MEDICAL VIROLOGY

INTRODUCTION TO VIRUSES

LECTURE 1

BY

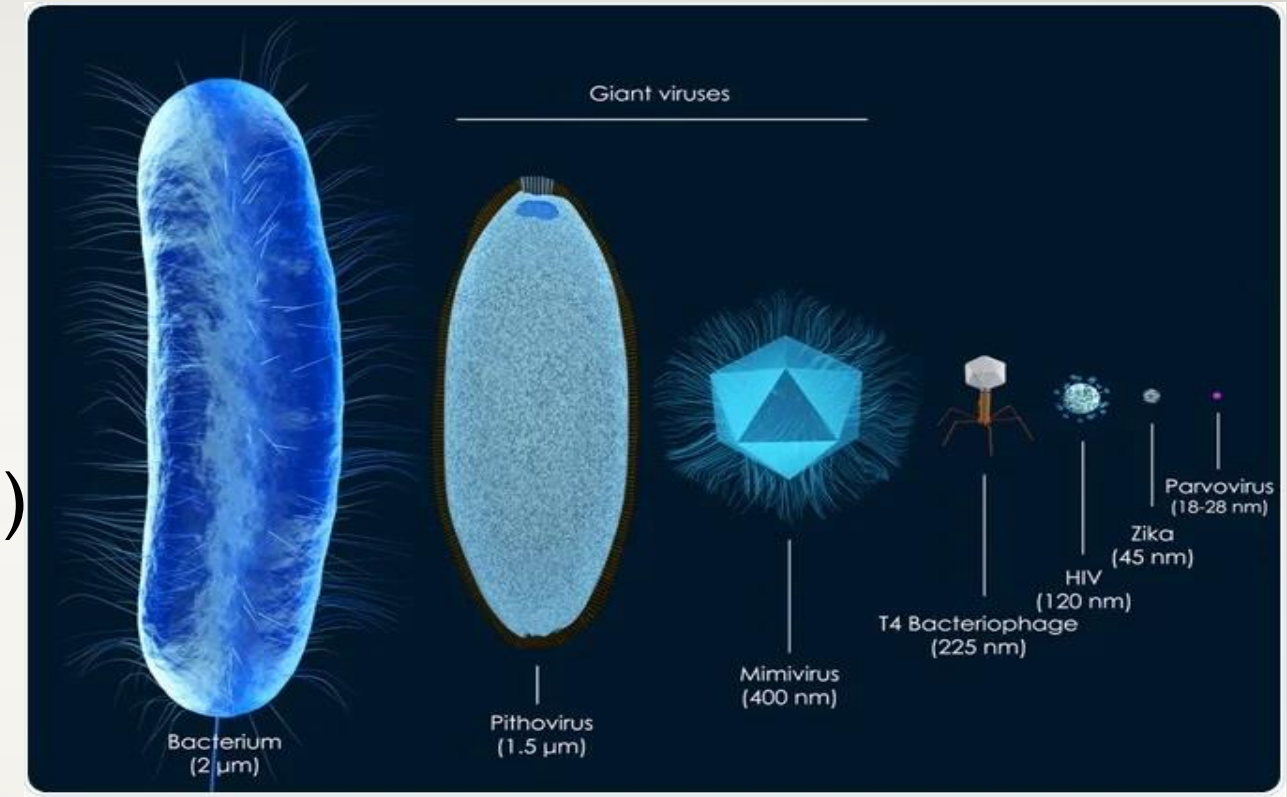
Assist. Prof. Dr. Luma Ghaeb

Viruses General Properties

1-Small size:

The smallest infectious agents
(20-300 nm in diameter)

Bacteria (300-1000nm); RBC (7500nm)



2. Genome:

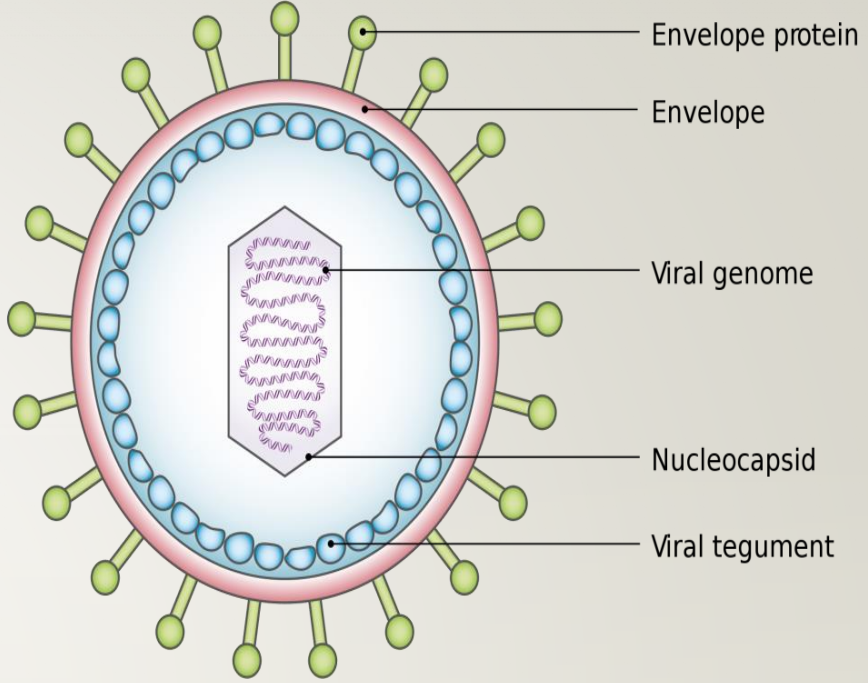
Either DNA or RNA

3. Metabolically inert:

- Do not posses active protein synthesizing apparatus
- Do not have a nucleus, cytoplasm, mitochondria or ribosomes
- No metabolic activity outside host: obligate intracellular parasites

Can replicate only inside living cells; NOT on inanimate media

Viruses classifications according to:



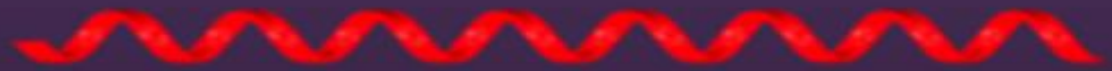
1-Genome:

- A core of DNA or RNA
- May be single-stranded (ss) or double stranded (ds)
- May be circular or linear
- single stranded genomes can be either (+) sense, or (-) sense, the sense strand is the one that can serve directly as mRNA and code for protein, so for these viruses, the viral RNA is infectious. The viral mRNA from - strand viruses is not infectious, since it needs to be copied into the + strand before it can be translated. Also there is ambisense RNA genome.

DNA VIRUS GENOMES RNA

Single Stranded

+ or -



Double Stranded

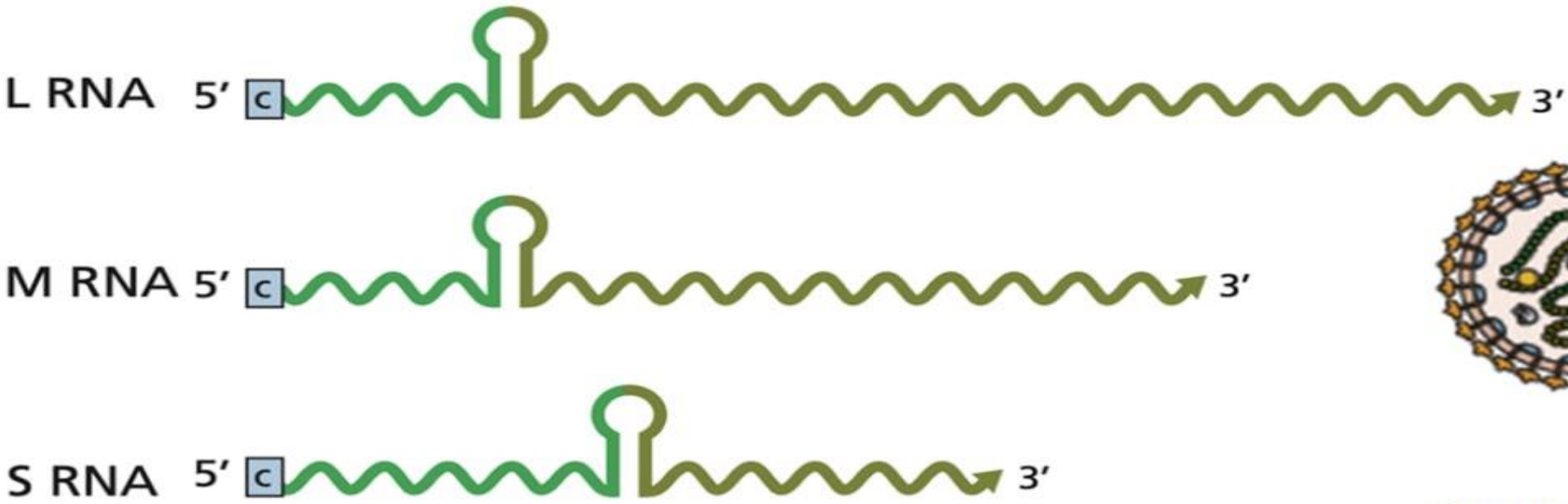
Segmented

Double Stranded Segmented

Ambisense RNA genomes

Ambisense (–) strand RNA

***Arenaviridae* (11 kb in 2 RNAs)**
***Peribunyaviridae* (12.4–16.6 kb in 3 RNAs)**



Arenaviridae
RNA pol in virus particle

RNA has both (+) and (-) components (Ambisense)

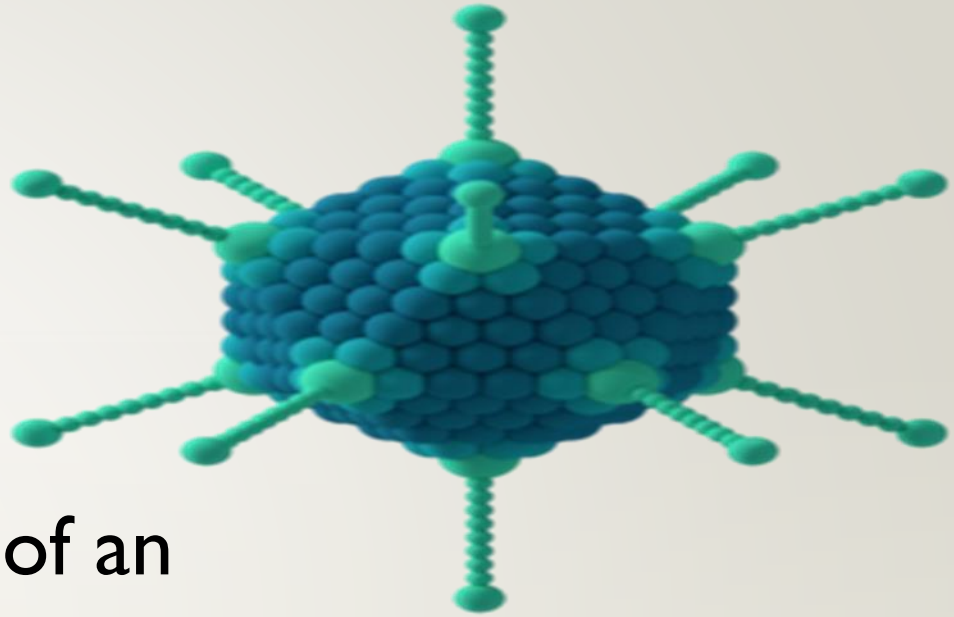
Viruses classifications

2- Capsid: protein coat surrounding the genome

- Provides structural symmetry
- Participates in attachment to susceptible host
- Facilitates transfer of viral nucleic acid in to host cell
- Protects the viral genome from nucleases in blood stream

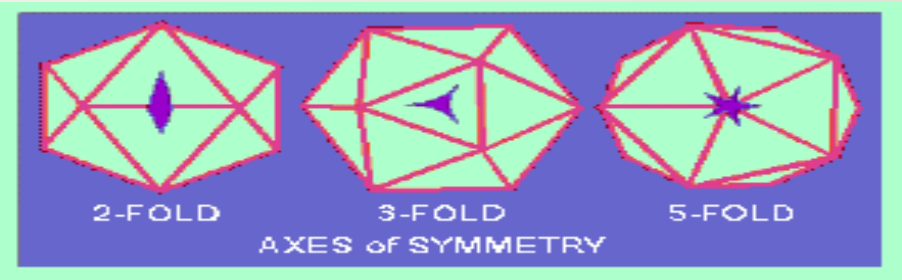
- **Capsomeres:** the structural units making up capsid: consist of one or several proteins

Viruses: Symmetry (Shapes)

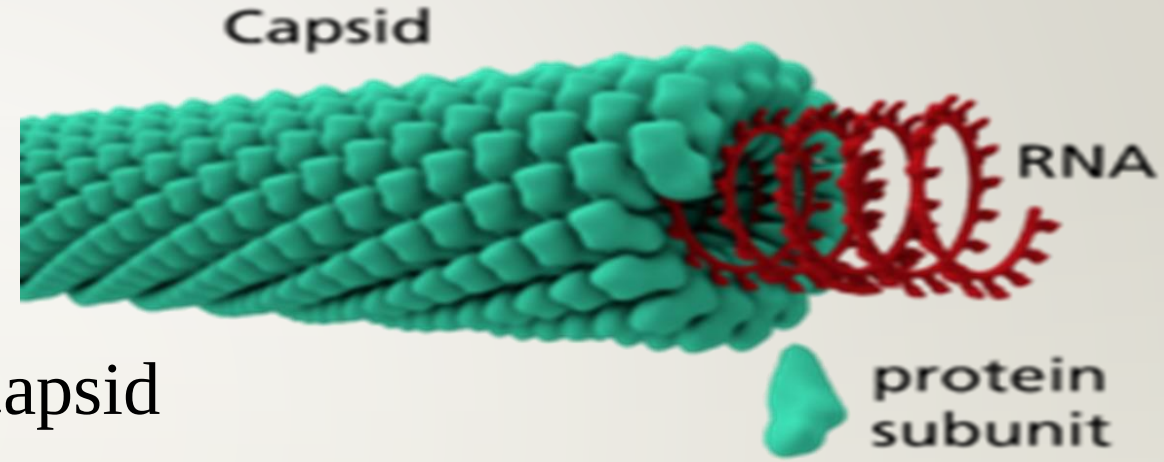


A) Cubic Symmetry (Icosahedral)

- Have exactly 60 subunits on the surface of an icosahedron
- Have fivefold, threefold and twofold rotational symmetry



Viruses: Symmetry (Shapes)



B) Helical Symmetry

- The virion contains an elongated nucleocapsid

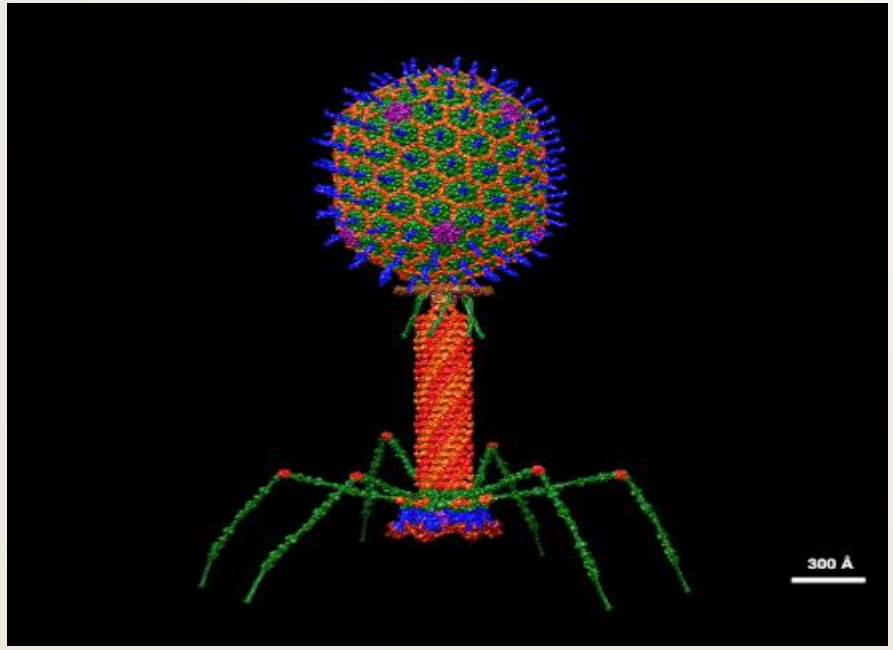
- The capsomeres are arranged round the spiral of nucleic acid

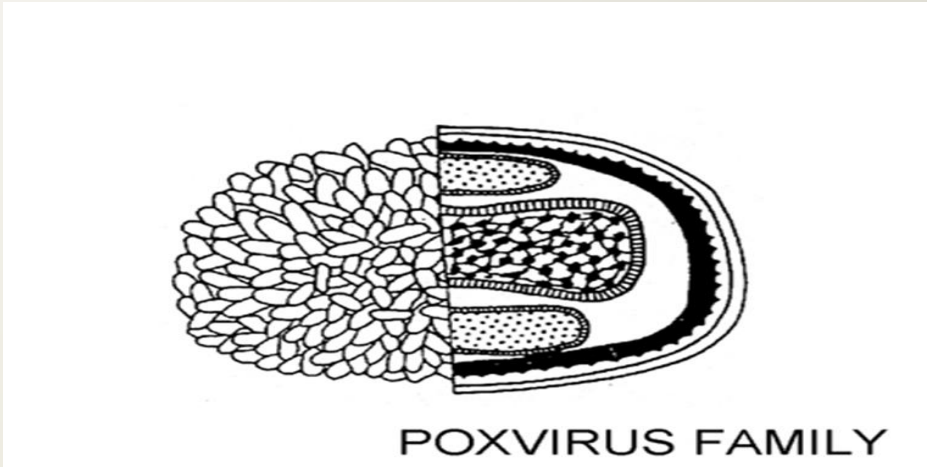
- Most helical viruses are enveloped

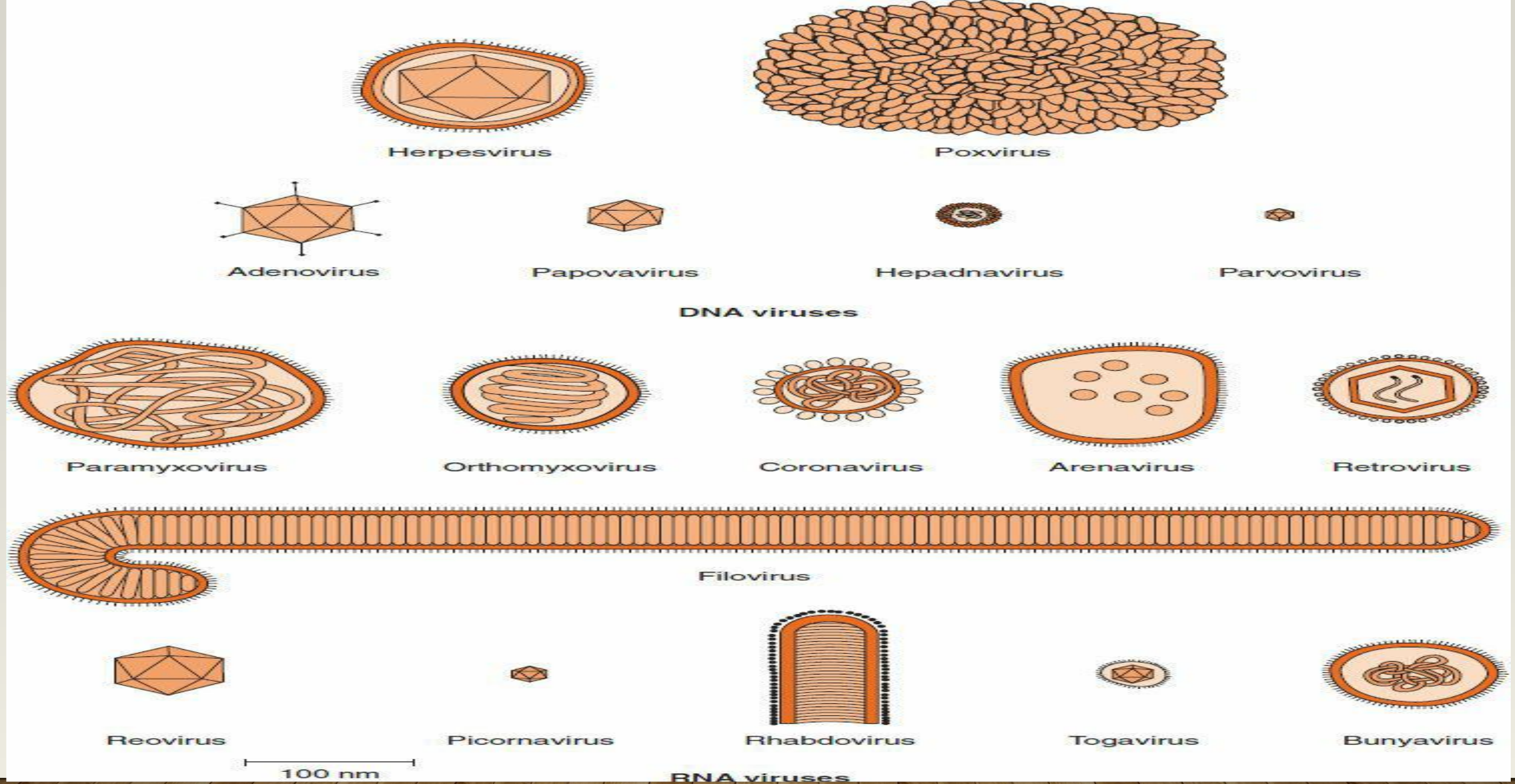
Viruses: Symmetry (Shapes)

C) Complex symmetry

Does not conform to cubic or helical symmetry






Herpesvirus
Poxvirus
Adenovirus
Papovavirus
Hepadnavirus
Parvovirus
DNA viruses
Paramyxovirus
Orthomyxovirus
Coronavirus
Arenavirus
Retrovirus
Filovirus
Reovirus
Picornavirus
Rhabdovirus
Togavirus
Bunyavirus
100 nm
RNA viruses

Viruses classifications

3- Envelope:

- A lipoprotein surrounding the capsid in some viruses
- May contain material of host cell as well as viral origin.
- Virus-encoded glycoproteins are exposed on the surface of the envelope
- Most human helical viruses are enveloped while icosahedral are either enveloped or non-enveloped.

Many enveloped viruses also contain matrix proteins, which are internal proteins that link the nucleocapsid to the envelope. They are very abundant (ie, many copies per virion). Some virions also contain other, non-structural proteins that are used in the viral life cycle. Examples of this are replicases, transcription factors, etc. These non-structural proteins are present in low amounts in the virion.

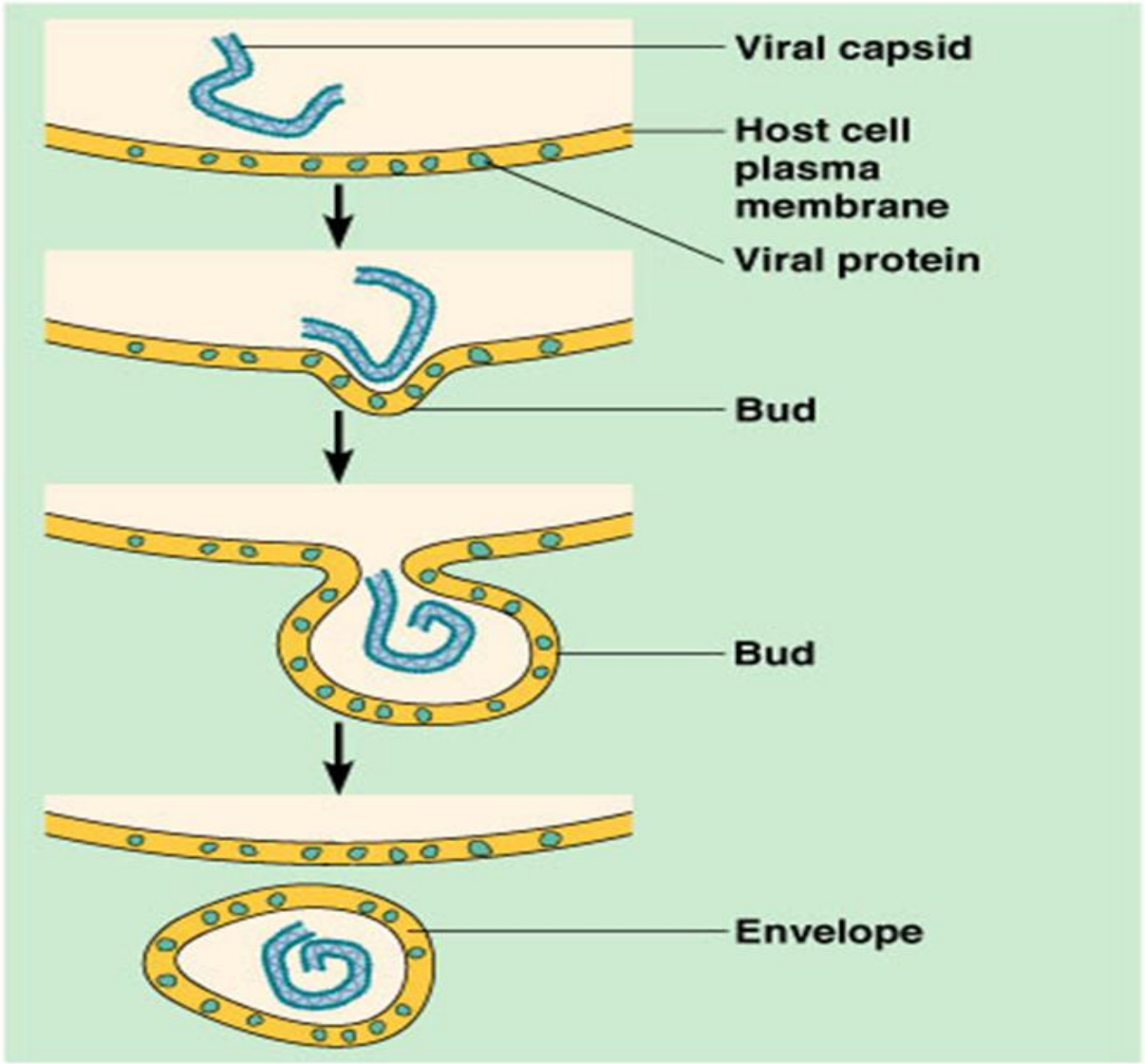
Enveloped viruses are formed by budding through cellular membranes, usually the plasma membrane but sometimes an internal membrane such as the ER, golgi, or nucleus. In these cases, the assembly of viral components (genome, capsid, matrix) occurs on the inside face of the membrane, the envelope glycoproteins cluster in that region of the membrane, and the virus buds out. This ability to bud allows the virus to exit the host cell without lysing, or killing the host. In contrast, non-enveloped viruses, and some enveloped viruses, kill the host cell in order to escape.

Nucleocapsid

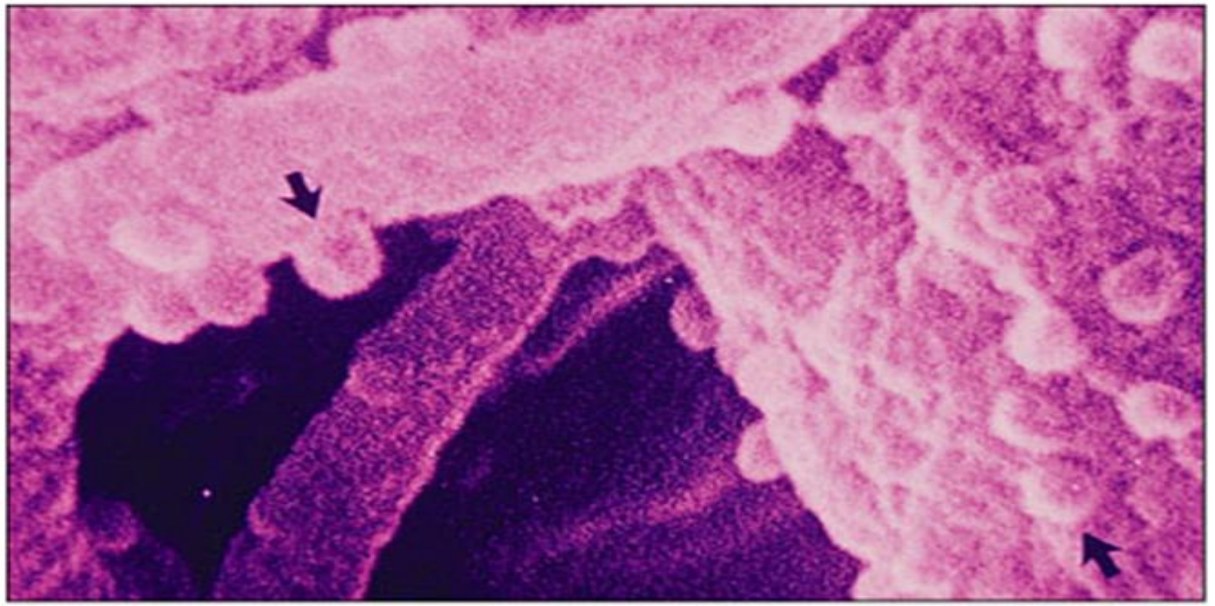
- The protein-nucleic acid complex

Virion

- The complete infective virus particle



(a) Release by budding

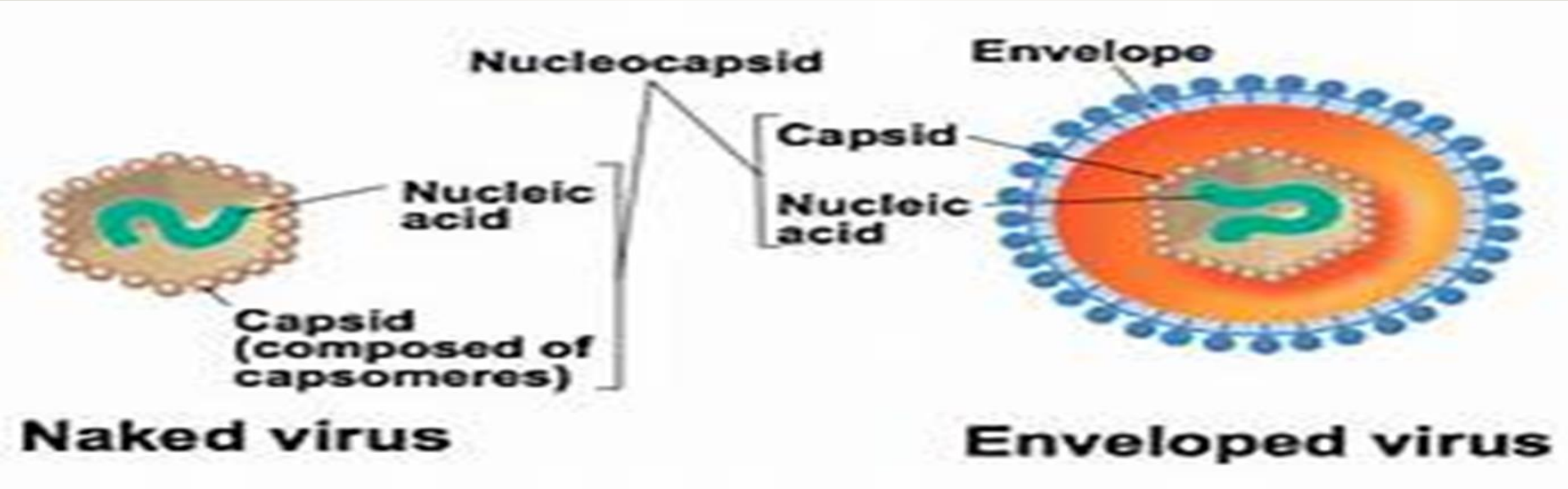


(b) *Alphavirus*

Viruses classification

Significance of Envelope

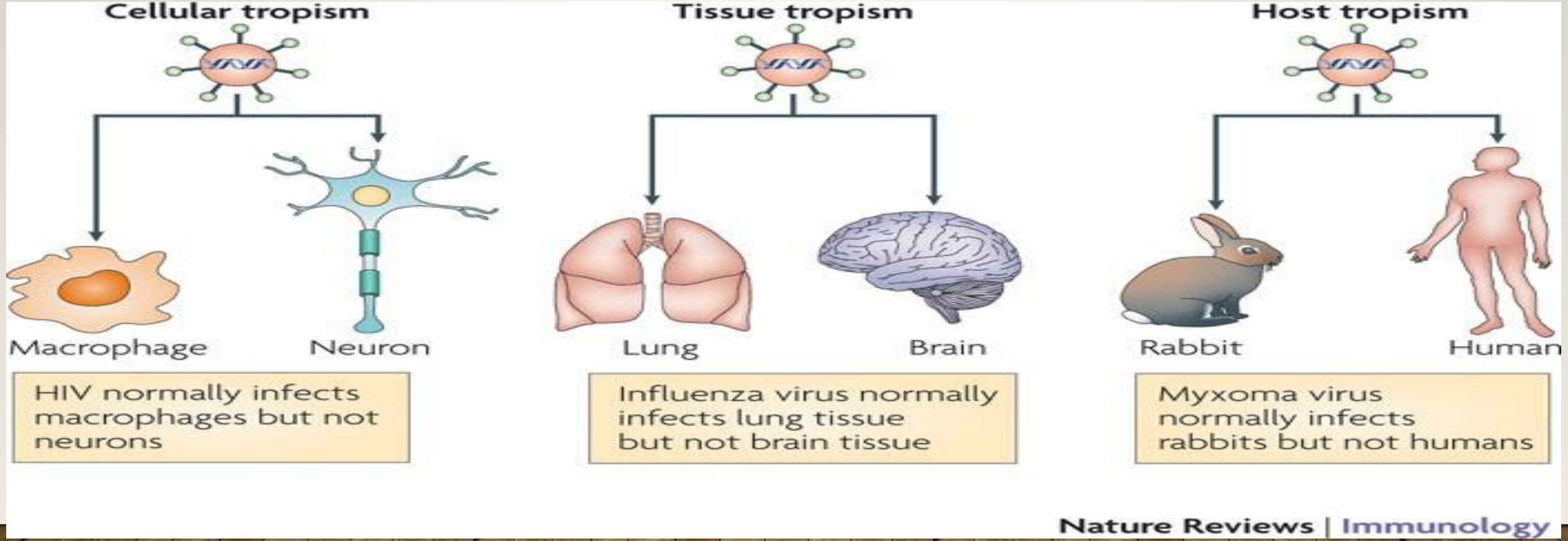
- Enveloped viruses are more unstable i.e. are more sensitive to heat, drying, detergents and alcohols.



Viruses classification

4- Biologic properties:

including natural host range & tissue tropisms , mode of transmission, vector relationships.



Transmission & Portal of Entry

Viruses are transmitted to the individual by many different routes, and their portals of entry are varied For example, person-to-person spread occurs by transfer of respiratory secretions, saliva, blood, or semen and by fecal contamination of water or food. The transfer of blood, either by transfusion or by sharing needles during intravenous drug use, can transmit various viruses (and bacteria). The screening of donated blood for human immunodeficiency virus, human T-cell lymphotropic virus, hepatitis B virus, hepatitis C virus, and West Nile virus has greatly reduced the risk of infection by these pathogens.

Portal of Entry	Virus	Disease
Respiratory tract[1]	Influenza virus	Influenza
	Rhinovirus	Common cold
	Respiratory syncytial virus	Bronchiolitis
	Epstein–Barr virus	Infectious mononucleosis
	Varicella-zoster virus	Chickenpox
	Herpes simplex virus type 1	Herpes labialis
	Cytomegalovirus	Mononucleosis syndrome
	Measles virus	Measles
	Mumps virus	Mumps
	Rubella virus	Rubella
	Hantavirus	Pneumonia
	Adenovirus	Pneumonia
	Parvovirus B19	Slapped cheeks syndrome
Gastrointestinal tract[2]	Hepatitis A virus	Hepatitis A
	Poliovirus	Poliomyelitis
	Rotavirus	Diarrhea
Skin	Rabies virus[3]	Rabies
	Yellow fever virus[3]	Yellow fever
	Dengue virus[3]	Dengue
	Human papillomavirus	Papillomas (warts)
Genital tract	Human papillomavirus	Papillomas (warts)
	Hepatitis B virus	Hepatitis B
	Human immunodeficiency virus	Acquired immunodeficiency syndrome (AIDS)
	Herpes simplex virus type 2	Herpes genitalis and neonatal herpes
Blood	Hepatitis B virus	Hepatitis B
	Hepatitis C virus	Hepatitis C
	Hepatitis D virus	Hepatitis D
	Human T-cell lymphotropic virus	Leukemia
	Human immunodeficiency virus	AIDS
	Cytomegalovirus	Mononucleosis syndrome or pneumonia
Transplacental	Cytomegalovirus	Congenital abnormalities
	Rubella	Congenital abnormalities
	Parvovirus B19	Hydrops fetalis

[1]Transmission of these viruses is typically by respiratory aerosols or saliva.

[2]Transmission of these viruses is typically by the fecal–oral route in contaminated food or water.

[3]Transmission of these viruses is typically by the bite of an infected animal.

Transmission can occur also between mother and offspring in utero across the placenta, at the time of delivery, or during breast feeding. Transmission between mother and offspring is called vertical transmission.
Person-to-person transmission that is not from mother to offspring is called horizontal transmission.

Type of Transmission	Virus
Transplacental[1]	Cytomegalovirus Parvovirus B19 virus Rubella virus
At time of birth[2]	Hepatitis B virus Hepatitis C virus Herpes simplex virus type 2 Human immunodeficiency virus[3] Human papillomavirus
Breast feeding	Cytomegalovirus Human T-cell lymphotropic virus

Animal-to-human transmission can take place either directly from the bite of a reservoir host as in rabies or indirectly through the bite of an insect vector, such as a mosquito, which transfers the virus from an animal reservoir to the person.

Virus	Animal Reservoir	Mode of Transmission	Disease
Rabies virus	In United States, skunks, raccoons, and bats; in developing countries, dogs	Usually bite of infected animal; also aerosol of bat saliva	Rabies
Hantavirus[1]	Deer mice	Aerosol of dried excreta	Hantavirus pulmonary syndrome (pneumonia)
Yellow fever virus	Monkeys	Bite of *Aedes* mosquito	Yellow fever
Dengue virus	Monkeys	Bite of *Aedes* mosquito	Dengue
Encephalitis viruses[2]	Wild birds (e.g., sparrows)	Bite of various mosquitoes	Encephalitis
SARS[3] coronavirus	Civet cat	Aerosol droplets	SARS
Avian influenza virus (H5N1)	Chickens and other fowl	Aerosol droplets, guano	Influenza

[1]Sin Nombre virus is the most important hantavirus in the United States.

[2]Important encephalitis viruses in the United States include eastern and western equine encephalitis viruses, West Nile virus, and St. Louis encephalitis virus.

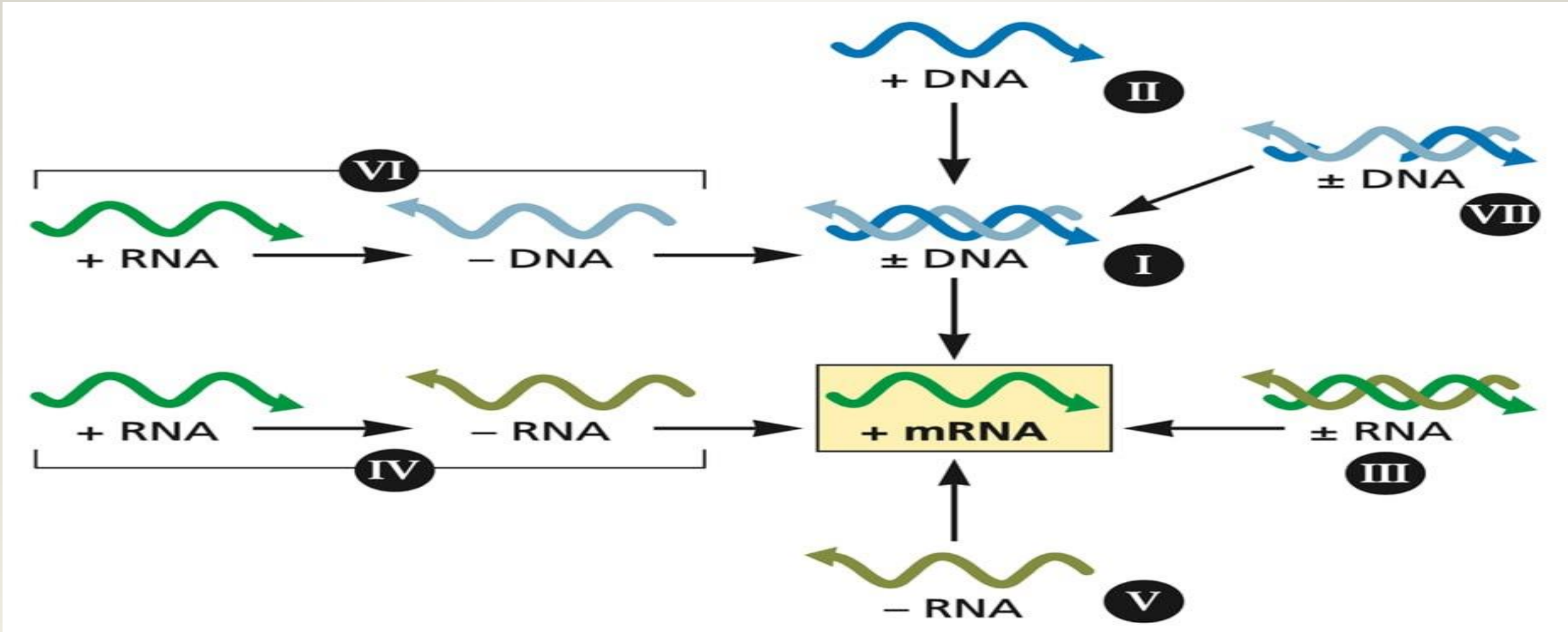
[3]SARS = severe acute respiratory syndrome.

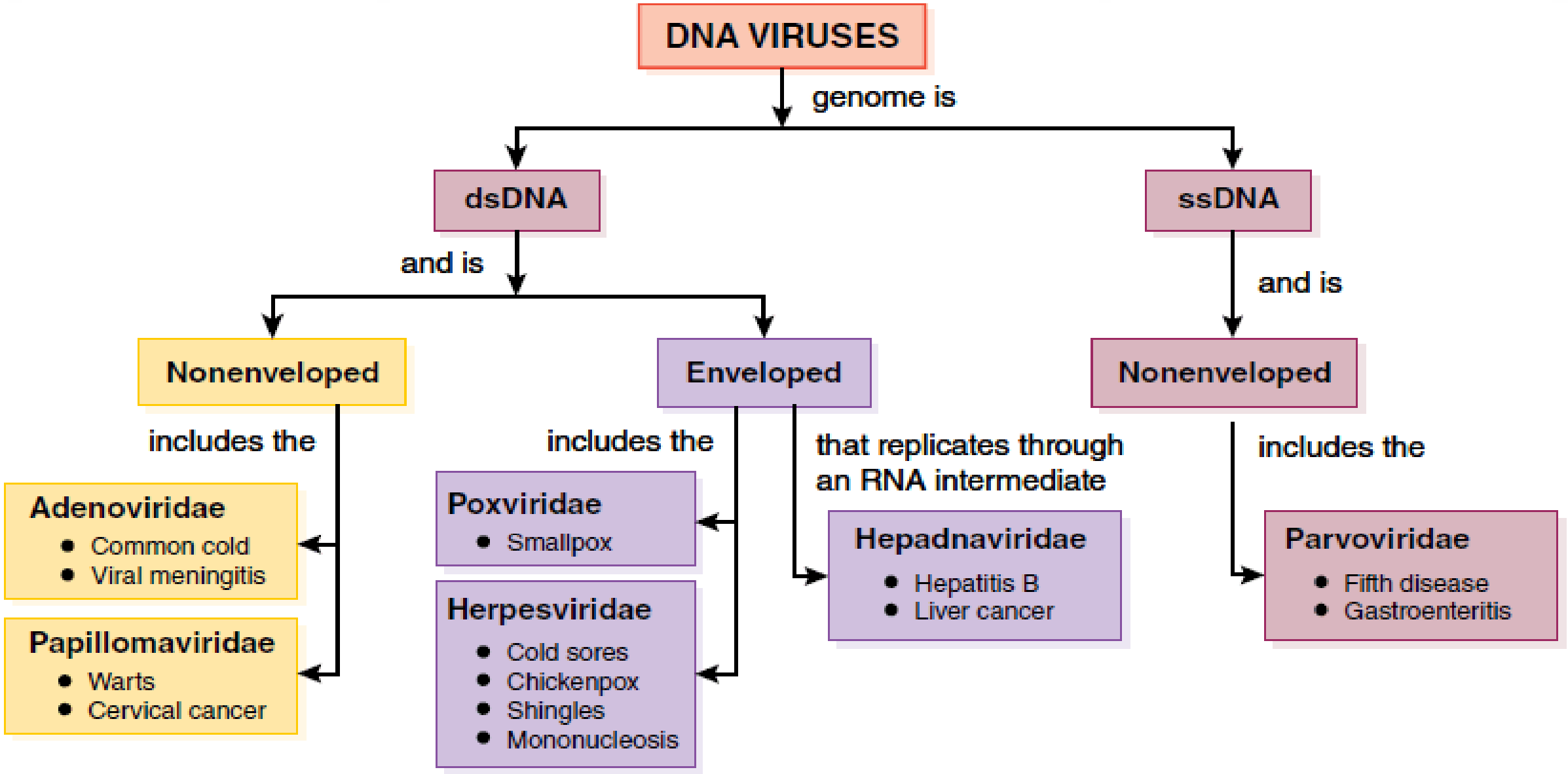
Virus Classification

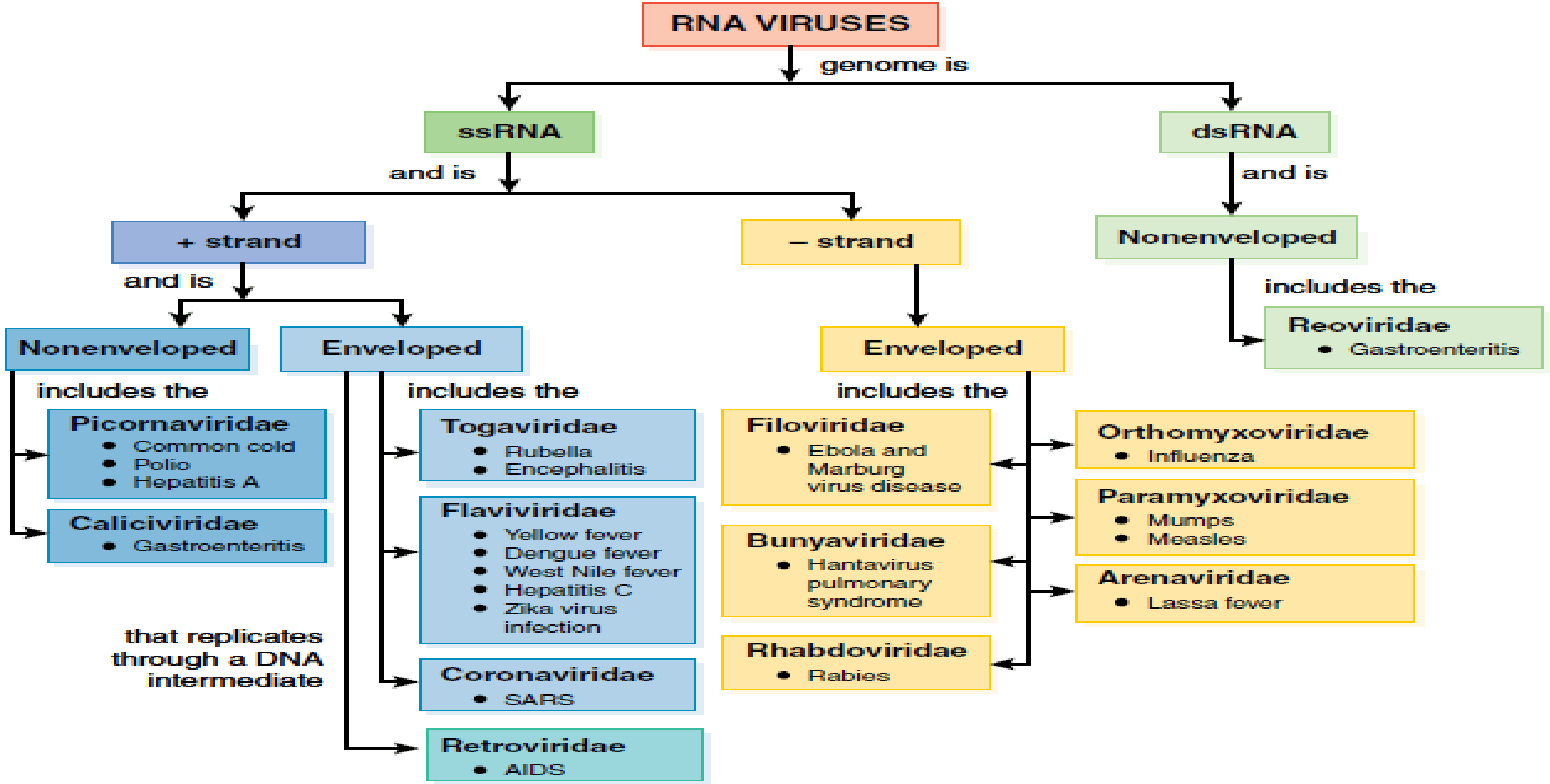
4 - Baltimore classification

To understand the features shared among different groups of viruses, a classification scheme is necessary. However, most viruses are not thought to have evolved from a common ancestor, so the methods that scientists use to classify living things are not very useful. Biologists have used several classification systems in the past, based on the morphology and genetics of the different viruses. However, these earlier classification methods grouped viruses based on which features of the virus they were using to classify them. **The most commonly-used classification method today is called the Baltimore classification scheme which is based on how messenger RNA (mRNA) is generated in each particular type of virus.** The surface structure of virions can be observed by both scanning and transmission electron microscopy, whereas the internal structures of the virus can only be observed in images from a transmission electron microscope.

Baltimore classification




DNA VIRUSES
genome is
dsDNA
ssDNA
and is
and is
Nonenveloped
Enveloped
Nonenveloped
includes the
includes the
that replicates through an RNA intermediate
includes the
Adenoviridae
Common cold
Viral meningitis
Papillomaviridae
Warts
Cervical cancer
Poxviridae
Smallpox
Herpesviridae
Cold sores
Chickenpox
Shingles
Mononucleosis
Hepadnaviridae
Hepatitis B
Liver cancer
Parvoviridae
Fifth disease
Gastroenteritis


RNA VIRUSES
genome is
ssRNA
and is
+ strand
and is
Nonenveloped
includes the
Picornaviridae
Common cold
Polio
Hepatitis A
Caliciviridae
Gastroenteritis
Enveloped
includes the
Togaviridae
Rubella
Encephalitis
Flaviviridae
Yellow fever
Dengue fever
West Nile fever
Hepatitis C
Zika virus infection
Coronaviridae
SARS
that replicates through a DNA intermediate
Retroviridae
AIDS
– strand
Enveloped
includes the
Filoviridae
Ebola and Marburg virus disease
Bunyaviridae
Hantavirus pulmonary syndrome
Rhabdoviridae
Rabies
Orthomyxoviridae
Influenza
Paramyxoviridae
Mumps
Measles
Arenaviridae
Lassa fever
dsRNA
and is
Nonenveloped
includes the
Reoviridae
Gastroenteritis

Virus Nomenclature

Using these and other criteria, the International Committee on Nomenclature of Viruses (ICTV) produced the following the hierarchical system for viral classification.

1) Orders (virales): Groupings of families of viruses that share common characteristics and are distinct from other orders and families.

2) Families (-viridae): Groupings of genera of viruses that share common characteristics and are distinct from the member viruses of other families.

3) Subfamilies (-virinae): Not used in all families, but allows for more complex hierarchy of taxa.

4) Genera (-virus): Groupings of species of viruses that share common characteristics and are distinct from the member viruses of other species.

5) Species (virus): The definition accepted by ICTV is "a virus species is defined as a polythetic class of viruses that constitutes a replicating lineage and occupies a particular ecological niche". A species can be further broken down into strains, variants, subspecies which desighnated by numbers, etc.

Order: Mononegavirales
Family: Paramyxoviridae
Genus: Rubulavirus
Species: Mumps virus

Human Parainfluenza virus 2
Human Parainfluenza virus 4

Atypical Virus-like Agents

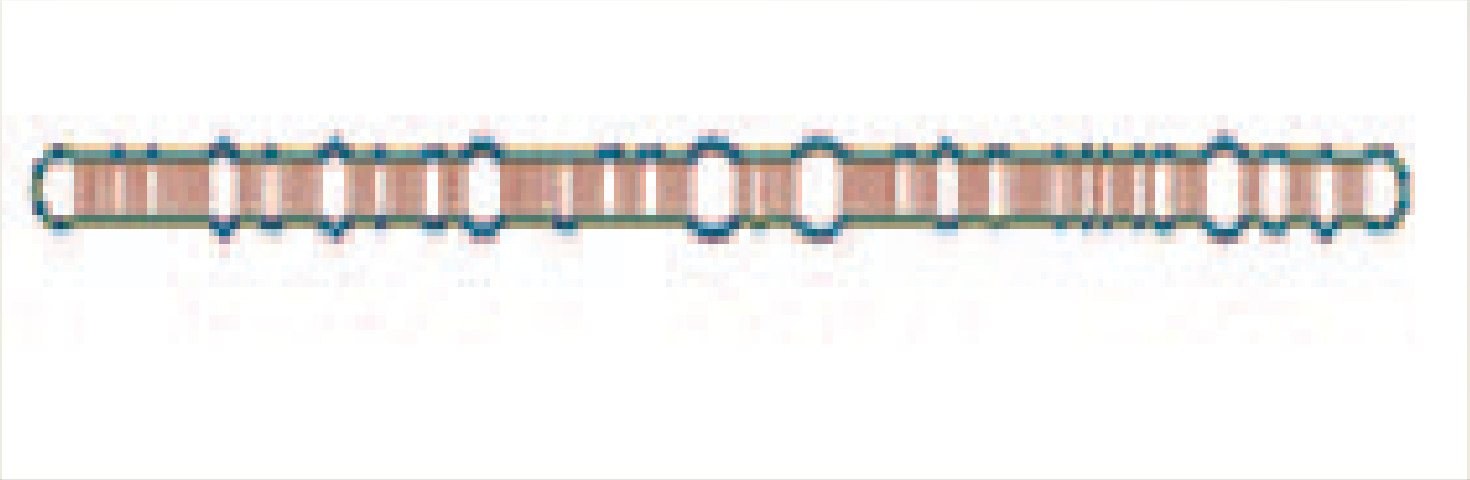
Satellites and viroids

Satellites and viroids have features which differentiate them from the better understood "conventional" viruses. However, they have features which are common to several viruses and they are often referred to **as subviral agents**. The similarities with conventional viruses have permitted a preliminary classification of viroids into families and genera.

Satellites are categorized by two forms, satellite viruses and satellite nucleic acid. Neither satellite viruses nor satellite nucleic acids encode the enzymes required for their replication and require coinfection with a conventional, helper, virus to provide the replicative enzymes However, unlike DI viruses, the sequence of satellite genomes is significantly different to that of the helper virus**. Satellite viruses encode the structural protein that encapsidate them but the satellite nucleic acids either encode only nonstructural proteins or no proteins at all. The satellite nucleic acids derive their structural proteins from the coinfecting helper virus.** In some cases the sequences of the immediate termini of satellite genomes are similar to those of the helper virus, suggesting that these regions are involved in replication as is frequently the case for the helper virus genomes.

The presence of a satellite or satellite virus may affect the replication of the helper virus and may also increase or decrease the severity of the disease caused by the helper virus. A satellite that is important because of its association with disease in humans is hepatitis delta virus (HDV). HDV is only found in association with hepatitis B virus (HBV) and is associated with enhanced pathogenicity of HBV. The HDV genome consists of a circular ssRNA molecule which is extensively base-paired and appears as a rod-like structure. HDV is unable to replicate without a helper virus (HBV) which provides the structural proteins which encapsidate the genome and allow HDV to be spread

Viroids are novel agents of disease in plants; their infectious material consists of a single circular ssRNA molecule with no protein component. Viroids, with genomes ranging in size from 246 to 400 nucleotides, are the smallest self-replicating pathogens known. Cause several plant diseases but are not implicated in human diseases



Prions

The "**proteinaceous infectious particle**," a name that was shortened to "prion" (pronounced "pree-on") have no RNA & DNA. Prions can enter the brain through infection, or they can arise from mutations in the gene that encodes the protein.

An abnormal form of a normally harmless protein found in the brain that is responsible for **a variety of fatal neurodegenerative diseases** of animals, including humans, called transmissible spongiform encephalopathies.

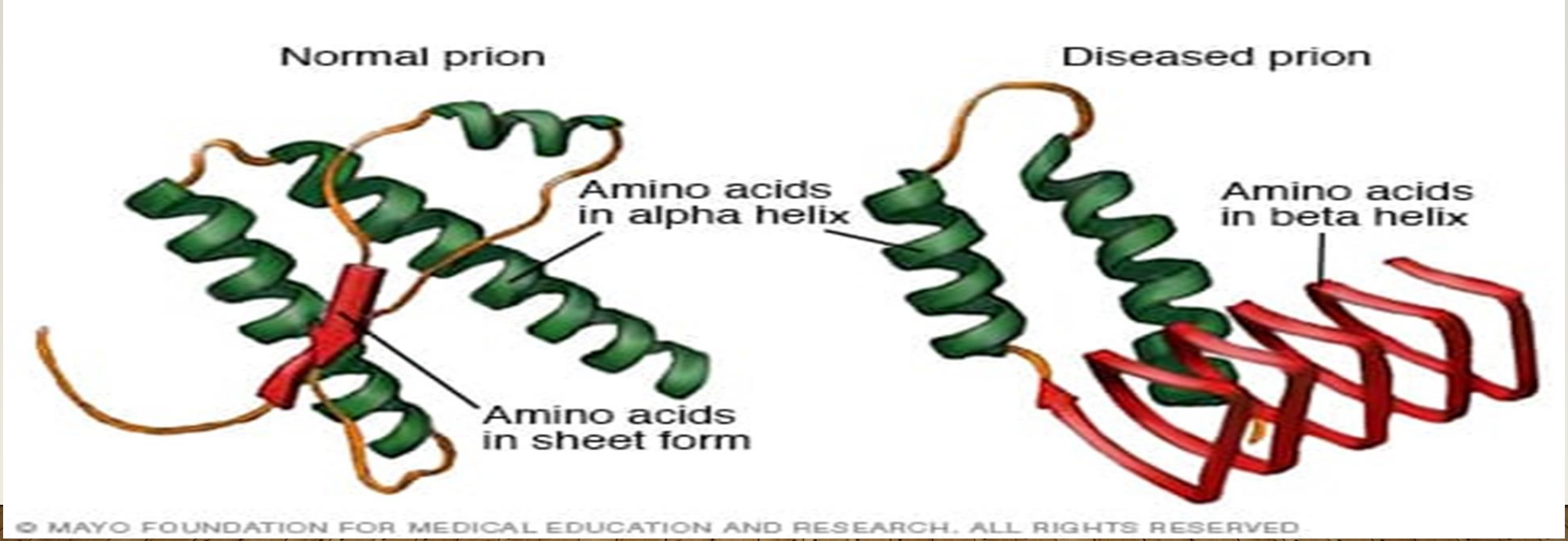
They can be:

- **Acquired** through contaminated food or medical equipment
- **Inherited** via mutations in the gene that codes for PrP
- **Sporadic**, where the misfolded PrP develops without any known cause

The normal protein structure($PrP^{C)}$ is thought to consist of a number of flexible coils called alpha helices. In the **prion protein** some of these helices are stretched into flat structures called beta strands **(**$PrP^{Sc)}$.

The normal protein conformation can be degraded rather easily by cellular enzymes called proteases, but the prion protein shape is more resistant to this enzymatic activity.

Thus, as prion proteins multiply, they are not broken down by proteases and instead accumulate within neurons, destroying them. Progressive neuron destruction eventually causes brain tissue to become filled with holes in a spongelike, or spongiform, pattern.



How Creutzfeldt-Jakob disease works

CAUSE

Creutzfeldt-Jakob disease is caused by abnormal proteins called prions that are not killed by standard methods for sterilizing surgical equipment.

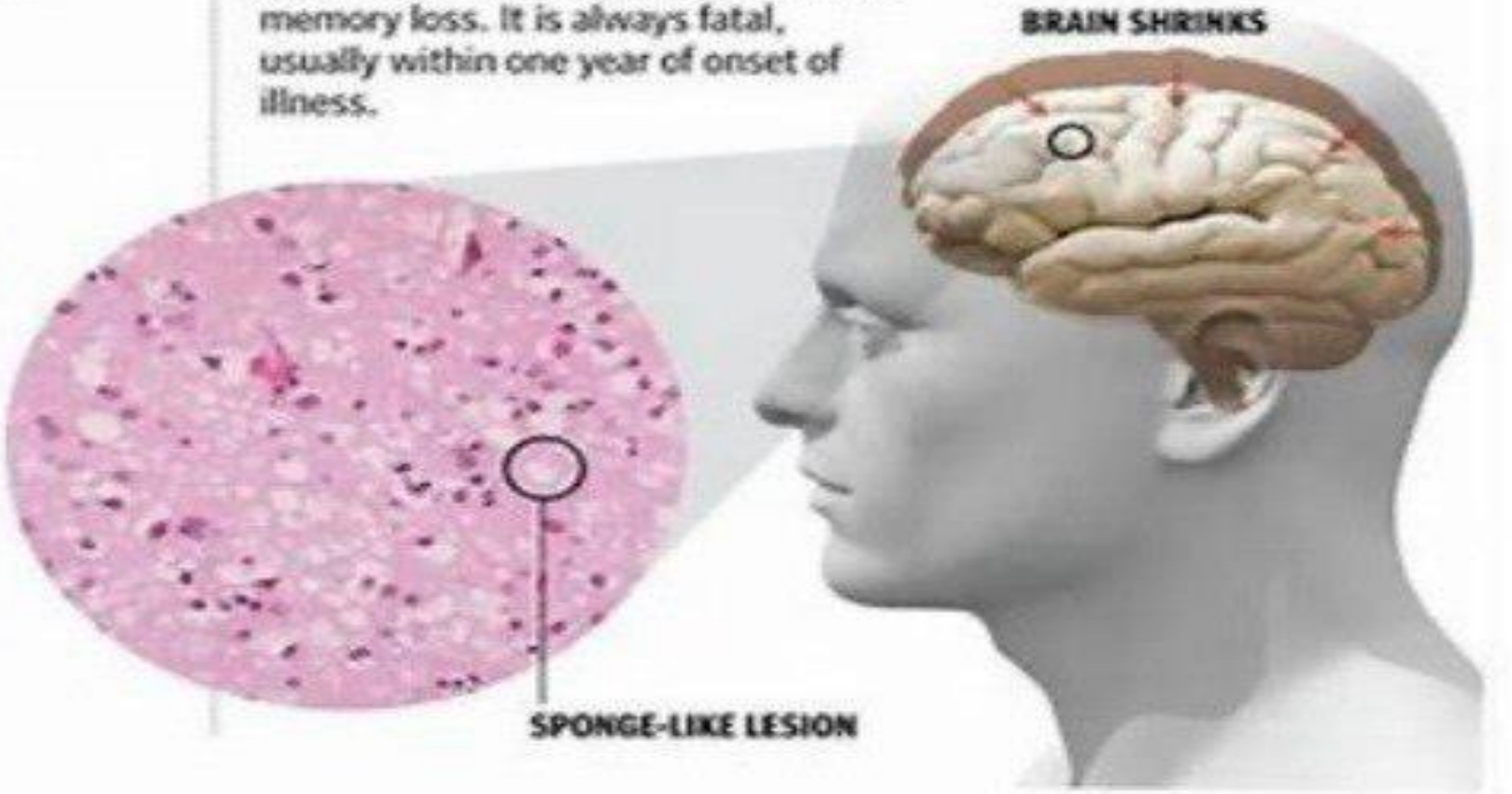
NORMAL HUMAN PROTEIN

DISEASE-CAUSING PRION

As prions build up in cells, the brain slowly shrinks and the tissue fills with holes until it resembles a sponge.

CONSEQUENCES

Those affected lose the ability to think and to move properly and suffer from memory loss. It is always fatal, usually within one year of onset of illness.



- **an MRI brain scan** – uses strong magnetic fields and radio waves to produce a detailed image of the brain, and can show up abnormalities particular to CJD
- **an EEG** – records brain activity and may pick up abnormal electrical patterns seen in sporadic CJD
- **a lumbar puncture** – a procedure where a needle is inserted into the lower part of the spine to draw out a sample of cerebrospinal fluid (which surrounds your brain and spinal cord) so it can be tested for a certain protein that indicates you may have CJD
- **a prototype blood test** for variant CJD has
- **tonsil biopsy** – a small piece of tissue can be taken from the tonsils and checked for the abnormal prions found in variant CJD (they're not present in other types of CJD)
- **genetic test** – a simple blood test to find out whether you have a mutation (fault) in the gene that produces normal protein; a positive result may indicate familial (inherited) prion disease

The specific symptoms of CJD may be treated by:

- treating ataxia (loss of physical co-ordination)
- treating urinary incontinence (loss of bladder control)
- treating bowel incontinence (loss of bowel control)
- treating dysphagia (swallowing difficulties)
- dystonia (muscle spasms and stiffness)
- blindness or vision loss