Viruses

CLS 212: Medical Microbiology

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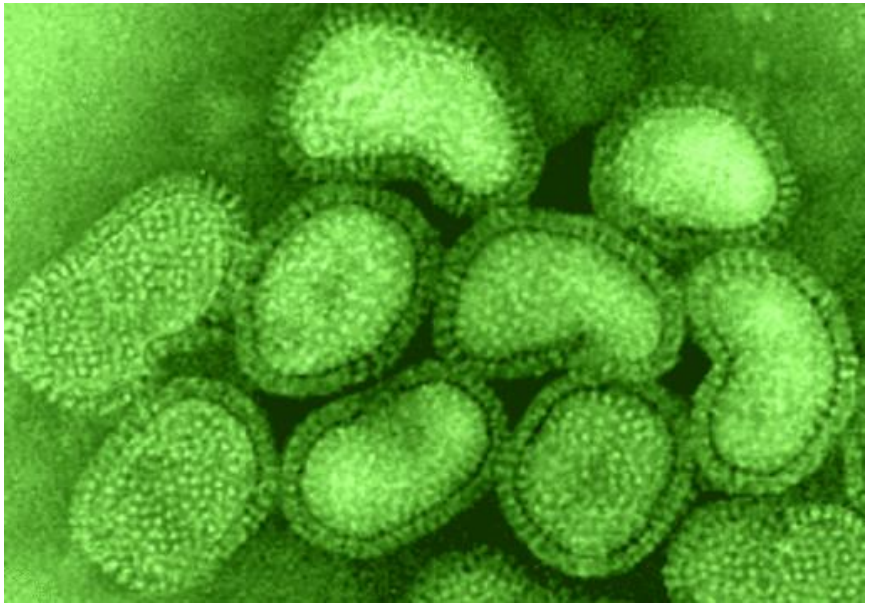
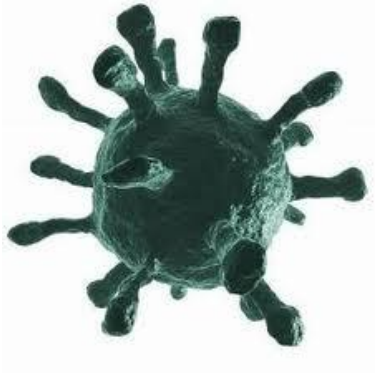
History

- 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.



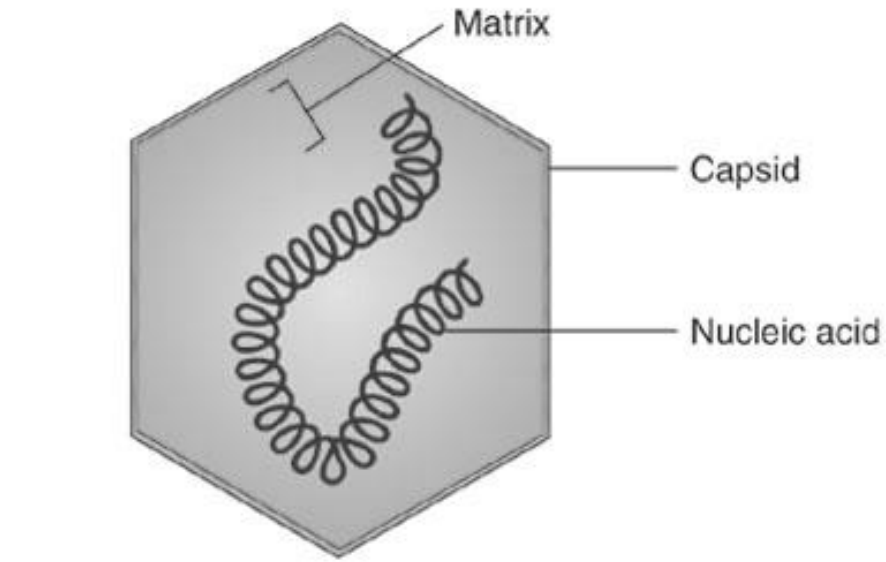
Introduction

- The study of viruses is called: Virology.
- Viruses are obligate intracellular pathogens that can infect all types of living organisms.
- Viruses that infect bacteria are called: **Bacteriophages.**
- Many human diseases are caused by viruses.
- Some viruses **“oncogenic viruses”** can even cause cancers **e.g.** leukemia, lymphoma..
- Virus particles can only be seen by an electron microscope.
- Most viruses range in sizes from 10-300 nanometers.

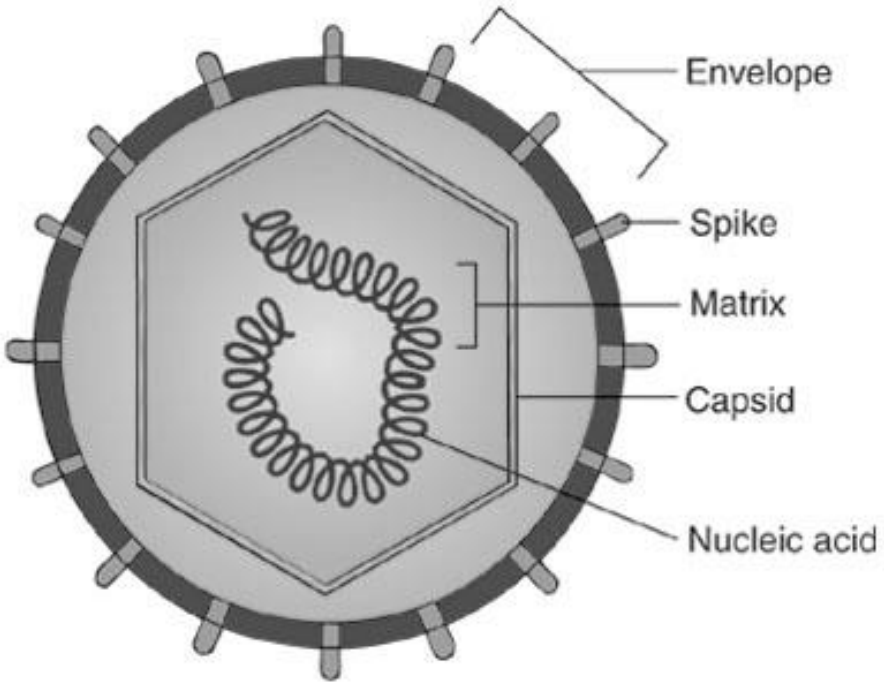


Structure of Viruses

1) Genome
2) Capsid
3) Envelope



(a) **Naked Nucleocapsid Virus**



(b) **Enveloped Virus**

I- Virus Genome

- The genetic material (nucleic acid) of viruses can be DNA or RNA, never both. DNA or RNA may be single stranded (ss) or double stranded (ds).

- Viruses are classified into 4 types according to the type of nucleic acid they have: ssDNA viruses, ssRNA viruses, ds DNA viruses, and ds RNA viruses.

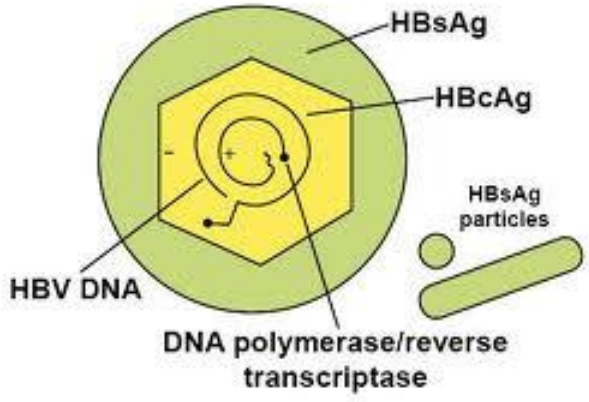
- The most common forms of viral genomes found in nature are ssRNA then dsDNA.

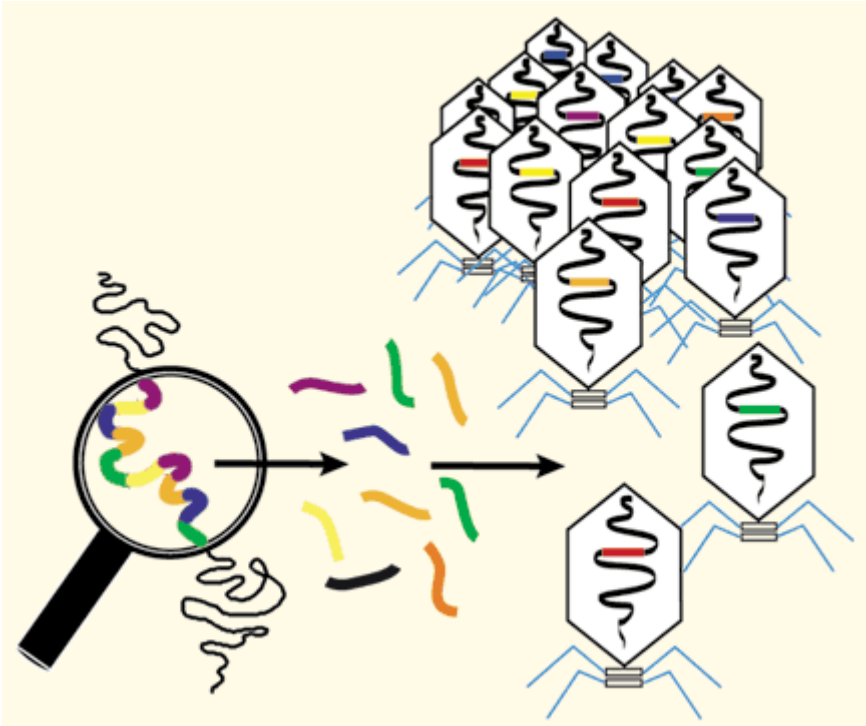
- **Genome size varies greatly between species.** The smallest viral genomes code for only 4 proteins (have a mass of about 10^6 Daltons); the largest code for several 100s of proteins (have a mass of about 10^8 Daltons).

I- Virus Genome

- For viruses with **RNA or single-stranded DNA**, the strands are said to be either **positive-sense** (called the + strand) or **negative-sense** (called the - strand), depending on whether it is complementary to the viral messenger RNA (mRNA).

- Viral genomes are usually circular but some are linear or segmented.



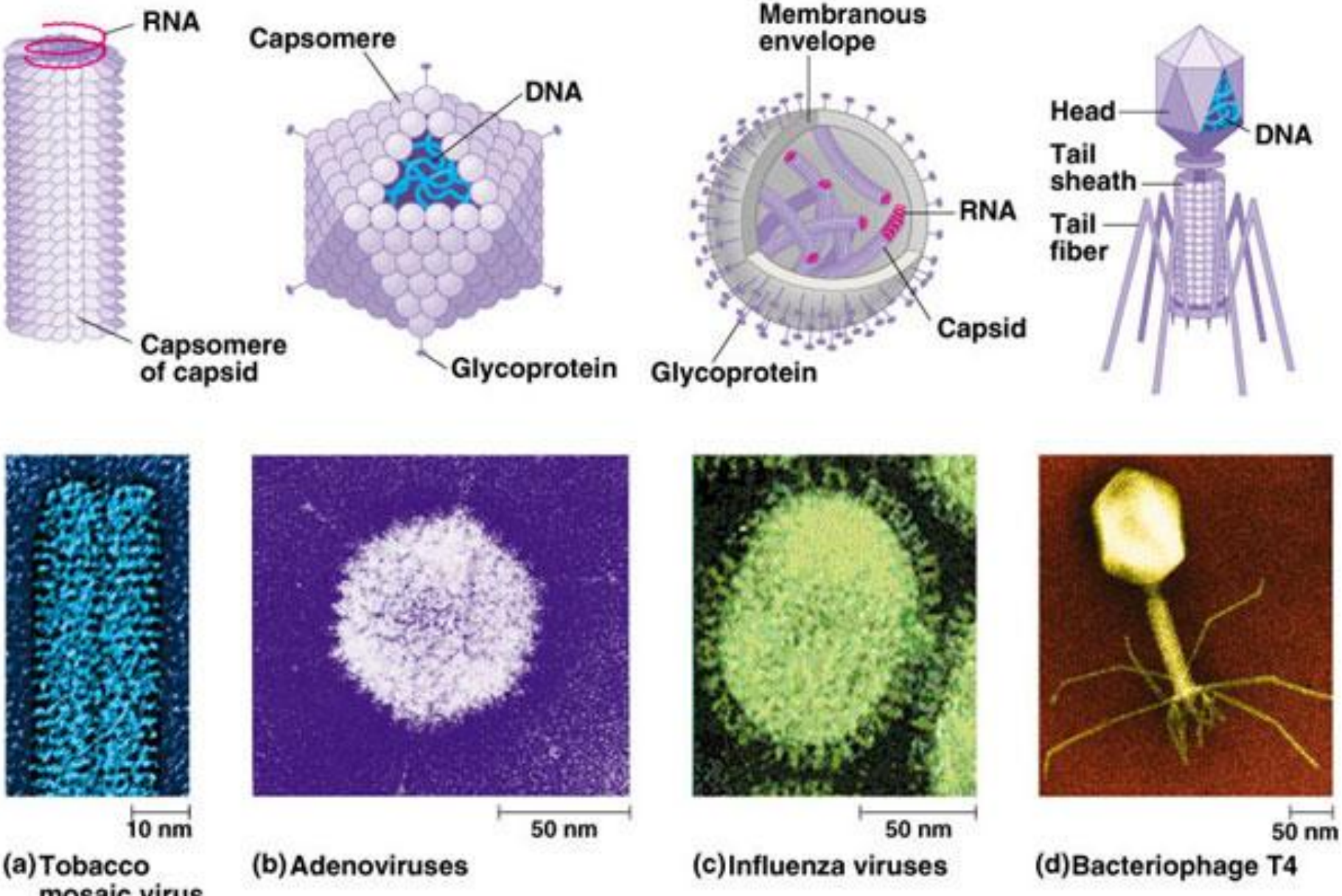


II. Capsid

- The protein coat inclosing the genome.
- The capsid is designed to give shape and protect the virus nucleic acid from environmental damage.
- It is composed of many small protein units called ***capsomeres.***
- 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. **Polyhedral:** many sided.
3. **Bullet shaped.**
4. **Spherical.**
5. **Complex:** combination of shapes.

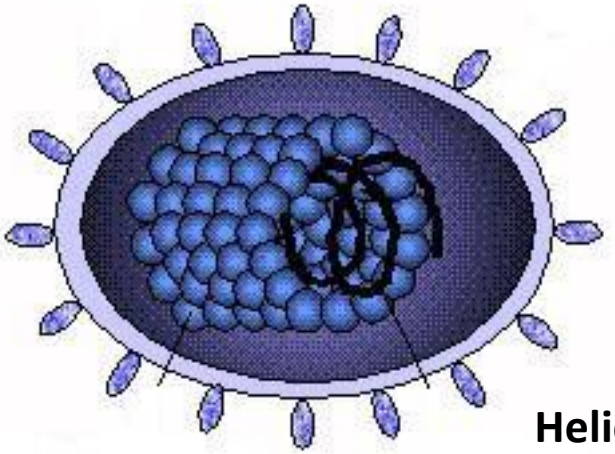


(a) Tobacco mosaic virus

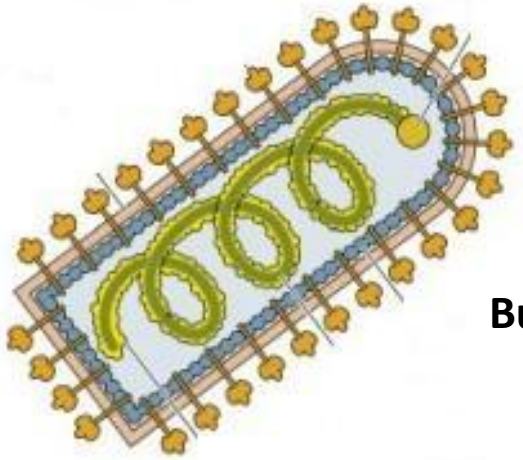
(b) Adenoviruses

(c) Influenza viruses

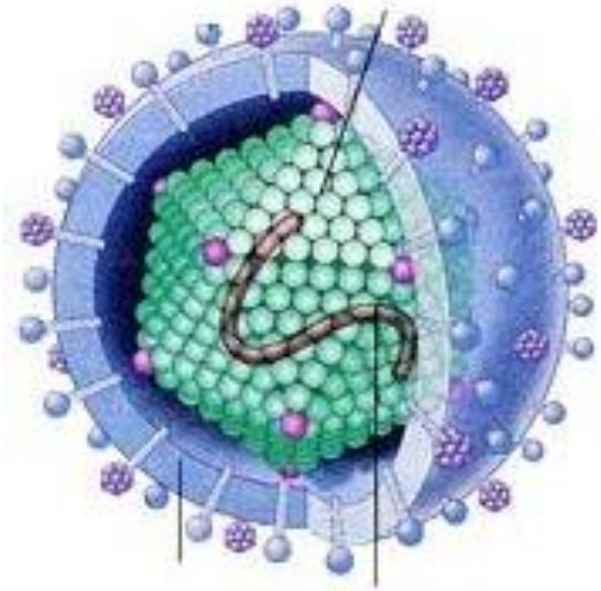
(d) Bacteriophage T4



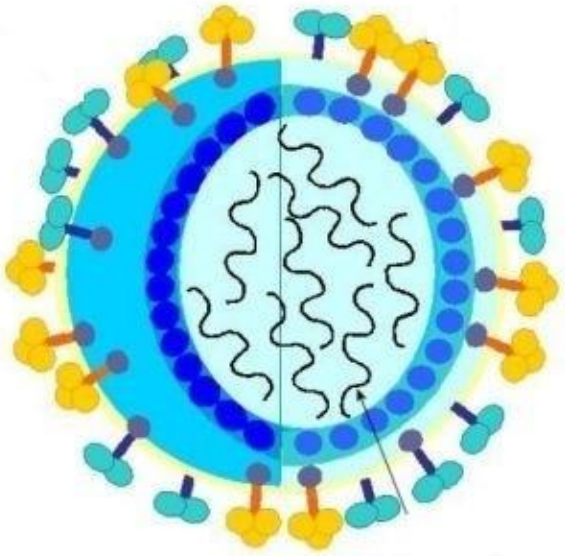
Helical Virus



Bullet-shaped Virus



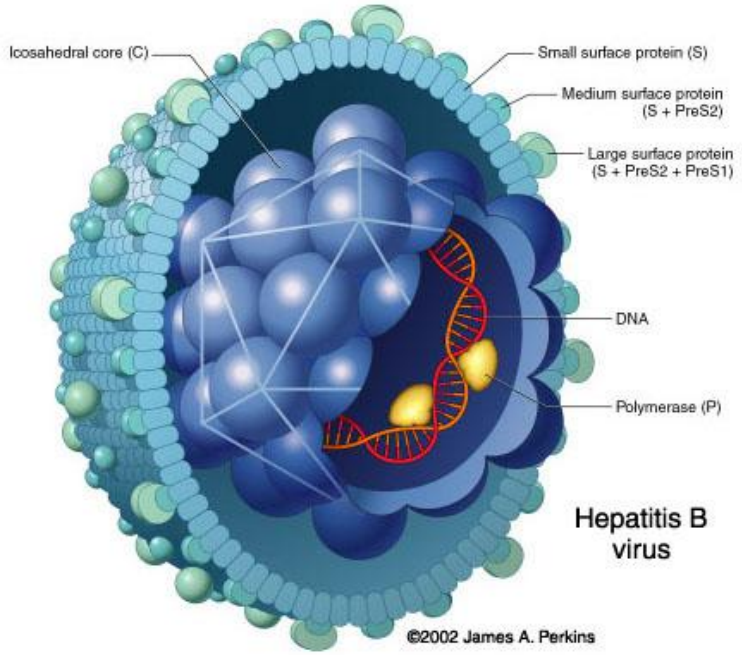
Polyhedral Virus



Spherical Virus

Virus Envelope

- A lipid bilayer membrane found in **some** viruses.
- It is derived from the host cell membrane or nuclear membrane during the release of the virus and never made by the viruses themselves.



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.

Taxonomy of Viruses

- **Order *(-virales)*** *being the highest* currently recognized.
- **Family *(-viridae)***
- **Subfamily *(-virinae)***
- **Genus *(-virus)***
- **Species *(-virus e.g. tobacco mosaic* virus*)***

- The Nobel Prize-winning biologist David Baltimore devised the **Baltimore classification system.**

Replication of Viruses

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

A. Early phase
- 1- Recognition
- 2- **Attachment** → **The most important step**
- 3- Penetration
- 4- Uncoating

B. Eclipse Phase (late)
- 5- Biochemical synthesis
- 6- Assembly of virus
- 7- Release

Replication of Viruses: *the early phase*

1- Recognition:

The virus should recognize the cell to be able to replicate within it. Which involves interaction between virial capsid proteins and receptors (protein or polysaccharide molecules) on the host cell membrane.

2- Attachment (adsorption):

Attachment of the virus to the receptor on the host cell.

3- Penetration:

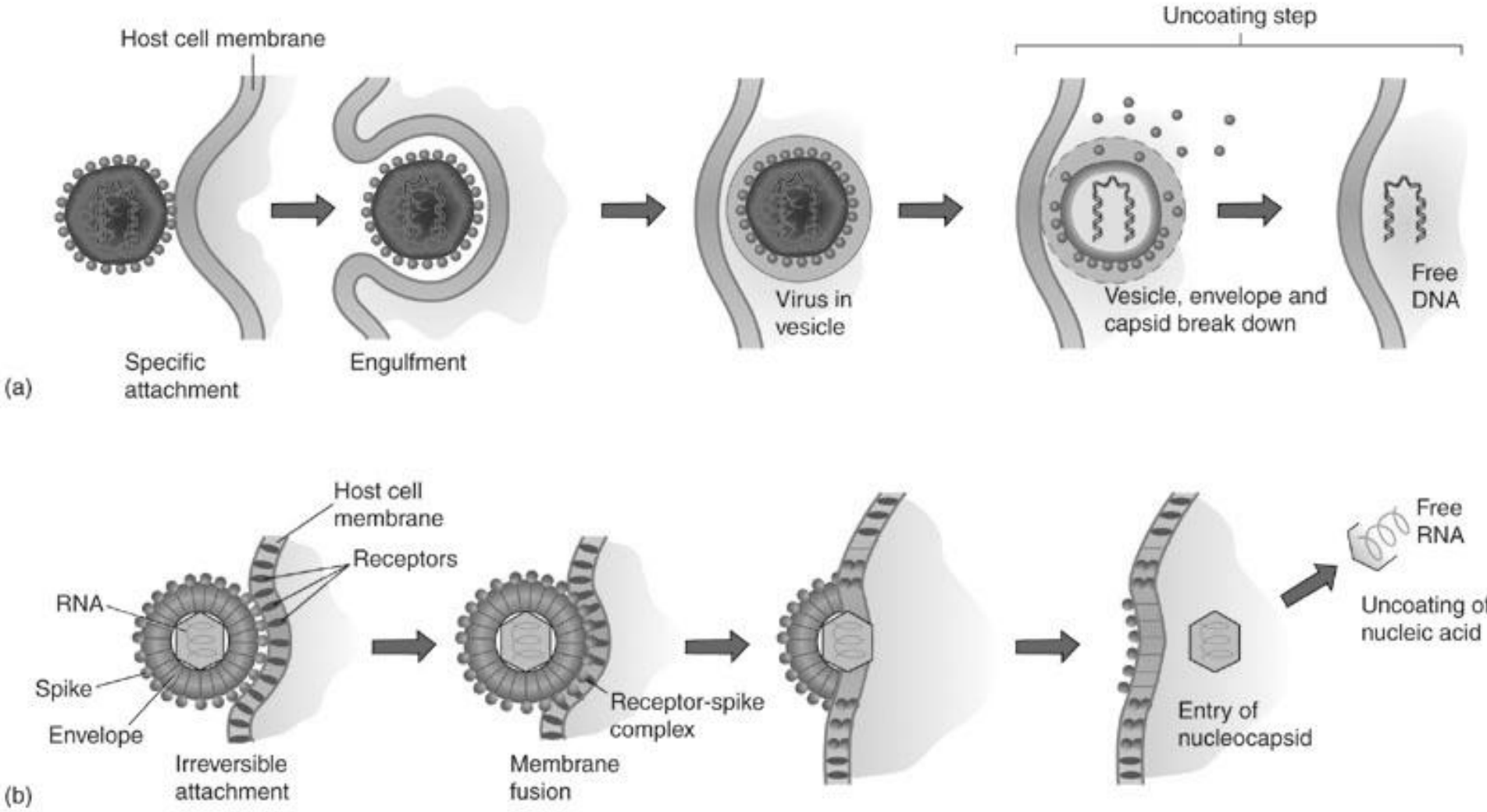
The entire virus enters the host cell. This process is temperature dependant (37C˚).

- Naked viruses: penetrate by endocytosis.
- Enveloped viruses: penetrate by fusion to plasma membrane.

4- Uncoating:

Removal of the coat (capsid) by the host cell proteolytic enzymes and the nucleic acid will be exposed.

Penetration Step



Replication of Viruses: *the Eclipse phase*

5- Biochemical synthesis: (formation of NA + capsid)

A- Early transcription followed by early translation for the production of viral mRNAs and nonstructural proteins.

B- Late transcription followed by late translation for the production of viral mRNAs and structural proteins.

C- Nucleic acid replication to produce copies of the original viral genome.

6- Assembly (maturation):

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

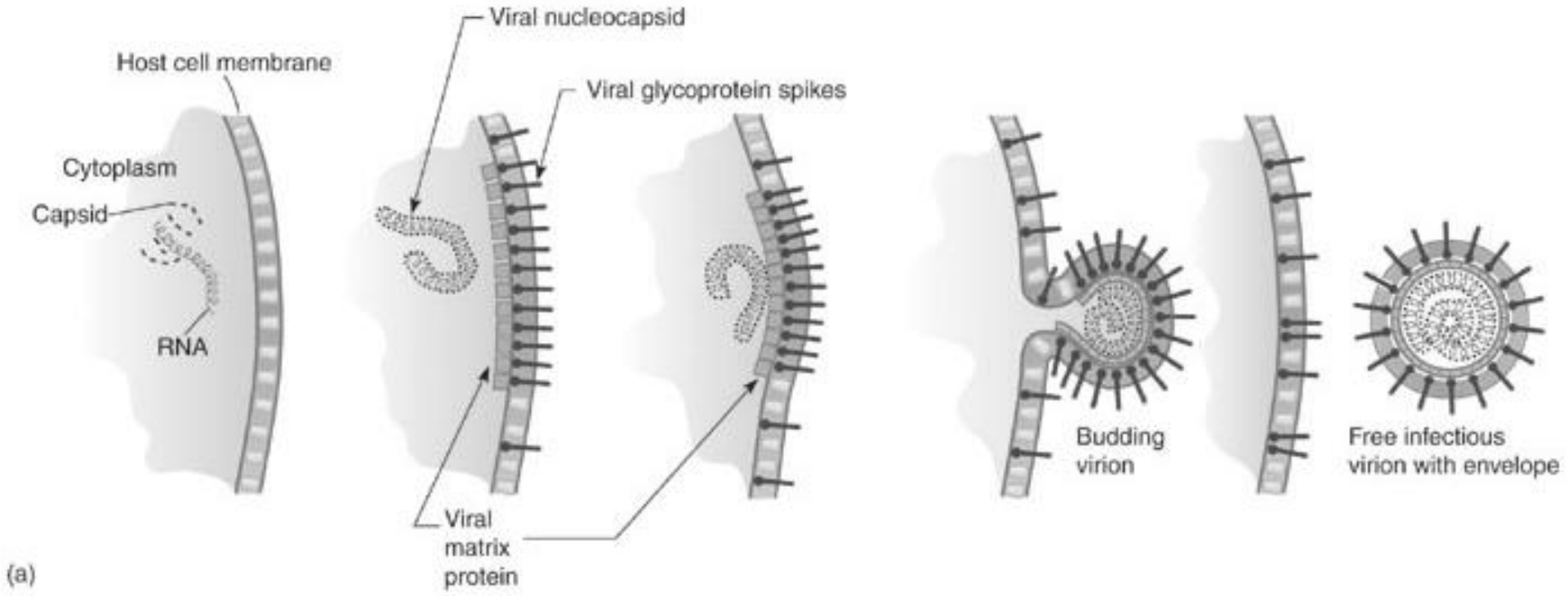
7- Release:

Escape of the complete virions from the host cell.

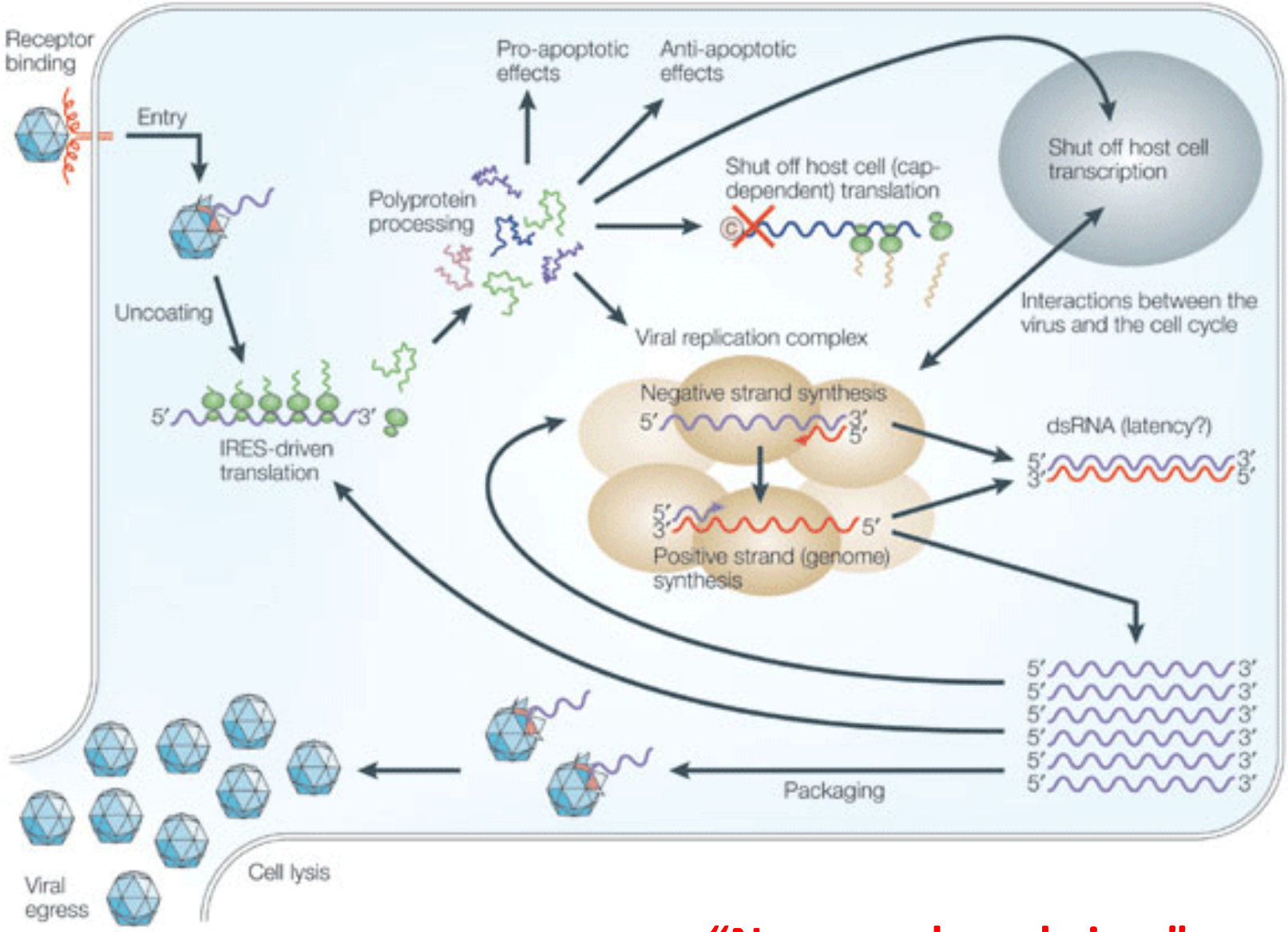
Naked viruses ⟶ Cell lysis (cell death).

Enveloped viruses ⟶ Budding.

Release of Enveloped Virus

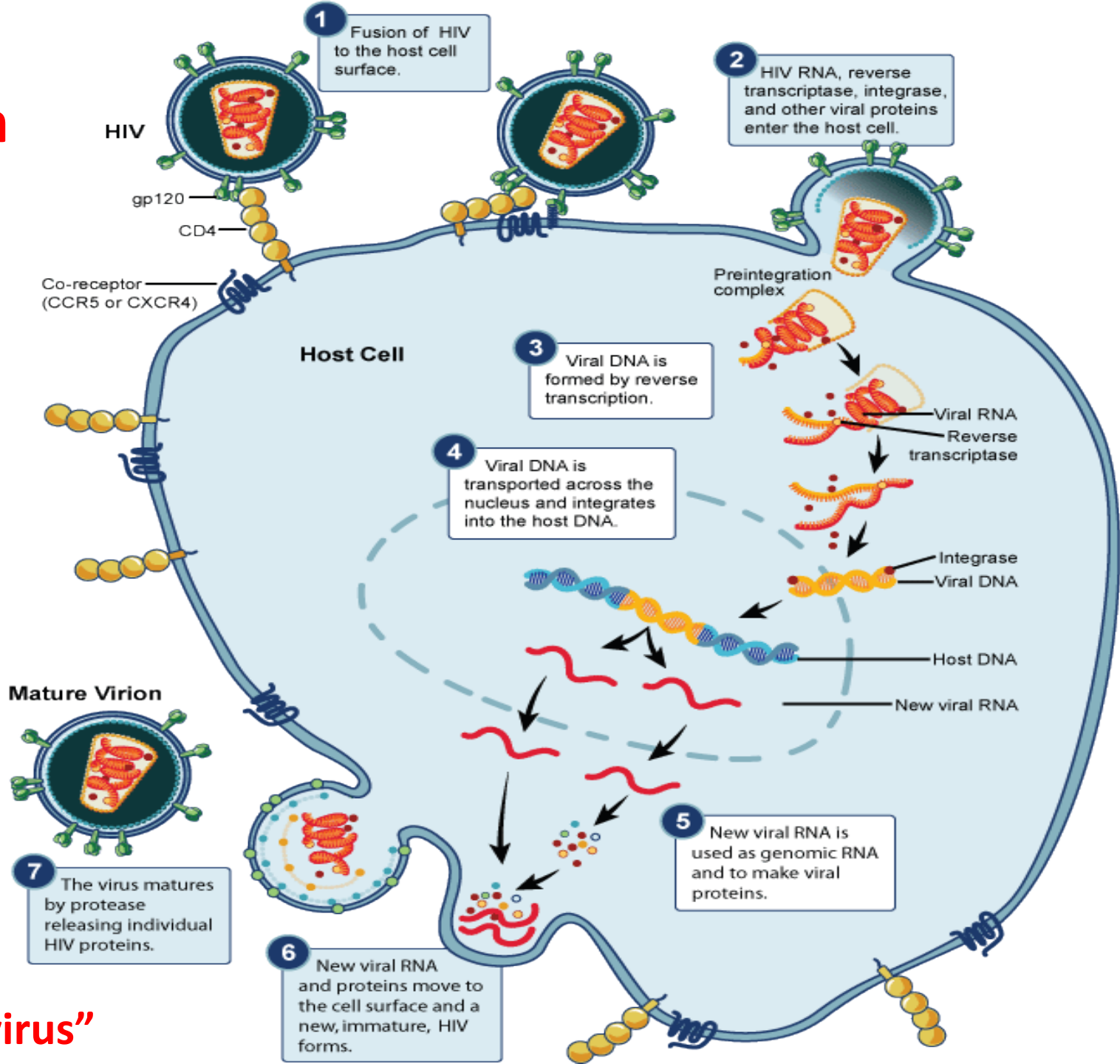


Replication of Picornavirus



“Non enveloped virus”

HIV Replication Cycle



"Enveloped virus"

Cell Response to Viral Infection

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

1- Lytic infection: Cell dies at the end of virus replicative cycle **(occurs in most RNA viruses).**

2- Persistent infection: Cell remains alive and continues to produce progeny virions **(e.g. measles virus, papilloma viruses, and other slow virus infections).**

3- Latent infections: cell remains alive but the virus cannot replicate, however, can be reactivated **(e.g. Herpes viruses).**

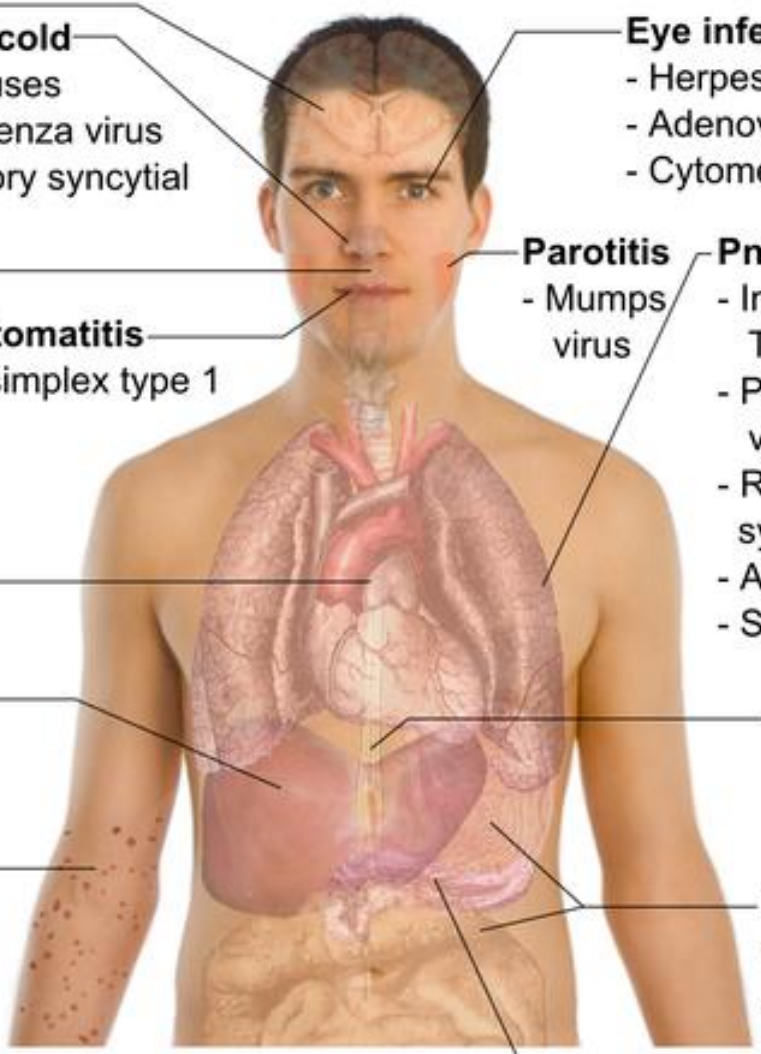
4-Transforming infection: the infected cell is transformed by the virus and the cell:

a- continues to produce progeny virions as in most RNA oncogenic viruses OR

b- do not produce progeny virions as in most DNA oncogenic viruses.

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

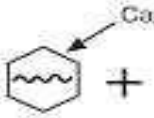
Pancreatitis
- Coxsackie B virus

RNA Viruses

Picornavirus

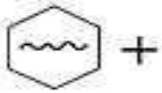
C = 32
22-30 nm

Astrovirus



C = 32?
30-35 nm

Calicivirus

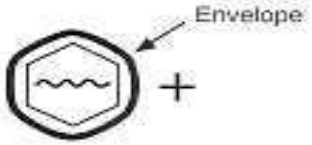


C = 32 (holes)
35-39 nm

Flavirus

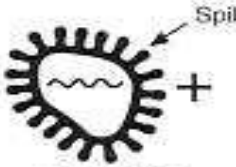
Icosahedral
45-50 nm

Togavirus



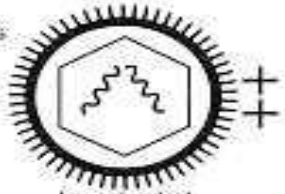
Icosahedral
70 nm

Coronavirus



Pleomorphic
120-160 nm

Retrovirus



Icosahedral
90-120 nm

Reovirus

C = 132
60-80 nm

Bunyavirus

90-120 nm

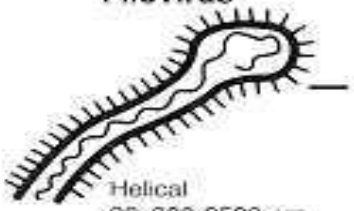
Orthomyxovirus

Helical, Pleomorphic
80-120 nm

Arenavirus

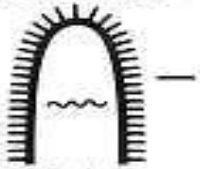
Pleomorphic
110-130 nm

Filovirus



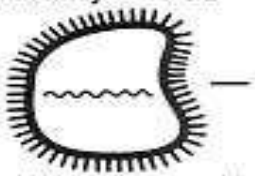
Helical
80x800-2500 nm

Rhabdovirus



Helical
60x180 nm

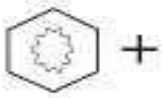
Paramyxovirus



Helical, Pleomorphic
150-300 nm

DNA Viruses

Circovirus

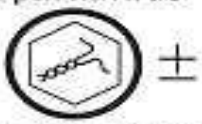


Icosahedral
17-22 nm

Parvovirus

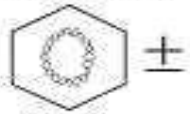
C = 12
18-26 nm

Hepadnavirus



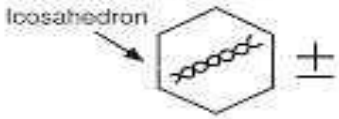
C = 180 Icosahedral
40-48 nm

Papovavirus



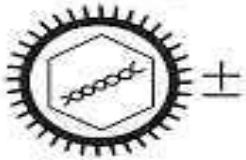
C = 72
45/55 nm

Adenovirus



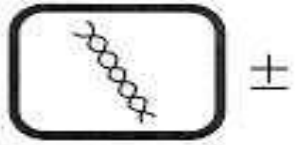
C = 252
75-80 nm

Herpesvirus

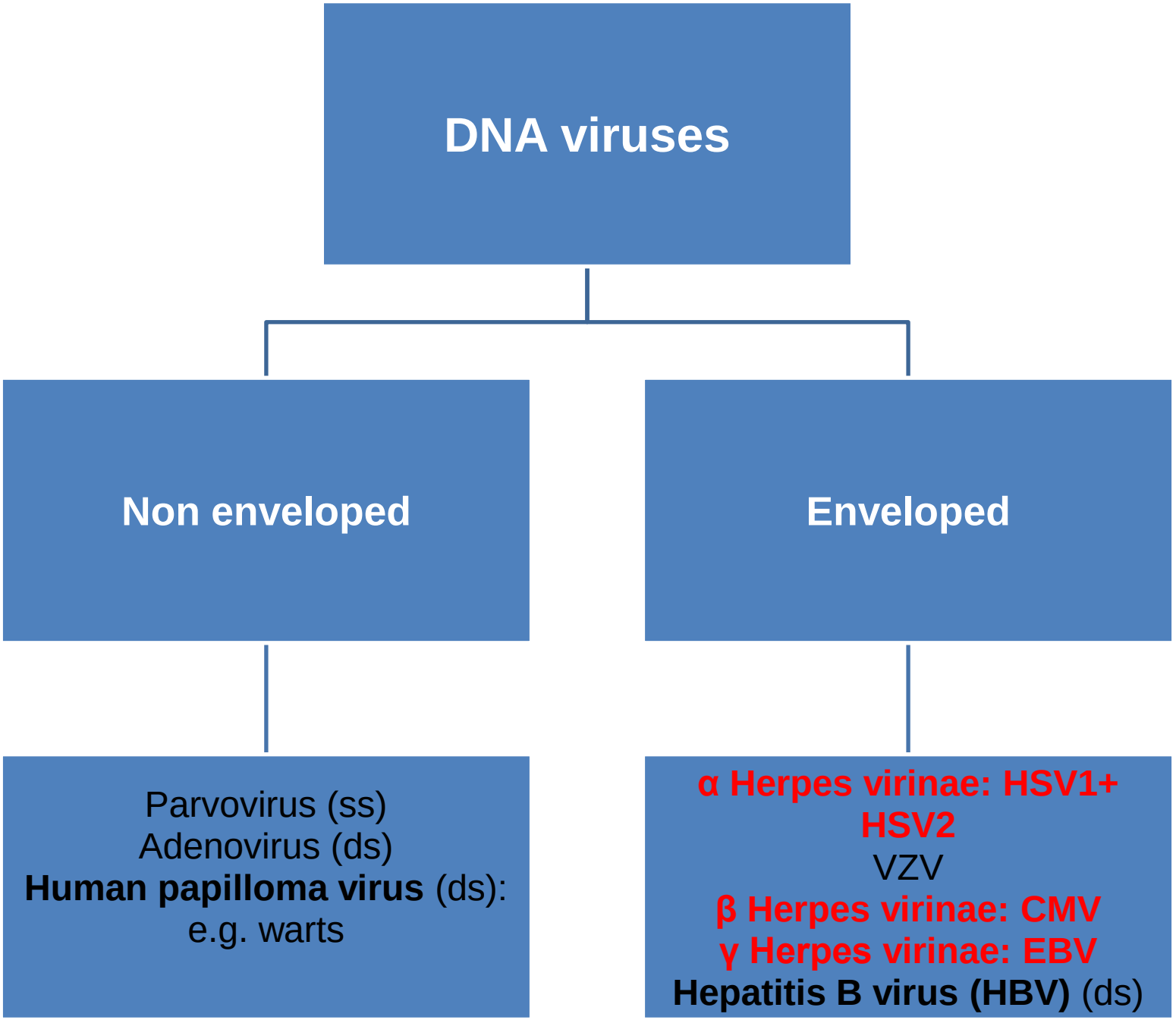


C = 162
150-200 nm

Poxvirus



Complex
240x300 nm


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)

Herpes Virus

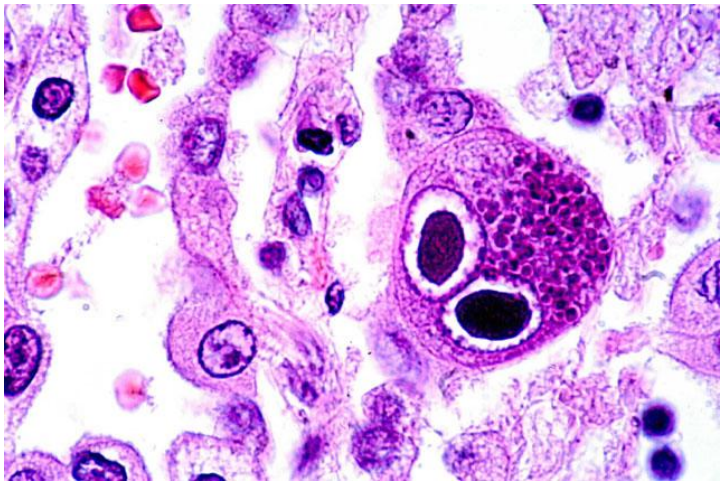
All herpes viruses share a characteristic ability to remain latent within the body over long periods.

α-Herpes Virinae

Herpes Simplex Virus1: Fever Blisters
Herpes Simplex Virus2: Genital Herpes

- Both are infection in the skin or mucus membranes of the mouth, lips or genitalia.
- **The 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.

β-Herpes Virinae

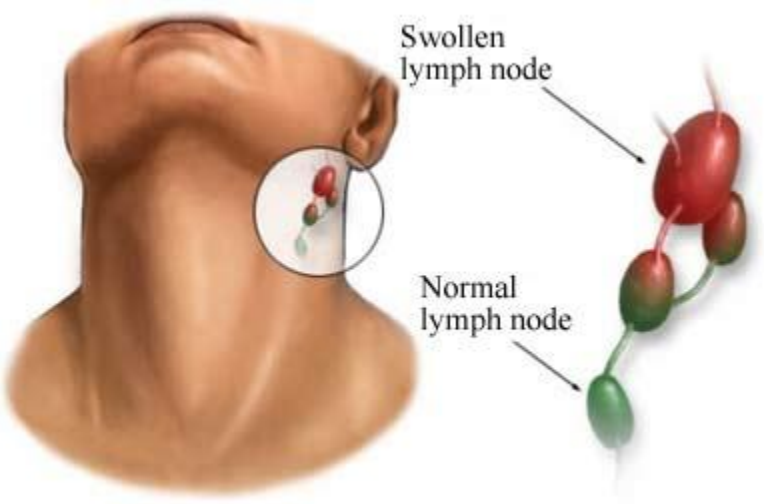


Cytomegalovirus (CMV)

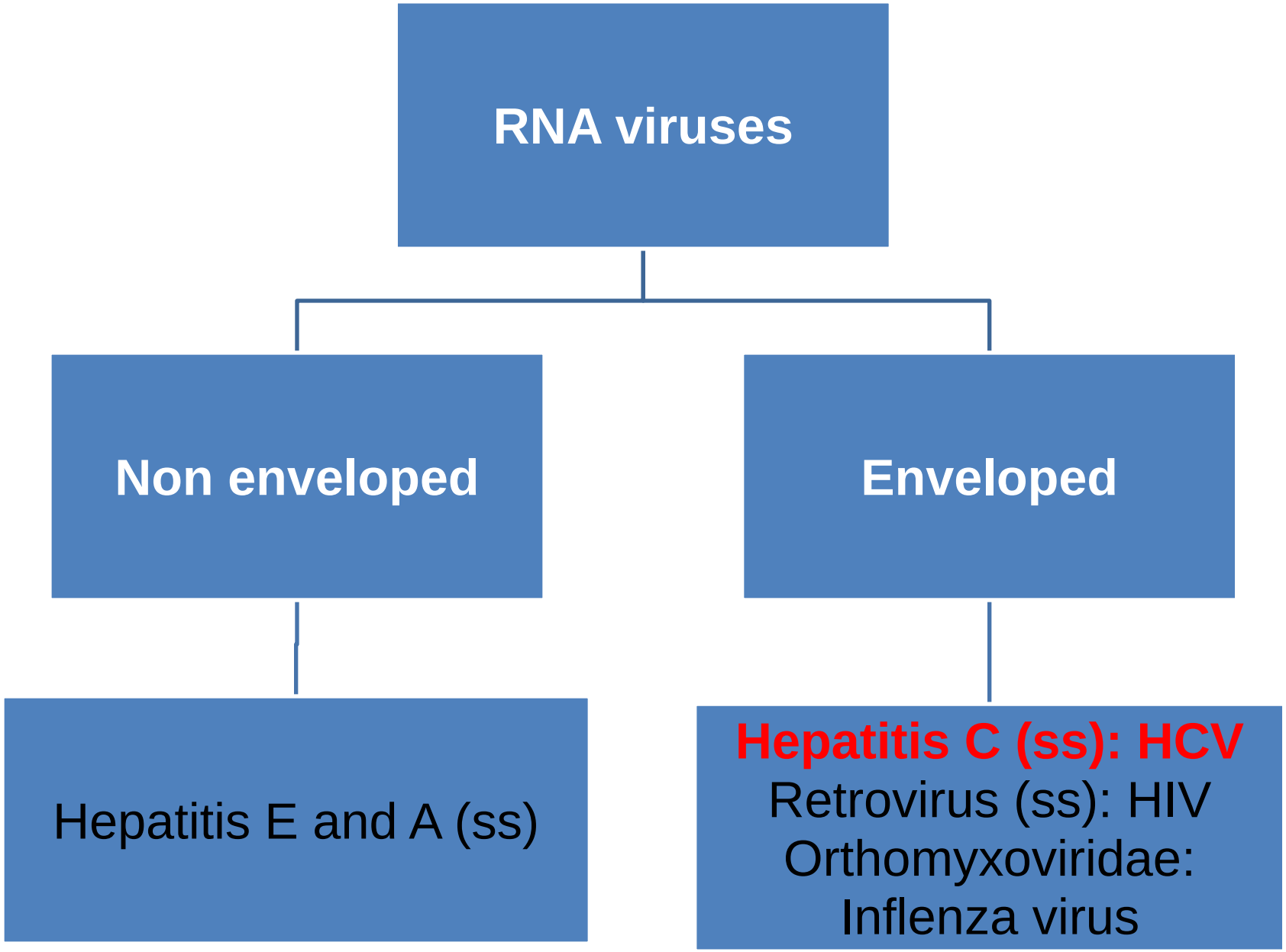
- It is called CMV because the infected **cells are greatly enlarged and multinucleated.**
- Initial infection commonly occurs during childhood.
- CMV infections are frequently associated with the **salivary glands.**
- The infection in children is usually **asymptomatic**; these viruses continue to shed the virus for months in virtually all body fluids (tears, urine, and saliva) without causing detectable damage or clinical illness.
- Some of them develop an **infectious mononucleosis/glandular fever-like syndrome** (Identical to that caused by EBV), with prolonged fever, and a mild hepatitis. A sore throat is common.
- After infection, the virus remains latent in the body for the rest of the person's life. Overt disease rarely occurs unless immunity is *suppressed* either by drugs, infection or old-age.
- **Transmission:** occurs from person to person through bodily fluids.

γ-Herpes Virinae

Epstein-Barr Virus



- **Cause:** infectious mononucleosis
  (kissing disease)
- **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 (ss): HCV
Retrovirus (ss): HIV
Orthomyxoviridae:
Inflenza virus

Hepatitis C Virus (HCV)

- A member of the family ***Flaviviridae*** that causes ***liver disease***, that might lead to liver cirrhosis then liver cancer.

- **HCV infection has 3 basic stages:**

1. **The incubation period:** average of 45 days.
2. **Acute infection:** lasts an average of 6 months and is **asymptomatic** (if symptomatic: decreased appetite, fatigue, abdominal pain, jaundice, itching, and flu-like symptoms)
3. **Persistent infection:** after 6 months often **asymptomatic** (if symptomatic: fatigue, flu-like symptoms, joint pains, itching, sleep disturbances, appetite changes, nausea, and depression).

- **Transmission:** by blood-to-blood contact (Blood transfusion, sexual intercourse, needle prick,..)

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.
- **E.g.**

  Aciclovir for Herpes simplex virus infections and **Lamivudine** for HIV and Hepatitis B virus infections.