Virology – Introduction
JU- 2nd Year Medical Students

By

Dr Hamed AlZoubi – Microbiology and Immunology Department – Mutah University.

MBBS (J.U.S.T)

MSc, PhD medical microbiology (UK).

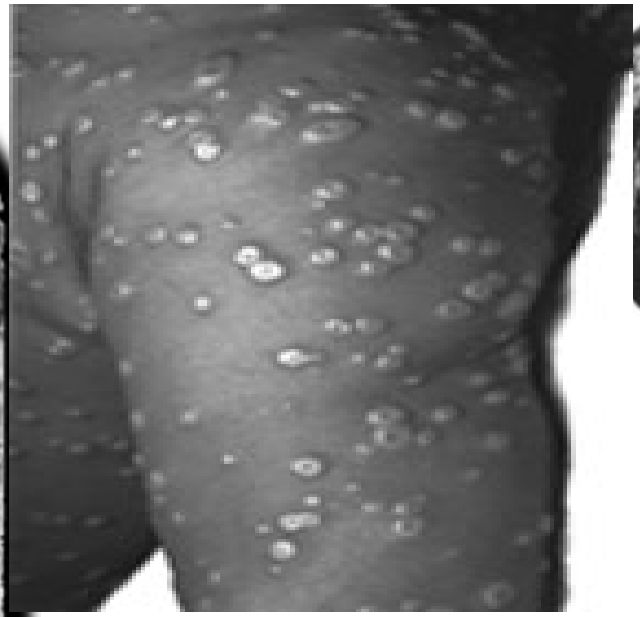
FRCPath (associate, medical microbiology).

Virology - introduction

- Contents:

1. History: Quick overview
2. Viral structure.
3. Viral classification (taxonomy) and nomenclature.
4. Range of diseases caused by viruses.
5. bacteriophages, Viroids, prions

History : more than 3000 years ago



Few months ago - year 2014

But also

Views

- Divinely created
- Outer space
- Conspiracy theory (man created)
- more speculations

- Simple free livings creatures preceded the development of more complicated ones such as bacteria- but an important thing is that viruses are cell dependent (could not be free),

Virology science development

- Virology as a science evolved after bacteriology, bacterial bigger size made them visible under light microscope
- Late 19th century, the term virus was used and it is a latin word means poisonous fluid
- Tobacco mosaic virus (plant infection) and animal hand foot mouth disease could be transmitted via filtrated (filters that retain bacteria) extracts.

Virology science development

- Can not be cultivated on usual bacterial media in laboratory
- Animals and plants were used initially to show infection, e.g dogs rabbits were used to develop vaccines for rabies and smallpox
- Expensive, not reproducible apart from animal rights.

- Later in 1950s the cell tissue and chick embryo together with **antibiotics** (contamination) were used to cultivate viruses in vitro
- Nowadays, E.M (1939) and molecular biology (isolate, clone and express viral genetics)
- Polio and Spanish flu viruses were *in vitro* constructed

Structure and general properties

- Why we need to know that:
- Many reasons such as:

- Necessary for identification

- Necessary to know how viruses replicate therefore we can interfere (prevent, control, treat…)

✓ enveloped or naked – resistance to heat, detergent and lipid solvents (alcohol)

✓ spikes for attachment - interfere

Structure and general properties

- ✓ Small size: 20-300nm diameter (Infiltrable)
- ✓ Genome: one kind of nucleic acid RNA or DNA
- ✓ Metabolically inert no mitochondria, cytoplasm, ribosomes...
- ✓ Replication: need living cells to replicate inside: utilize (KIDNAP) cellular replication mechanisms

Viral structure

Four major structures:

1. Viral nucleic acid RNA or DNA
2. Viral proteins
3. Capsid
4. Envelop (not all viruses have it)

Shapes, under EM, are frequently described using terms such as spherical, rod, bullets or bricks

The shape is determined by the capsomers(Morphological units) arrangement of the Capsid

Viral structure/Viral nucleic acid

1. Can be DNA or RNA, not both.

2. Single or double stranded:

All RNA viruses are single stranded except Reoviruses which are ds RNA.

All DNA viruses are double stranded except Parvoviruses which are ss DNA.

3. Linear or sometimes circular/supercoiled as in Papilloma and polyoma viruses (ds supercoiled DNA).

Nucleic acid

4. DNA is always a single molecule, while RNA can exist as a single or several molecules as in Orthomyxoviruses and Reoviruses (segments).

5. Viral genome is a haploid (one copy) except in Retroviruses which have two copies of their RNA genome (diploid).

6. RNA can be of positive or negative polarity (in comparison to the mRNA).

Nucleic acid

Negative polarity:

- ✓ RNA has an opposite symmetry to the mRNA (not translatable)
- ✓ Carry RNA dependent RNA polymerase to copy it into positive symmetry RNA.
- ✓ Directly non infectious to in vitro cells ? Why

Positive polarity

- ✓ RNA translated directly by the cellular ribosome
- ✓ do not carryenzymes (Except retroviruses which carry reverse transcriptase)
- ✓ Directly infectious to cells in vitro

Genomic size

- RNA usually smaller and more fragile than DNA viruses
- Each 1000 bp = kilobases
- For **single-stranded genomes, the** notation **kb is used.**
- **For double-stranded genomes, numbers are**expressed as kilobase pairs (**kbp).**

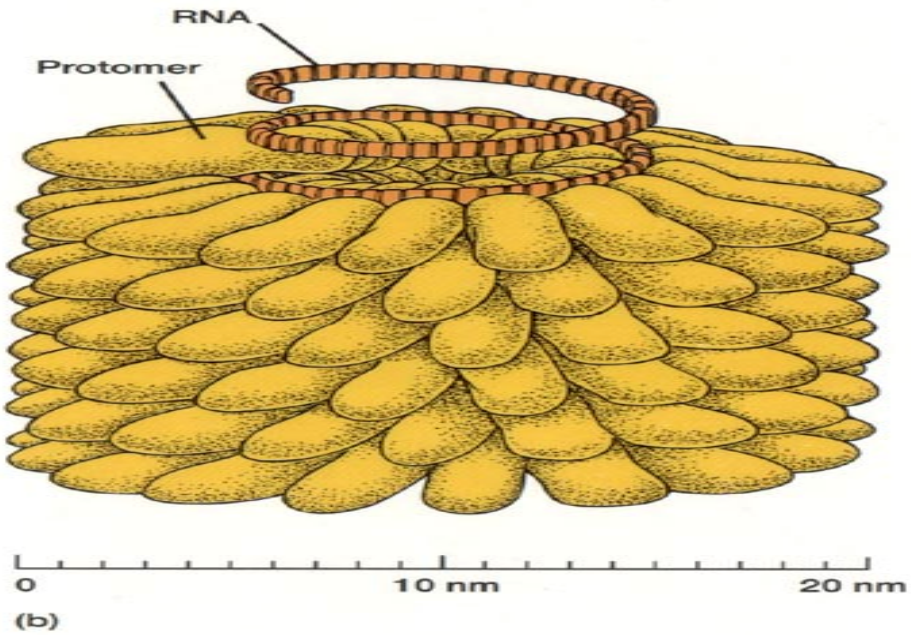
Capsid

- A shell which surrounds the nucleic acid.
- It mediates viral adsorption and penetration to cells and it protects the viral genome.
- It consists of capsomers (spherical shape of polypeptide strands), which is arranged in a geometric symmetry.
- three major forms of symmetry can be seen under electron microscope:

Icosahedral (spherical), helical (Rod shapes) and complex.

Helical symmetry

- In viruses with helical symmetry, the protein molecules of the nucleocapsid are arranged like the steps of the spiral staircase and the nucleic acid fills the central core.



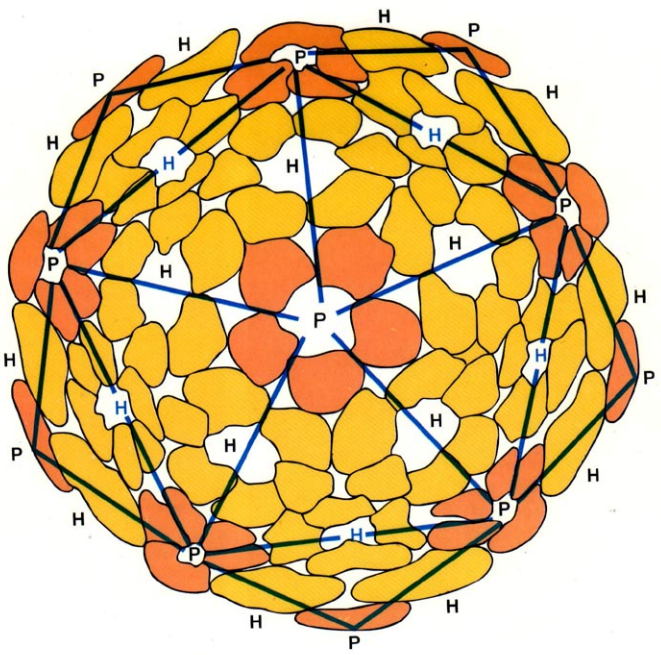
Icosahedral

- An Icosahedron is a solid shape consisting of 20 triangular faces arranged around the surface of a sphere. It has 12 vertices and 30 edges.

- Since protein molecules are irregularly shaped and are not regular equilateral triangles, the simplest icosahdral capsids are built up by using three identical subunits to form each triangular face.

- This means that (60) identical subunits are required to form a complete capsid.

The icosahedral formation is the one that permits the greatest number of capsomeres to be packed in a regular fashion to form the capsid



49 **The Structure of an Icosahedral Capsid**
Figure 17.13

Envelop

- It is a lipoprotein (host cell lipid + viral proteins).

✓ lipid bilayer usually punched off from the cell membrane during budding.

o **Glycoproteins**

Transmembrane proteins of two types:-

- **External glycoproteins** (spikes) - attachment to cell receptors .
- **Transport channel proteins**

They enable the virus to alter permeability of the membrane(M2 of influenza) .

- The protein between the capsid and the envelop is called the matrix protein.

Envelop

- Enveloped viruses are more sensitive to heat, detergents and lipid solvents such as alcohol and ether than nonenveloped viruses.

- Some viruses have an envelop and some do not (naked).

- Naked viruses released from cell by cell lysis, while enveloped viruses are released by either budding or lysis.
- Nucleocapsid ± envelop = virion

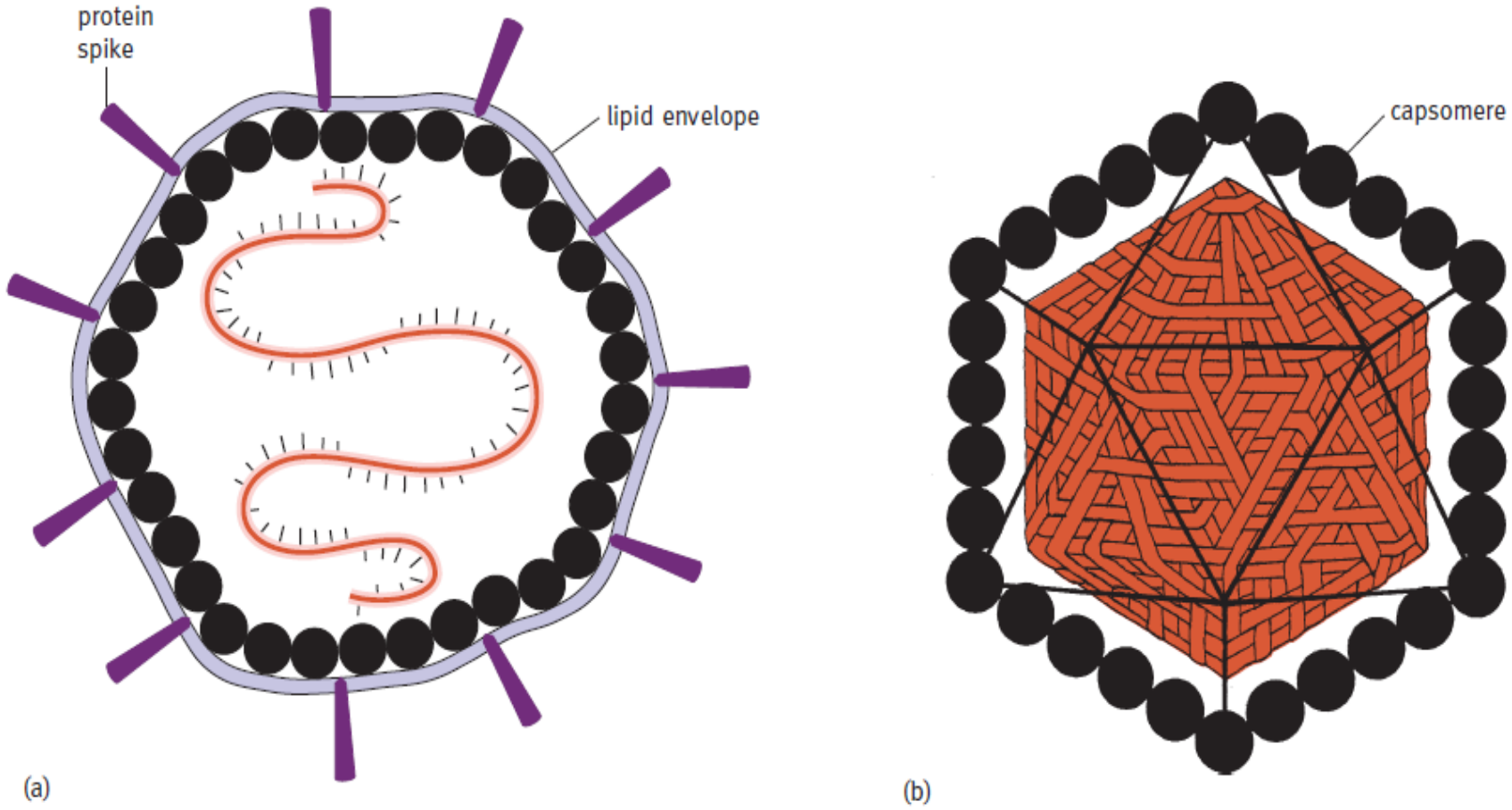


Fig. 2.1 Stylized structures of helical and icosahedral viruses. **(a)** A helical virus. The nucleocapsid is in the form of a spiral staircase, the viral nucleoproteins forming the 'steps' surrounding the nucleic acid. These viruses are often pleomorphic, with a lipid envelope, through which protrude protein spikes. **(b)** An icosahedral virus. The 20-sided protein shell (capsid) encloses the nucleic acid, which is in a non-helical configuration and may be packaged as a condensed or crystal structure. Little is known about the exact packaging of nucleic acids in virus particles.

Influenza virus – structure
For more details see textbook

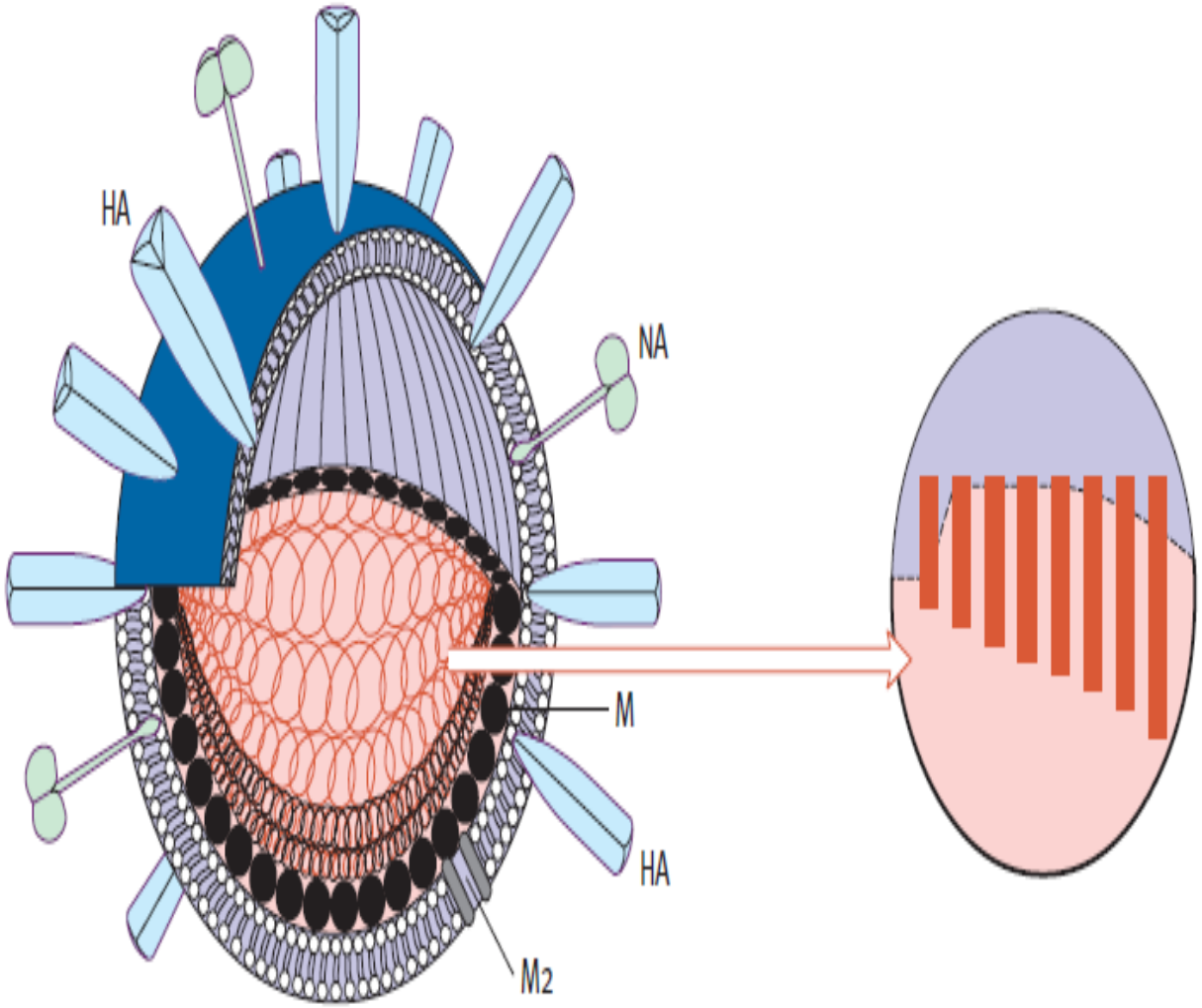


Fig. 2.2 Structural features of influenza virus. The spikes of HA and NA protrude from the lipid bilayer; beneath this is a layer of M protein, which in turn encloses the segmented RNA genome, each segment of which is covered with the nucleocapsid protein and has attached additional structural proteins PB1, PB2, and PA, which are involved in genome replication. 'Pores' of M2 penetrate through the lipid and function as ion channels.

Properties of naked capsid viruses

Component

Protein.

Properties

Is environmentally stable to the following:
- Temperature
- Acid
- Proteases
- Detergents
- Drying

Is released from cell by lysis.

Consequences

Can be spread easily (on fomites, from hand to hand, by dust, by small droplets).
Can dry out and retain infectivity.
Can survive the adverse conditions of the gut.
Can be resistant to detergents and poor sewage treatment.
Antibody may be sufficient for immunoprotection.

From Medical Microbiology, 5th ed., Murray, Rosenthal & Pfaller, Mosby Inc., 2005, Box 6-4.

Properties of enveloped viruses

Components

Membrane.
Lipids.
Proteins.
Glycoproteins.

Properties

Is environmentally labile—is disrupted by the following:
- Acid
- Detergents
- Drying
- Heat

Modifies cell membrane during replication.
Is released by budding and cell lysis.

Consequences

Must stay wet.
Cannot survive the gastrointestinal tract.
Spreads in large droplets, secretions, organ transplants, and blood transfusions.
Does not need to kill the cell to spread.
May need antibody and cell-mediated immune response for protection and control.
Elicits hypersensitivity and inflammation to cause immunopathogenesis.

From Medical Microbiology, 5th ed., Murray, Rosenthal & Pfaller, Mosby Inc., 2005, Fig. Box 6-5.

Viral proteins

1. Structural proteins

- Capsid proteins: protection and receptor attachment
- Proteins associated with the genome (nucleoproteins)

2. non structural proteins (transiently coded enzymes necessary for replication but not ultimately backed in the virion)

Morphology

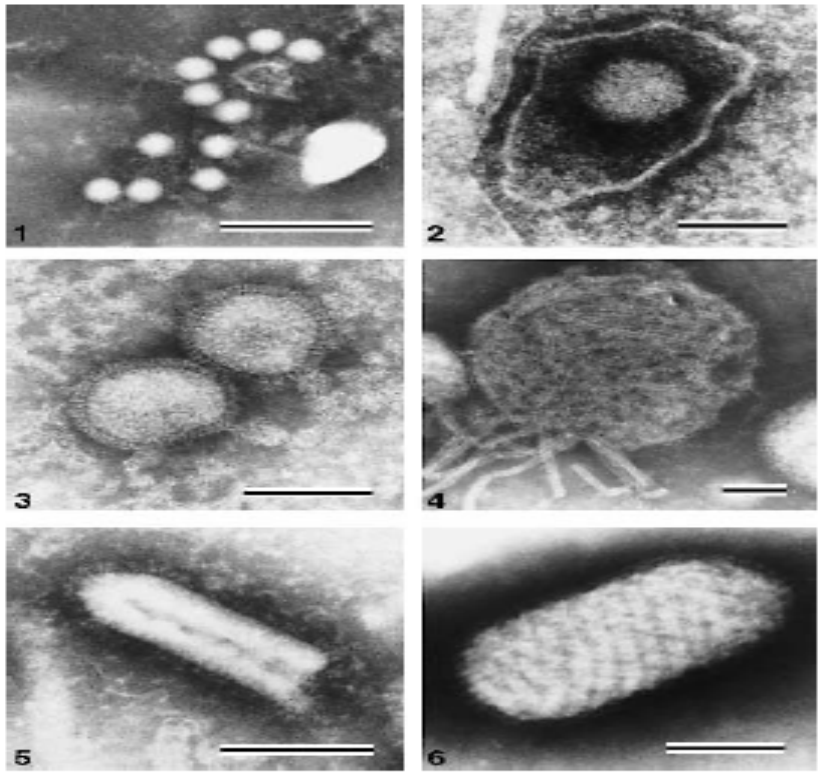


Figure 1.1 MORPHOLOGICAL FORMS OF VIRUSES: 1. poliovirus, naked RNA virus with cubic symmetry; 2. herpesvirus, enveloped DNA virus with cubic symmetry; 3. influenzavirus, enveloped RNA virus with helical symmetry; 4. mumps virus, enveloped RNA virus with helical symmetry—the helical nucleocapsid is being released; 5. vesicular stomatitis virus, morphologically similar to rabies virus; 6. orfvirus, also with a complex symmetry. Bars represent 100 nm (Electron micrographs courtesy of E. Kjeldsberg)

Classification

- The following are the main criteria used for the classification of viruses:

1. the type of nucleic acid (DNA or RNA);
2. the number of strands of nucleic acid and their physical construction (single- or double-stranded, linear, circular, circular with breaks, segmented);
3. polarity of the viral genome-RNA viruses: ‘positive-stranded’ ‘negative-stranded’;
4. the symmetry of the nucleocapsid;
5. the presence or absence of a lipid envelope.

DNA viruses

Family	Genome	Capsid	Envelop	Enzyme
Poxviridae	ds linear	Complex	yes	DNA dependent RNA polymerase
Herpesviridae	ds linear	Icosahedral	yes	DNA polymerase
Adenoviridae	ds linear	Icosahedral	No	X
Polyomaviridae	ds circular	Icosahedral	No	X
Papillomaviridae	ds circular	Icosahedral	No	X
Parvoviridae	ss linear	Icosahedral	No	X
Hepadnaviridae	ds (partial) circular	Icosahedral	yes	DNA polymerase (RT activity)

Abbreviations: ss: single stranded, ds: double stranded, RT: reverse transcriptase

Negative RNA viruses

Family	Genome	Capsid	Envelop	Enzyme
Bunyaviridae	ss circular /segmented	helical	yes	yes
Arenaviridae	ss circular/segmented*	helical	yes	yes
Orthomyxoviridae	ss linear/segmented	helical	yes	yes
Paramyxoviridae	ss linear	helical	yes	yes
Rhabdoviridae	ss linear	helical	yes	yes
Filoviridae	ss linear	helical	yes	yes
Reoviridae	ds linear/segmented	Icosahedral	No	yes
Deltaviridae	ss circular	Icosahedral	yes	unknown

The enzyme is RNA dependent RNA polymerase, * ambisense

Positive RNA viruses

Family	Genome	Capsid	Envelop	Enzyme
Retroviridae	ss linear /segmented	Icosa	yes	reverse transcriptase
Coronaviridae	ss linear	helical	yes	No
Togaviridae	ss linear	Icosa	yes	No
Flaviviridae	ss linear	Icosa	yes	No
Caliciviride	ss linear	Icosa	No	No
Hepeviridae	ss linear	Icosa	No	No
Picornaviridae	ss linear	Icosa	No	No
Astroviridae	ss linear	Icosa	No	No

NOMENCLATURE - ICTV

- According to:
- The type of disease they cause (e.g. herpesviruses)
- acronyms, for example papovaviruses (*papilloma–polyoma–vacuolating agent)* picornaviruses (*pico, small; rna, ribonucleic acid*
- morphological features of the virion, (e.g. coronaviruses, which have a halo or corona of spikes).
- The place where they were first isolated (e.g. Coxsackie, Marburg)
- after their discoverers (e.g. Epstein–Barr virus (EBV)).

Range of viral disease

- Very wide: asymptomatic-death
- Tissue tropism and host specificity
- One virus: many syndromes
- One syndrome: many viruses e.g respiratory

Bacteriophages and viriods

- Bacteriophages: viruses infect bacteria
- Viriods:

- usually plant pathogens
- short ssRNA genome.
- *coconut cadang–cadang viroid*
- HDV is a human defective virus

Prions - **proteinaceous infectious particles**

- Caused by a mutant normal human protein PrP^{c} >PrP^{sc} (Chr 20) Occurs in human and animals
- These proteins has no nucleic acid and can ccumulate in brain - toxic
- cause Creutzfeldt–Jakob disease (CJD) and other spongiform encephalopathies affecting both humans and animals

Prions

Transmission:

- Ingestion
- Iatrogenic e.g blood transfusion, dura mater transplants and surgery (brain, tonsils, appendix and spleen)
- Occurrence:
- Spradic - CJD
- Acquired
- ✓ Ingestion (variant KJD), iatrogenic, Kuru, inherited

The End