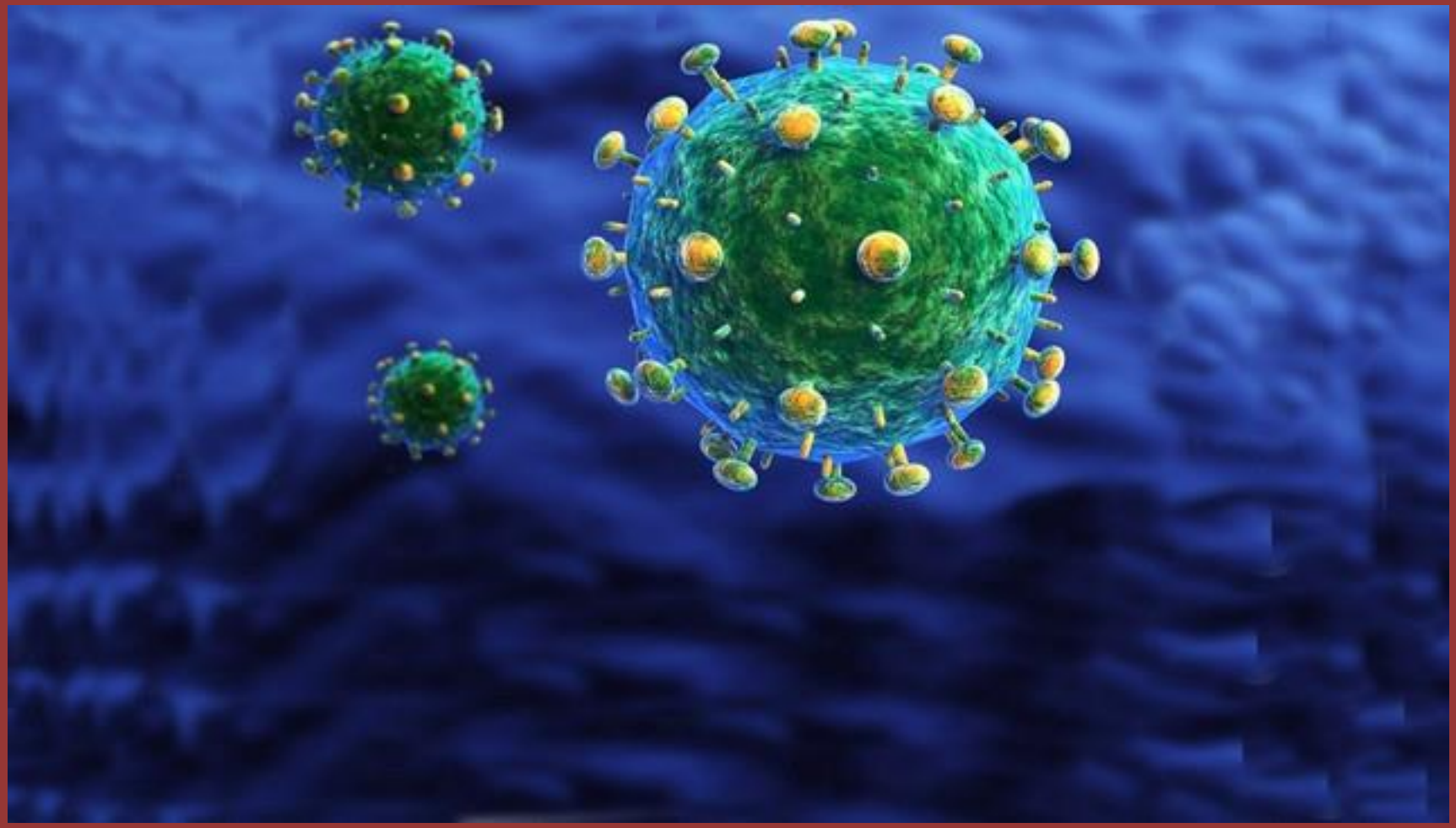


Viruses

History

- Through the 1800s, many scientists discovered that something smaller than bacteria could cause disease and they called it virion (*Latin word- poison*)
- In the 1930s, after the invention of **electron microscopes**, viruses finally could be seen.
- The first photographs of viruses were obtained in 1940.

Study of Viruses - Virology

- **Viruses are:**
- 1. Acellular
- 2. Obligate intracellular parasites
- 3. No ATP generating system
- 4. No Ribosomes or means of Protein Synthesis

- Viruses that infect bacteria are called: **Bacteriophage**
- Many human diseases are caused by viruses e.g

  AID

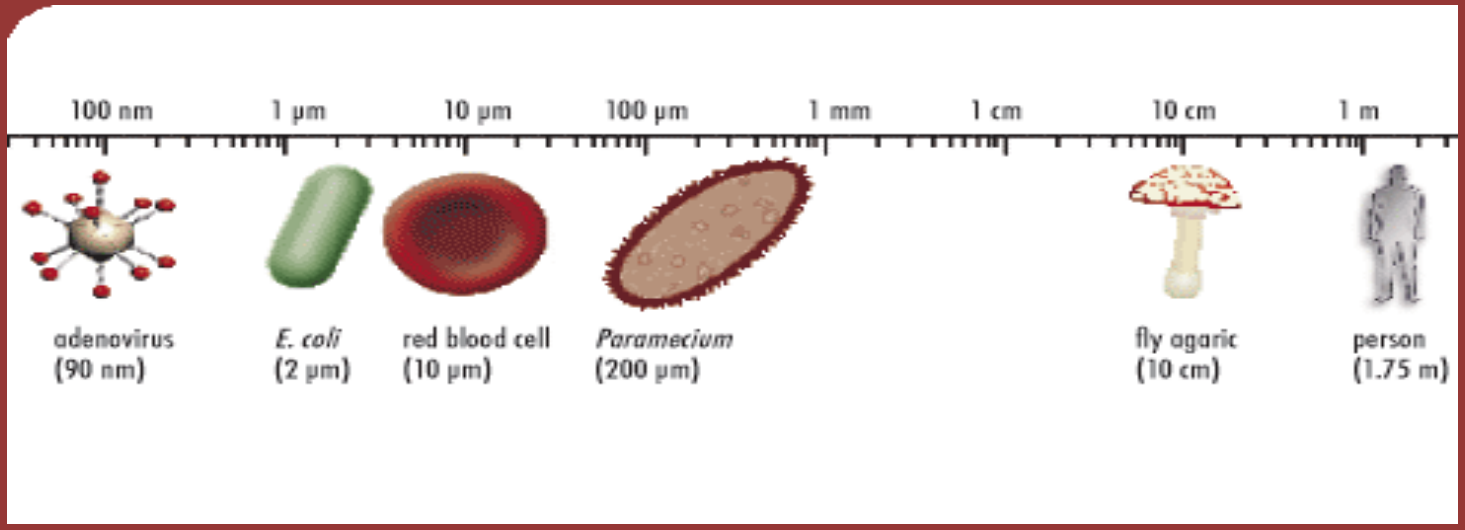
  Hepatitis

  Influenza

  SARS

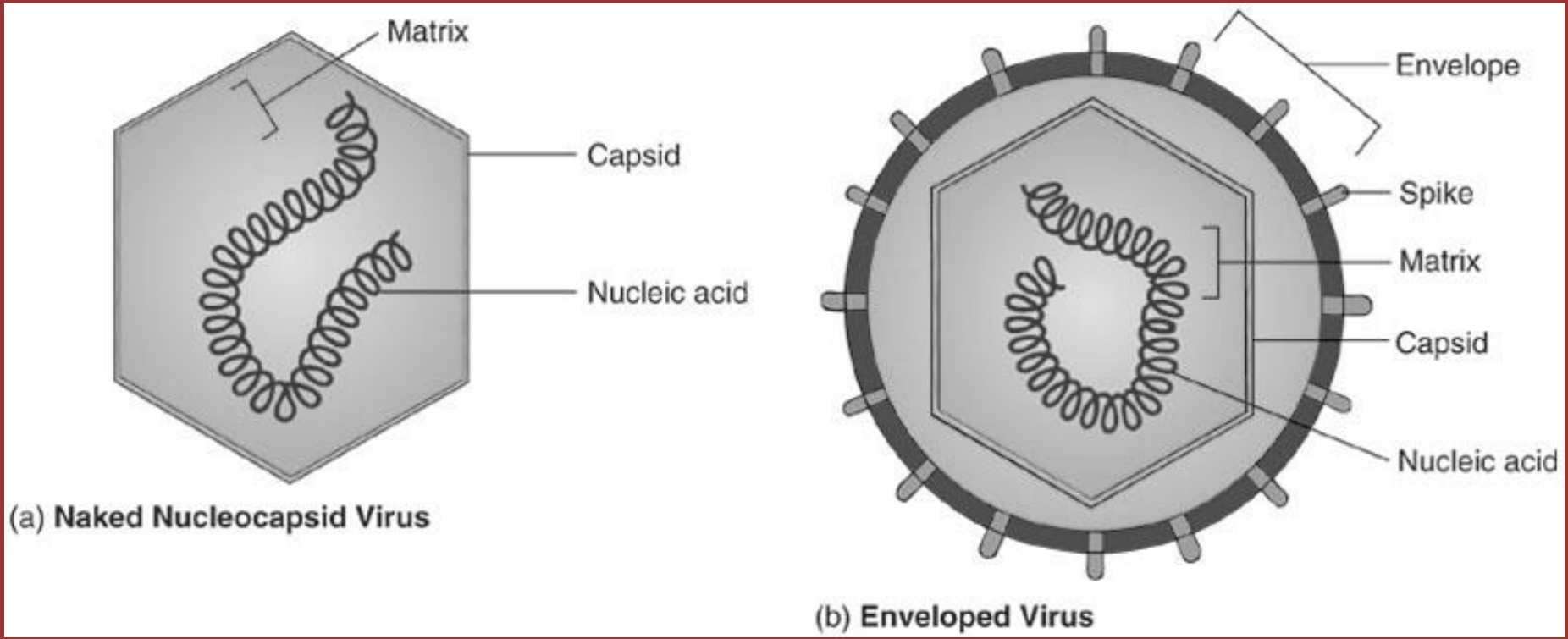
- Some viruses “**oncogenic viruses**” can even cause cancers **e.g.** leukemia, lymphoma..

Viral size



- Virus particles can only be seen by an electron microscope
- Most viruses range in sizes from 10-300 nanometers.

Structure of virus



Structure of Viruses

1) Genome:

The nucleic acid material containing the genetic information and its either DNA or RNA.

2) Capsid:

A protein structure designed to protect the genome. It is composed of many small protein units called ***capsomeres.***

3) Envelope:

A lipid bilayer membrane found in some viruses. It is derived from the host cell membrane or nuclear membrane and never made by the viruses themselves.

I- Virus Genome

Viruses have either DNA or RNA

Viral NA are usually circular but some are linear.

Both DNA or RNA can be Single Strand (ss) or Double Strand (ds)

Viruses have four categories based on that

1. ss DNA viruses
2. ds DNA viruses → most common.
3. ss RNA viruses → most common.
4. ds RNA viruse

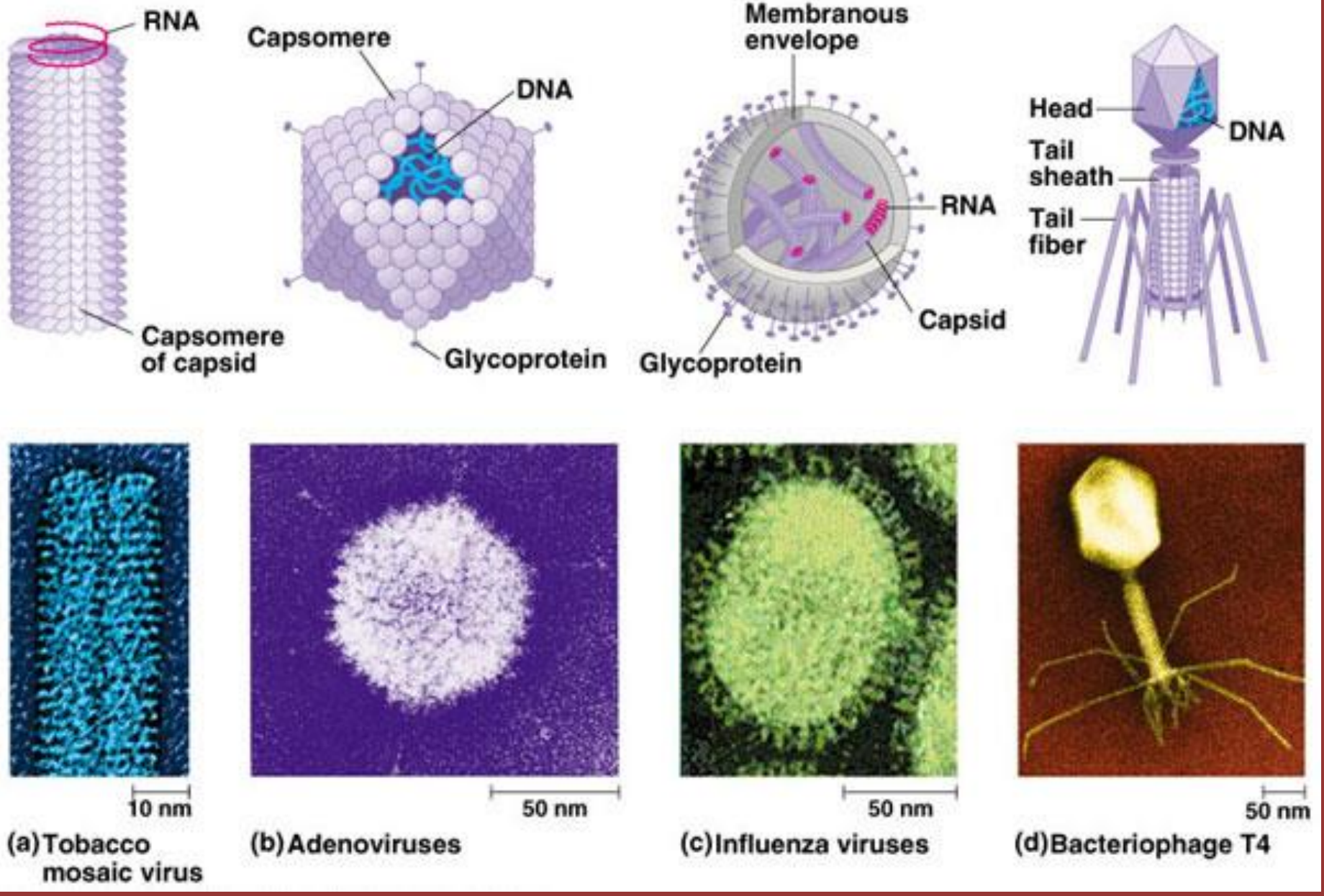
Contains several genes that are responsible for the production of **non-structural protein** (enzymes and regulatory proteins)
and **structural proteins** (proteins incorporated in the structure of the progeny virus)

II. Capsid

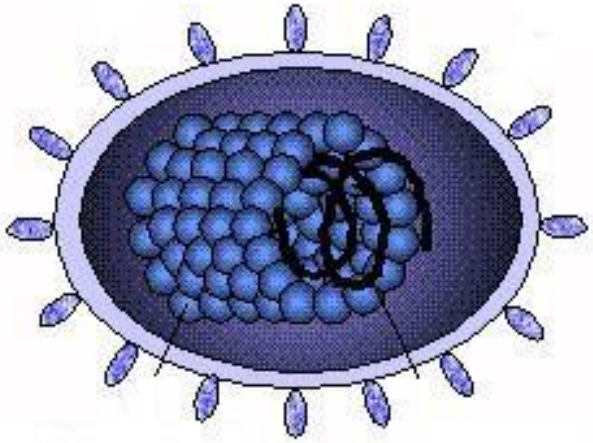
- The protein coat inclosing the genome.
- The capsid is designed to give shape, size, and protect the virus nucleic acid from environmental damage.
- Capsid and Nucleic Acid are called "**neocleocapsid**" or "naked virus".

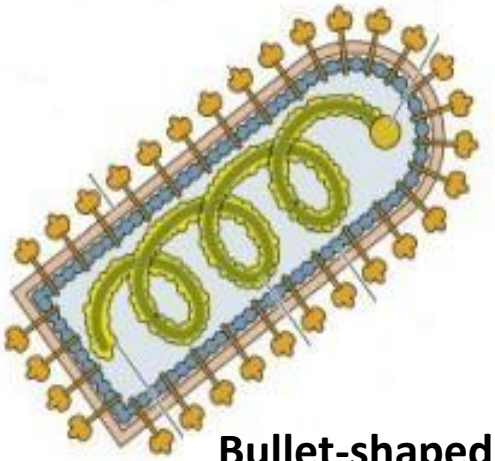
- **Capsids of viruses have different shapes and symmetry. They can be:**

1. **Helical:** coiled tubes.
2. **Icosahedral:** many sided.
3. **Bullet shaped.**
4. **Spherical.**
5. **Complex:** combination of shapes.

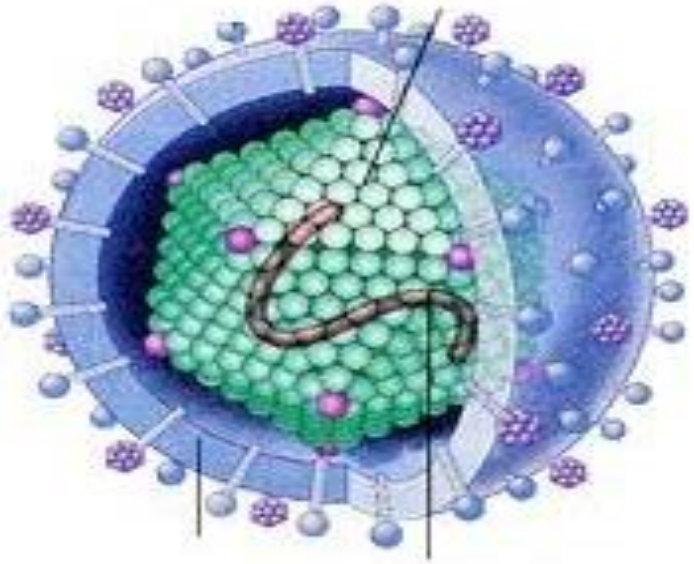

RNA
Capsomere of capsid
Capsomere
DNA
Glycoprotein
Membranous envelope
RNA
Capsid
Glycoprotein
Head
DNA
Tail sheath
Tail fiber
10 nm
(a) Tobacco mosaic virus
50 nm
(b) Adenoviruses
50 nm
(c) Influenza viruses
50 nm
(d) Bacteriophage T4

Helical Virus

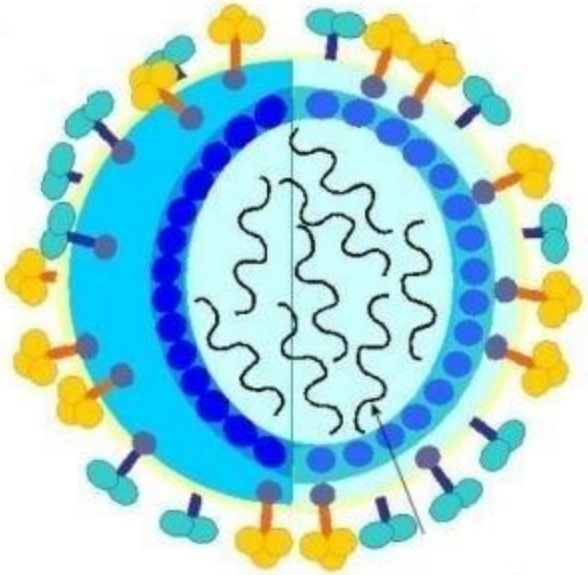




Bullet-shaped Virus



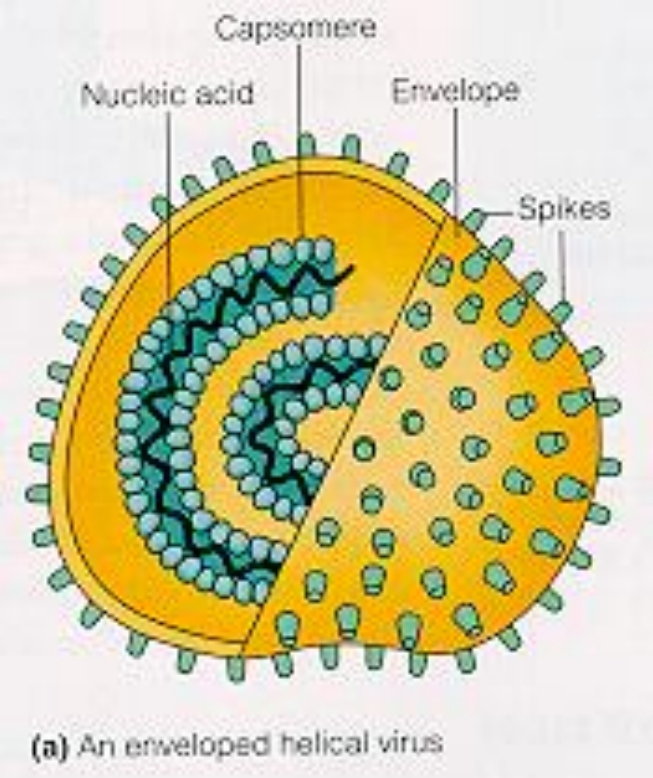
Polyhedral Virus



Spherical Virus

III. Envelope

- Lipid containing membrane surrounding the nucleocapsid used in *defining a viral family*
- The virus that is not enveloped is referred to as *a naked virus*
- Often there are projecting spikes of glycoprotein which are important as viral attachment protein to host cell or erythrocytes



Atypical Virus-Like Agents

Viroids

- Naked RNA without protein coat or envelop
- Plant pathogens

Prions

- Composes of entirely of protein
- Have no DNA or RNA
- Cause fatal neurological disease in animals such as **Mad cow disease** and **Creutzfeldt-Jacob disease** (CJD) in human

Classification of Viruses

Viruses are classified by the following characteristics:

1. Type of genetic material (DNA or RNA).
2. Shape of capsid.
3. Number of capsomeres.
4. Size of capsid.
5. Presence or absence of an envelope.
6. Type of host that it infects.
7. Type of disease that it produces.
8. Target cells.
9. Immunologic or antigenic properties.

Three problems every virus must solve

1) How to reproduce during its “visit” inside the cell.

- ✓How to:
  - ◆copy its genetic information
  - ◆produce mRNA for protein production

2) How to spread from one individual to another.

3) How to evade the host defenses.

Virus Replication

- The ability of viruses to infect or invade the target cell and multiply inside it and subsequent escape outside the cell.

1) **Attachment (adsorption) :**

Adsorption involves attachment of viral surface proteins or spikes to the cell surface receptor proteins

2) **Penetration:**

The entire virus enters the cells.

3) **Un-coating:**

Release of the viral genome from its protective capsid to enable the viral nucleic acid to replicate.

Virus Replication

4) **Biosynthesis:**

This step result in the production of pieces /parts of viruses (e.g. viral DNA and viral proteins)

(genome replication and genome expression)

5) **Assembly :**

The viral parts are assembled to create complete virions inside the host cell

6) **Release:**

Escape of the complete virions from the host cell.

Naked viruses → Cell lysis (cell death).

Enveloped viruses → Budding.

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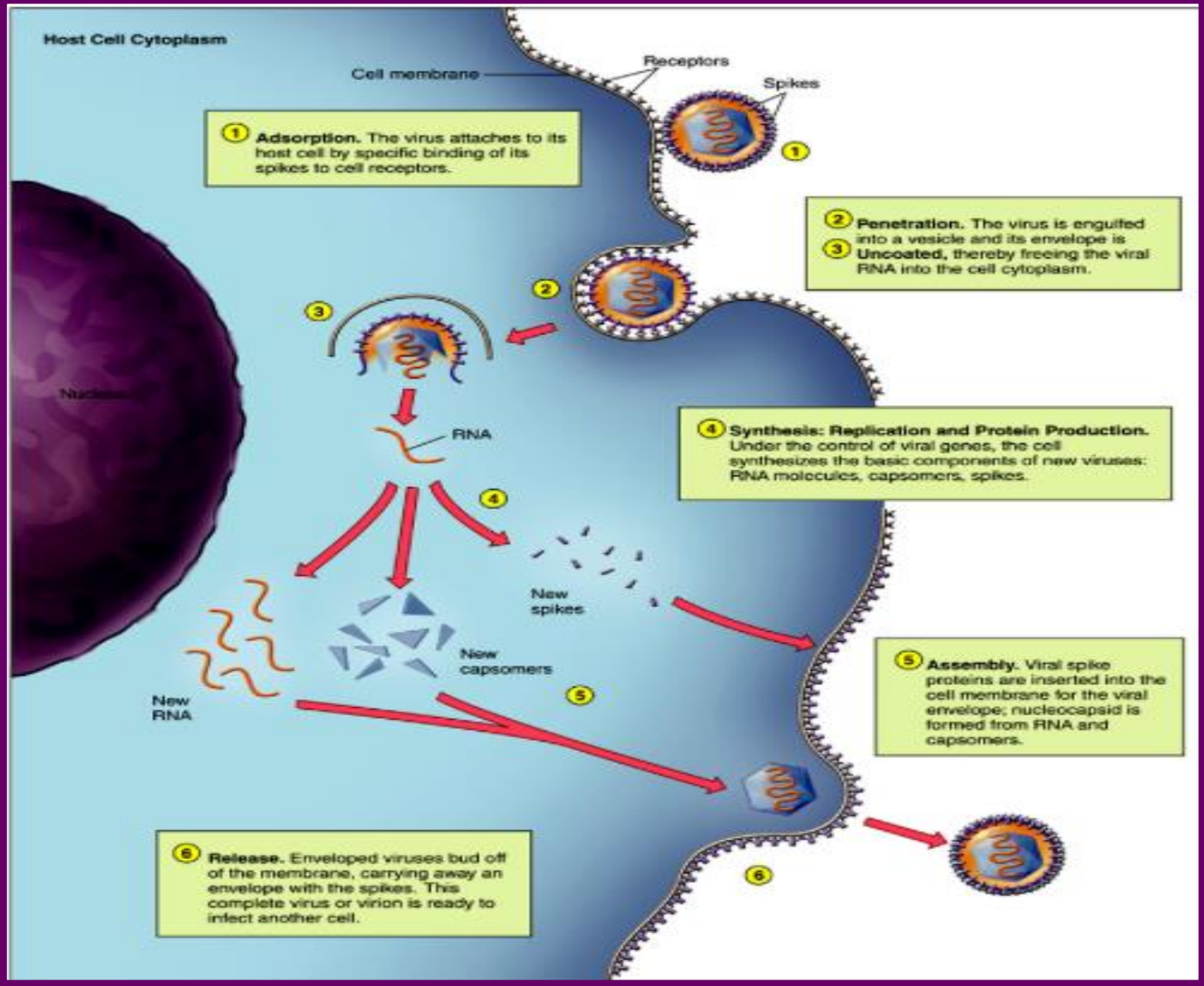
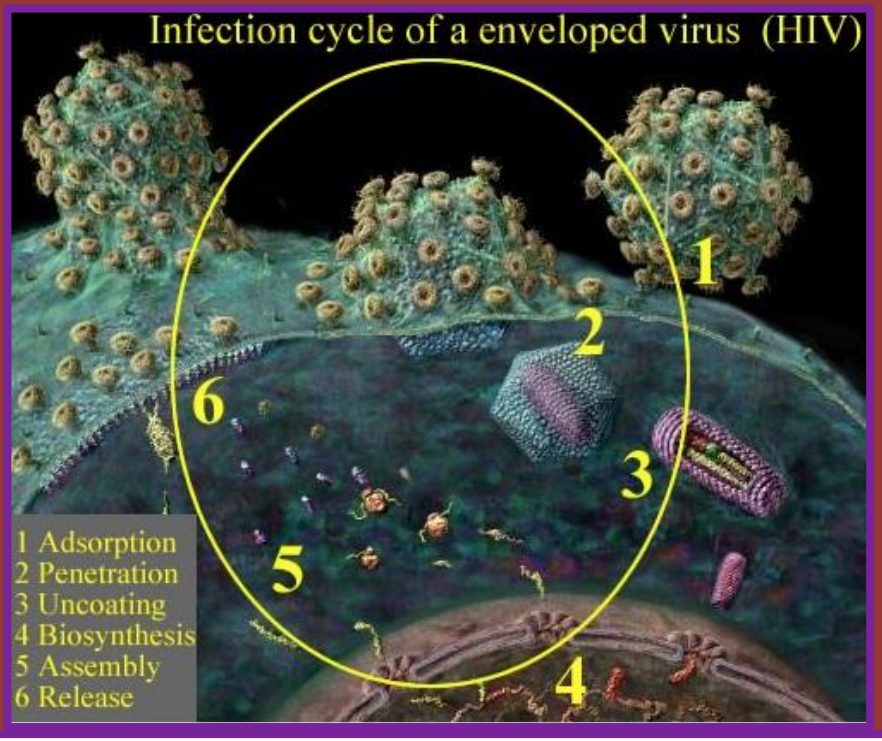
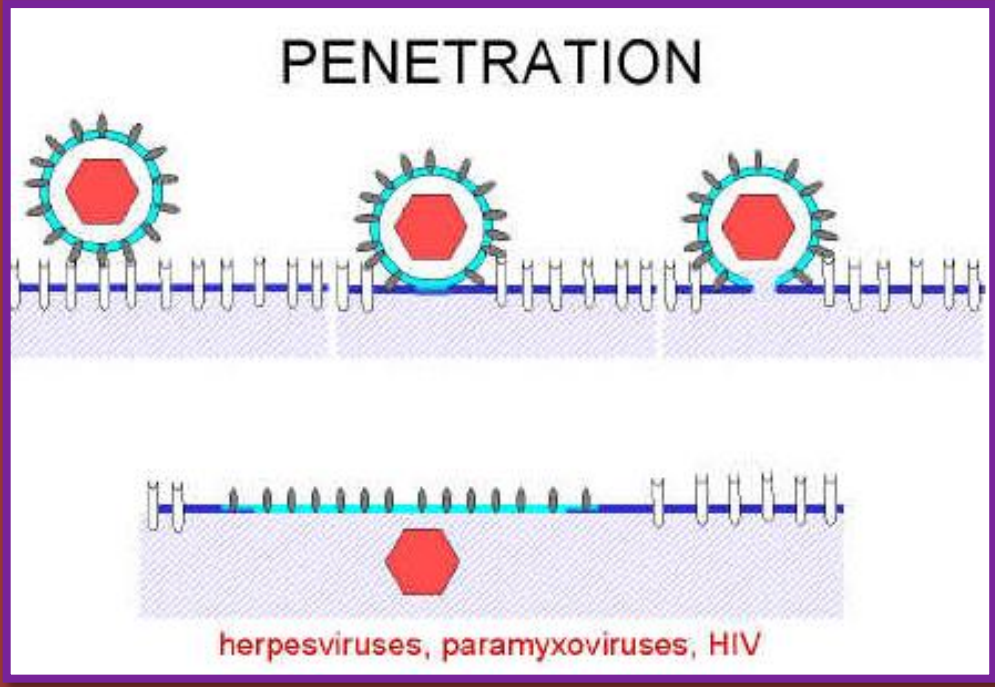

Host Cell Cytoplasm
Cell membrane
Receptors
Spikes
1 Adsorption. The virus attaches to its host cell by specific binding of its spikes to cell receptors.
2 Penetration. The virus is engulfed into a vesicle and its envelope is
3 Uncoated, thereby freeing the viral RNA into the cell cytoplasm.
RNA
4 Synthesis: Replication and Protein Production. Under the control of viral genes, the cell synthesizes the basic components of new viruses: RNA molecules, capsomers, spikes.
New spikes
New capsomers
New RNA
5 Assembly. Viral spike proteins are inserted into the cell membrane for the viral envelope; nucleocapsid is formed from RNA and capsomers.
6 Release. Enveloped viruses bud off of the membrane, carrying away an envelope with the spikes. This complete virus or virion is ready to infect another cell.

Penetration Step

A. Some enveloped viruses fuse directly with the plasma membrane. Thus, the internal components of the virion are immediately delivered to the cytoplasm of the cell. (enveloped viruses)



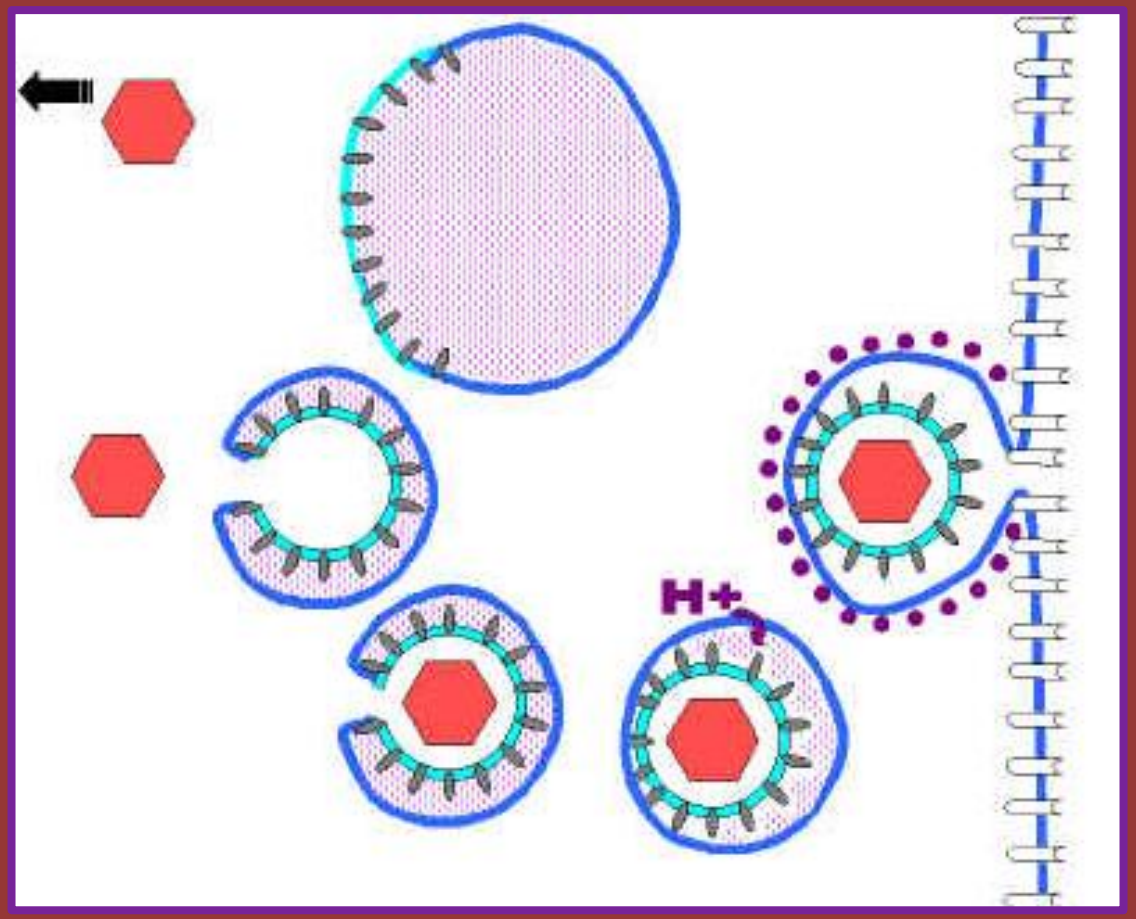


Penetration Step

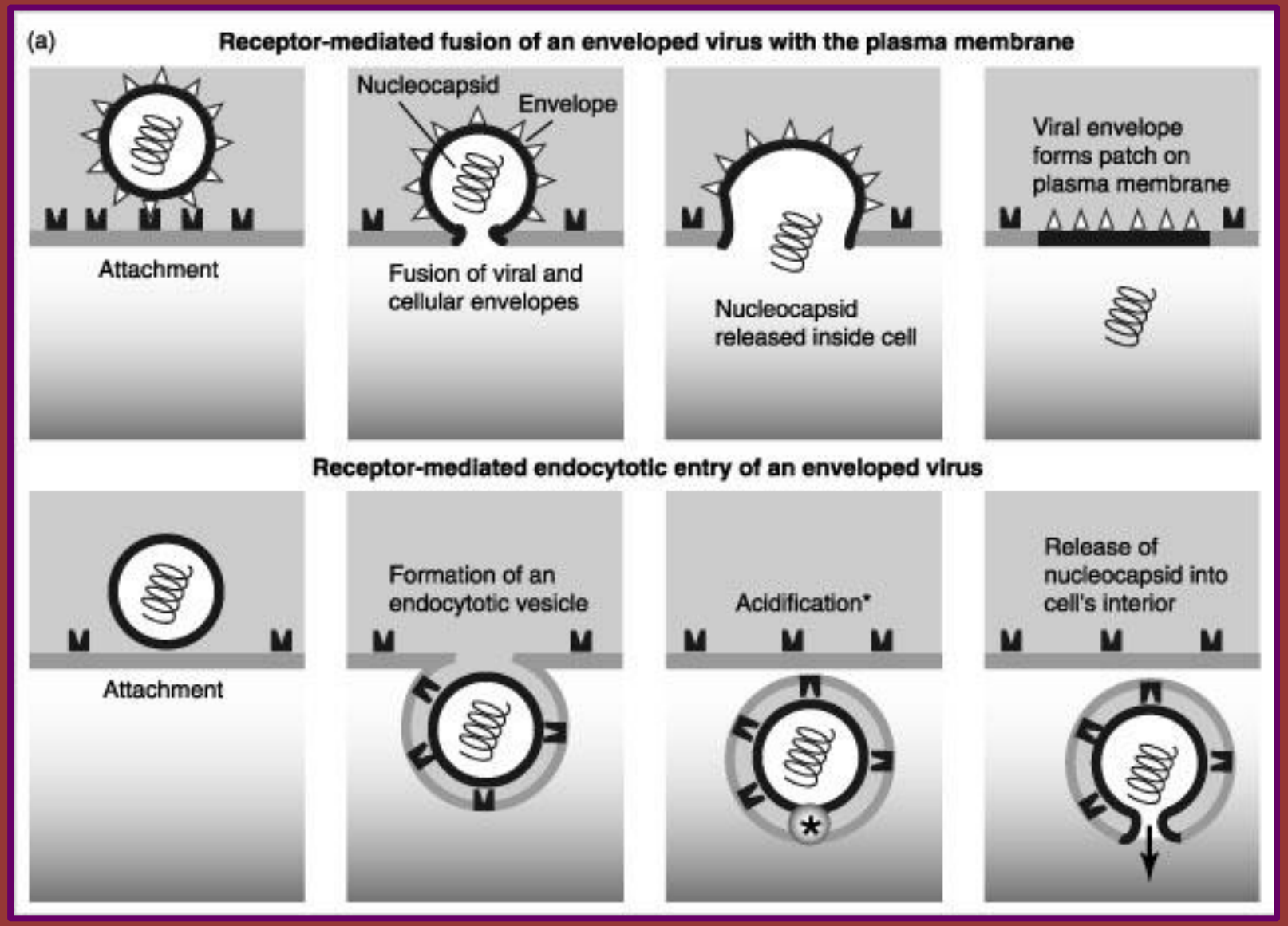
B. Entry via endosomes at the cell surface.

Some viruses are unable to fuse directly with the plasma membrane. These viruses are taken into endosomes. Then internal components of the virus is released into the cytoplasm of the cell .

(both enveloped and non-envelope viruses)

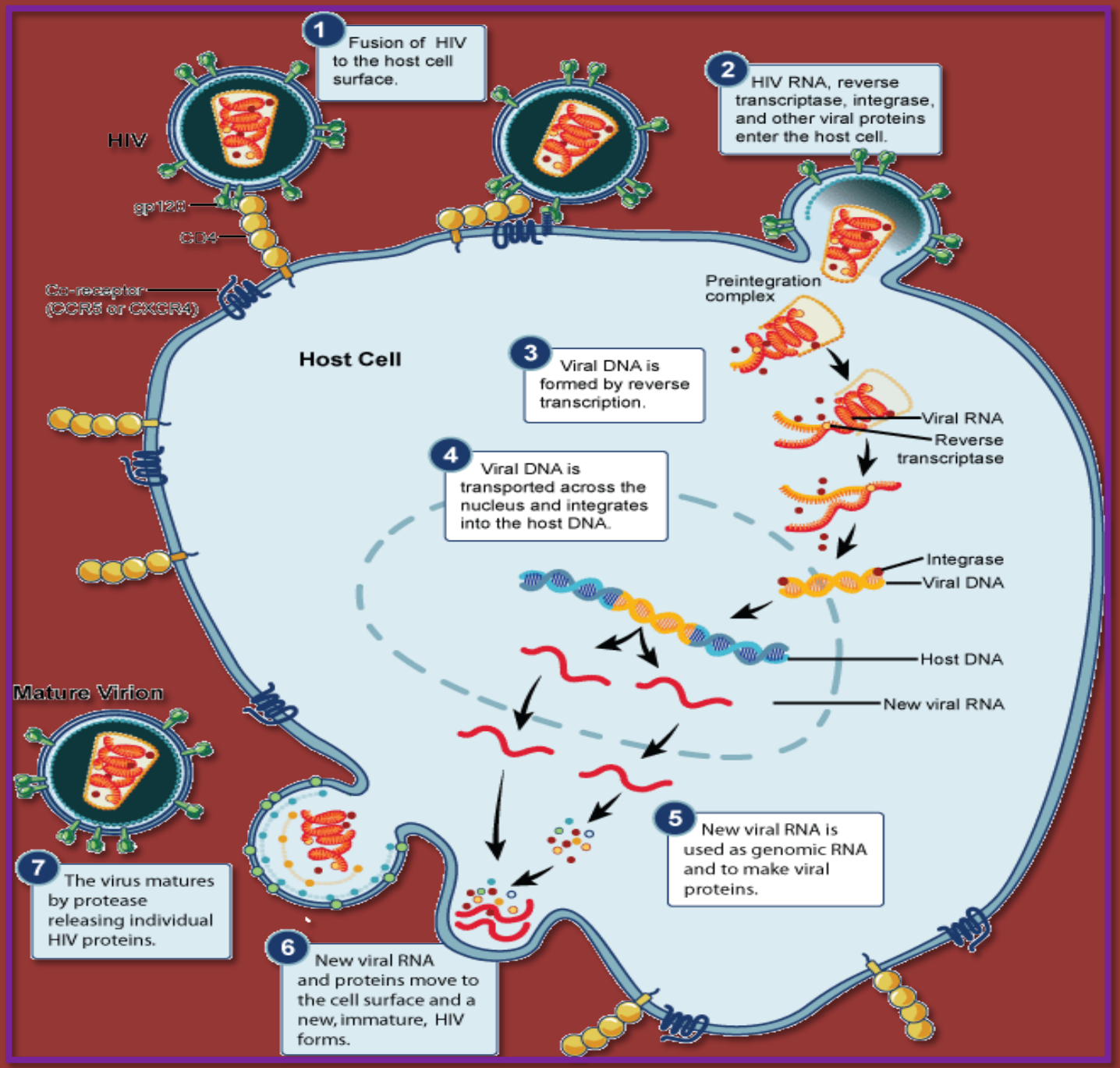


Penetration Step

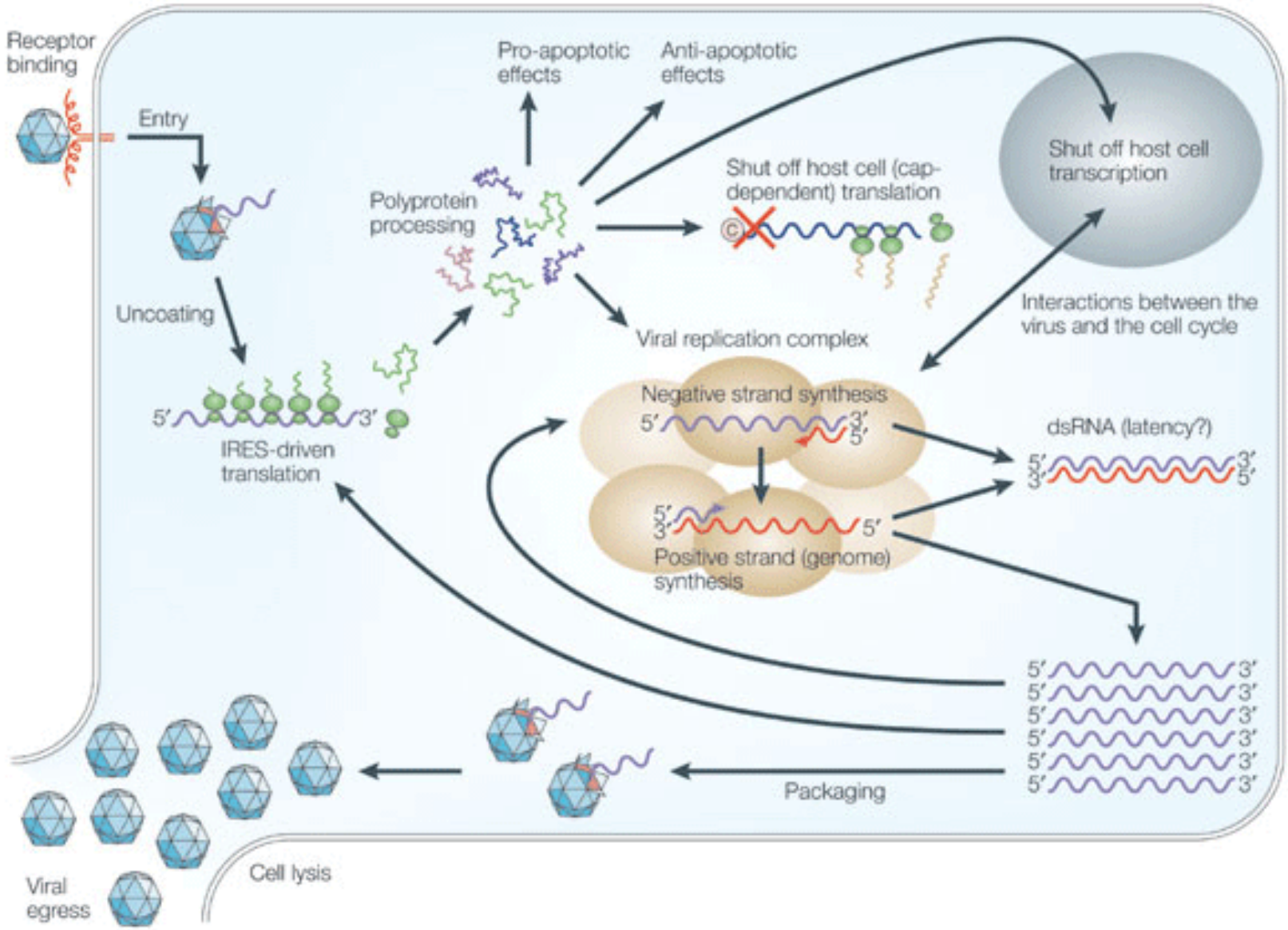


Replication Cycle of HIV virus.

e.g. enveloped virus.

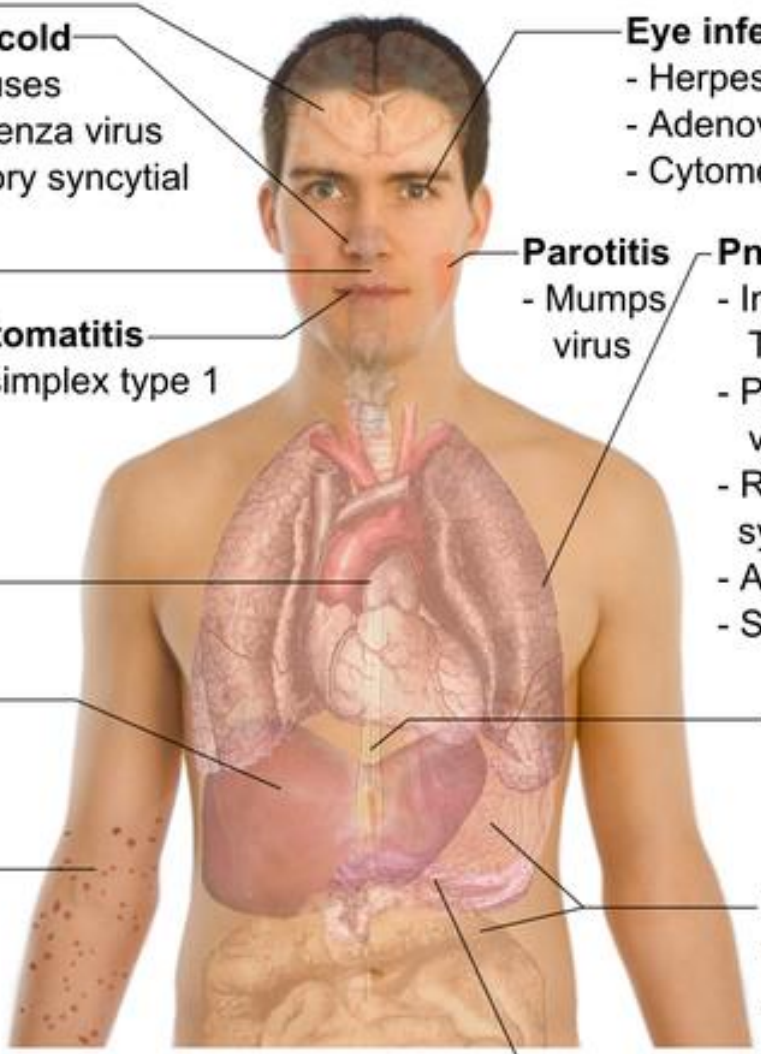


Replication Cycle of Picornavirus e.g. non-enveloped virus



Overview of

Viral infections



Encephalitis/ meningitis
- JC virus
- Measles
- LCM virus
- Arbovirus
- Rabies

Common cold
- Rhinoviruses
- Parainfluenza virus
- Respiratory syncytial virus

Eye infections
- Herpes simplex virus
- Adenovirus
- Cytomegalovirus

Parotitis
- Mumps virus

Pneumonia
- Influenza virus, Types A and B
- Parainfluenza virus
- Respiratory syncytial virus
- Adenovirus
- SARS coronavirus

Pharyngitis
- Adenovirus
- Epstein-Barr virus
- Cytomegalovirus

Gingivostomatitis
- Herpes simplex type 1

Cardiovascular
- Coxsackie B virus

Hepatitis
- Hepatitis virus types A, B, C, D, E

Myelitis
- Poliovirus
- HTLV-I

Skin infections
- Varicella zoster virus
- Human herpesvirus 6
- Smallpox
- Molluscum contagiosum
- Human papillomavirus
- Parvovirus B19
- Rubella
- Measles
- Coxsackie A virus

Gastroenteritis
- Adenovirus
- Rotavirus
- Norovirus
- Astrovirus
- Coronavirus

Sexually transmitted diseases
- Herpes simplex type 2
- Human papillomavirus
- HIV

Pancreatitis
- Coxsackie B virus

The OutCome of Viral Infections

The range of structural and biochemical effects that viruses have on the host cell is extensive. These are called ***cytopathic effects.***

- **Lytic Infection** → Host cell dies at the end of virus replicative cycle (e.g. influenza & polio)

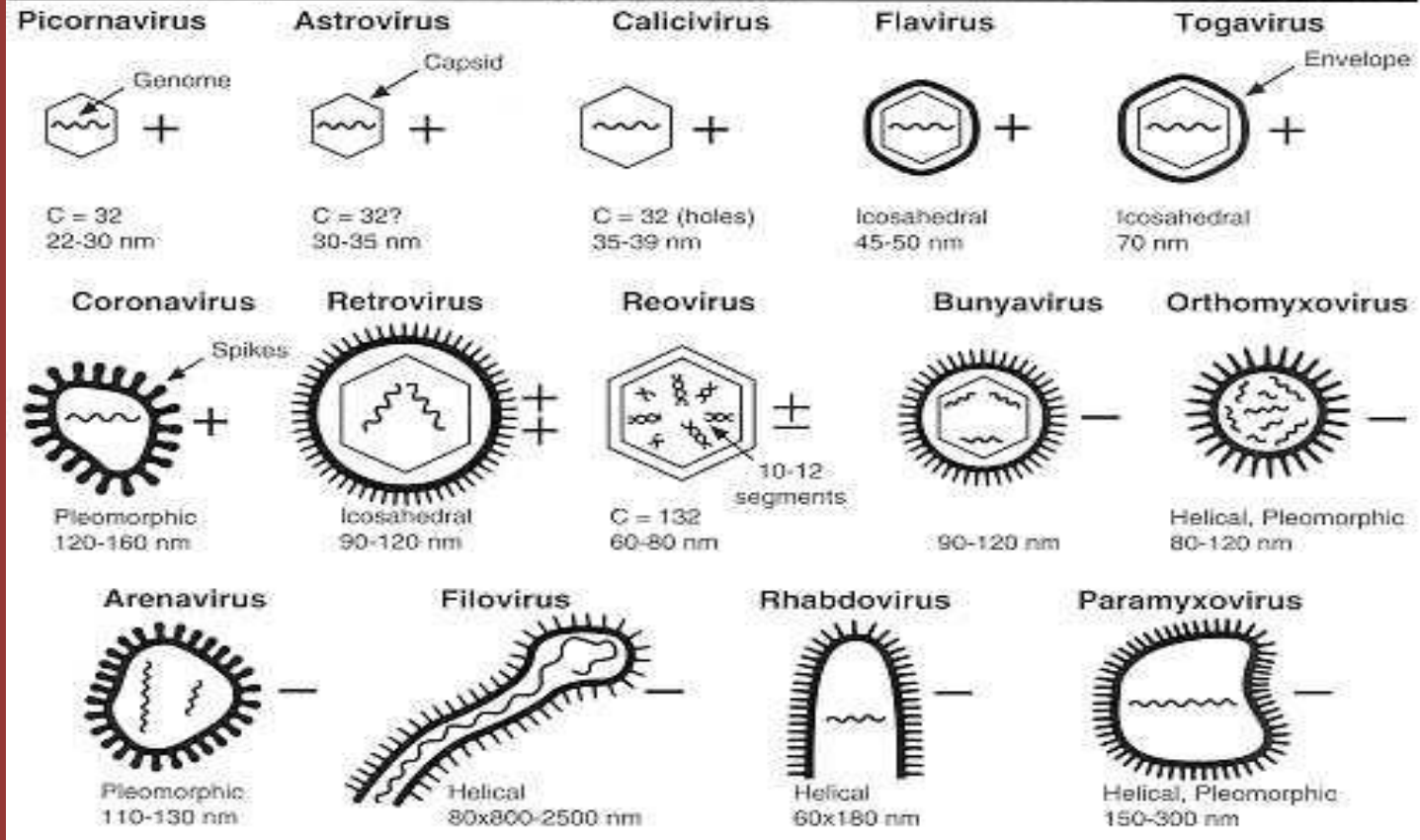
- **Persistent Infection** → Host cell remains alive and continues to produce progeny virions. (e.g. Hepatitis B infections)

The OutCome of Viral Infections

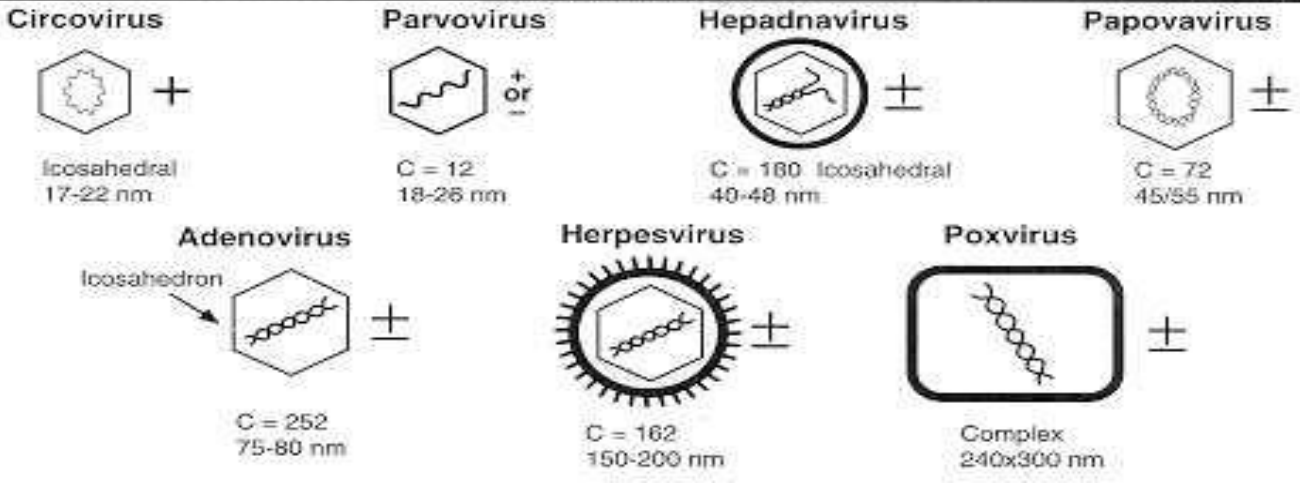
- **Latent Infections** → Host cell remains alive, and viruses enter a dormant state where it dose not replicate until some trigger causes them to activate and replicate again. (e.g. HIV & Herpes infections).

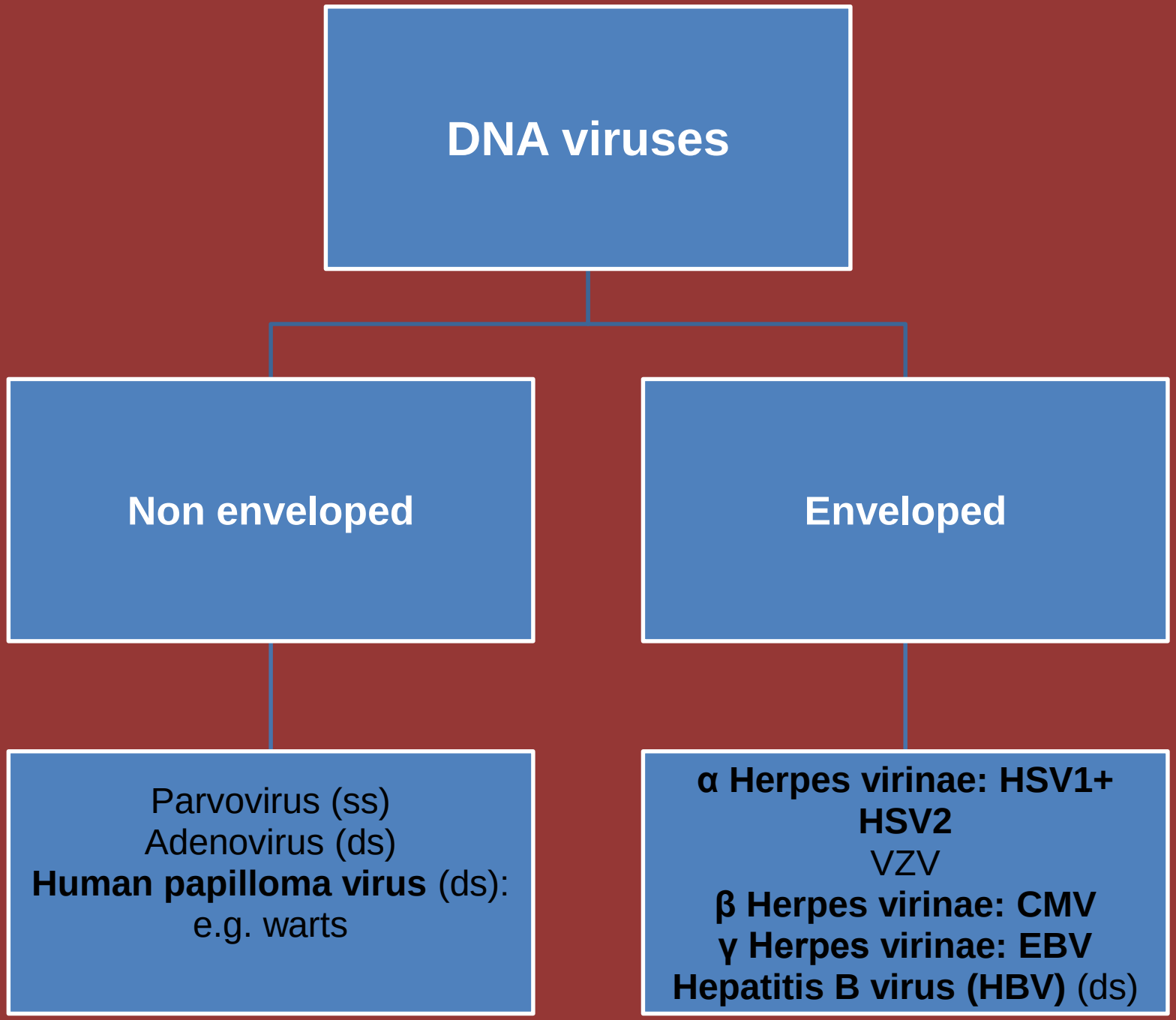
- **Transformation Infections** → Infected host cell is transformed by the virus. (those are viruses that carry oncogenes which my lead to cancer in host cells. They can be DNA or RNA viruses) (e.g. HBV, HCV).

RNA Viruses



DNA Viruses




DNA viruses
Non enveloped
Enveloped
Parvovirus (ss)
Adenovirus (ds)
Human papilloma virus (ds):
e.g. warts
α Herpes virinae: HSV1+
HSV2
VZV
β Herpes virinae: CMV
γ Herpes virinae: EBV
Hepatitis B virus (HBV) (ds)

α-Herpes Virinae

Herpes Simplex Virus Type 1: Fever Blisters

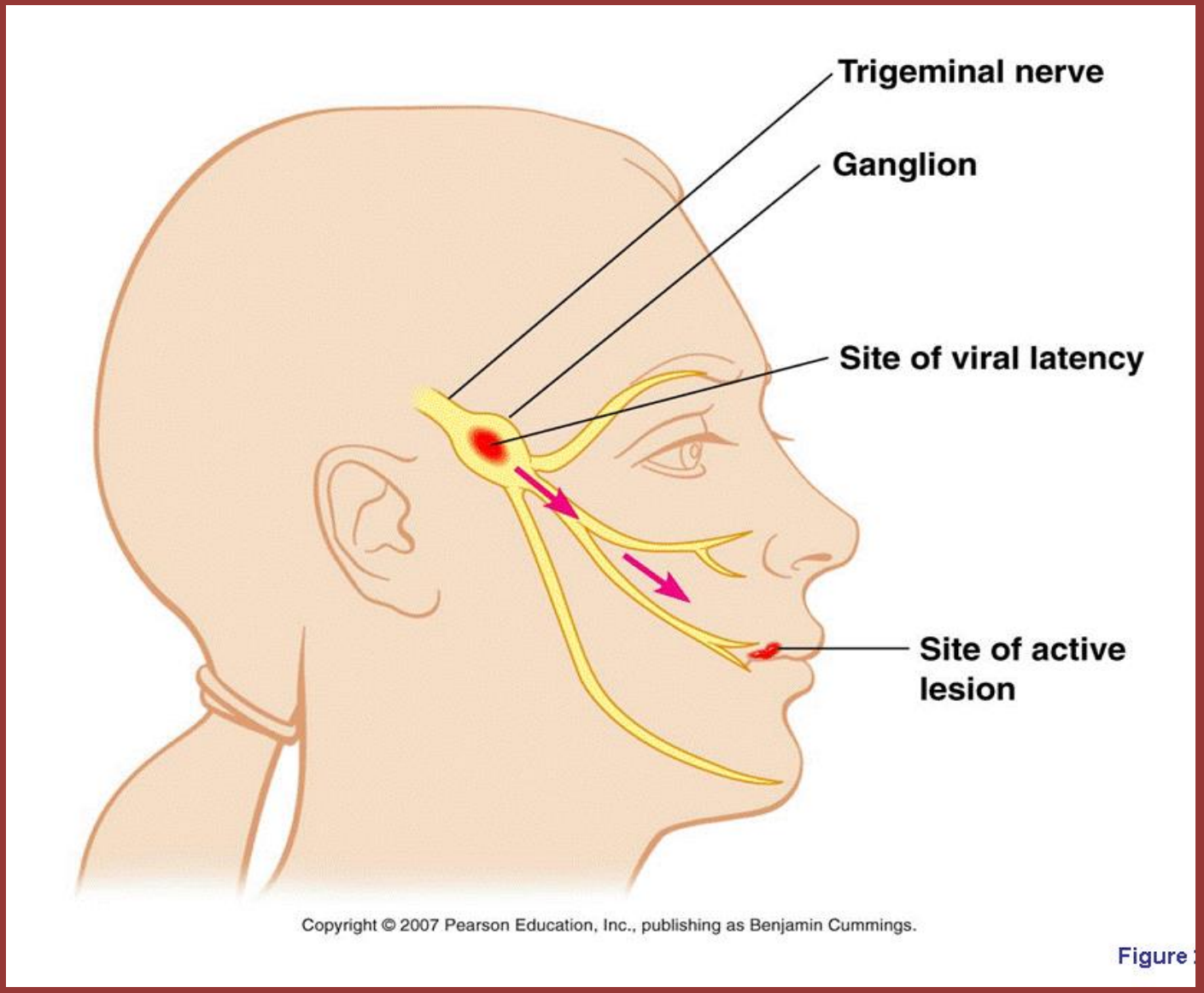
Herpes Simplex Virus Type 2: Genital Herpes

- Both are infection in the skin or mucus membranes of the mouth, lips or genitalia.
- ***Primary infection:*** a lesion called **Blister** which is watery and cause itching.
- When the blister is healed the virus shed to the nerve to hide from the immune system.
- ***latent infection:*** Recurrent infection can happen when there is a decrease in the immunity.

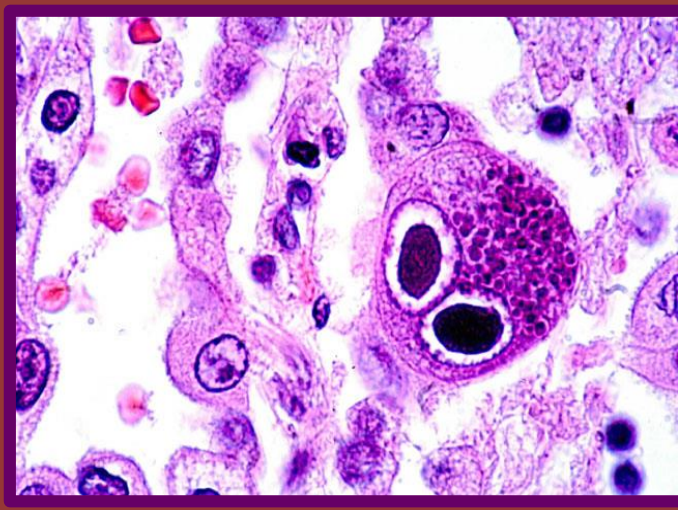
Transmission:

transmitted through close contact with infected person who is shedding virus from the skin.

Latency of HSV-1



β-Herpes Virinae

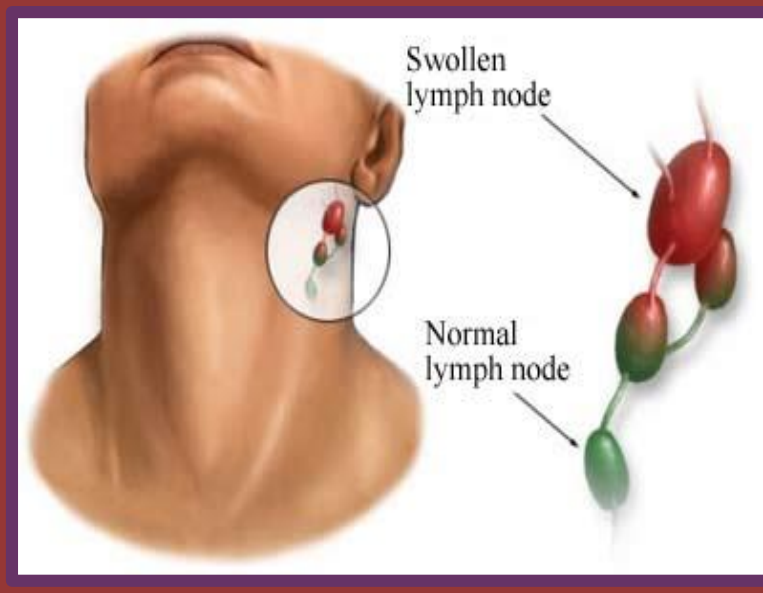


- It is called CMV because the infected **cells are greatly enlarged and multinucleated.**
- Initial infection commonly occurs during childhood.
- **The infection in infants or children is usually asymptomatic**; they continue to shed the virus for months in virtually all body fluids (tears, urine, and saliva) without causing detectable damage or clinical illness.
- **The primary infection in immuno-competent persons presents as mononucleosis-like syndrome which soon resolves. Most of them remain asymptomatic for life.**
- After infection, the virus remains latent in the body for the rest of the person's life. Disease rarely occurs unless immunity is *suppressed* either by drugs, infection (HIV) or old-age, immuno-suppressive drugs.

Transmission:

occurs from person to person through bodily fluids (e.g. **urine, saliva, blood, or breast milk)**

γ-Herpes Virinae

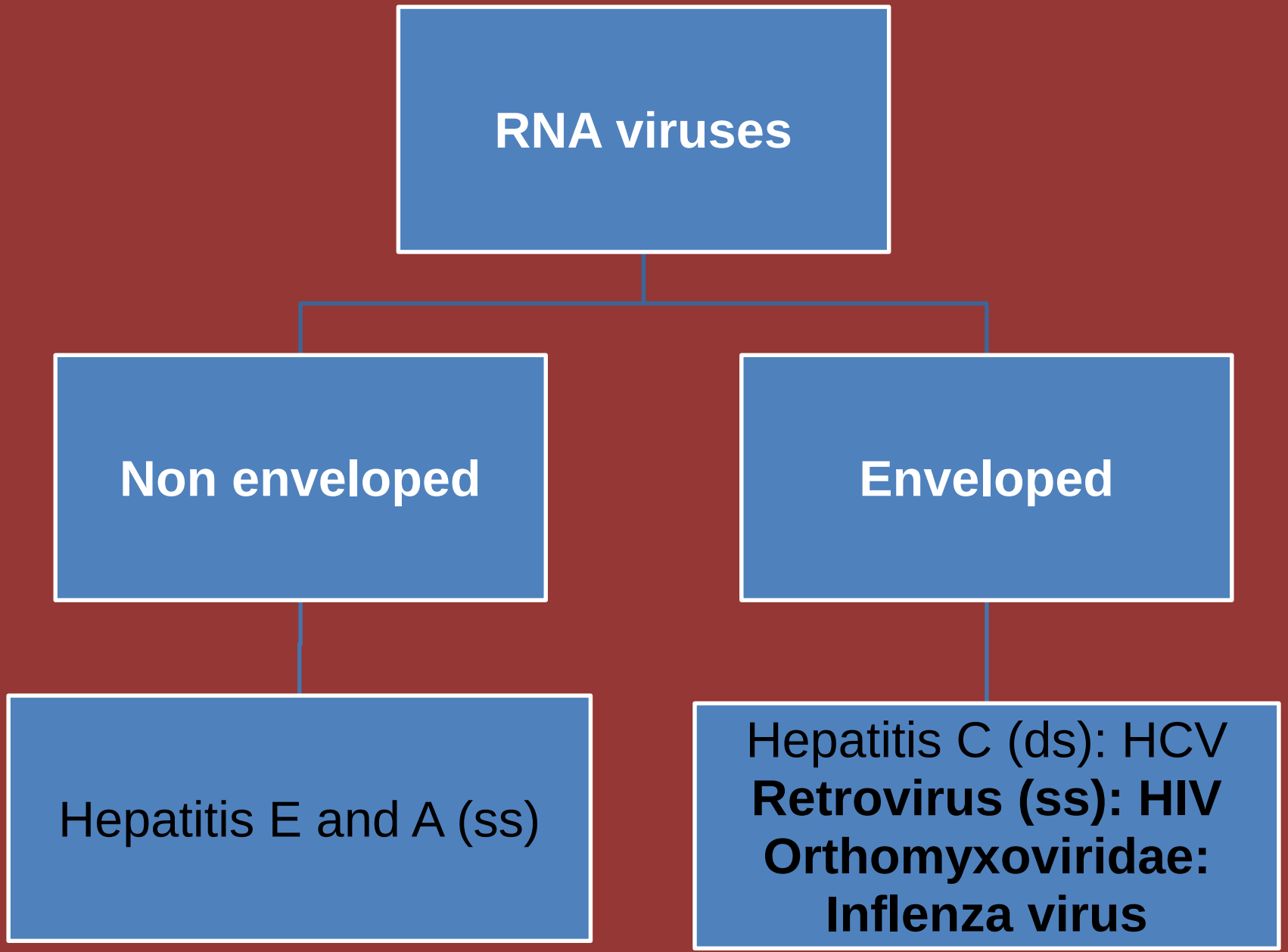


Epstein-Barr Virus (kissing disease)

- **Cause:** infectious mononucleosis
- **Symptoms:** fever, sore throat and swollen lymph glands. Sometimes, a swollen spleen or liver involvement may develop. infectious mononucleosis is almost never fatal.
- Although symptoms of infectious mononucleosis usually resolve in 1 to 2 months, **EBV remains dormant** or latent in a few cells in the throat and blood for the rest of the person's life. Periodically, the virus **can reactivate** and is commonly found in the saliva of infected persons. This reactivtion usually occurs without symptoms of illness. Epstein-barr can reoccur at any time especially after illness or stress.

Transmission:

by intimate contact with saliva that contains the virus.


RNA viruses
Non enveloped
Enveloped
Hepatitis E and A (ss)
Hepatitis C (ds): HCV
Retrovirus (ss): HIV
Orthomyxoviridae:
Inflenza virus

Influenza virus

There are 3 types of inflenza viruses:

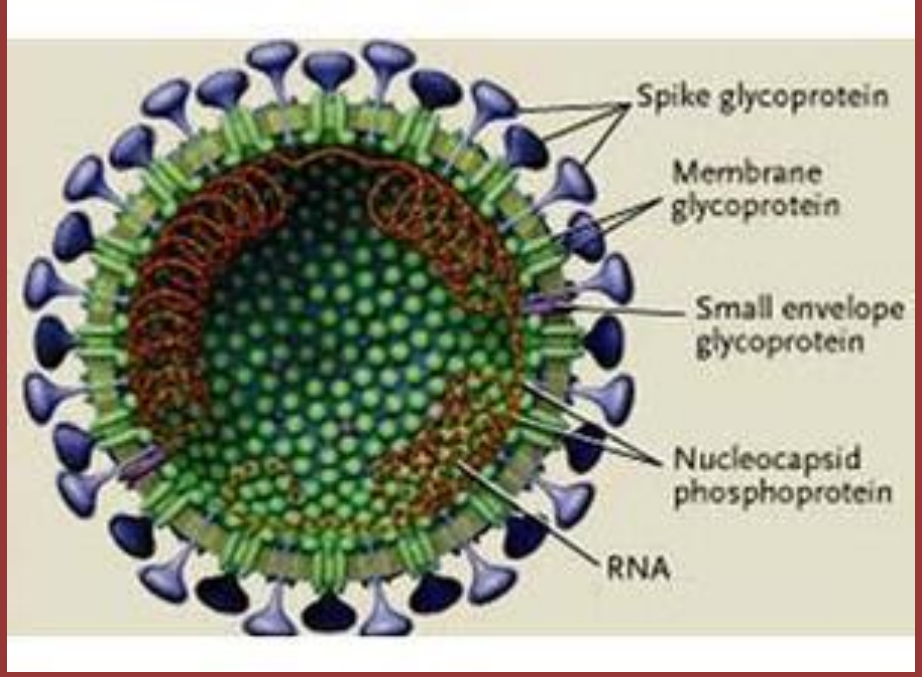
- Influenzavirus A: causes of all flu pandemics and infect humans, other mammals and birds
- Influenzavirus B: infect humans and seals
- Influenzavirus C: infect humans and pigs

Inflenza A:

the most virulent human pathogens among the three influenza types and causes the most severe disease.

- There are several types of protein from(Hemagglutinin) H1 to H5 and (Neureminidase) N1 to N5 giving several kind of infections that transmit between animals and human, such as bird flu, swine flu and many others.

Corona Virus



- Enveloped positive strand RNA virus
- Coronaviruses are named for the crown-like spikes on their surface
- Human CoVs isolated in the 1960s

- Six human CoVs (HCoVs) have been identified :

  - HCoV-229E
  - HCoV-OC43
  - HCoV-NL63
  - HCoV-HKU1
  - **SARS-CoV**
  - Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

- First identified in Saudi Arabia (September 2012)
- Different from any other corona virus previously found in people
- Spread from an infected person to others through:

  - The air by coughing and sneezing

  - Close personal contact, such as touching or shaking hands.

Symptoms & Complications

Most people confirmed to have MERS-CoV infection have had severe acute respiratory illness with:

- Fever
- Cough
- Shortness of breath
- Some people also had gastrointestinal symptoms including diarrhea and nausea/vomiting.
- Complications, such as pneumonia and kidney failure

- Incubation period for MERS 2-14 days

- People with pre-existing medical conditions, more likely to become infected with MERS, or have a severe case

- Pre-existing conditions from reported cases included diabetes; cancer; and chronic lung, heart, and kidney disease.

- No vaccine currently available

Treatment is supportive and based on the patient's clinical condition.

Prevention of Viral Infections: Vaccines

- Vaccines are available to prevent over 13 viral infections of humans.
- **Types of Vaccines**

1. **Live vaccines (attenuated):** contain weakened forms of the virus, which do not cause the disease but triggers immunity. Live vaccines can be dangerous when given to people with a weak immunity (immuncompromised). **e.g.** MMR vaccine

2. **Killed vaccines:** contain killed, but previously virulent, micro-organisms that have been destroyed with chemicals, heat, radioactivity or antibiotics. **e.g.** influenza vaccine

3. **Subunit vaccines:** produced by biotechnology and genetic engineering techniques. These vaccines use only the capsid proteins of the virus. **e.g.** Hepatitis B vaccine

Treatment of Viral Infections: Antiviral Drugs

- Until recent years, there were no drugs for the treatment of viral infections.
- Antiviral drugs are difficult to develop and use because viruses are produced within host cells.
- Antiviral drugs work by inhibiting viral replication inside cells.

Independent reading

Viral Hepatitis