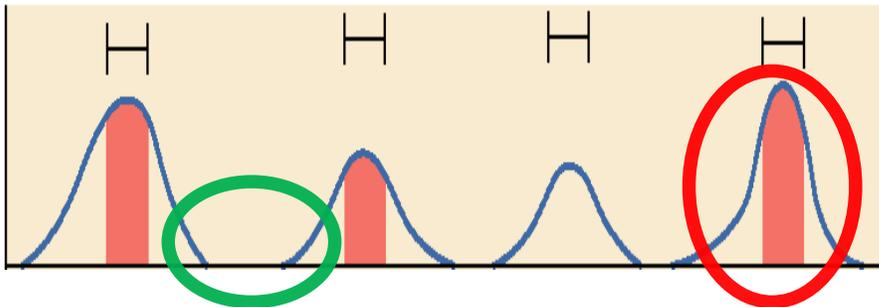
- Drop in immunity
- Stress

# Pathogenesis of Viral Infection

## 3. Latent persistent infections:

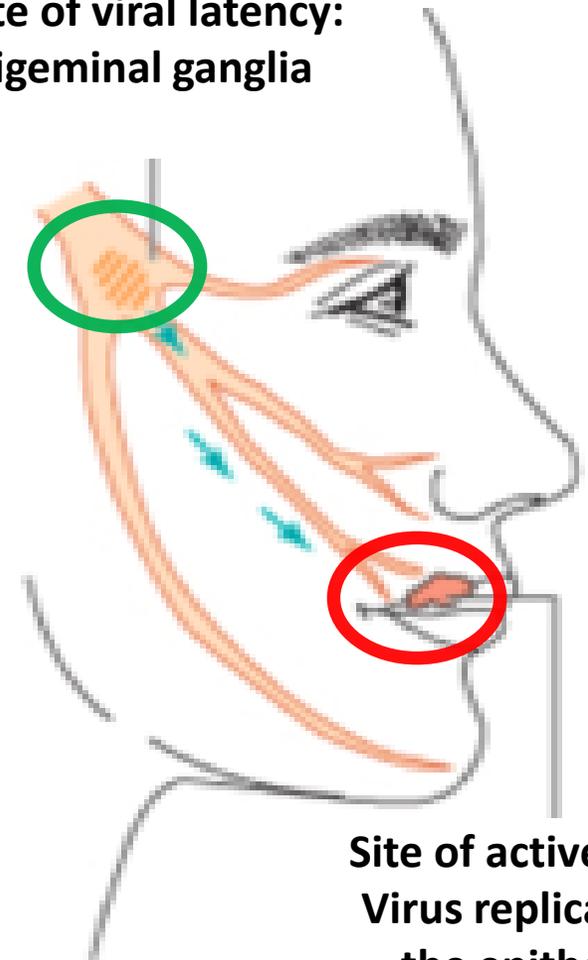
Site of herpes simplex  
Viral latency:

Trigeminal ganglia



Transport along  
peripheral sensory nerves

Site of viral latency:  
Trigeminal ganglia

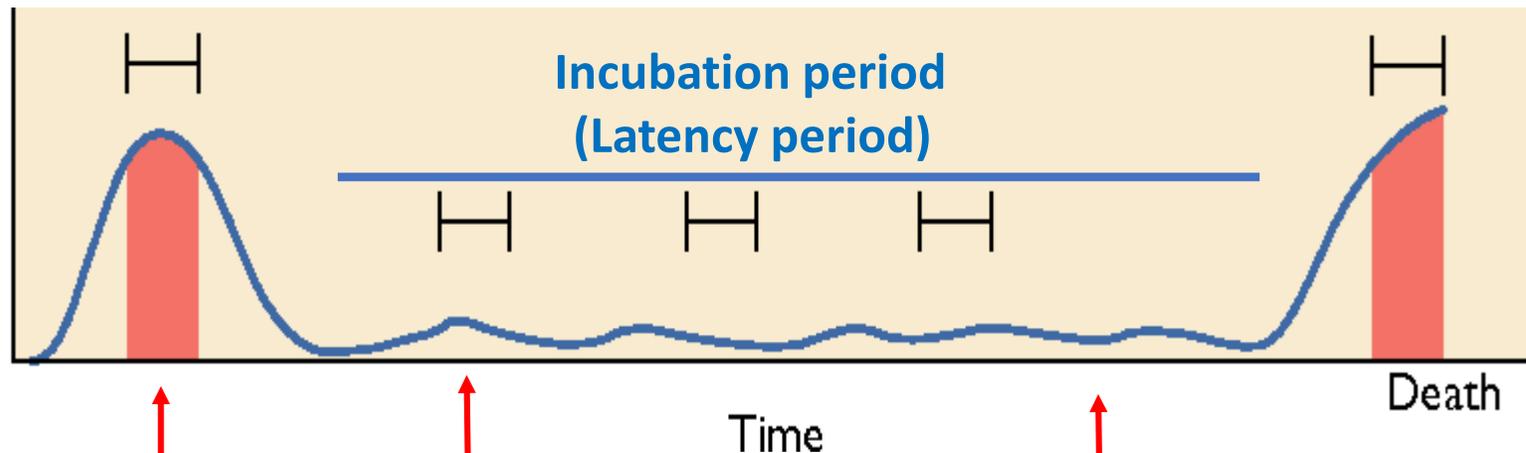


Site of active lesion:  
Virus replication in  
the epithelium

# Pathogenesis of Viral Infection

## 4. Slow persistent infections:

- Starts with acute infection.
- Then the symptoms subside but the amount of virus never goes to baseline.
- There is a struggle between the virus and the immune system.
- Example: HIV



If the immune system drops the symptoms appear

Virus can be detected during the incubation period because it doesn't reach the base line

## Mechanisms of Viral Persistence

- Antigenic variation
- molecular mimicry
- Restricted gene expression
- Down-regulation of MHC class I expression, resulting in lack of recognition of infected cells e.G. Adenoviruses
- Down-regulation of accessory molecules involved in immune recognition e.G. By EBV.
- Infection of immune privilege sites within the body e.G. HSV in sensory ganglia in the CNS
- Direct infection of the cells of the immune system itself e.G. Herpes viruses, retroviruses (HIV) - often resulting in immunosuppression

## Cell Tropism

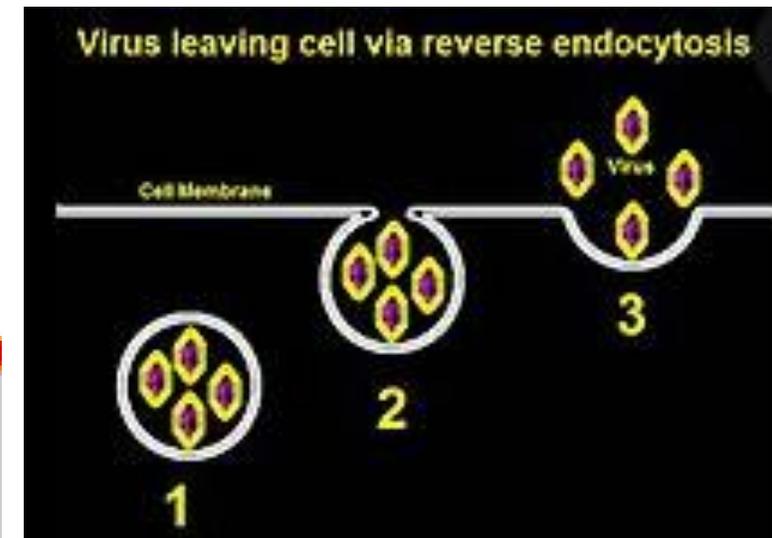
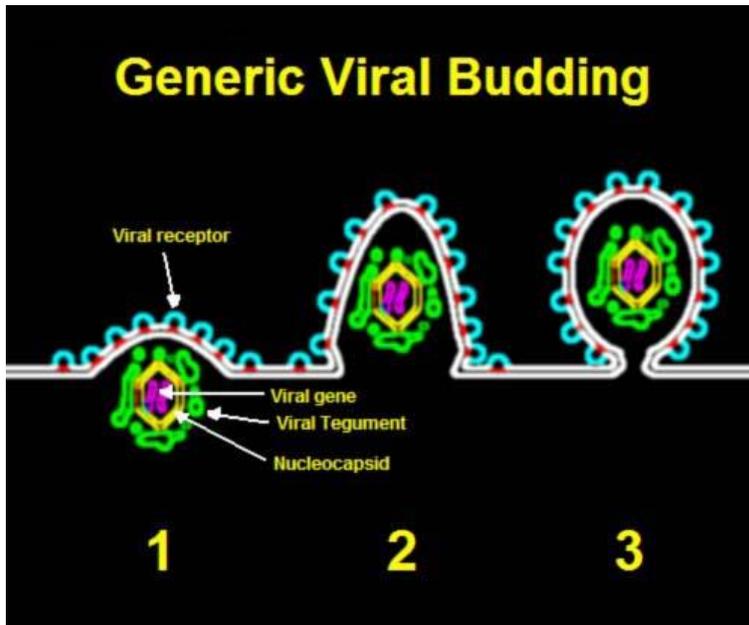
Viral affinity for specific body tissues (tropism) is determined by

- Cell receptors for virus.
- Cell transcription factors that recognize viral promoters and enhancer sequences.
- Ability of the cell to support virus replication.
- Physical barriers.
- Local temperature, pH, and oxygen tension enzymes and non-specific factors in body secretions.
- Digestive enzymes and bile in the gastrointestinal tract that may inactivate some viruses.

# Pathogenesis of Viral Infection

## Virus Shedding

- Once replication has been completed and the host cell is exhausted of all resources in making viral progeny, the viruses may begin to leave the cell by several methods



# Pathogenesis of Viral Infection

## Damage caused by the virus

viruses can destroy cells through a variety of mechanisms.

1. direct cytopathic effects to disrupt cellular functions through releasing enzymes to degrade host metabolic precursors,
2. or releasing proteins that inhibit the synthesis of important host factors, proteins, DNA and/or RNA

**THANKS**