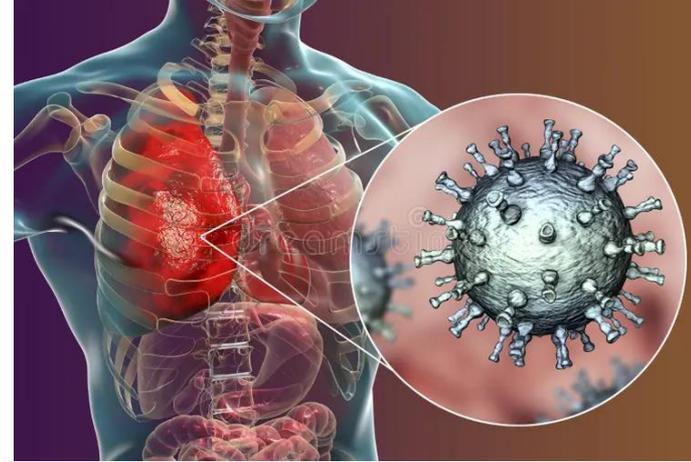


# Virology III



## Lecture 24

Dr. Samer Y. Alqaraleh  
PhD. Nanobiotechnology (Microbiology)

Faculty of Dentistry

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# Persistent Infections

- **Persistent infections** - cell harbors the virus and is not immediately lysed.
- Can last weeks or host's lifetime; several can periodically reactivate – **chronic latent state**
  - Measles virus – may remain hidden in brain cells for many years
  - Herpes simplex virus – cold sores and genital herpes
  - Herpes zoster virus – chickenpox and shingles

# Viral Damage

- Some animal viruses enter the host cell and permanently alter its genetic material resulting in cancer – **transformation** of the cell.
- Transformed cells have an increased rate of growth, alterations in chromosomes, and the capacity to divide for indefinite time periods resulting in tumors.
- Mammalian viruses capable of initiating tumors are called **oncoviruses**
  - Papillomavirus – cervical cancer
  - Epstein-Barr virus – Burkitt's lymphoma

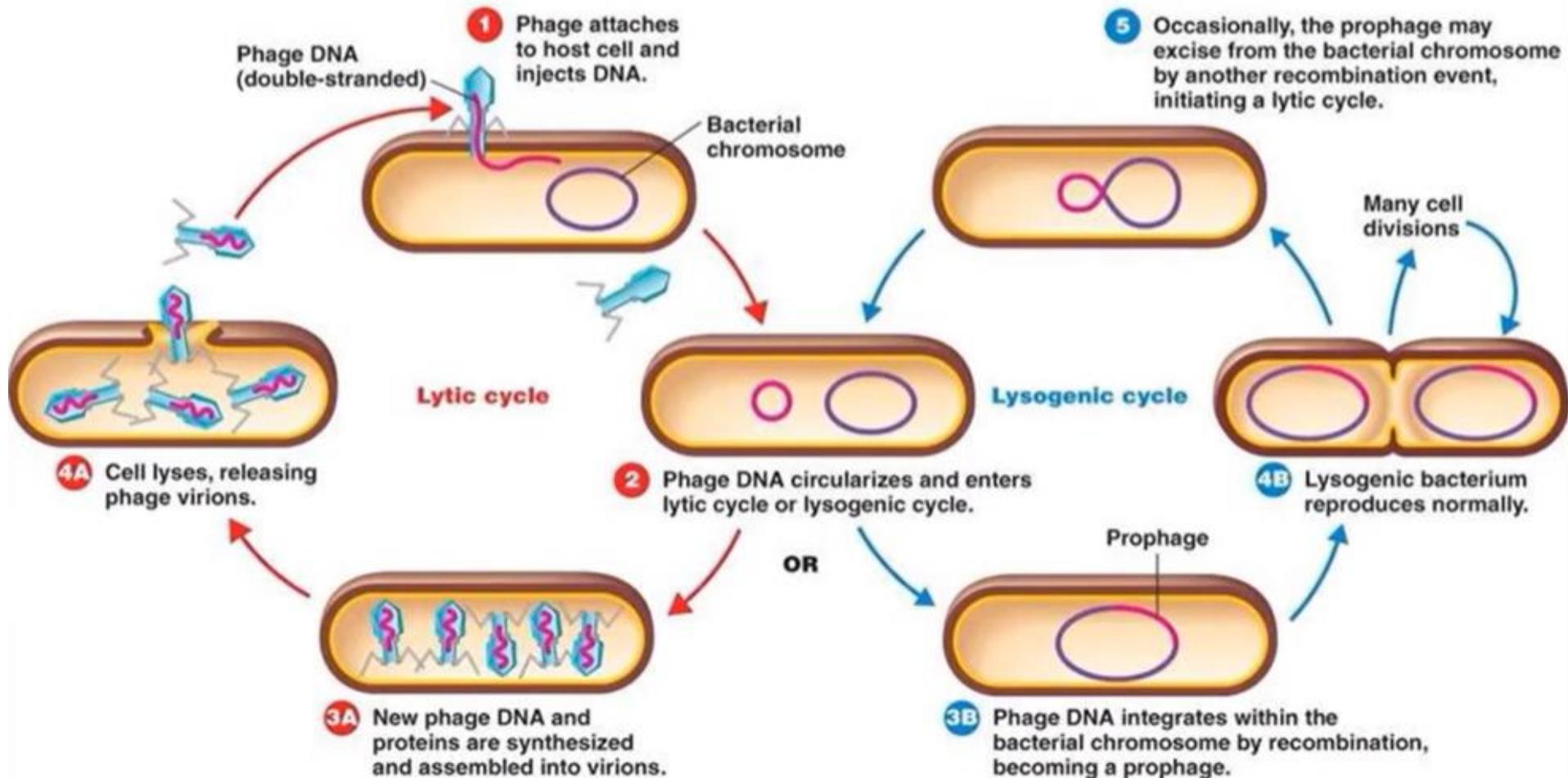
# Multiplication Cycle in Bacteriophages

- **Bacteriophages** – bacterial viruses (phages)
- Most widely studied are those that infect *Escherichia coli* – complex structure, DNA
- Multiplication goes through similar stages as animal viruses.
- Only the nucleic acid enters the cytoplasm - uncoating is not necessary
- Release is a result of cell lysis induced by viral enzymes and accumulation of viruses - **lytic cycle**

# Steps in Phage Replication

1. **Adsorption** – binding of virus to specific molecules on host cell.
2. **Penetration** – genome enters host cell
3. **Replication** – viral components are produced
4. **Assembly** – viral components are assembled
5. **Maturation** – completion of viral formation
6. **Lysis & Release** – viruses leave the cell to infect other cells, called **lytic cycle**.

# Lytic and Lysogenic Cycles



# Lysogeny: The Silent Virus Infection

- Not all phages complete the lytic cycle.
- Some DNA phages, called **temperate phages**, undergo adsorption and penetration but don't replicate.
- The viral genome inserts into bacterial genome and becomes an inactive **prophage** – the cell is not lysed.
- **Prophage** is retained and copied during normal cell division resulting in the transfer of temperate phage genome to all host cell progeny – **lysogeny**
- **Induction** can occur resulting in activation of lysogenic prophage followed by viral replication and cell lysis.

# Lysogeny

- Lysogeny results in the spread of the virus without killing the host cell.
- Phage genes in the bacterial chromosome can cause the production of toxins or enzymes that cause pathology – **lysogenic conversion**
  - *Corynebacterium diphtheriae*
  - *Vibrio cholerae*
  - *Clostridium botulinum*

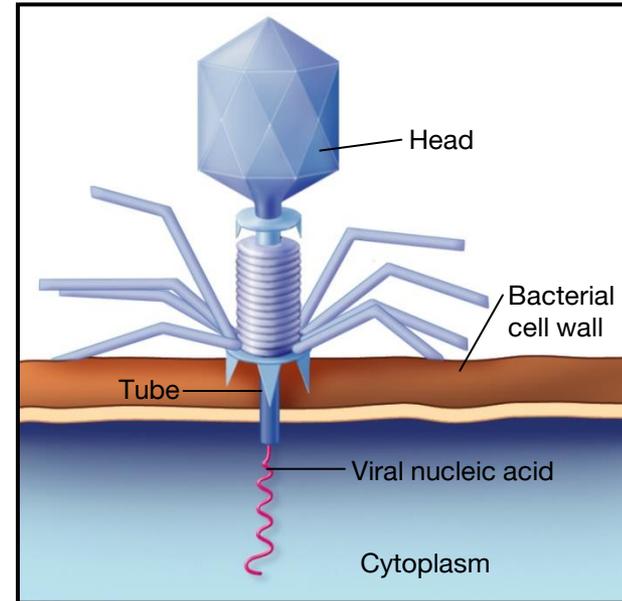
# Comparison of Bacteriophage and Animal Virus

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**TABLE 6.4** Comparison of Bacteriophage and Animal Virus Multiplication

	Bacteriophage	Animal Virus
<b>Adsorption</b>	Precise attachment of special tail fibers to cell wall	Attachment of capsid or envelope to cell surface receptors
<b>Penetration</b>	Injection of nucleic acid through cell wall; no uncoating of nucleic acid	Whole virus is engulfed and uncoated, or virus surface fuses with cell membrane; nucleic acid is released.
<b>Synthesis and Assembly</b>	Occurs in cytoplasm Cessation of host synthesis Viral DNA or RNA replicated Viral components synthesized	Occurs in cytoplasm and nucleus Cessation of host synthesis Viral DNA or RNA replicated Viral components synthesized
<b>Viral Persistence</b>	Lysogeny	Latency, chronic infection, cancer
<b>Release from Host Cell</b>	Cell lyses when viral enzymes weaken it.	Some cells lyse; enveloped viruses bud off host cell membrane.
<b>Cell Destruction</b>	Immediate	Immediate or delayed



# How do we grow viruses?

**Obligate intracellular parasites  
– what do they need to grow?**

They require appropriate cells to replicate.

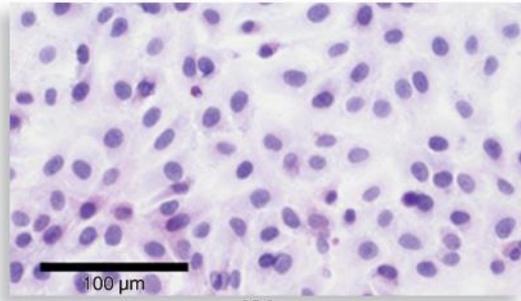
# Techniques in Cultivating and Identifying Animal Viruses

- Obligate intracellular parasites that require appropriate cells to replicate
- Methods used:
  - **Cell (tissue) cultures** – cultured cells grow in sheets that support viral replication and permit observation for cytopathic effects
  - **Bird embryos** – incubating egg is an ideal system; virus is injected through the shell
  - **Live animal** inoculation – occasionally used when necessary

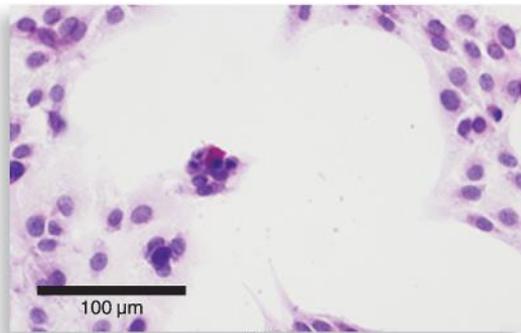
# Methods for Growing Viruses

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(a)



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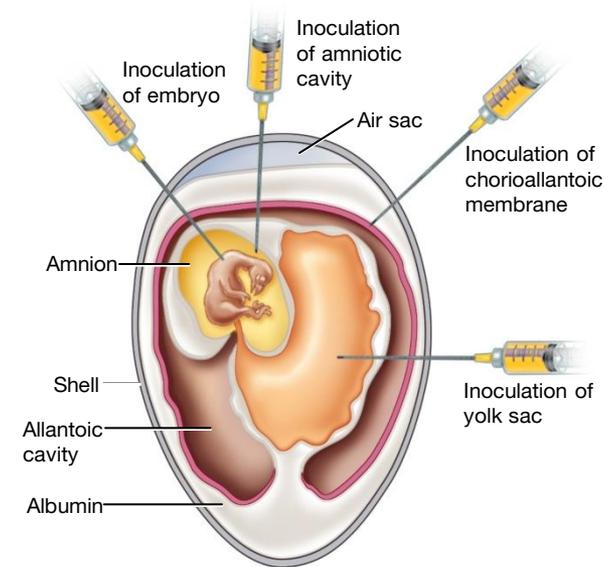
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(a)

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(b)

# Prions and Other Infectious Particles

**Prions** - misfolded proteins, contain no nucleic acid

- Extremely resistant to usual sterilization techniques
- Cause transmissible spongiform encephalopathies
  - fatal neurodegenerative diseases

Common in animals:

- **Scrapie** in sheep and goats
- **Bovine spongiform encephalopathies** (BSE), mad cow disease
- Humans – **Creutzfeldt-Jakob Syndrome** (CJS), fatal neurodegenerative disorder

# Other Noncellular Infectious Agents

- ❖ **Satellite viruses:** Are subviral agents.
  - dependent on other viruses for replication.
  - Have their own genome.
  - Lack essential genes needed for replication.
  - Use proteins or enzymes supplied by the helper virus.
    - Adeno-associated virus (AAV) – replicates only in cells infected with **adenovirus**.
    - Delta agent (Hepatitis D virus, HDV) – naked ssRNA expressed only in the presence of **hepatitis B virus**
- ❖ **Viroids** – short pieces of RNA, no protein coat; only been identified in plants.

# Anti-viral drugs

1) Prevent attachment

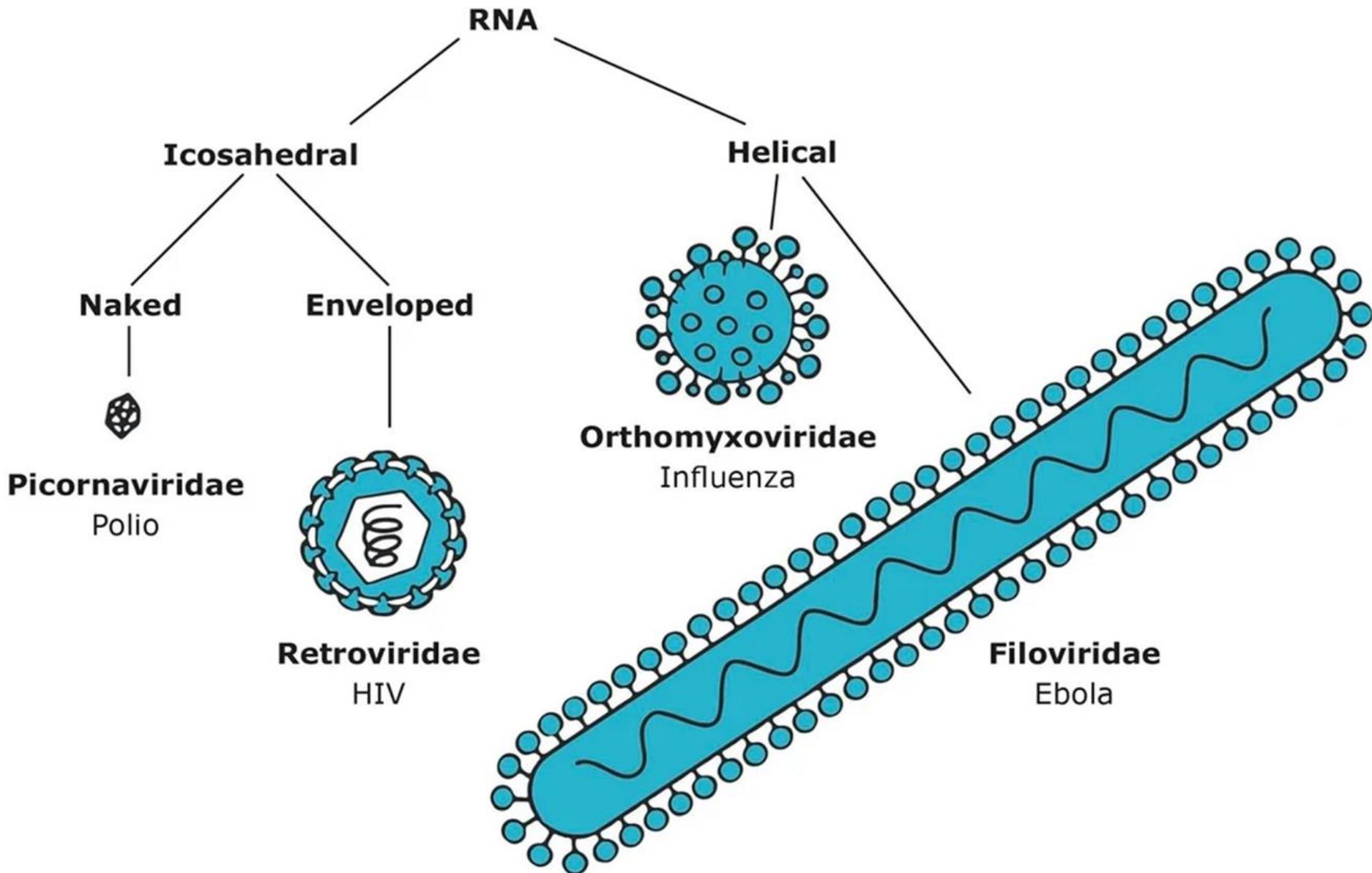
2) Prevent Uncoating; **Rimantadine**

3) Prevent Replication; **Acyclovir** (Block DNA polymerase), **Ribavirin** inhibits mRNA translation

4) Prevent release; **Tamiflu**

# Grouping viruses

- ✓ Viruses are grouped according to the type of genetic code they carry – either DNA or RNA.
- ✓ By the shape of their capsid.
- ✓ Originally viruses were grouped and named according to the disease they cause, even if they are not closely related.
  
- For example - **Hepatitis A is an RNA virus**  
- **Hepatitis B is a DNA virus**
- But they both cause liver disease.
  
- ✓ Nowadays, viruses are grouped by their shared characteristics



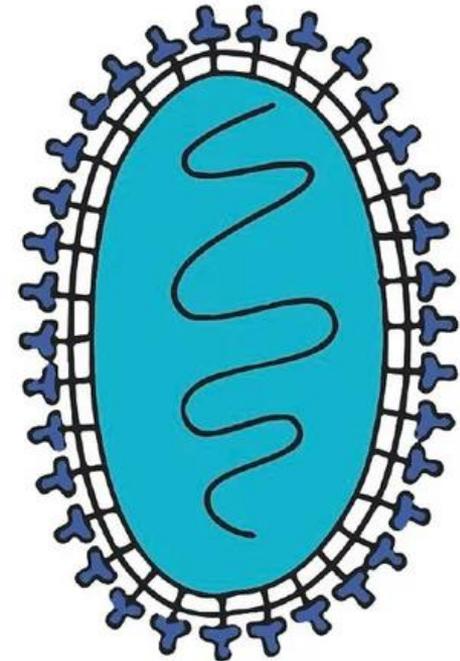
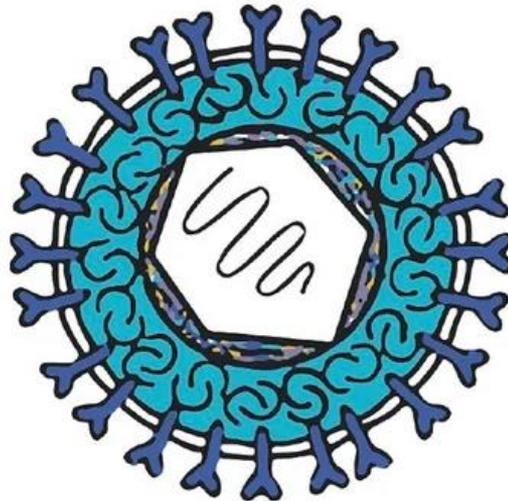
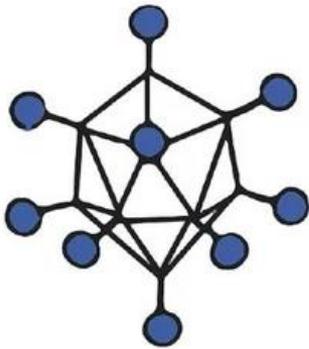
**DNA**

**Icosahedral**

**Helical/Complex**

**Naked**

**Enveloped**



**Adenoviridae**  
Tonsillitis

**Herpesviridae**  
Glandular fever

**Poxviridae**  
Smallpox

# DNA VIRUSES

## ❖ Most DNA viruses

- Are double-stranded (dsDNA, like human DNA)
- Have icosahedral symmetry
- Replicate in the nucleus
- Are linear

## ❖ Exceptions\*\*\*

- **Parvoviridae**
  - only 1 strand of DNA (ssDNA)
- **Poxviridae**
  - no icosahedral symmetry, surrounded by complex structural proteins.
  - replicates in cytoplasm
- **Papilloma, polyoma, and hepadna**
  - are non-linear (circular)

# The DNA viruses are "HHAPPPy"

## ❖ Enveloped DNA viruses

- Herpesviridae
- Hepadnaviridae
- Poxviridae



**dsDNA**

## ❖ Naked DNA viruses

- Adenoviridae
- Polyomaviridae
- Papillomaviridae
- Parvoviridae



**ssDNA**



# Herpesviridae (Herpes Family)

## ❖ General characteristics

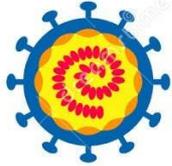
- Herpein = **Creep**
- Large, **enveloped DNA viruses** with **icosahedral capsid**
- **Double-stranded, linear DNA**
- Replicate in the **nucleus**
- Establish **latent infections** with periodic reactivation.
- Humans are the natural host for most members.
- Similar morphology.
- Response to antiviral drug (Acyclovir).



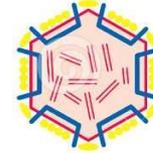
Polyomaviridae  
Papillomaviridae



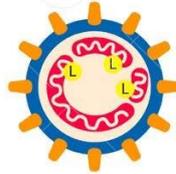
Herpesviridae



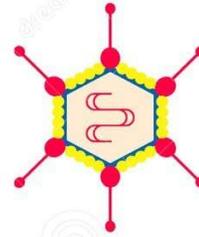
Paramyxoviridae



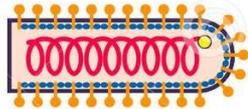
Reoviridae



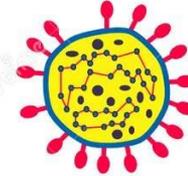
Bunyaviridae



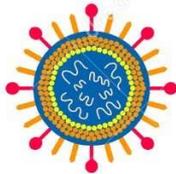
Adenoviridae



Rhabdoviridae



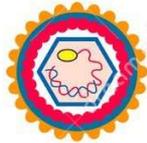
Arenaviridae



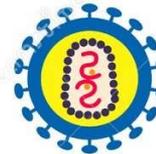
Orthomyxoviridae



Caliciviridae



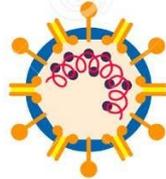
Hepadnaviridae



Retroviridae



Togaviridae



Coronaviridae



Parvoviridae



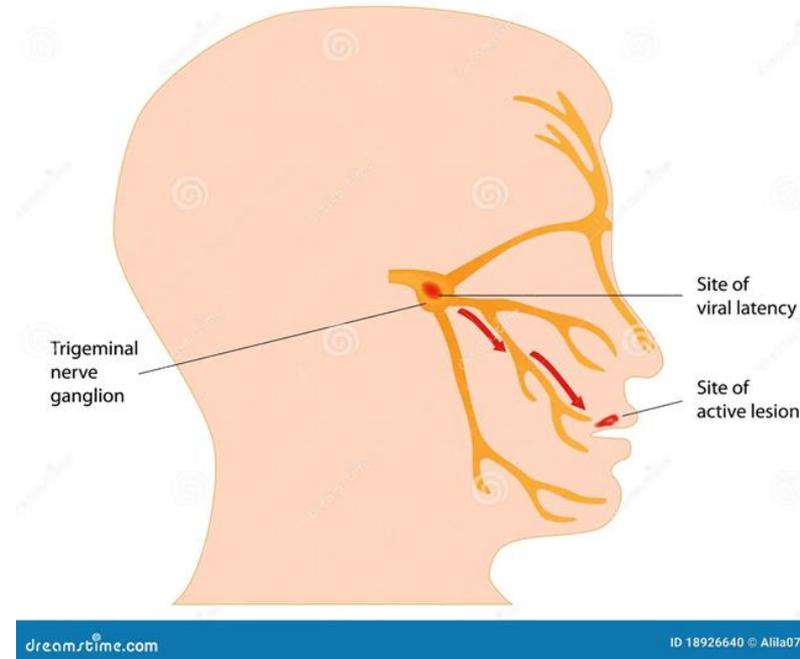
Filoviridae



Flaviviridae

## ❖ Clinical importance

- **Primary infection** → active viral replication and symptoms
- Lifelong infection due to **latency** → viral genome persists in host cells without infection.
- Severe disease in **immunocompromised patients**.
- Some members are **oncogenic**.
- Reactivation causes **secondary** (recurrent) disease → triggered by stress, immunosuppression, fever, UV light



# Classification of Human Herpesviruses

## 1. **Alphaherpesvirinae**

- Fast replication
- Establish latency in sensory nerve ganglia

Virus	Disease
Herpes simplex Viruses (HSV-1)	Oral herpes, gingivostomatitis
Herpes simplex Viruses (HSV-2)	Genital herpes
Varicella-Zoster virus (VZV) or (HHV-3)	Chickenpox(varicella) & shingles (zoster)

# Classification of Human Herpesviruses

## 2. **Betaherpesvirinae**

- Slow replication
- Latency mainly in monocytes & glands

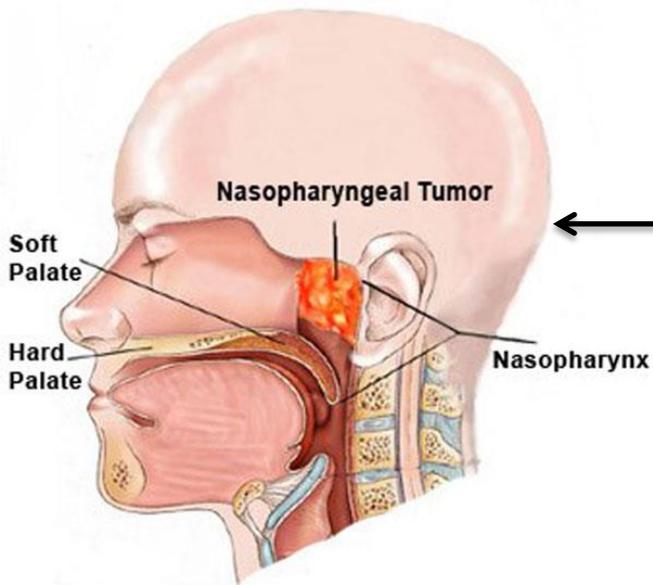
Virus	Disease
Cytomegalovirus (CMV) or (HHV-5)	Congenital infections, retinitis
HHV-6	Roseola infantum
HHV-7	Febrile illness in children



### 3. Gammaherpesvirinae

- Infect **lymphocytes**
- Associated with **cancers**

Virus	Disease
Epstein-Barr virus (EBV) or (HHV-4)	Burkitt lymphoma, nasopharyngeal carcinoma
HHV-8	Kaposi sarcoma



# Diagnosis

- ✓ Specimen
- ✓ Visualize by EM
- ✓ PCR (most sensitive)
- ✓ Serology (IgM/IgG) by **ELISA** (Enzyme-Linked Immunosorbent Assay)
- ✓ Viral culture
- ✓ Cytopathic effects, e.g: by using Giemsa stain to seen Giant cells under LM.