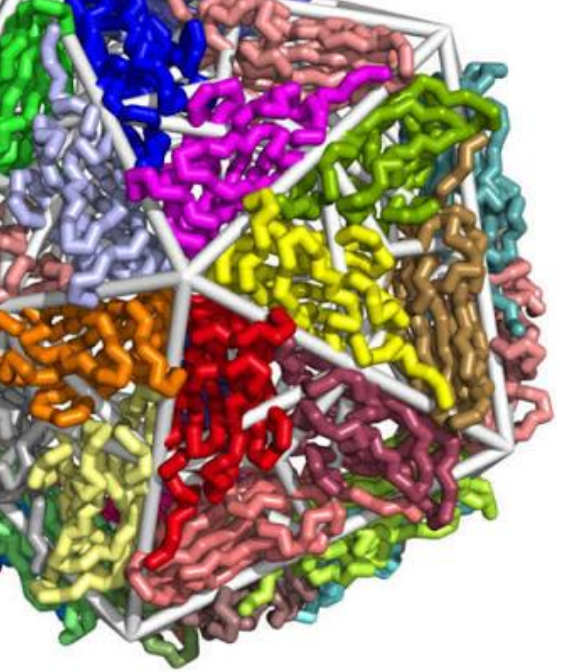
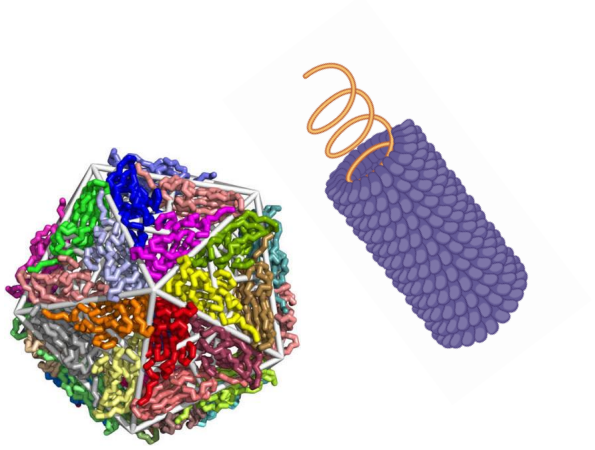


# Viral Structure, Classification & Replication

**Summer Term**
**Lecture no. 3**

**Asst. Prof. Dr. Tola A. Faraj**



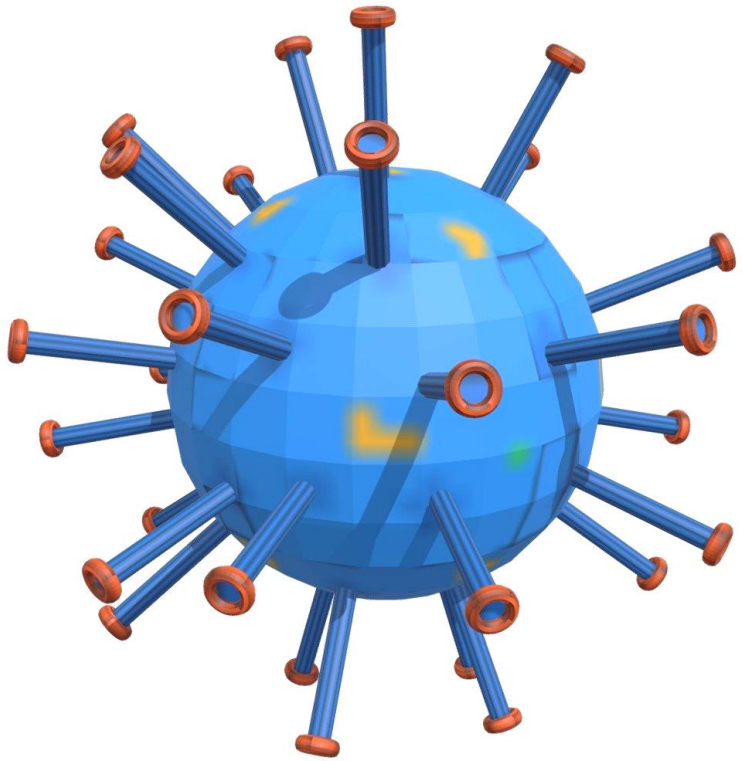
# Outline_

- ❑ Viral Architecture _
- ❑ Baltimore Classification Scheme _
- ❑ The Lytic Replication Cycle _
- ❑ Cytopathic Effects (CPE) _

# ✔ Viral Architecture _

## 1. The Virion Definition

- A **virion** is an infectious, obligate intracellular parasite consisting of genetic material packaged within a protein coat. Viruses lack metabolic machinery, ribosomes, and autonomous energy production.



| Feature | **Virion** | **Virus** |
| --- | --- | --- |
| **Definition** | A single, fully assembled, mature physical particle outside a host cell. | The entire model/lifecycle of the infectious agent, including active replication inside a cell. |
| **State** | Inactive and extracellular (floating outside the cell). | Active and intracellular (hijacking a host cell's machinery). |
| **Primary Role** | Protect the genetic material and transmit it to a new host. | Reproduce, mutate, and manipulate host systems. |

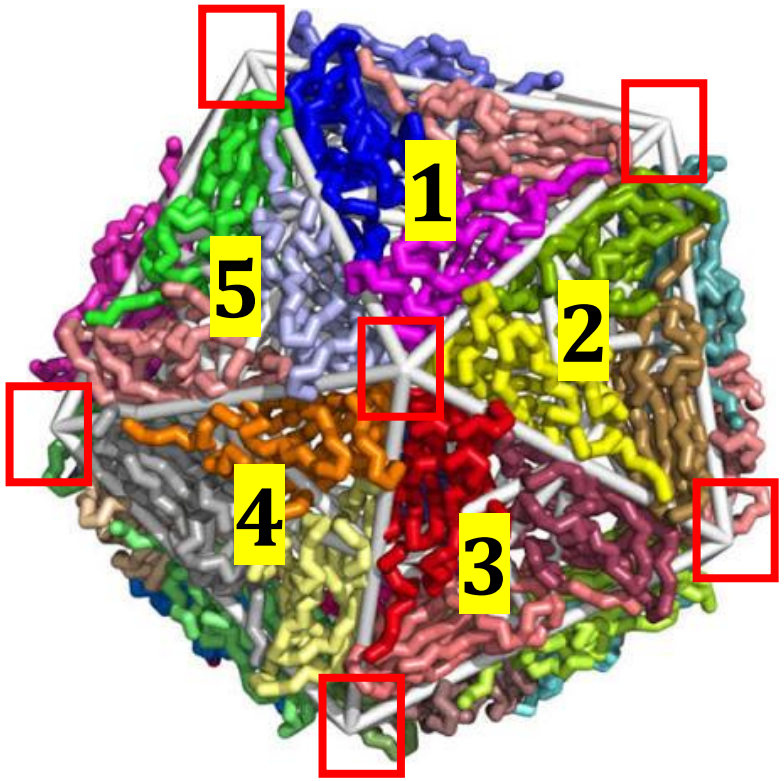
## 2. Capsids and Symmetry

- The **capsid** is a protein shell that protects the viral genome and facilitates host cell recognition in non-enveloped viruses.
- Capsids are constructed from protein subunits called **capsomeres**.

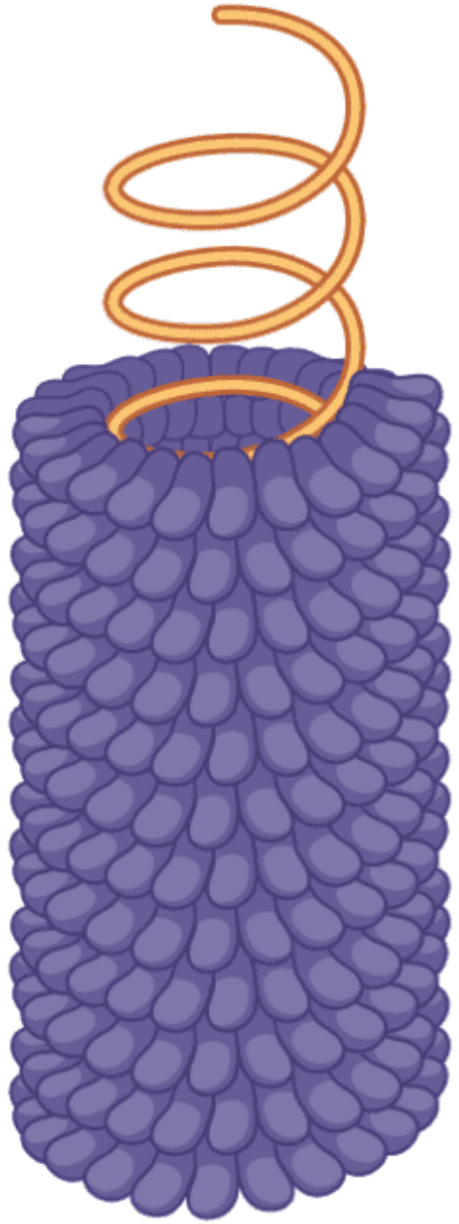
1. **Icosahedral Symmetry**
2. **Helical Symmetry**
3. **Complex Symmetry**

## ✔ **Icosahedral Symmetry**:

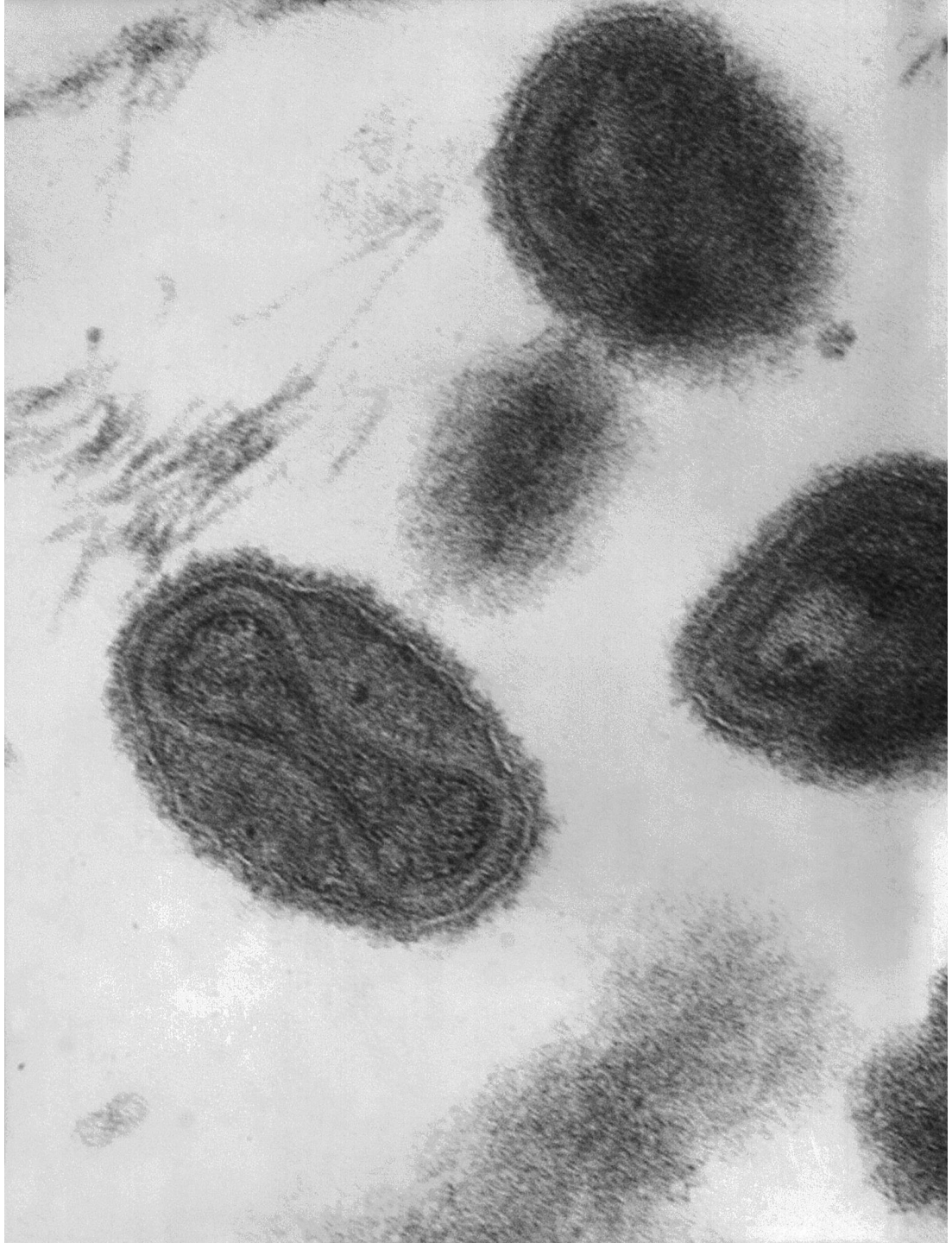
- A regular polyhedron with 20 triangular faces and 12 vertices.
- Provides **maximum internal volume** with the minimum number of protein subunits (thermodynamically efficient).
- *Examples:* Adenovirus, Poliovirus.



- **Helical Symmetry:**
  - Protein subunits bind directly to the nucleic acid, coiling into a ribbon-like spiral.
  - All human viruses with helical symmetry are enveloped.
  - *Examples:* Influenza virus, Rabies virus, Ebola virus.



- **<u>Complex Symmetry</u>:**
  - Structures that fit neither purely icosahedral nor helical models.
  - *Example:* Poxviruses (brick-shaped with lateral bodies and a core membrane).



## 3. The Envelope: Structure & Origin

- ***Composition*:** Lipid bilayer derived from host cellular membranes (plasma membrane, ER, or Golgi) via **budding**, combined with viral transmembrane glycoproteins.
- ***Function*:** Host cell receptor binding, entry via membrane fusion, and evasion [avoidance] of immediate host immune recognition.

## ❑ *Stability Contrast*

| Feature | Non-Enveloped (Naked) Viruses | Enveloped Viruses |
|---|---|---|
| ❑ **Outer Boundary** | Protein capsid | Lipid bilayer membrane |
| ❑ **Environmental Stability** | High (resistant to heat, desiccation/drying, acid, detergents) | Low (sensitive to heat, drying, detergents, ether) |
| ❑ **Transmission** | Fecal-oral, fomites, contaminated water | Direct contact, respiratory droplets, blood/body fluids |
| ❑ **Example** | Norovirus, Rotavirus | Influenza virus, HIV, SARS-CoV-2 |

## 4. Viral Genome Diversity

Viruses violate [break up] the universal cell rule where DNA is the sole genetic material. Viral genomes can be:

- **DNA:** Single-stranded (ssDNA) or Double-stranded (dsDNA); Linear or Circular.
- **RNA:** Single-stranded (ssRNA) or Double-stranded (dsRNA); Monopartite (single molecule) or Segmented (multiple distinct fragments, e.g., Influenza).
- **RNA Polarity:**
  - **Positive-sense (+ssRNA):** Can function directly as mRNA in the host cell (5' → 3' orientation). Pure genomic RNA is infectious on its own.
  - **Negative-sense (-ssRNA):** Complementary to mRNA (3' → 5’ orientation). Must be transcribed into +ssRNA by a viral RNA-dependent RNA polymerase (RdRp) carried inside the virion before translation can occur.

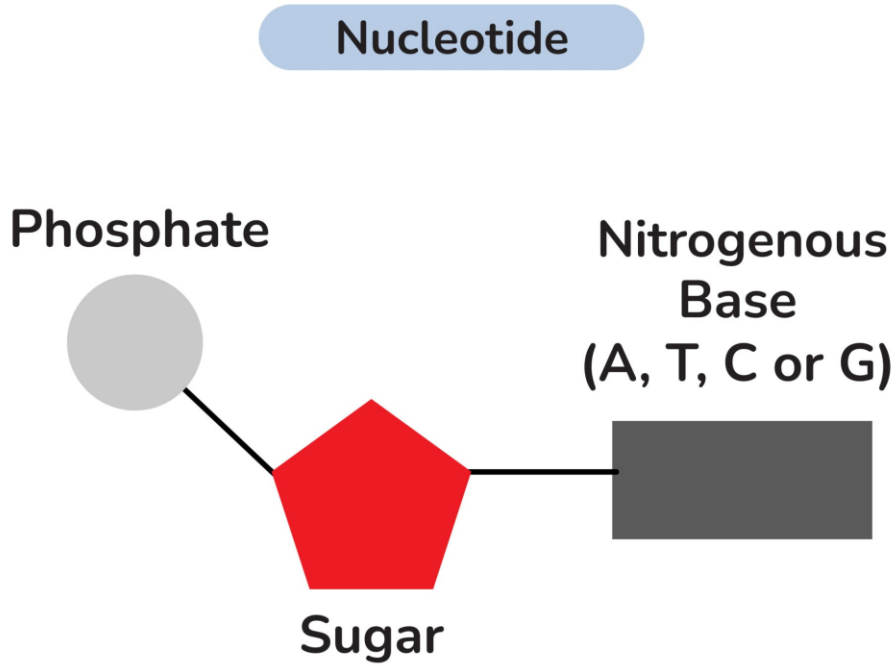
# ✔ Baltimore Classification Scheme _

- ❑ Developed by David Baltimore in 1971, this system categorizes viruses into **seven classes** based on their mechanism of mRNA synthesis. Every virus must produce 5' capped, translation-competent mRNA (+ssRNA) to be read by host ribosomes.

✔ **mRNA** (messenger ribonucleic acid) is a vital molecule that **carries genetic instructions** from a cell's DNA to → its protein-making machinery.

DNA $\xrightarrow{\text{Replication}}$ DNA $\xrightarrow{\text{Transcription}}$ RNA $\xrightarrow{\text{Translation}}$ Protein

- **Replication** preserves the **master code** so new cells inherit an exact genetic **copy**.
- **Transcription** rewrites a specific DNA instructions manual into → a **portable RNA message**.
- **Translation decodes** the triplets of nucleotides (codons) in RNA into a chain of **amino acids** that folds into a 3D functional protein.



## ✔ The Seven Baltimore Classes

**Class I: dsDNA Viruses**

- *Strategy:* Uses host or viral RNA Polymerase II to **transcribe dsDNA directly into mRNA**.
- *Examples:* Herpesviridae, Poxviridae, Adenoviridae.

**Class II: ssDNA Viruses**

- *Strategy:* Must synthesise a **complementary DNA strand first using host DNA polymerase to form a dsDNA intermediate**, which is then transcribed.
- *Examples:* Parvoviridae (e.g., Parvovirus B19).

**Class III: dsRNA Viruses**

- *Strategy:* The genomic dsRNA **cannot** be translated. The viral **RNA-dependent RNA polymerase (RdRp)** transcribes the negative strand of the dsRNA into mRNA.
- *Examples:* Reoviridae (e.g., Rotavirus).

**Class IV: +ssRNA Viruses**

- *Strategy:* Genome **acts directly as mRNA** and is translated immediately upon entry. One of the first proteins translated is viral RdRp, which synthesizes a -ssRNA template to produce more +ssRNA genomes.
- *Examples:* Coronaviridae, Flaviviridae, Picornaviridae.

**Class V: -ssRNA Viruses**

- *Strategy:* The genomic RNA is **complementary to mRNA**. The virion **must carry packaged RdRp protein** inside the capsid to transcribe the -ssRNA into mRNA upon entering the cell.
- *Examples:* Orthomyxoviridae (Influenza), Rhabdoviridae (Rabies), Filoviridae (Ebola).

**Class VI: +ssRNA-RT Viruses (Retroviruses)**

- *Strategy:* Diploid +ssRNA genome. Uses virion-packaged **Reverse Transcriptase (RT)** to convert +ssRNA into a cDNA hybrid, then dsDNA. The dsDNA integrates into the host chromosome via **Integrase** to form a provirus, which is then transcribed by host RNA Polymerase II.
- *Examples:* Retroviridae (HIV-1, HTLV-1).

**Class VII: dsDNA-RT Viruses (Gapped dsDNA)**

- *Strategy:* Gapped [incomplete] dsDNA genome. Transcribed into an RNA intermediate (**pgRNA**) [pregenomic RNA] by host RNA Polymerase II. The viral Reverse Transcriptase then copies the RNA intermediate back into gapped dsDNA inside the developing capsid.
- *Examples:* Hepadnaviridae (Hepatitis B Virus).

# ✔ The Lytic Replication Cycle _

Viral replication occurs through six **[6]** distinct, sequential stages:

## Step 1: Attachment (Adsorption)

- High-affinity specific binding between viral **Attachment Proteins** (VAPs) and host cell **receptors/co-receptors.**
- *Determinant of Tropism:* Species and tissue specificity depend entirely on receptor expression.
- *Examples:*
  - HIV: GP120 binds CD4 (primary receptor) and CCR5/CXCR4 (co-receptors) on T-helper cells.
  - Influenza: Hemagglutinin (HA) binds sialic acid residues on respiratory epithelial cells.
  - SARS-CoV-2: Spike (S) protein binds ACE2.

## Step 2: Entry (Penetration)

**For Enveloped Viruses:**

- *Direct Membrane Fusion:* Viral envelope fuses directly with the host plasma membrane at neutral pH (e.g., HIV).
- *Receptor-Mediated Endocytosis:* Virion is internalized into an endosome. Acidification of the endosome triggers conformational changes in viral proteins, inducing envelope-endosome fusion (e.g., Influenza).

**For Non-Enveloped Viruses:**

- *Receptor-Mediated Endocytosis followed by pore formation or endosomal disruption* (e.g., Poliovirus inserts its genome through a membrane channel).

## Step 3: Uncoating

- Disassembly of the capsid shell to release the viral nucleic acid into the host cytoplasm or nucleus.
- Triggered by conformational changes.

## Step 4: Replication & Gene Expression

- **Transcription & Translation:**
  - **Production of viral mRNAs** to hijack host ribosomes.
  - **Early Gene Products:** Non-structural proteins (e.g., viral polymerases, transcription factors, immune-evasion factors).
  - **Late Gene Products:** Structural proteins (e.g., capsomeres, envelope glycoproteins).
- **Genome Replication:**
  - DNA viruses typically replicate in the **nucleus** using host machinery (Exception: *Poxviruses* replicate in the cytoplasm using their own machinery).
  - RNA viruses typically replicate in the **cytoplasm** using viral RdRp (Exception: *Orthomyxoviruses* replicate in the nucleus).

## Step 5: Assembly (Maturation)

- Packaging of newly synthesized viral genomes into structural capsid proteins.
- Driven by self-assembly interactions or specific packaging signals.

## Step 6: Release

- **Lysis:** Typical of non-enveloped viruses. Disruption of host membrane integrity causes cell destruction and releases all progeny virions simultaneously [at once].
- **Budding:** Typical of enveloped viruses. Capsid interacts with viral glycoproteins localized at cell membranes (plasma, Golgi, or ER), taking part of the host membrane as an envelope. Allows continuous release without immediate host cell death.

# ✔ Cytopathic Effects (CPE) _

- **Cytopathic Effects (CPE)** refer to morphological, biochemical, and structural changes observed in host cells → following viral infection.

- CPE is an essential **diagnostic parameter** in classical cell culture virology.

# Common Types of CPE

1. **Cell Lysis & Detachment**:
   - Destruction of cytoskeleton and cell-cell junctions causes infected cells to round up, shrink, lose adherence, and lyse.
   - *Observed in:* Enteroviruses, Rhinoviruses.

2. **Syncytia Formation (Giant Multinucleated Cells)**:
   - Enveloped viruses express fusion proteins on the host plasma membrane during replication, causing adjacent [next to] cells to fuse into a single massive cell with dozens of nuclei.
   - *Observed in:* Respiratory Syncytial Virus (RSV), Measles virus, HIV.

**3. <u>Inclusion Bodies</u>:**

- Dense, microscopic intracellular structures representing sites of active viral replication, assembly, or aggregated viral proteins.

**4. <u>Transformation (Oncogenesis)</u>:**

- Loss of contact inhibition, rapid proliferation, altered cell morphology, and immortalization driven by viral oncogenes.
- *Observed in:* Human Papillomavirus (HPV), Epstein-Barr Virus (EBV).


# Thank You!