L:7 Virology

Introduction

By

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Virology : is the science that deal with the study of viruses, and focuses on the following aspects of viruses: their structure, classification and evolution, their ways to infect host cells & reproduction, their interaction with host organism physiology and immunity, laboratory diagnosis, and their use in in production of vaccines and therapy. Viral infections are the most common cause of human disease, it responsible for at least 60% of the illness. A few viruses can produced cancer

- Viruses effect on all life forms, including human, animals, plants, fungus and bacteria - They damage or kill the cells that they infect

- **Virus are extremely small infective agents,** ultramicroscopic**. obligatory intracellular. A complete particle, or virion** , has much simpler structure than a cell. It essentially consist of a block of genetic material (either **DNA or RNA** but not both) surrounded by proteinaceous coat that protects it from the environmental damage and aid in its transmission from host to host, the protein coat of virus is called the **capsid. The capsid** composed from subunits called **capsomers,** designed to protect the genome, the capsid and nucleic acid called **Nucleocapsid.** Virus have the capacity for infecting and replicating in animal, plant & bacteri. The virus was coined by Pasteur, is from the Latin word for poison.

- The pathogenicity of a virus depends on structural and functional characteristics. There are two major structures of viruses
  - **Enveloped virus**
  - **Naked or non enveloped virus** (virus is not enveloped)

An important structural feature used in defining a viral family is the presence or absence of a lipid-containing membrane (the envelope) surrounding the nucleocapsid. The nucleocapsid is flexible and coiled within the envelope, resulting in most such viruses appearing to be roughly spherical. However, the cellular membrane proteins are replaced by virus-specific proteins, conferring virus-specific antigenicity upon the particle

- **Envelope is lipoprotein** in nature (Lipid and proteins),
- ***The envelope is derived from host cell membrane when virus is released by budding**.

***Enveloped viruses are more sensitive** to **damage by harsh environments** (**heat**, **drying**, **detergent** & **lipid solvents such as alcohol** & **ether**) than non-enveloped virus therefore, it transmitted by the respiratory, parenteral, and sexual routes. Nonenveloped viruses are more stable to hospital environmental conditions and often transmitted by the fecal-oral route.

- **Peplomers** (**Envelope spikes**):
- These are glycoprotein projections, bind to cell surface proteins (Hemagglutinin, Neuraminidase)
- **Virion**: is a complete virus particle combining these structural elements.

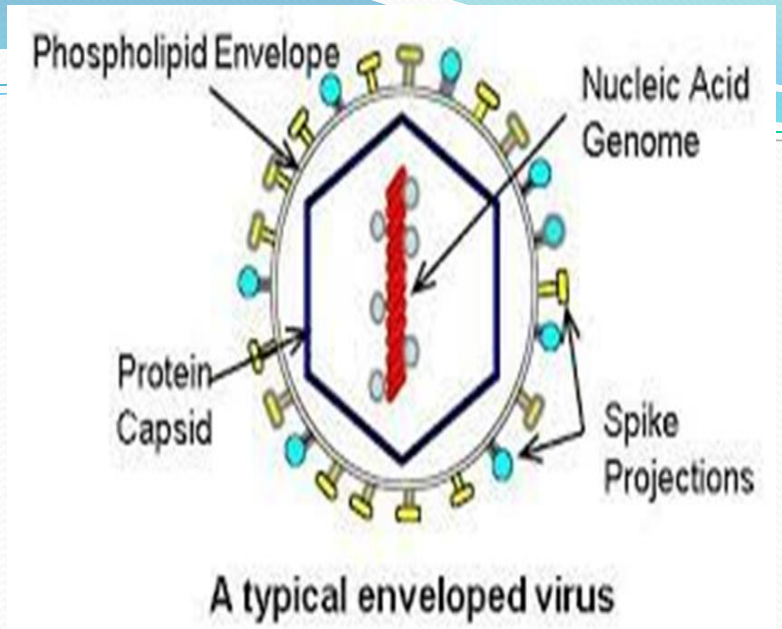
- **Prions**: This infectious protein without nucleic acid, causes animal & human diseases **(Mad Cow)**

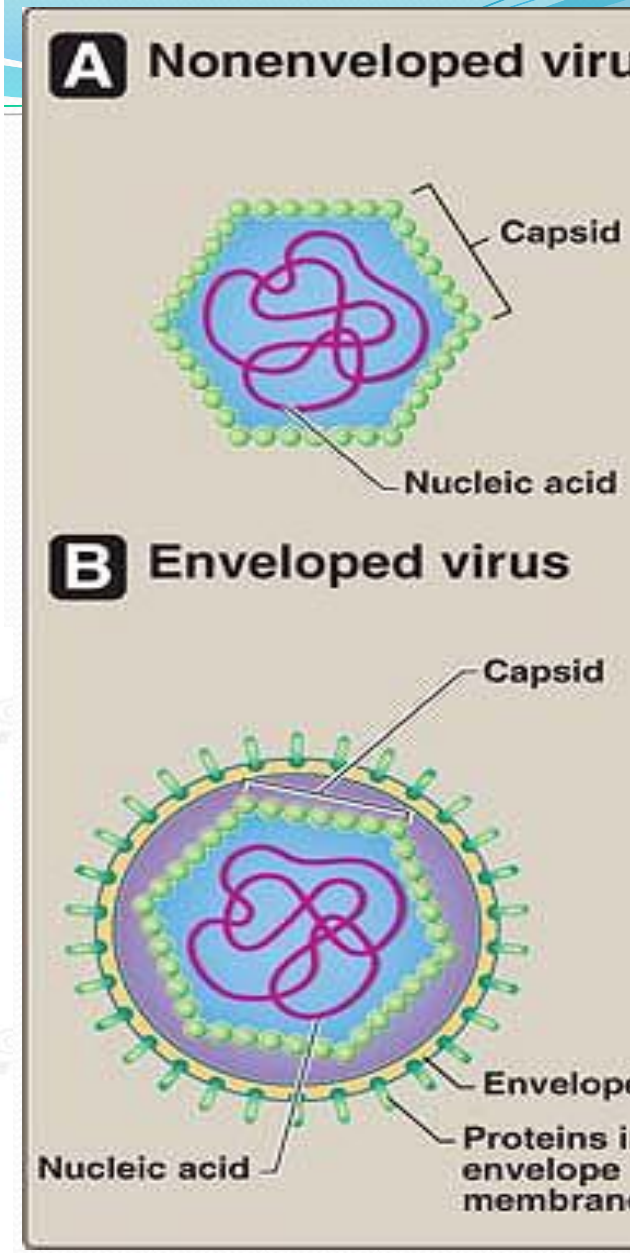
- **Viriod**: This infectious nucleic acid without protein.

Infectious RNA molecules, causes plant diseases & transmitted like virus

•Viruses have a host range: adapted to specific organisms that is, viruses infect specific cells or tissues of specific hosts

***Viral specificity**: refers to the specific kinds of cells a virus can infect. It is regulated by the specificities of attachment, penetration and replication of the virus (Receptors Properties of viruses)





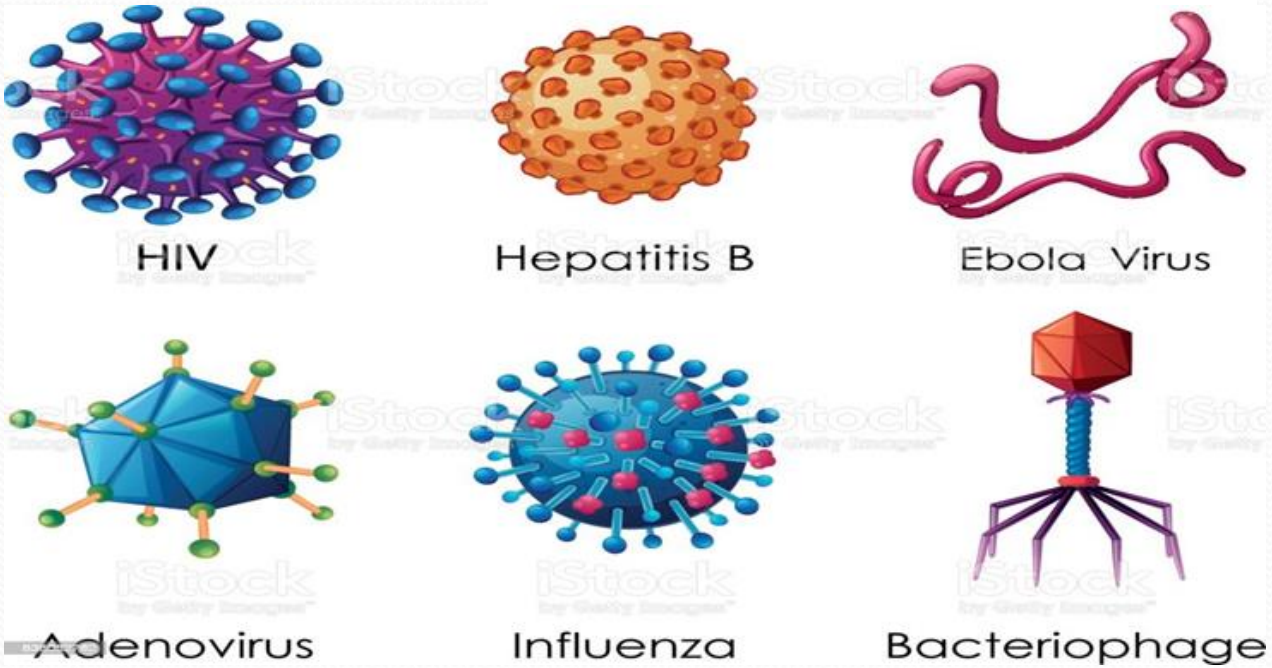
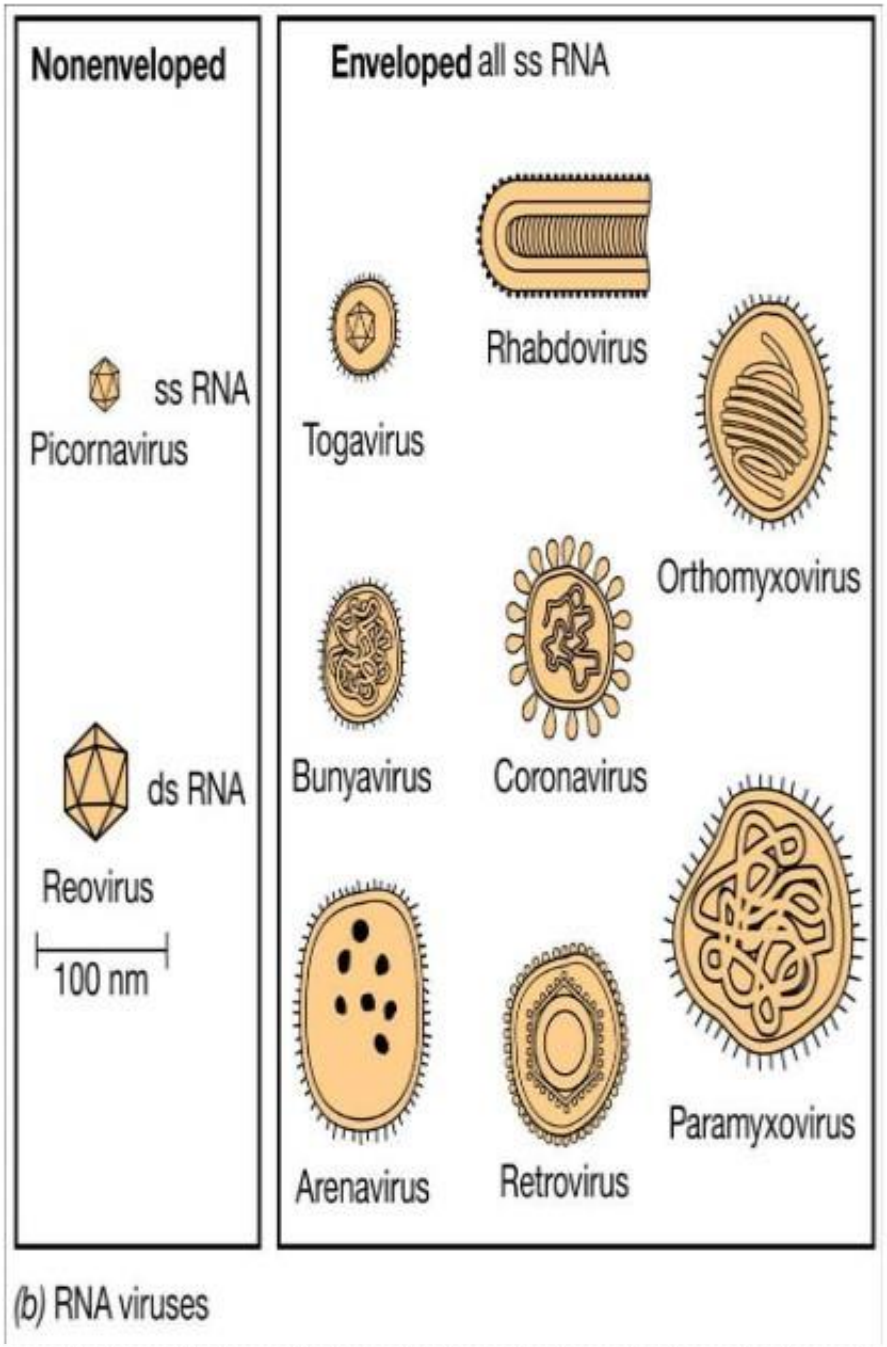


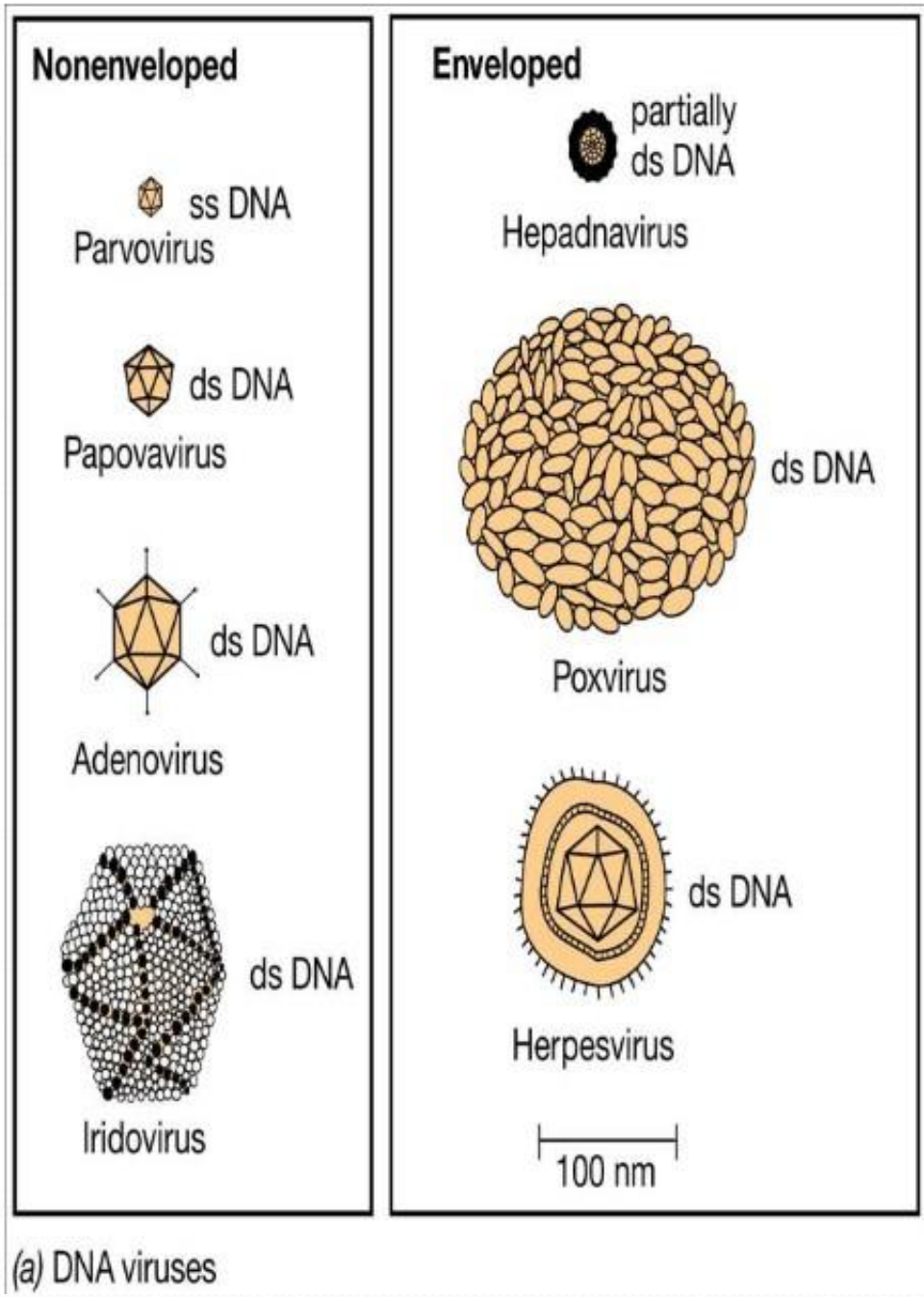
Figure show viruses

Genome of N A of virus

1. **DS RNA**
2. **SS RNA**
3. **DS DNA**
4. **SS DNA**

The type of nucleic acid found in the virus particle is perhaps the most fundamental and straightforward of viral properties. It may be RNA or DNA, either of which may be single-stranded (ss) or double-stranded (ds). The most common forms of viral genomes found in nature are **ssRNA and dsDNA**. However, **both dsRNA and ssDNA genomes are found in viruses of medical** significance. Single-stranded viral RNA genomes are further subdivided into those of positive polarity (**+RNA**: that is, of **messenger RNA sense, which can therefore be used as a template for protein synthesis**), and those of negative polarity or are antisense (**- RNA**: that is, **complementary to messenger RNA sense,** which cannot therefore be used directly as a template for protein synthesis). Viruses containing these two types of RNA genomes are commonly referred to as positive-strand and negative-strand RNA viruses, respectively.


Nonenveloped
Enveloped all ss RNA
ss RNA
Picornavirus
Togavirus
Rhabdovirus
Orthomyxovirus
Bunyavirus
Coronavirus
ds RNA
Reovirus
100 nm
Arenavirus
Retrovirus
Paramyxovirus
(b) RNA viruses


Nonenveloped
Enveloped
ss DNA
Parvovirus
partially ds DNA
Hepadnavirus
ds DNA
Papovavirus
ds DNA
Poxvirus
ds DNA
Adenovirus
ds DNA
Herpesvirus
ds DNA
Iridovirus
100 nm
(a) DNA viruses

The general properties of viruses:

1.The virus contains one type of nucleic acid, either RNA or DNA but never both

2. *All viruses have a protein coat (capsid) that surrounds and protects the nucleic acid core.

3. *Some viruses have a lipid envelope or membrane surrounding a nucleocapsid core. *The source of the envelope is from the membranes of the host cell.

4. Viruses are not cells; do not possess cellular organelles as, mitochondria, ribosomes or other cellular components

5. ***They do not encode their own protein synthesis machinery (ribosomes) and energy-generating metabolic pathways. **They depend upon protein synthetic machinery of host cells

6. *Viruses replicate or multiply only within living cells (Viruses are obligate intracellular)

7. They are unaffected by antibiotics. - Antibiotic have no effect on viruses, but antiviral drugs have been developed to treat life-threatening infections.

The general properties of viruses:

8. They are sensitive to interferon

9.*Viruses do not reproduce by binary fission, but they replicate by complex process in the living cells that they infect

10.***Viruses do not grow (have constant size and shape)

11.* Ultra-filterable, very small size, i.e. they are not retained by bacteria-proof filters.

12.*Viruses are very small units with diameters of about 16 nm to over 300 nm as poxviruses

13.*Ultramicroscopic, can only be seen with electron microscope

14. They possess the genes to invade and regulate the metabolic activity of host cells. e.g// • Ex. Hepatitis B (4 genes) and herpesviruses (100 genes)

15.*They have genetic information encoding their structural components,

16. Some of the viruses also possess genes that code for several regulatory active proteins (such as trans-activators) and enzymes (e.g. proteases and polymerases. e.g. RNA dependent- RNA polymerase

- **<u>Structure and symmetry of virus:</u>**
- **Type of symmetry of the virus capsid, capsids normally have one of three shapes**
- 1.**icosahedral** (as in the poliovirus).
- 2-**helical** (as in the tobacco mosaic virus)
- 3.**complex**(as in the bacteriophages , or phages).
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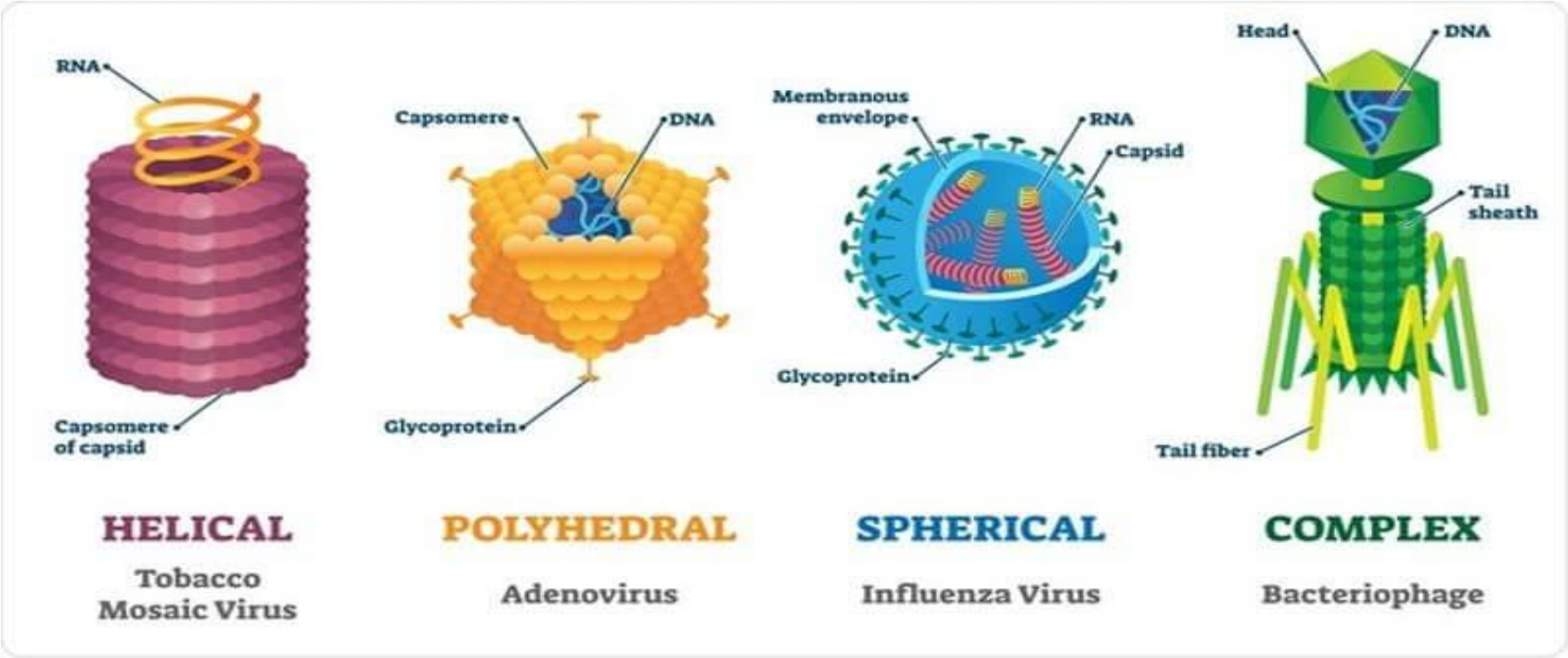


Figure show viral shapes

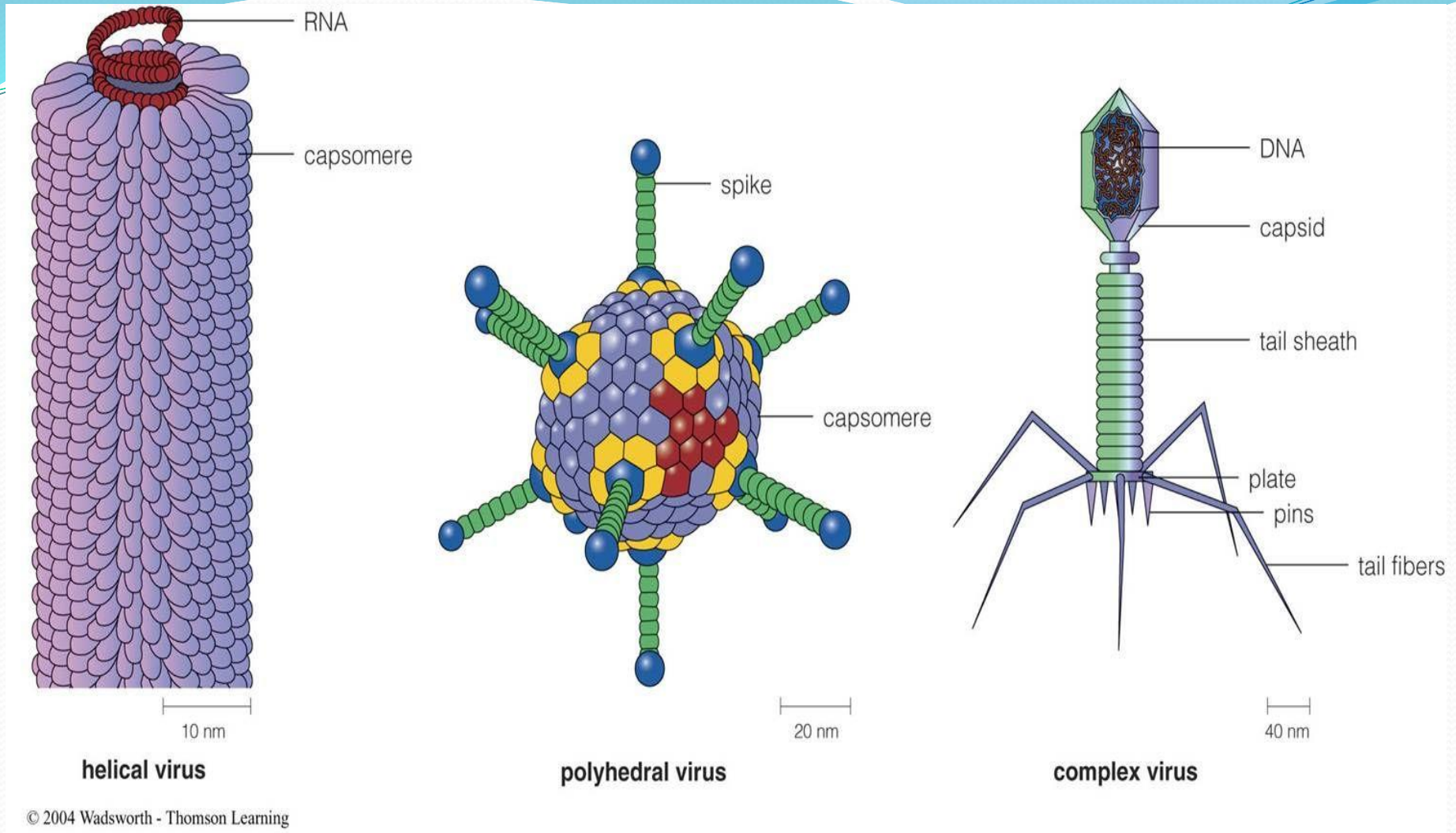


Figure show viral nucleocapsid symmetry

- **Method of replication**

These groups are designated by **Roman numerals** and discriminate viruses depending on their mode of replication and genome type

General Steps in Viral Multiplication (Viral production, Replication):- Viruses multiply only in living cells.

The host cell must provide the energy and protein synthetic machinery

****The virus replication occurs in six main stages:**

1. **Attachment or Adsorption :** is a specific binding between viral capsid protein and specific receptors on the host cellular receptors.

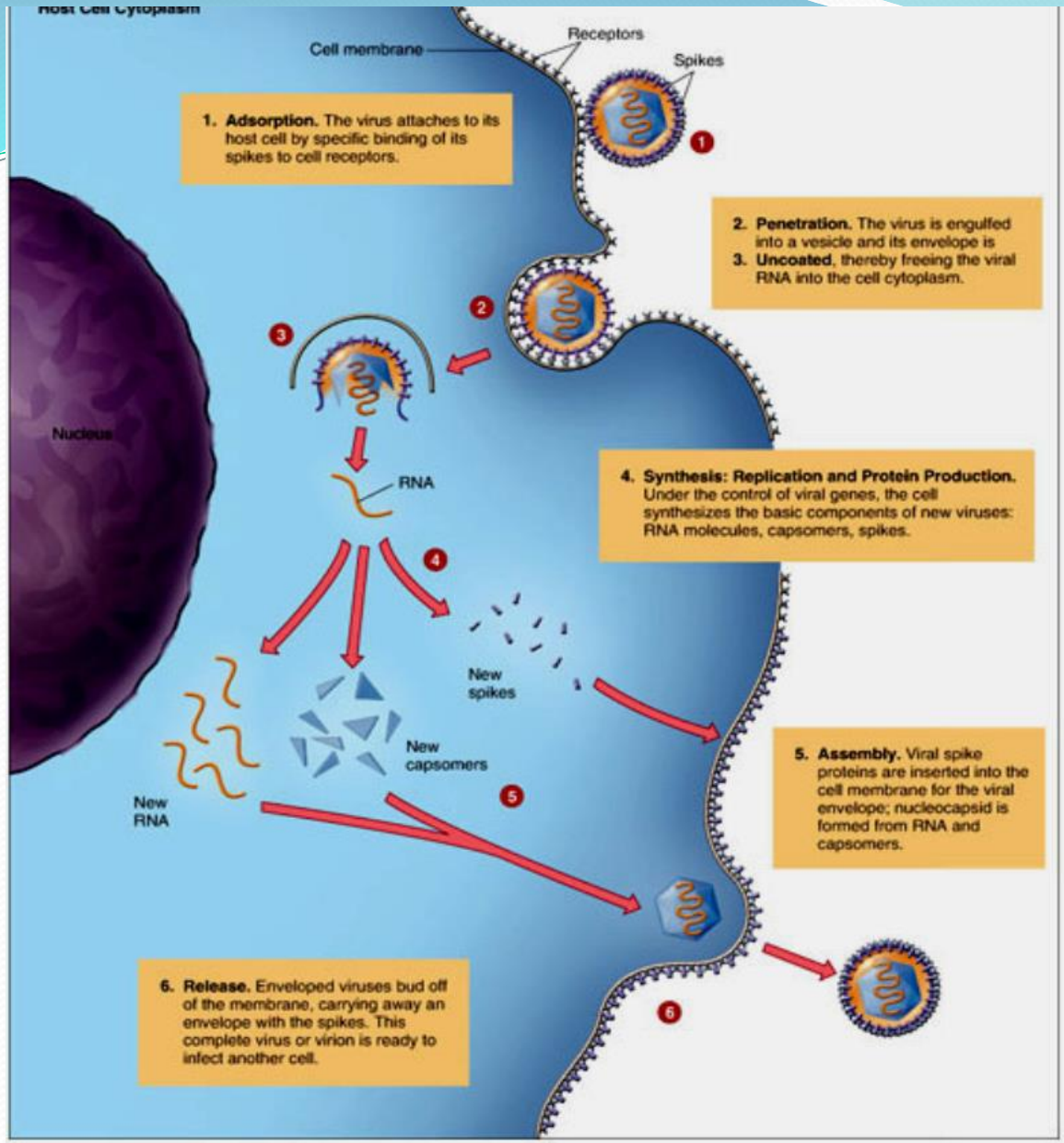
2.**Penetration**: viruses enter the host cell through receptor-mediated endocytosis or membrane fusion

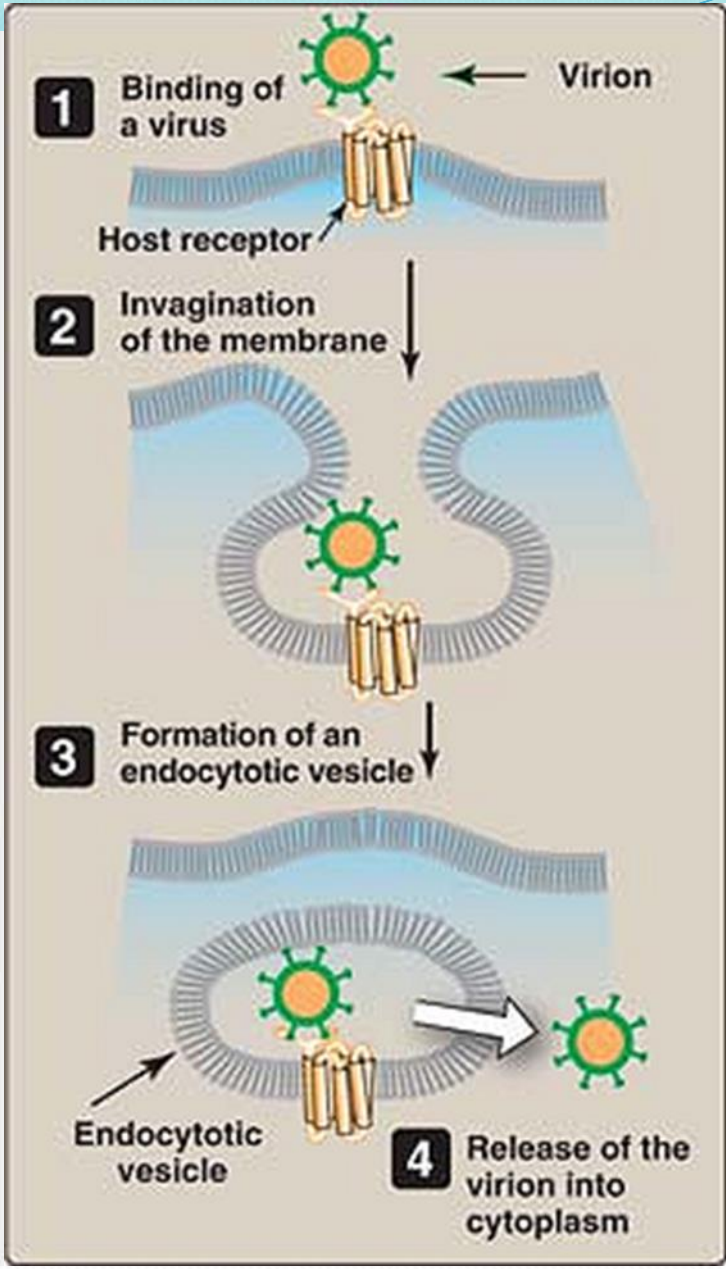
3.**Uncoating:** the viral capsid is degraded by viral enzyme or host enzymes thus releasing the viral genomic nucleic acid

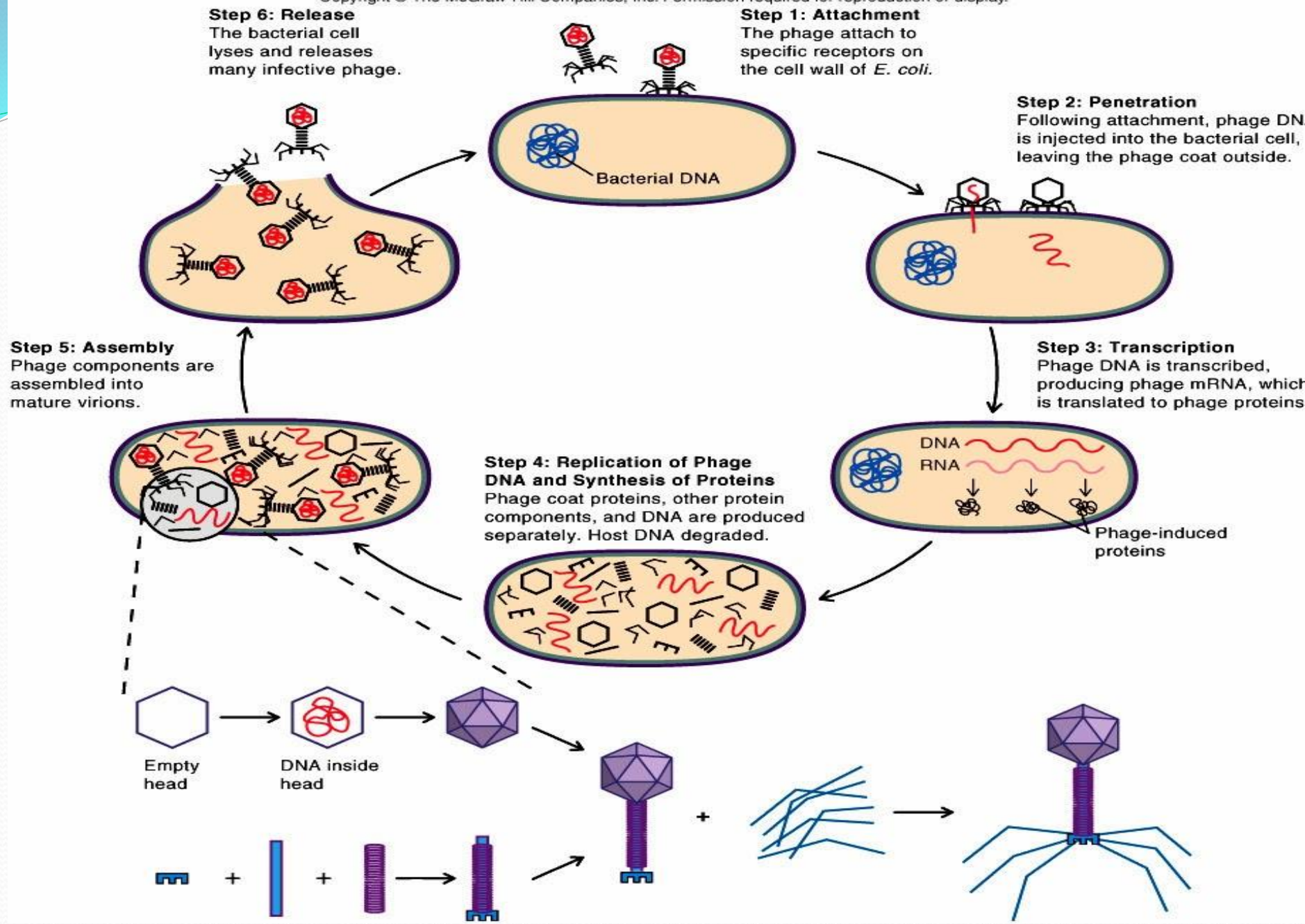
4.**Replecation:** synthesis of viral messenger RNA (mRNA) for viruses except positive sense RNA viruses

5.Assemble: viral protein synthesis, assemble of viral protein and genome

6.Release: viruses are released from the host cell by lyses. Enveloped viruses (e,g, HIV) typically are released from the host cell by budding .


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.
Nucleus
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.


1
Binding of a virus
Virion
Host receptor
2
Invagination of the membrane
3
Formation of an endocytotic vesicle
Endocytotic vesicle
4
Release of the virion into cytoplasm



Once the virus infects a given cell, there are two cycles that the virus can follow:

1)The lytic cycle: (cytocidal infection) involves using the organelles and machinery of the cell to assemble new viruses, which eventually **ruptures the cell** and releases the virions into the outside environment.

2)The lysogenic cycle: Some viruses undergo a **lysogenic cycle** (dormant or latent) where the viral genome is incorporated by genetic recombination into a specific place in the host's chromosome. The viral genome is then known as a "**provirus**", The viral genome is mostly silent within the host. But when reactivated in response to environmental stimuli (e.g., heat, ultraviolet irradiation, or chemotherapy) cause cell lysis and release of viral progeny. E.g. AIDS (HIV infection). E.g. Bacteriaphages

****Effects of viruses on host cell:**

Cytopathic effects (CPE): (Morphologic Effects) : is the changes in cell morphology caused by infecting virus for e.g. rounding of the infected cell, fusion with adjacent cells to form a syncytia (polykaryocytes), and the appearance of nuclear or cytoplasmic inclusion bodies.

Effects on Cell Physiology: The interaction of virus with the cell membrane may change the physiological parameters of infected cells, including movement of ions, formation of secondary messengers, and activation cascades leading to altered cellular activities.

Effects on cell biochemistry: Many viruses inhibit the synthesis of host cell macromolecules, including DNA, RNA, and protein and cellular transcriptional activity.. etc.

Genotoxic Effects: Following virus infection, breakage, fragmentation, rearrangement and/or changes in the number of chromosomes may occur.

Biologic Effects: Virus-specified proteins may alter the cell's antigenic or immune properties, shape, and growth characteristics.

Persistent Infections:

In a persistent infection the virus is not eliminated from all of the host tissues after initial infection or the acute phase of disease.

****There are several types of persistent infection:

1)Latent Infection: Some viruses undergo a **lysogenic cycle** (dormant) where the viral genome is incorporated by genetic recombination into a specific place in the host's chromosome. The viral genome is then known as a "provirus", The viral genome is mostly silent within the host. But when reactivated in response to environmental stimuli (e.g., heat, ultraviolet irradiation, or chemotherapy) cause cell lysis and release of viral progeny. E.g. AIDS (HIV infection)

2)Chronic Infection: The cellular effects of chronic infection are usually the same as those of acute cytocidal infections, except that production of progeny may be slower, and limited to a few cells. The long-term cellular changes may result in severe disease, immune suppression. e.g. HCV infection

3)Slow Infection: This type of virus-cell interaction is characterized by a prolonged incubation period, and slow progression of cellular injury and disease. e.g. measles

4)Transforming Infections: DNA or RNA tumor viruses may mediate multiple changes that convert a normal cell into a malignant phenotype.

Viral-like particles (VLPs):

•VLPs are nanoscale structures made up of assembled viral proteins that lack viral genetic material (not real virus) and are therefore non-infectious. If a person is vaccinated with VLPs then an immune response is generated as if the immune system has been presented with a real virus.

VLPs are dispersed nanomaterials that can be produced in a variety of systems, including mammals, plants, insects, and bacteria.

•VLPs can be exploited as carriers for the delivery of bio- and nanomaterials, such as drugs, and vaccines

VLP types:

**Application of VLPs is their potential in vaccinology where they can offer several advantages over conventional vaccine approaches, because of

1. *Their size and shape, which resembles the actual size and shape of native viruses,

2. *VLPs can efficiently elicit the immune responses

3. *VLPs lacking viral genomes, there is no potential for replication within the target cells, which improved safety especially for immune-compromised or elderly vaccines

4. *VLPs can stimulate both humoral and cellular immune response.

Sub-viral particles (viroid and prion):

1. Viroids:

**Plant viruses resemble animal viruses in many aspects:

*Plant viruses are morphologically similar to animal viruses, and they have similar types of nucleic acid

***Some plant diseases are caused by viriod

****viroids;** are short pieces of naked RNA,The RNA does not code for any proteins. Thus viroids have been pathogens **only** for plants

2. Prions:

A few infectious diseases are caused by prions.

*In 1982, American neurobiologist **Stanley Prusiner** proposed that proteinaceous infectious particle caused a **neurological disease in sheep called scrapie**

*The infectivity of scrapie-infected brain tissue is reduced by **treatment with proteases** but **not** by treatment with **radiation**, suggesting that the infectious agent is **pure protein**.

*Prion **not affected** by **Radiation,** and **chemical agents**

Sub-viral particles (viroid and prion):

*Caused nine animal diseases, All nine are **neurological diseases** called **spongiform encephalopathies** because large vacuoles develop in the brain , including the“**mad cow disease**”that emerged in cattle in Great Britain in 1987.

The human diseases are :

***kuru**, **Creutzfeldt-Jakob disease (CJD),**

*** Gerstmann-SträusslerScheinker syndrome,**

***Fatal familial insomnia.**

***These diseases run in families, which indicates **a possible genetic cause**.

*They cannot be purely inherited, **because** mad cow disease arose from **feeding scrapie-infected sheep meat to cattle**, and the new (bovine) variant was transmitted to humans who ate **undercooked beef** from infected cattle.

* CJD has been **transmitted with transplanted nerve tissue and contaminated surgical instruments**.

*These diseases are caused by the conversion of a **normal host glycoprotein** called **PrPC into** an **infectious form** called **PrPSc**

Viruses can be classified according to

1. ***the host cell they** infect:

a.* animal viruses

b. *plant viruses

c. *fungal viruses

d. *bacteriophages: (viruses infecting bacteria which include the most complex viruses).

*Another classification is based mainly on characteristics of structure of the viral particles, including:

a. ***capsid** shape, or symmetry (icosahedral , helical or complex).

b. *envelope: Presence or absence of lipid envelope. (enveloped, or naked)

c. *the **type of nucleic acid (DNA or RNA, double stranded (ds) or single stranded (ss)**,

d. the process of replication.

Baltimore classification : Baltimore classification (first defined in 1971): Named after David Baltimore, a Nobel Prize-winning biologist.

**Transmission of Viruses:

1. **Respiratory transmission** (Droplet contact) e.g. Influenza A, common cold
2. **Faecal-oral transmission**: Enterovirus (HAV)
3. **Iatrogenic transmission** due to medical procedures, e.g: transplantation of infected material and blood transfusion e.g. HBV, or HCV
4. **Sexual Transmission:** HIV
5. **Animal or insect vectors**: Rabiesvirus

Vaccine can produce lifelong immunity and prevent viral infection

The types Vaccines

1) **live, attenuated microorganisms;**

2) killed microorganisms

3) microbial extracts

4) vaccine conjugates

5) inactivated toxins (toxoids)

6)DNA vaccine

Family	Viruses	Type of NA	Diseases
Pox viruses	Variola	DNA	Smallpox, humanPox, Monkey Pox, Cowpox, Vaccina Virus
herpes viruses	Herpes simplex type1&2	DSDNA	Cold, genital sores, encephalitis
	Varicella-zoster	DSDNA	Chickenpox, shingles
	Cytomegalovirus	DSDNA	Cytomegalic inclusion disease of neonates, pneumonia in immunocompromised patients
	Epstein- Barr (EB)	DSDNA	Infectious mononucleosis (cancer)
Adeno viruses	Adeno viruses	DNA	Sore throat, conjunctivitis, hemorrhagic cystitis
Papova viruses	Papilloma	DNA	Warts, cervical cancer
Hepadna viruses	Hepatitis B	DSDNA	Hepatitis B, liver cancer
Flaviviridae	Hepatitis C	SSRNA	Hepatitis
Hepadna viruses	Hepatitis D	SSRNA	Hepatitis
Picorna viruses	Hepatitis A	SSRNA	Hepatitis
Hepeviridae	Hepatitis E	SSRNA	Hepatitis
Reo viruses	Rota viruses	DSRNA	Causes diarrhea in infant
oncovirus or oncogenic viruses. tumor virus	Hepatitis C, adenovirus, papillomavirus Epstein–Barr virus	DNA, RNA	cause cancer

Family	Viruses	Type of NA	Diseases
Picorna viruses	rhino viruses	RNA	Common cold
Retero viruses (HIV)	Human immuno- deficiency viruses	SSRNA	AIDS
Rhabdo viruses	rabies viruses	RNA	Causes human rabies
paramyxo viruses	Mumps	RNA	sterility. encephalitis, swelling of the parotid glands
	Measles	RNA	(rash, maculopapules)
	Respiratory Syncytial Virus RSV (Pneumvirus)	RNA	influenza
orthomyxovirus	Influenza A,B ParaInfluenza	RNA SSRNA	influenza
Matonaviridae	Rubella	SSRNA	Causes measles in children (rash)
Ebola virus	Ebola virus	RNA	Hemorrhagic fever
Zika virus	Zika virus	DNA	Guillain-Barre syndrome
Corona virus	Corona virus	SSRNA	Respiratory failure, Common cold
Picornaviridae	Polio virus	SSRNA	Poliomyelitis

Antiviral Chemotherapy (Prevention and Treatment of Viral Infection)

Although public health measures and vaccines are the most effective ways to control many viral infections, preventive measures have not succeeded for numerous viral diseases. For some of these diseases, antiviral drugs have been developed. Antiviral drugs have been highly successful, saving lives and relieving suffering, especially for human infected with immunodeficiency virus (HIV). Because viruses are obligate intracellular parasites, antiviral agents must be capable of selectively inhibiting viral functions without damaging the host. There is a need for antiviral drugs active against viruses for which vaccines are not available or not highly effective

Types of Antiviral Agents

1- Nucleoside and Nucleotide Analogs

2- Reverse Transcriptase Inhibitors

3- Protease Inhibitors

4- Integrase Inhibitors

5- Fusion Inhibitor