

Properties, Classification, Nomenclature, Structure, and Composition of Viruses

BSc Biomedical Sciences
Fourth Year

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What is a Virus?

- A virus is a very small, non-cellular parasite of cells.
 - Its genome is composed of either DNA or
 - RNA, enclosed in a protein coat.
 - Nucleic acid + Protein = Virus
- Viruses are dependant on host cell
 - Building-blocks such as amino acids and nucleosides;
 - Protein-synthesizing machinery (ribosomes);
 - Energy, in the form of adenosine triphosphate (ATP).

Nature of Viruses

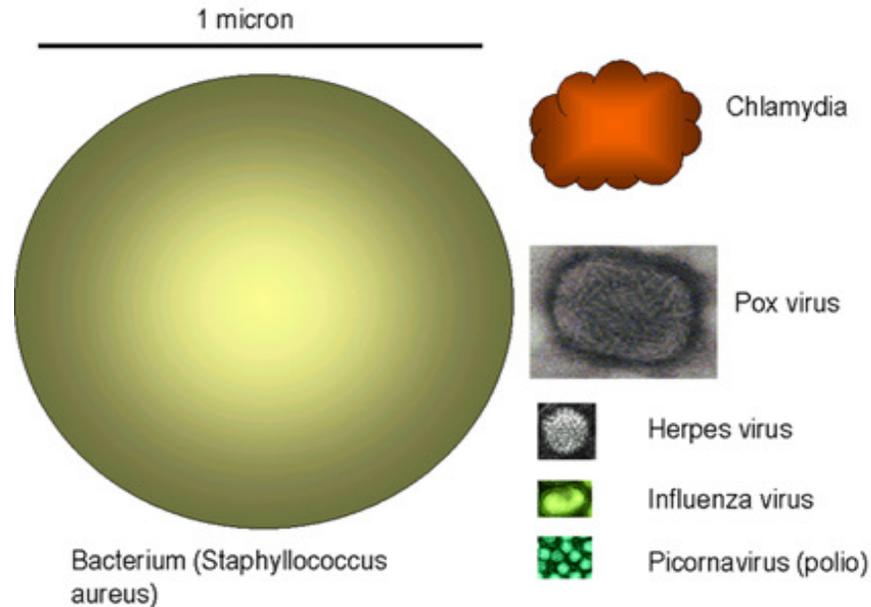
- Viruses are heterogeneous class of agents varying in:
 - Morphology and size
 - Chemical composition
 - Host Range
 - Effect on cells or host
 - Replication Strategies

General Characteristics Of Viruses

- Viruses consist of a genome either DNA or RNA but never both.
- Viruses multiply (replicate) only inside the host cells.
 - They absolutely depend on the host's metabolic system to produce viral genomes, proteins, glycoproteins and assemble progeny virions.
- The virus genome directs the synthesis of virion components with an appropriate host cell.
- Progeny virus particles are produced by assembly of newly made viral components.
- Progeny virus particles spread infection to new cells.

General Characteristics of Viruses

- Viruses are smaller than bacteria.



- Viruses lack cellular organelles, such as mitochondria and ribosomes.
- Viruses do not multiply in chemically defined media.
- Viruses do not undergo binary fission.

How Do Viruses Differ From Other Microorganisms?

Comparisons Between Viruses and Other Microorganisms

	Growth on artificial media	Division by binary fission	Whether they have both DNA and RNA	Whether they have ribosomes	Whether they have muramic acid	Their sensitivity to antibiotics
Bacteria	Yes	Yes	Yes	Yes	Yes	Yes
Mycoplasma	Yes	Yes	Yes	Yes	No	Yes
Rickettsia	No	Yes	Yes	Yes	Yes	Yes
Chlamydia	No	Yes	Yes	Yes	No	Yes
Viruses	No	No	No	No *	No	No

* The arenavirus family (an RNA virus family) appears to package ribosomes 'accidentally'. The packaged ribosomes appear to play no role in viral protein synthesis.

Virus Structure

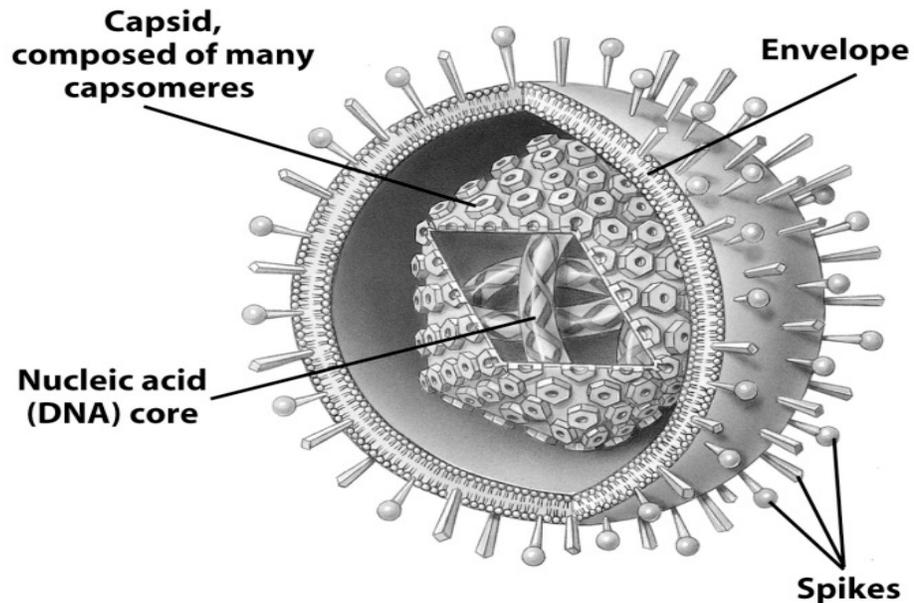
- Basically viruses consist of nucleic acid and protein.

Building Blocks:

- Capsomers - Protein subunits consisting of a single polypeptide or several identical or different protein molecules visible by electron microscopy as clumps or clusters on the virion.
- Capsid - The protective protein coat that surrounds nucleic acid.
 - It varies in complexity among various virus families.
 - As protection of the viral genome
 - As the site of receptors necessary for naked viruses to initiate infection
 - As the stimulus for antibody production
 - As the site of antigenic determinants important in some serologic tests
- Nucleocapsid - The structure consisting nucleic acid and the capsid.
 - This is the complete, functional virion among non-enveloped viruses.

Virus Structure

- **Viral Membrane, envelope**
 - The outermost component of enveloped viruses, surrounding the nucleocapsid.
- **Viral Glycoproteins**
 - Are surface projections which serve to attach virions to specific receptor sites on susceptible host cell surfaces



Terminology

- Defective virus
 - This virus cannot replicate by its own, it requires helper virus.
 - E.g. Hepatitis D virus, Sarcoma virus
- Viroids
 - Consist solely of a single molecule of circular RNA without a protein coat or envelope
- Prions
 - Infectious protein particles composed solely of proteins
- Virions
 - Complete virus particle

Genetic Content of Viruses

DNA Viruses

- Almost all DNA viruses which infect animals contain double-stranded DNA (dsDNA).
 - Exceptions include *Parvoviridae* and the *Circoviridae*.

RNA Viruses

- Almost all RNA viruses contain single-stranded RNA (ssRNA).
- Exceptions include the *Reoviridae* e.g. Rotavirus which contain dsRNA
- RNA viruses can be broadly subdivided as follows:
 - Viruses with positive strand (+) RNA genome (Positive sense), i.e. genomes of the same polarity as the mRNA e.g. picornaviruses & caliciviruses.
 - Viruses with negative strand (-) RNA genome (negative sense) i.e. genome of opposite polarity to mRNA e.g. *Rhabdoviridae*, *Paramyxoviridae* etc.

Uses of Viruses

- Vaccine development
- Gene therapy
- Tools to investigate host cells
- Phage typing of bacteria
- Antibacterial agent
- Pesticides

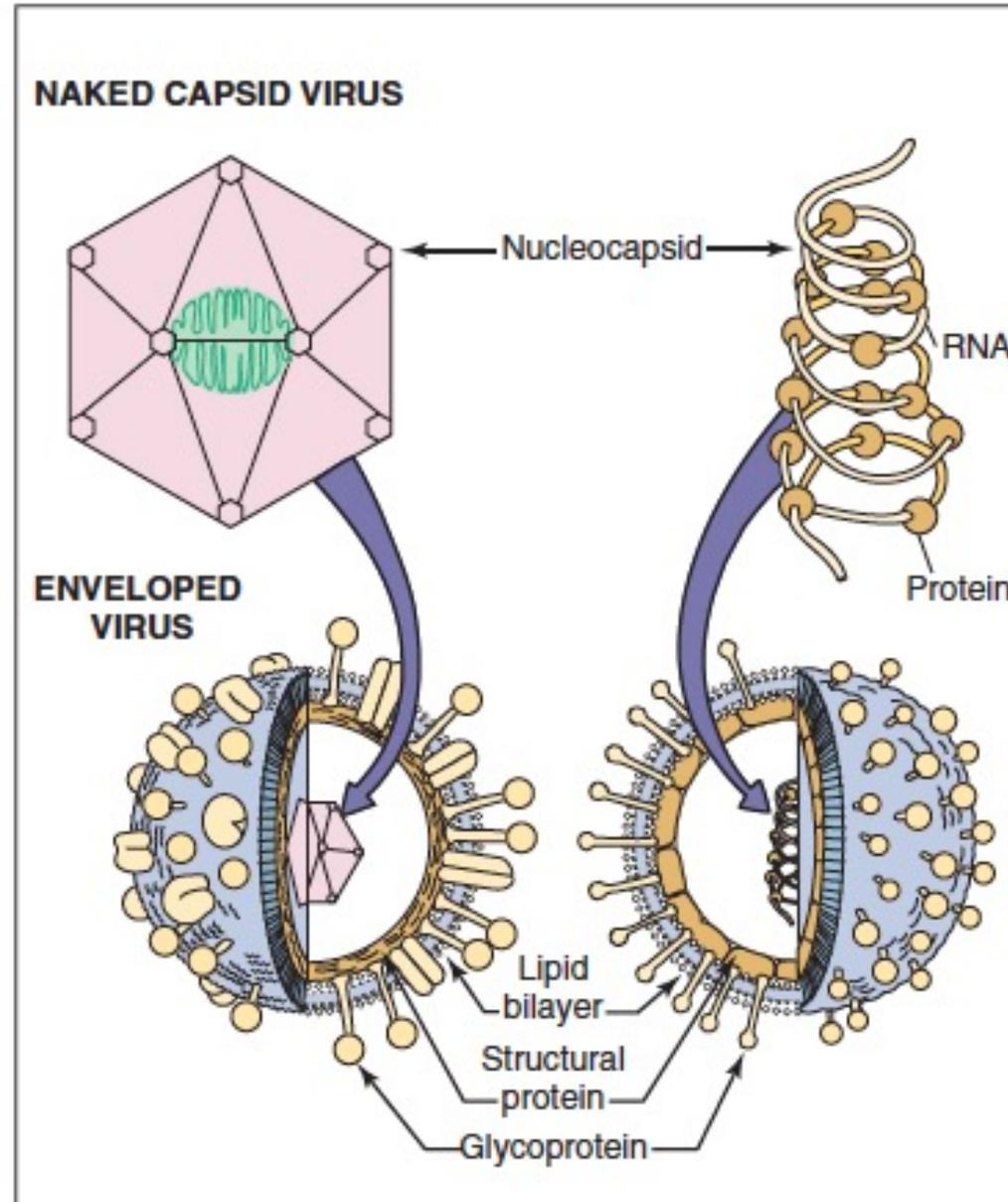
Virion Nucleocapsid Structure

- Nucleocapsids with helical (rod-like) symmetry.
 - Protein subunits are arranged helically around the nucleic acid to form a coiled ribbon like structure with helical e.g. tobacco mosaic virus, paramyxoviruses etc.
- Nucleocapsids with icosahedral (sphere like) symmetry.
 - The nucleic acid is condensed and forms the central portion of the quasispheric nucleocapsid e.g. adenoviruses and picornaviruses
 - It is characterised by 5:3:2 fold rotational symmetry.
- Nucleocapsids with complex symmetry.
 - These are regular structures but the nature of the symmetry is not fully understood e.g. poxviruses

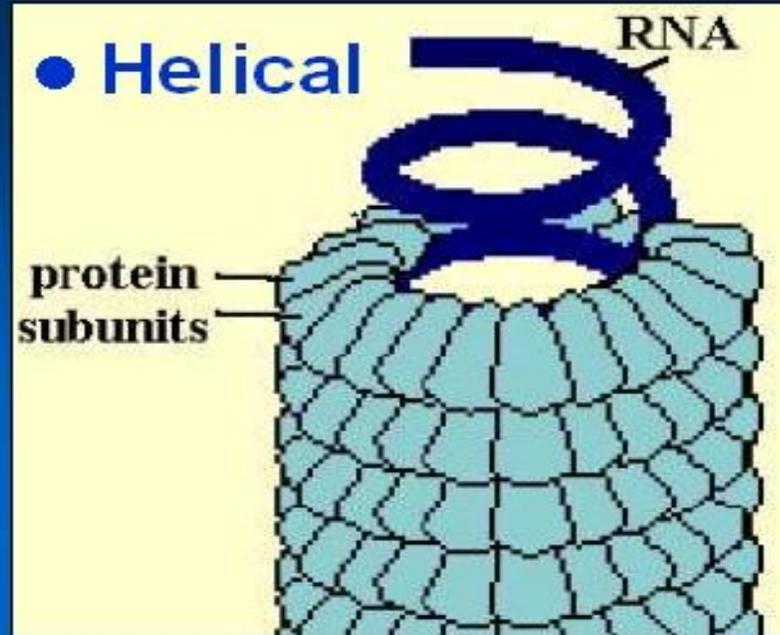
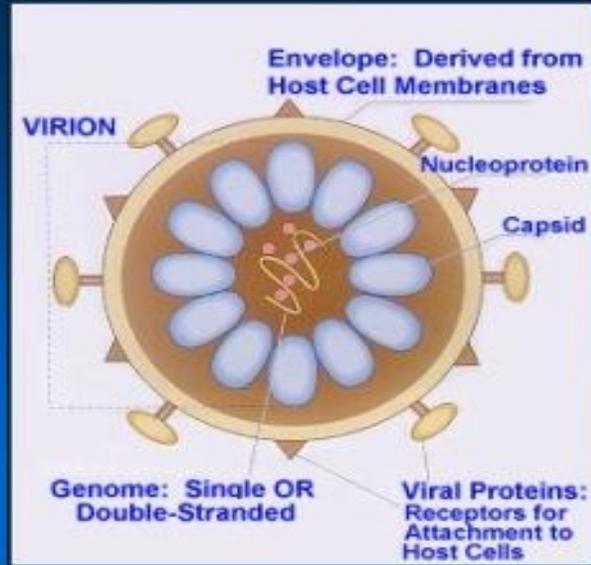
Five Basic Structural Forms Of Viruses In Nature

- Naked icosahedral
 - e.g. poliovirus, adenovirus, hepatitis A virus
- Naked helical
 - e.g. tobacco mosaic virus, so far no human viruses with this structure known
- Enveloped icosahedral
 - e.g. herpes virus, yellow fever virus, rubella virus
- Enveloped helical
 - e.g. rabies virus, influenza virus, parainfluenza virus, mumps virus, measles virus
- Complex e.g. poxvirus

Structure of Viruses



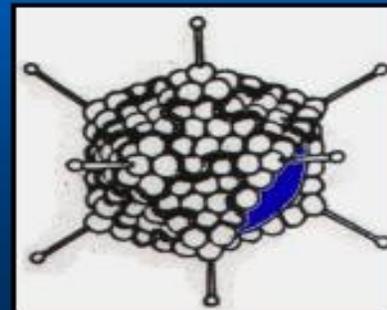
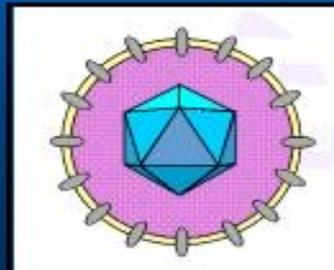
Structure of Viruses



Virus Structure

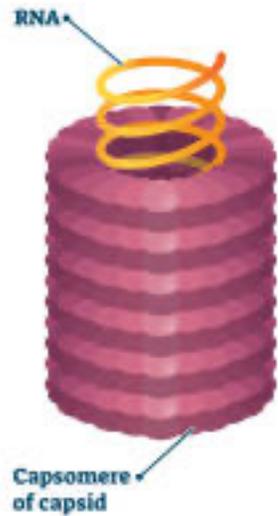
● Icosahedral

Herpesvirus:
Icosahedral
with
envelope



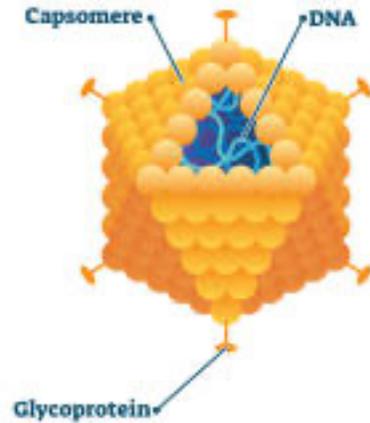
Adenovirus:
Icosahedral
No envelope

TYPES OF VIRUSES



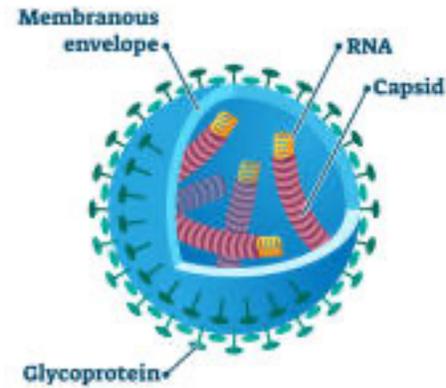
HELICAL

Tobacco
Mosaic Virus



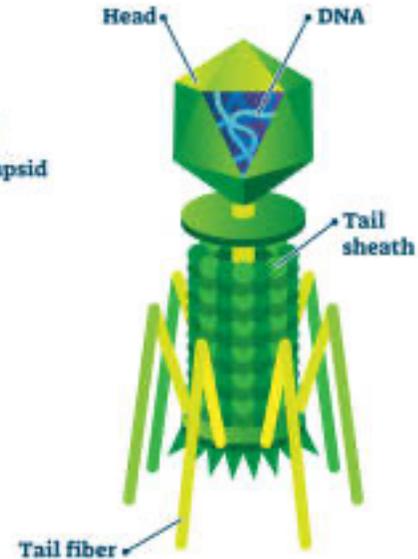
POLYHEDRAL

Adenovirus



SPHERICAL

Influenza Virus



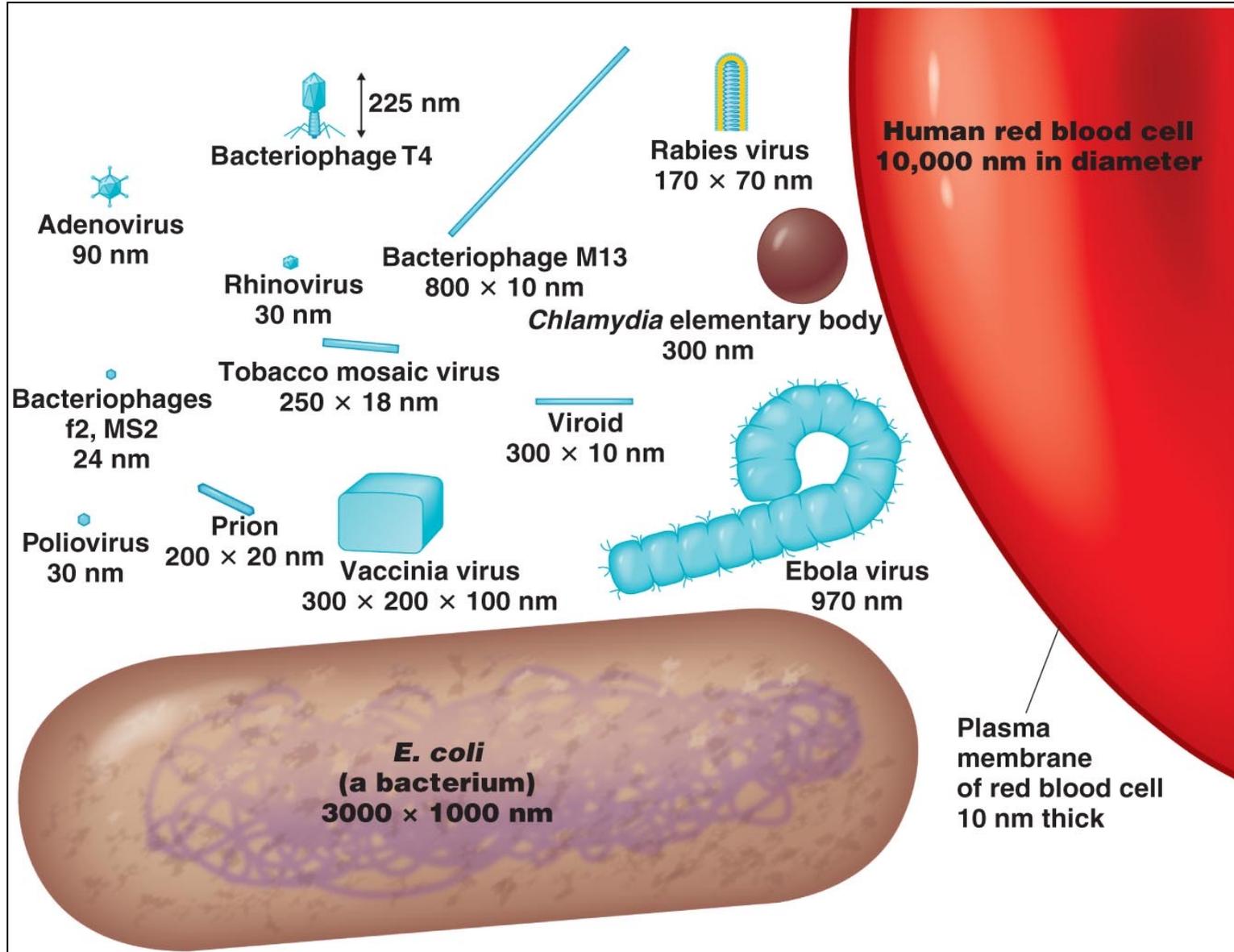
COMPLEX

Bacteriophage

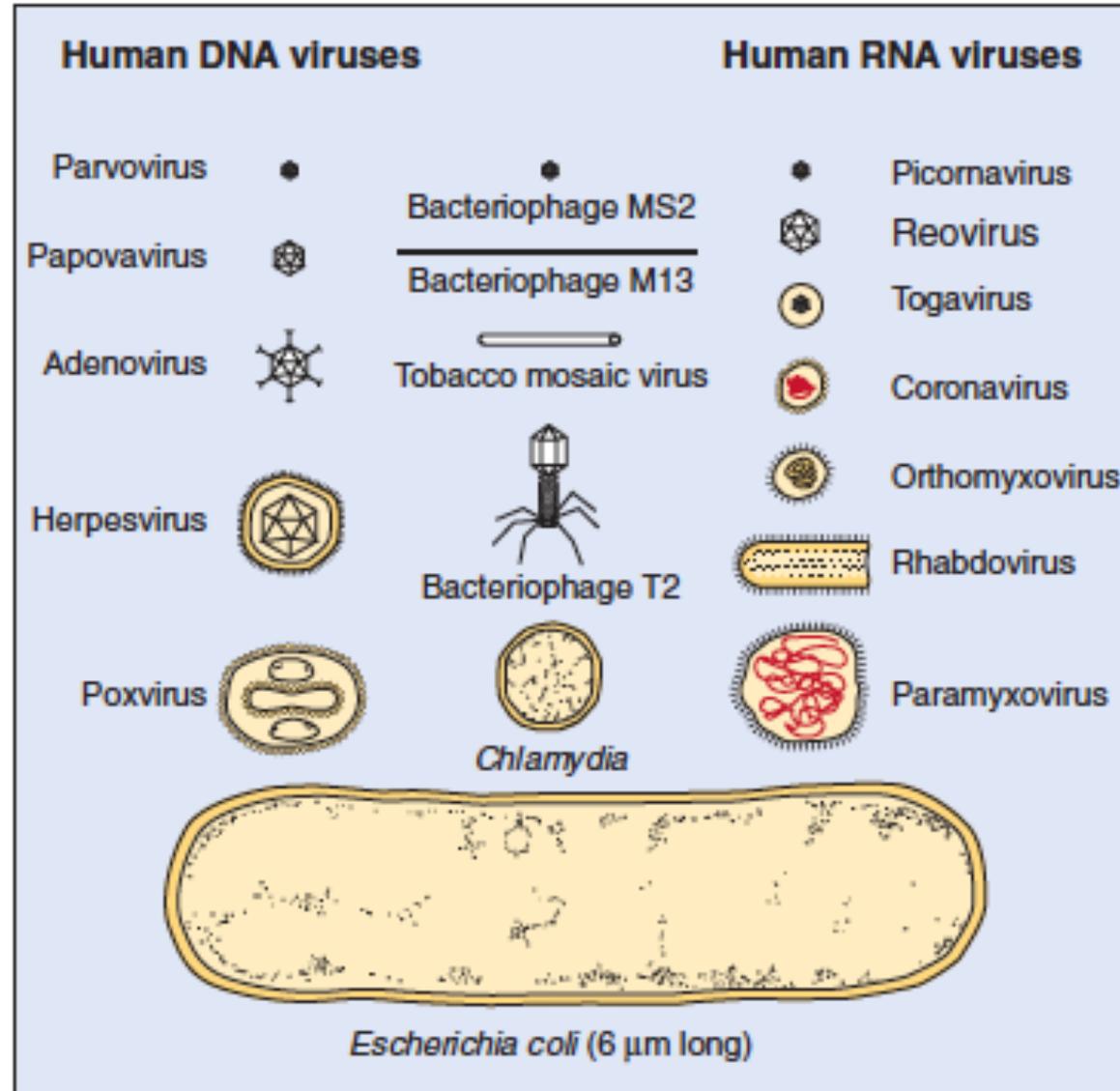
Relative Sizes of Viruses

- The size of Viruses range from:
 - Smallest (about 20nm) parvoviruses.
 - Largest (300-450 x 170-260nm) poxviruses
 - Some filamentous viruses such as Marburg and Ebola filoviruses may reach close to 1000nm length, about 80nm in diameter.
 - In general enveloped viruses are larger than non-enveloped viruses.

Relative Sizes of Viruses



Relative Sizes of Viruses



Criteria of Classification

Nomenclature of Viruses

- Various approaches have been used in the nomenclature of viruses (do not obey the binomial nomenclature).
- They can be grouped based
 - Disease, target tissue, means of transmission, vector etc
- Named after the diseases they cause
 - e.g. Measles virus, smallpox virus (poxvirus)
- Named after the places where the disease was first reported
 - e.g. Newcastle disease virus, Ebola virus, Norwalk virus, Bunyaviridae

Nomenclature of Viruses

- Host and signs of disease
 - e.g. Tobacco mosaic virus, cauliflower mosaic virus, brome mosaic virus
- Latin and Greek words
 - E.g. *Coronaviridae* - "crown", *Parvoviridae* - "small"
- Virus discoverers
 - E.g. Epstein-Barr virus
- How they were originally thought to be contracted
 - E.g. dengue virus ("evil spirit"), influenza virus (the "influence" of bad air)

Nomenclature of Viruses

- Body parts from where they were first isolated
 - E.g. Adenoviruses (adenoids), reoviruses (respiratory, enteric, orphan)
- Means of transmission
 - E.g. Respiratory Viruses, Enteric viruses
- Vector
 - E.g. arboviruses, arthropod-borne viruses
- Combinations of the above
 - E.g. Rous Sarcoma virus

Classification of Viruses

- The most consistent and current classification is based on:
 - Structure
 - Size of the virus, morphology and nucleic acid (genome)
 - Biochemical characteristics
 - Structure and mode of replication
 - Disease
 - Encephalitis and hepatitis viruses
 - Means of transmission
 - Arboviruses spread by insects
 - Host cell (Host range)
 - Animal, plant or bacteria viruses
 - Tissue or organ tropism - adenovirus and enteroviruses

Classification of Viruses

- Classification systems adopted by the international committee on taxonomy of viruses (ICTV) have emphasised the viral genome as the primary determinant for viral taxonomy.
 - Classification = viral genome

Criteria

- Nucleic acid - RNA or DNA
 - Non-segmented or segmented
 - If genome is ssRNA, can it function as mRNA?
- Virion Structure - Symmetry (icosahedral, helical or complex)
 - Enveloped or non-enveloped

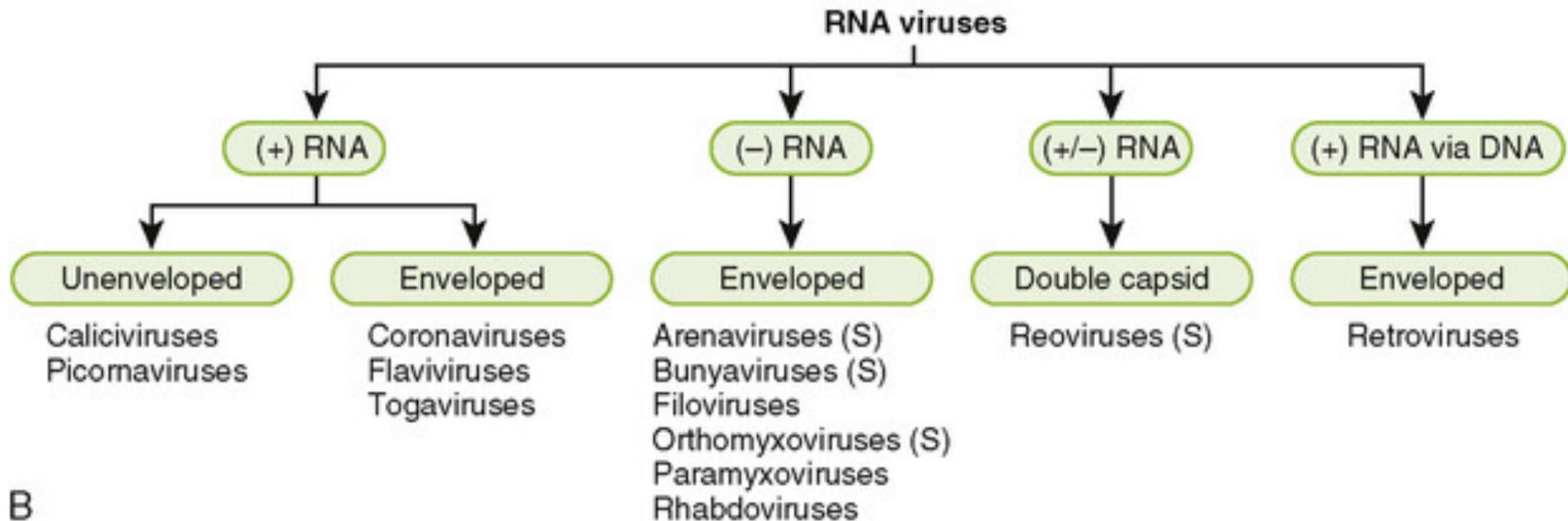
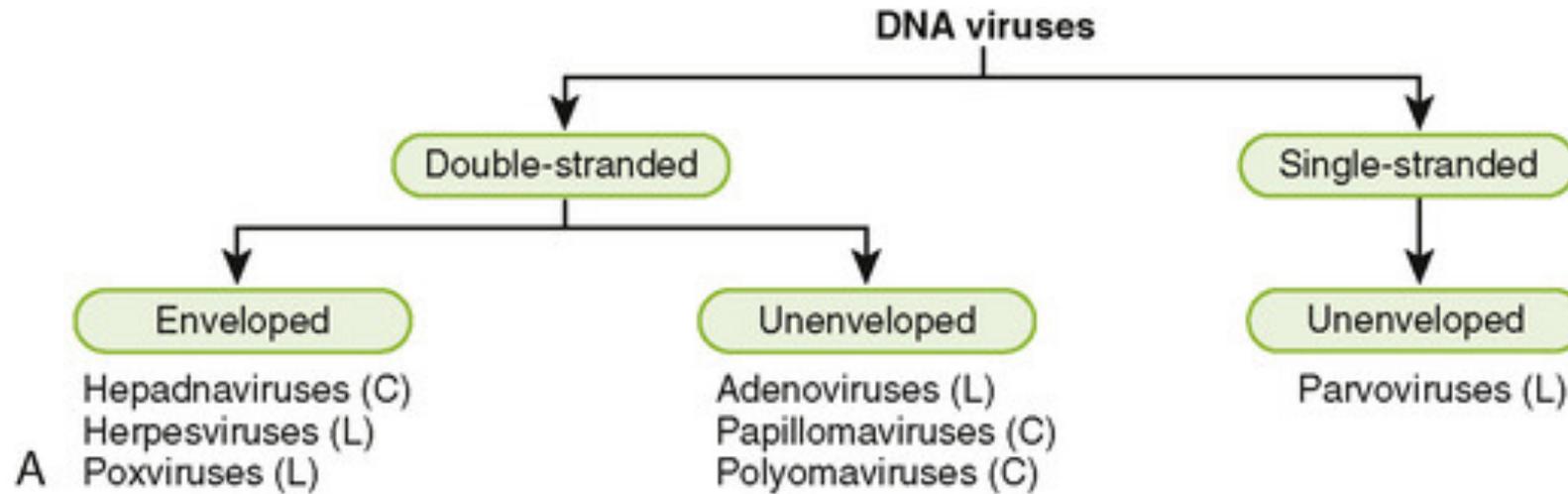
Nomenclature of Viruses

- Taxonomic groups - family, subfamily, genus and species
- The names of virus **families (family)** are italicized - End in Latin suffix - *viridae*
- The **genera (genus)** end in the suffix - *virus*
- The **species** - English common name

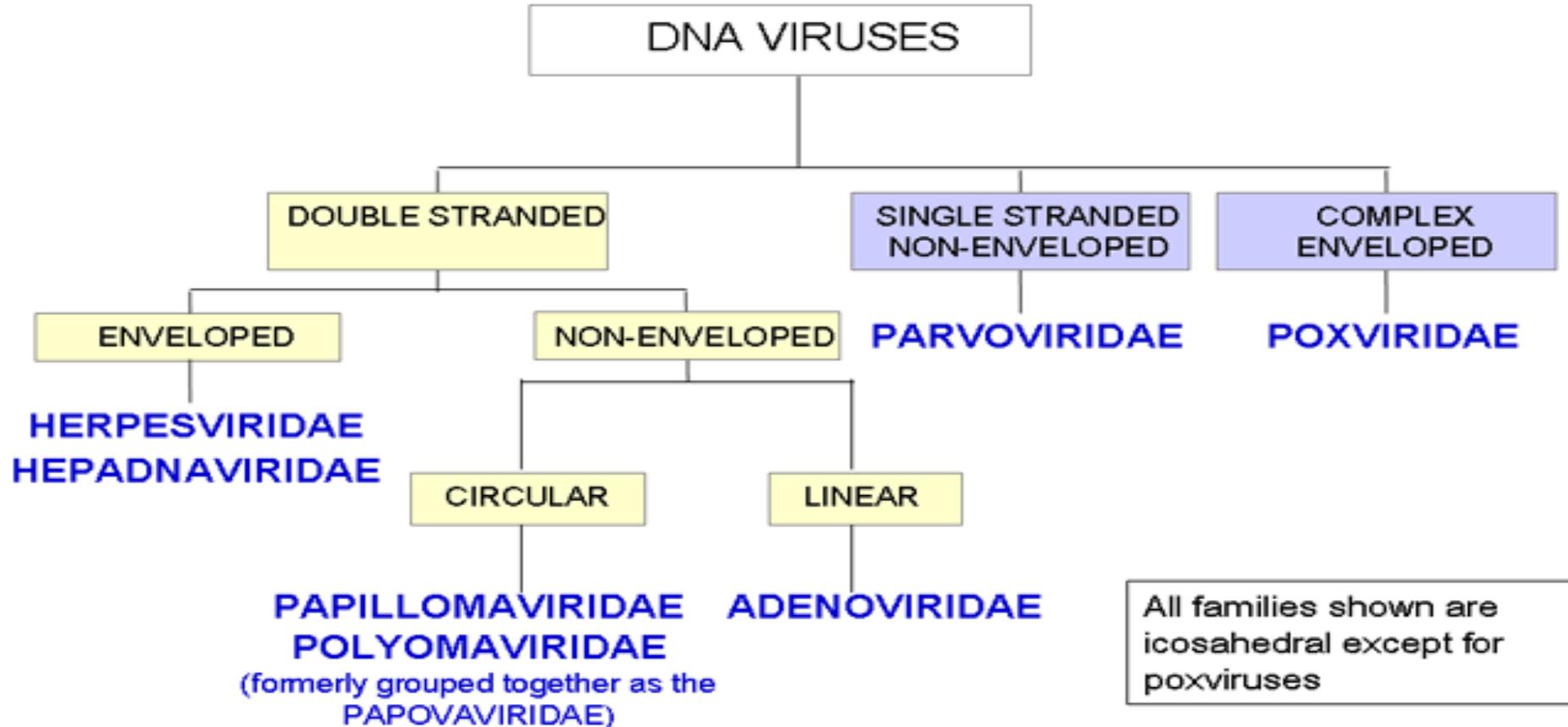
Table 10.1 Taxonomic groups of viruses

Taxonomic group	Suffix	Example 1	Example 2	Example 3
Family	<i>-viridae</i>	<i>Myoviridae</i>	<i>Paramyxoviridae</i>	<i>Coronaviridae</i>
Subfamily	<i>-virinae</i>	–	<i>Paramyxovirinae</i>	–
Genus	<i>-virus</i>	<i>T4-like viruses</i>	<i>Morbillivirus</i>	<i>Coronavirus</i>
Species	–	<i>Enterobacteria phage T4</i>	<i>Measles virus</i>	<i>Severe acute respiratory syndrome virus</i>

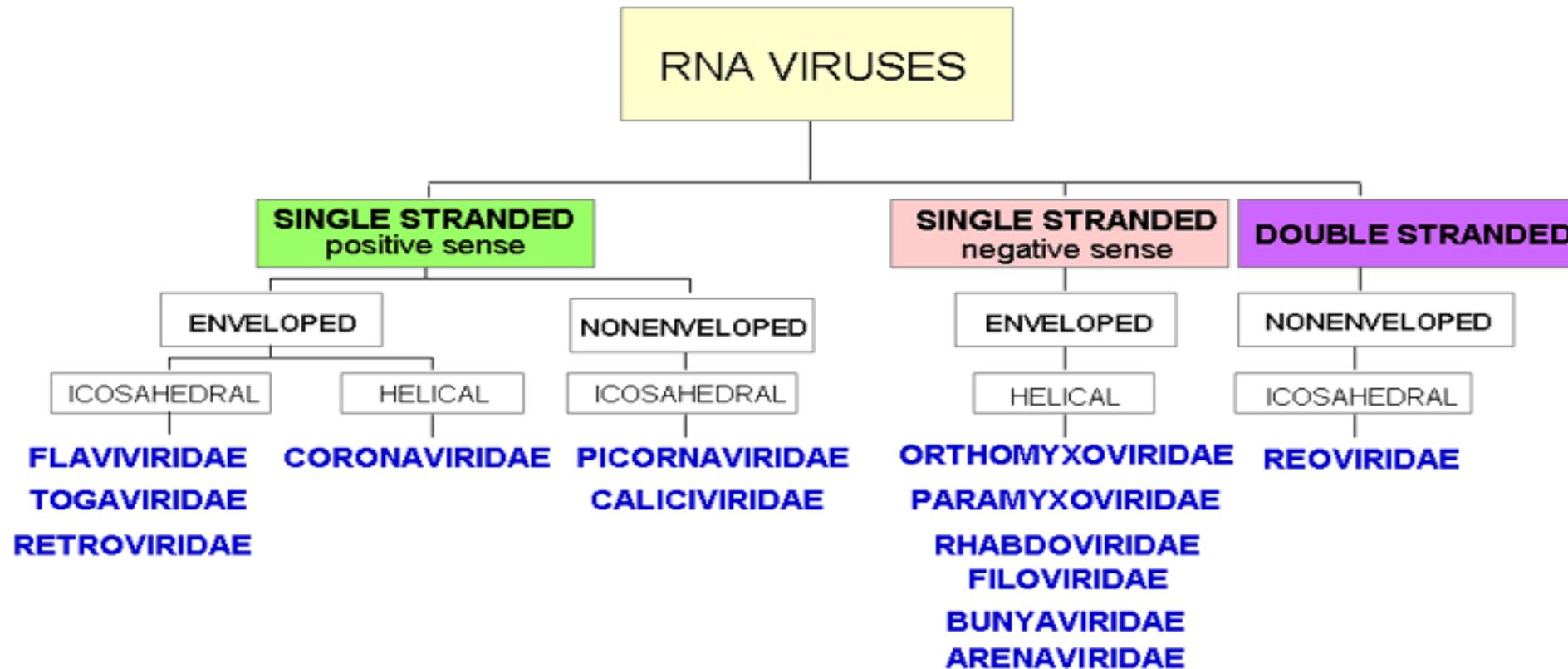
Classification of Viruses

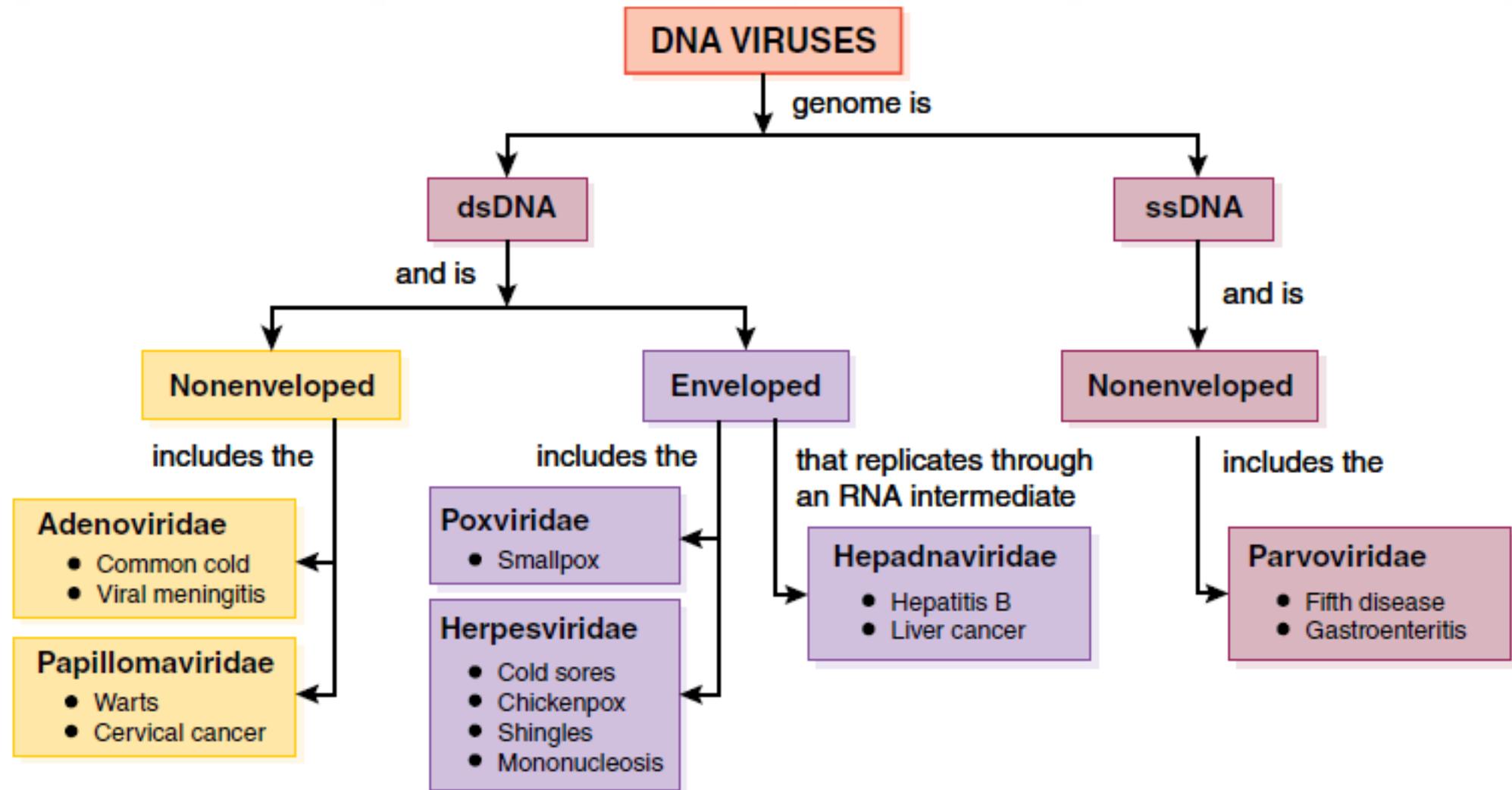


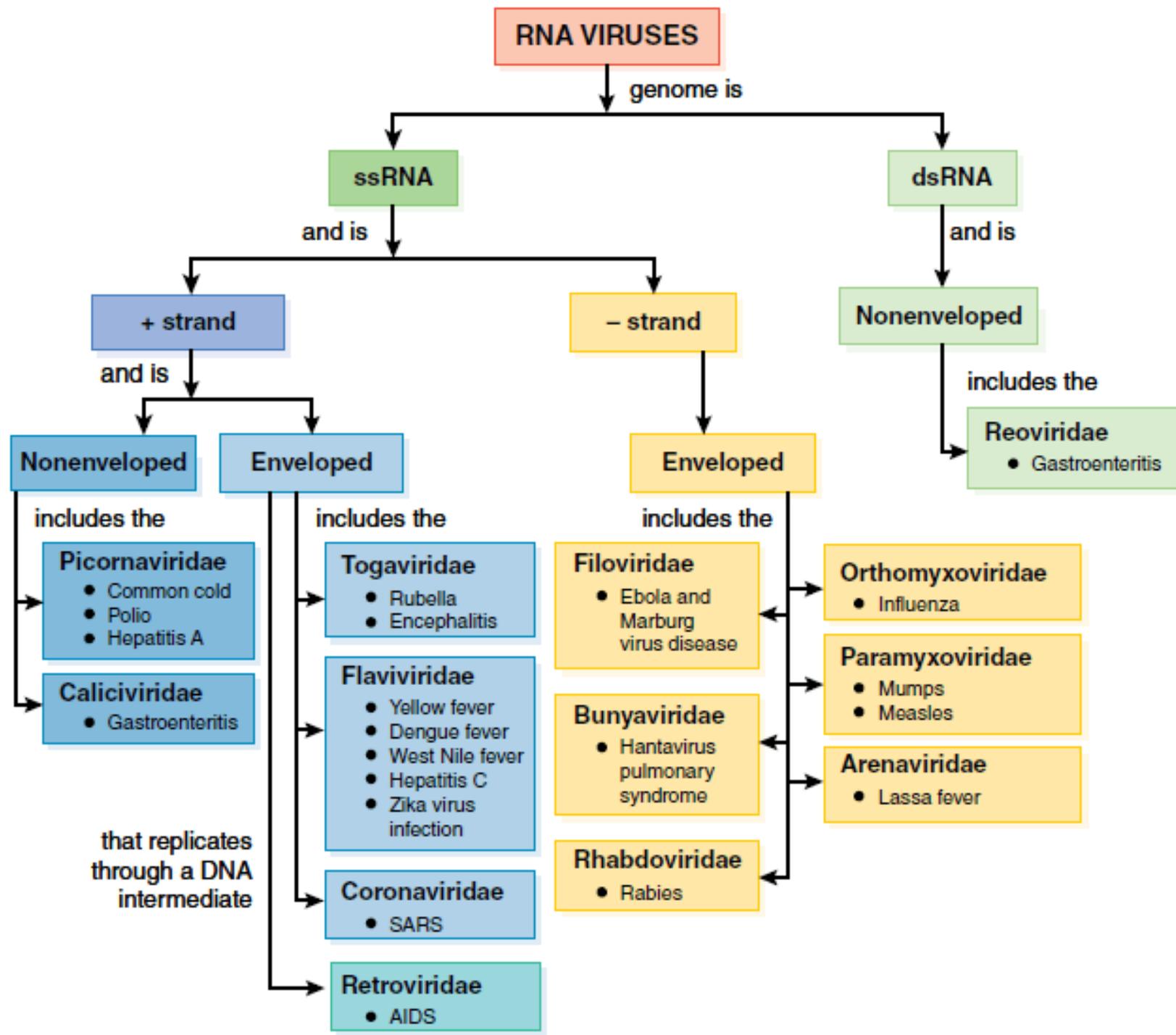
Classification of Viruses



Classification of Viruses







Baltimore Classification of Viruses

- The division of the viruses into classes based on **genome type** and **mode of replication and transcription**
 - Suggested by David Baltimore - Seven Baltimore classes.
 - Major groups of viruses are distinguished first by their nucleic acid content as either DNA or RNA
 - RNA and DNA viruses can be single-stranded (ssRNA, ssDNA) or double-stranded (dsRNA, dsDNA)

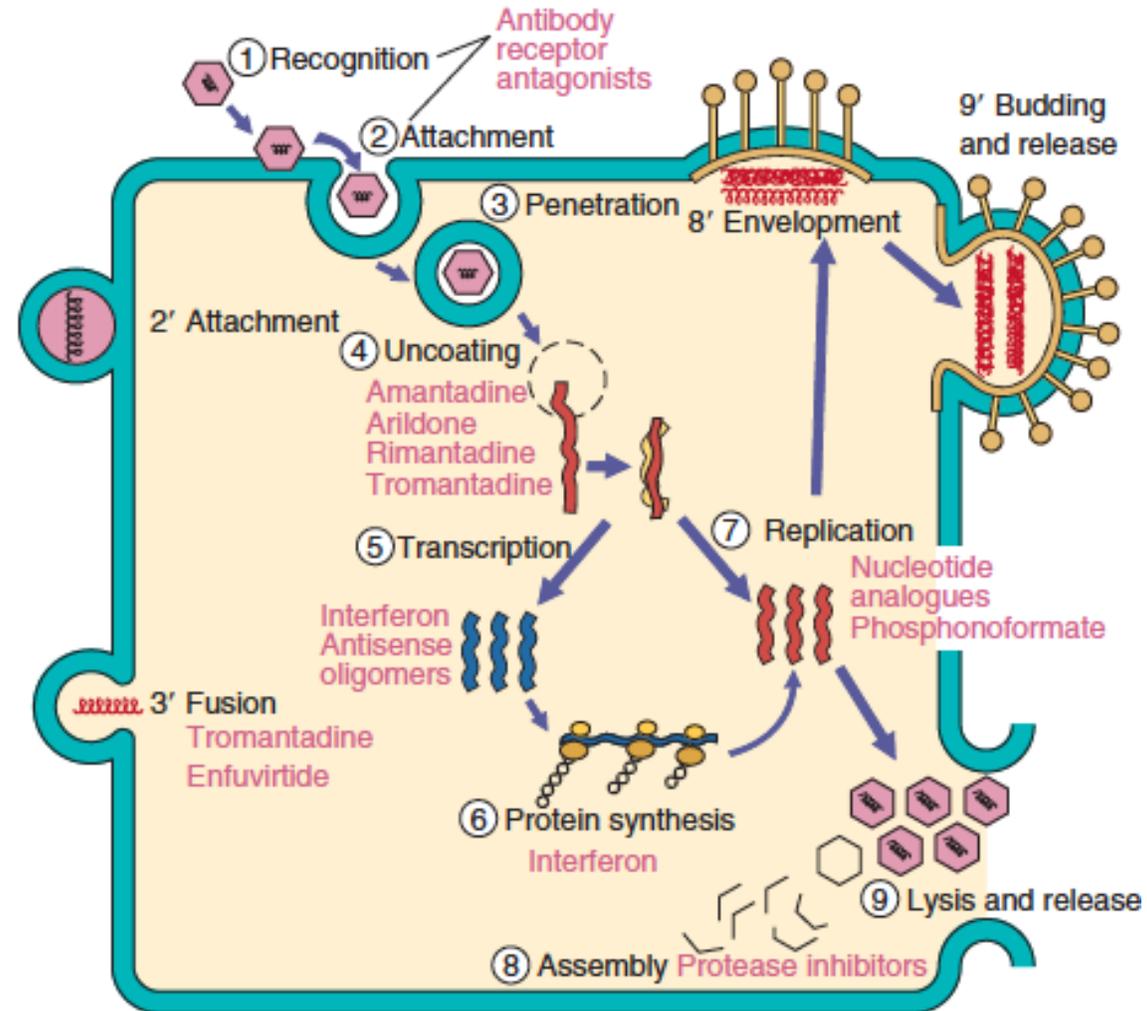
Seven Class Baltimore Classification of Viruses

Class	Description of genome and replication strategy	Example of bacterial virus	Example of animal virus
I	Double stranded DNA genome	Lambda, T4	Herpesviruses, Poxvirus
II	Single stranded DNA genome	ØX174	Parvoviruses
III	Double stranded RNA genome	Ø6	Reoviruses
IV	Single stranded RNA genome plus sense	MS2	Picornaviruses, Togaviruses
V	Single stranded RNA genome minus sense		Orthomyxoviruses, Rhabdoviruses
VI	Single stranded RNA genome that replicates with DNA intermediate		Retrovirus
VII	Double stranded DNA genome that replicates with RNA intermediate		Hepadnaviruses e.g. Hepatitis B virus

Viral Replication

- Viruses replicate by a process of separate synthesis of:
 - nucleic acid and protein
 - followed by their assembly into mature virions and not by binary fission as in cellular microorganisms.
- The major steps in viral replication are the same for all viruses.
- The host cell acts as a factory providing:
 - The substrates, energy and machinery necessary for the synthesis of viral genomes and replication.

Viral Replication



Other major targets:

Nucleotide biosynthesis and mutation: ribavirin

Thymidine kinase (drug activation): acyclovir, penciclovir

Neuraminidase: zanamivir, oseltamivir

Steps in Viral Replication

1. Recognition of the target cell
2. Attachment or adsorption
3. Penetration
4. Uncoating
5. Macromolecular Synthesis
 - a. Early mRNA & nonstructural protein synthesis
 - b. Replications of genome
 - c. Late mRNA & structural protein synthesis
 - d. Posttranslational modification of proteins
6. Assembly of virus
7. Budding of enveloped viruses
8. Release of virus

Recognition of & Attachment to the Target Cell

- Viruses must recognize and bind to specific cellular receptors on the surface of the cell. Receptors on the cell may be proteins, carbohydrates on glycoproteins or glycolipids.
 - This forms the basis of the host specificity of viruses not only species but also on cell types.
 - For example some viruses can only infect only a single species such as (measles, polioviruses-human) while other viruses (rabies virus) are able to infect the cells of a wide variety of animals that possess appropriate receptor sites (host range).
 - Susceptible target cell defines **tissue tropism** (e.g. neurotropic, lymphotropic etc.)

Examples of Viral Attachment Proteins

Virus Family	Virus	Viral Attachment Protein
Picornaviridae	Rhinovirus	VP1-VP2-VP3 complex
Adenoviridae	Adenovirus	Fiber protein
Reoviridae	Reovirus	σ -1
	Rotavirus	VP7
Togaviridae	Semliki Forest virus	E1-E2-E3 complex gp
Rhabdoviridae	Rabies virus	G protein gp
Orthomyxoviridae	Influenza A virus	HA gp
Paramyxoviridae	Measles virus	HA gp
Herpesviridae	Epstein-Barr virus	gp350 and gp220
Retroviridae	Murine leukemia virus	gp70
	Human immunodeficiency virus	gp120

gp, Glycoprotein; *HA*, hemagglutinin.

Examples of Viral Receptors

Virus	Target Cell	Receptor*
Epstein-Barr virus	B cell	C3d complement receptor CR2 (CD21)
Human immunodeficiency virus	Helper T cell	CD4 molecule and chemokine coreceptor
Rhinovirus	Epithelial cells	ICAM-1 (immunoglobulin superfamily protein)
Poliovirus	Epithelial cells	Immunoglobulin superfamily protein
Herpes simplex virus	Many cells	Herpesvirus entry mediator (HVEM), nectin-1
Rabies virus	Neuron	Acetylcholine receptor, NCAM
Influenza A virus	Epithelial cells	Sialic acid
B19 parvovirus	Erythroid precursors	Erythrocyte P antigen (globoside)

CD, Cluster of differentiation; *ICAM-1*, intercellular adhesion molecule; *NCAM*, neural cell adhesion molecule.

*Other receptors for these viruses may also exist.

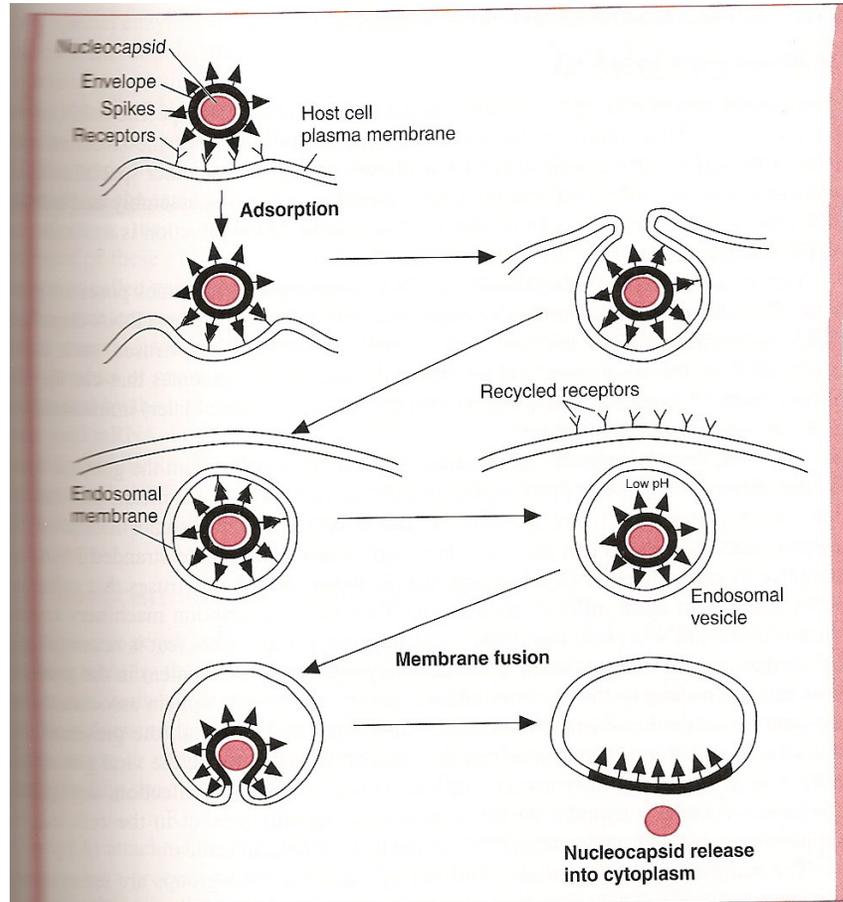
Penetration

- The second stage in virus replication, is entry of the virus into the host cell.
- Interaction of the vital attachment proteins (VAPs) & cell receptors initiates virus internalisation into the cell.
- Internalisation is dependant on the virion structure.
 - Most non-enveloped viruses enter the cell through **receptor-mediated endocytosis** or by **veropexis**.
 - Enveloped viruses fuse their membranes with cellular membranes to deliver the nucleocapsid or genome into the cytoplasm.
 - The optimum pH determines whether penetration occurs at the cell surface at neutral pH or by endocytosis

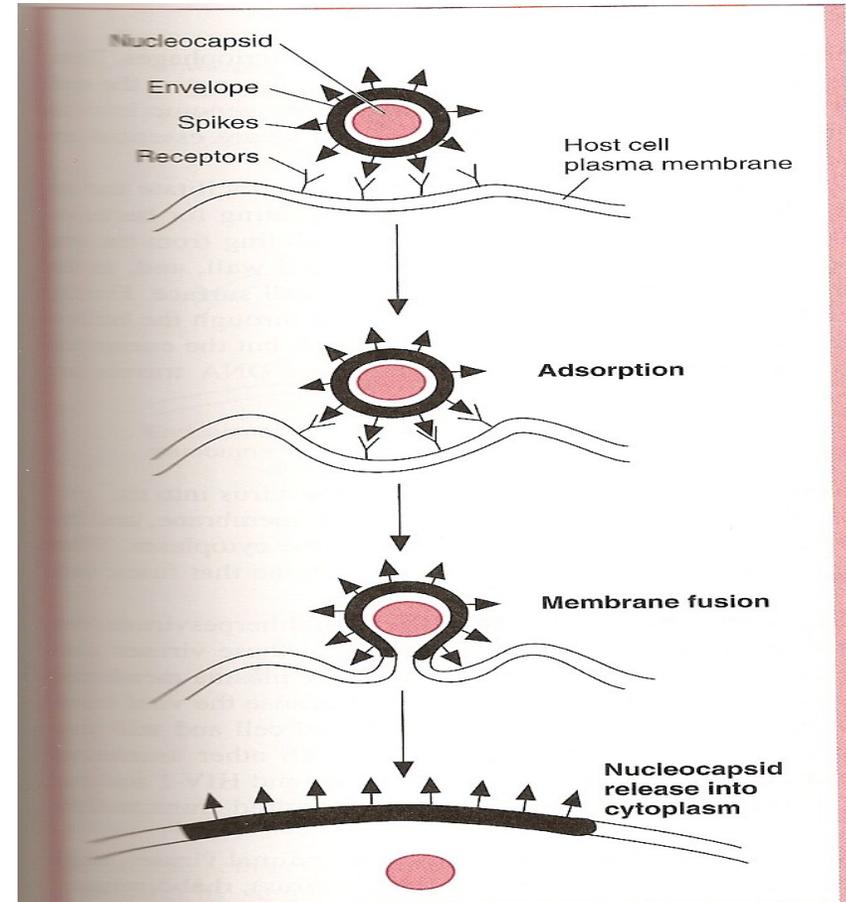
Penetration

- Entry by endocytosis
 - The virus is attached to specific receptors on the membrane which are underlined by the protein clathrin.
 - The virus is invaginated in a clathrin-coated pit which becomes a coated vesicle.
 - Fusion of the vesicle with cellular endosome and subsequently with lysosomes lead to low Ph.
 - The resulting acidity causes viral surface to fuse with lysosomal membrane releasing the viral nucleocapsid.
- Entry by fusing with the plasma membrane
 - 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.

Entry of Enveloped Viruses.



A. Entry via endocytosis



B. Entry by fusing with the plasma membrane

Uncoating and Eclipse

- Signifies the physical separation of the viral nucleic acid from the viral protein.
 - Nucleic acid has to uncoat sufficiently, so that virus replication can begin.
 - Some viruses do not completely uncoat though they replicate e.g. poxvirus.
- Eclipse phase last until infectious virions are made.

Macromolecular Synthesis

- Replication of viral nucleic acid and eventual assembly of progeny virion occur either in the nucleus or cytoplasm of the cells.
 - All DNA viruses except the **poxviruses** replicate DNA in the nucleus.
 - All RNA viruses except the **orthomyxoviruses** replicate in the cytoplasm.
- Mechanisms of viral Replication
 - Virus Specific mRNA in RNA virus infections
 - In infections with some RNA viruses e.g. picornaviruses, togaviruses and coronaviruses, the infecting viral RNA act directly as mRNA.
 - Other RNA viruses e.g. orthomyxoviruses, paramyxoviruses rhabdoviruses and reoviruses possess an RNA-dependant RNA polymerase which transcribe a complimentary copy of the viral RNA to act as mRNA.

Macromolecular Synthesis

- Mechanisms of viral Replication
 - Virus Specific mRNA in DNA infections
 - The genetic information of most DNA viruses is transcribed to mRNA in the cell nucleus by cellular RNA polymerase.
 - The exception is the poxvirus which have the DNA-dependent RNA polymerase in there virion core which is necessary because poxvirus replicates in the cytoplasm.
 - Retroviruses replication
 - A virion enzyme, RNA-dependent DNA polymerase (reverse transcriptase) uses the viral RNA as a template to synthesize a complimentary DNA copy which is then integrated into the cellular chromosome.
 - This provirus is transcribed by cellular RNA polymerase to produce mRNA.

Virus Maturation

Virus Maturation - involves 3 stages

- Assembly
 - When sufficient concentrations of viral structural proteins and nucleic acid have been made, they are assembled into progeny virus particles.
- Release
 - Progeny virus maybe released due to cell lysis mostly for non-enveloped viruses or if enveloped my bud from the cell.

Replication of Viruses

Virus Maturation

- Acquisition of virus envelope
 - The enveloped viruses obtain their envelopes when the nucleocapsid buds through the cell membrane.
 - Before budding, virus specific glycoproteins replace glycoproteins in the cell membranes so that the enveloped virus has an eventual structure which is very similar to a cell membrane but contain viral glycoproteins.

Thank you

for listening

Questions???

Thanks !!!