
Virology

General properties

Viruses are the smallest obligate intracellular infective agents containing only one type of nucleic acid (DNA or RNA) as their genome.

They have no metabolic activity outside the living cells.

They do not possess a cellular organisation and lack the enzymes necessary for protein and nucleic acid synthesis.

Viral genome (nucleic acid) diverts the host's metabolism to synthesise a number of virus specific macromolecules required for the production of virus progeny.

They multiply by a complex process and not by binary fission.

They do not grow in inanimate media. They are resistant to antibiotics

- The size of viruses ranges from 20 to 300 nm in diameter.
- The largest virus is the smallpox virus (300 nm) and the smallest is the parvovirus (20 nm)

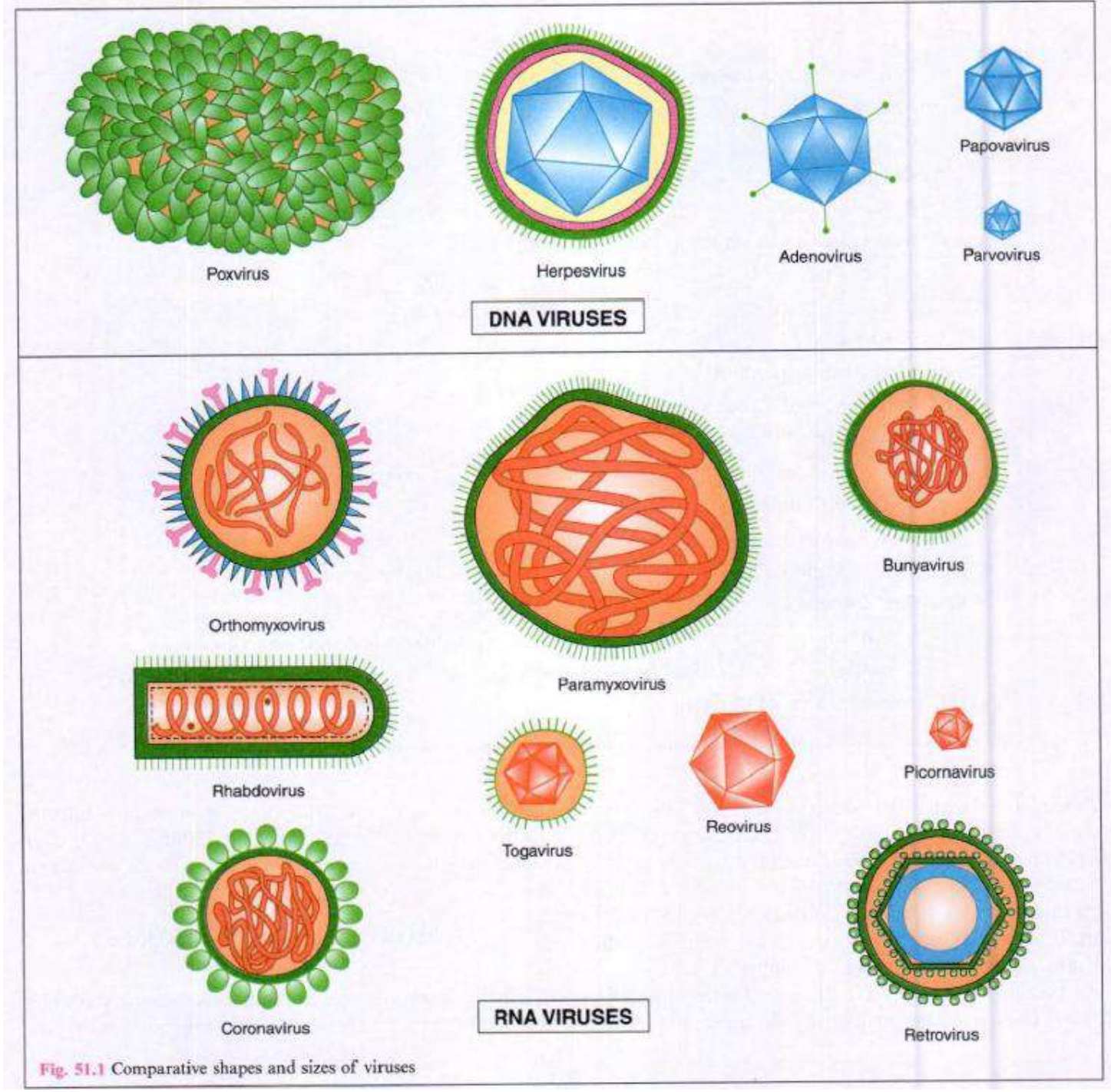
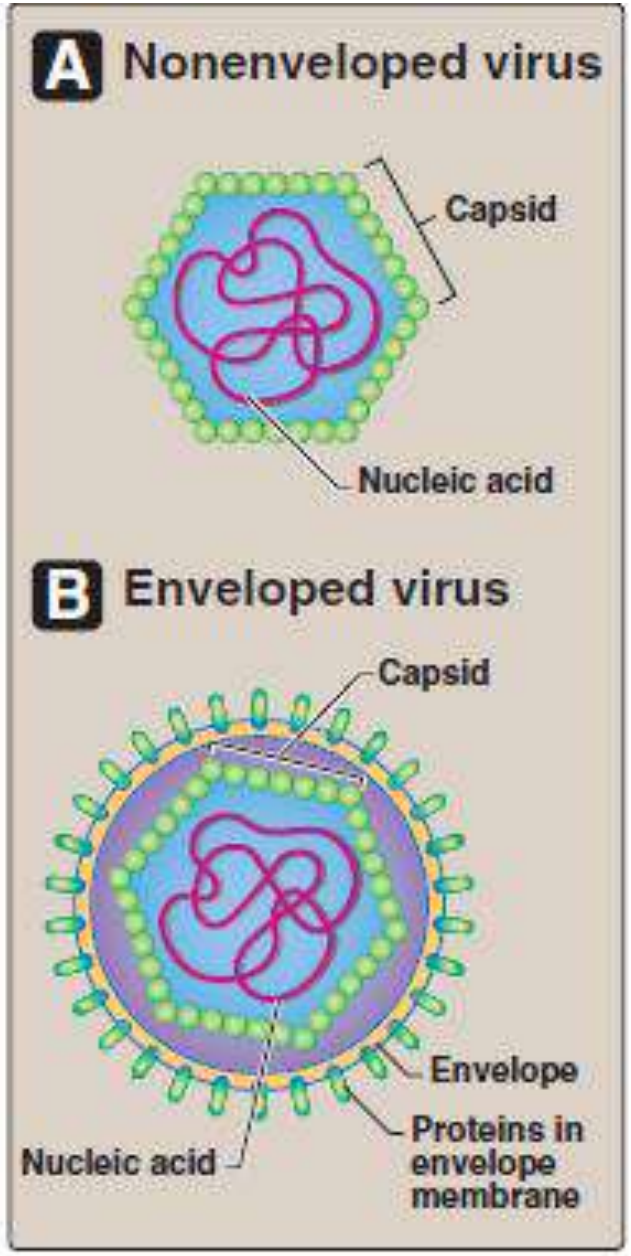


Fig. 51.1 Comparative shapes and sizes of viruses

OVERVIEW

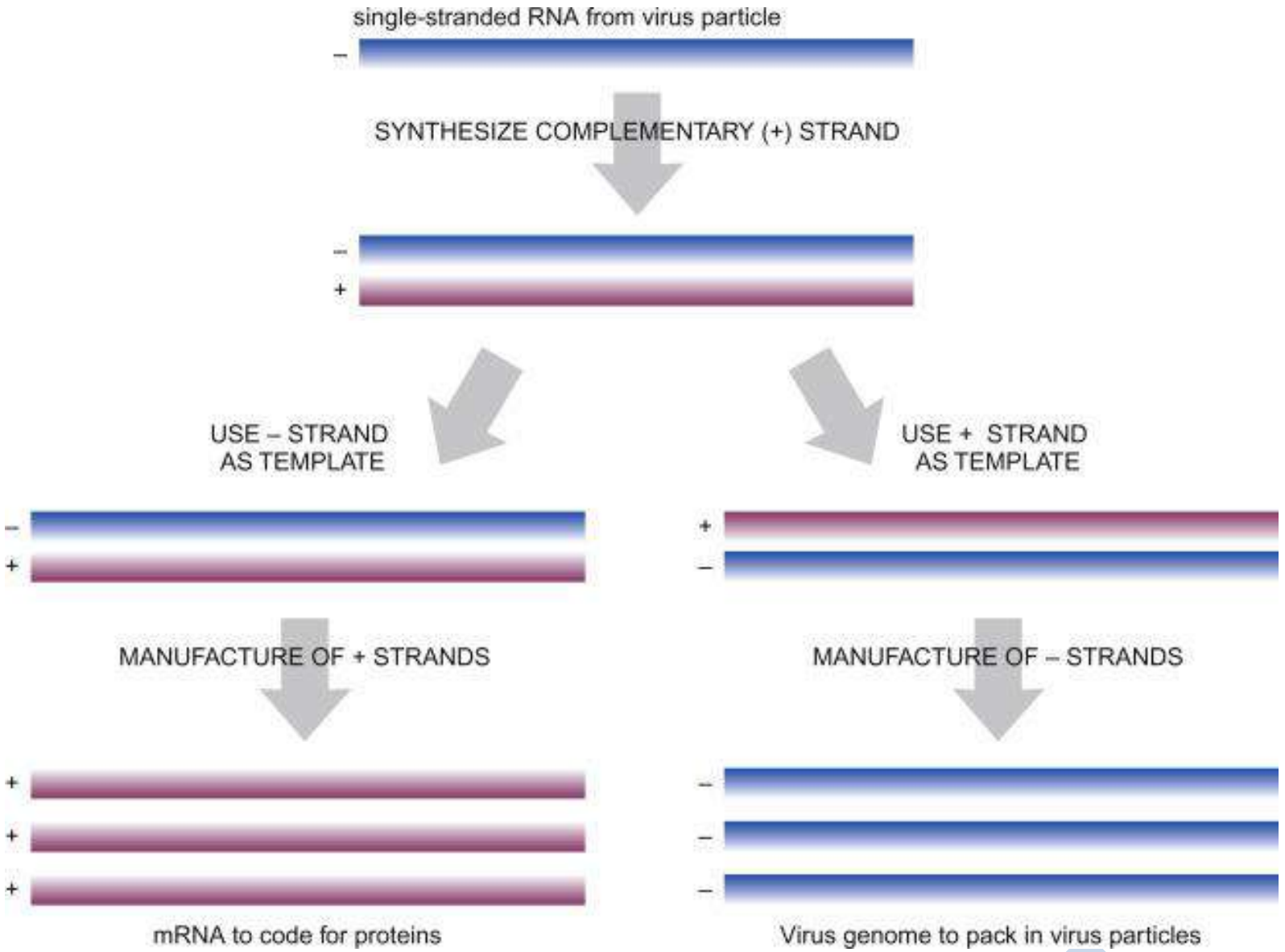
- A virus is an infectious agent that is minimally constructed of two components:
  - a genome consisting of either ribonucleic acid (RNA) or deoxyribonucleic acid (DNA), but not both
  - a protein-containing structure (capsid) designed to protect the genome
- Many viruses have additional structural features, for example, an envelope composed of a protein-containing lipid bilayer, whose presence or absence further distinguishes one virus group from another
- A complete virus particle combining these structural elements is called a virion.

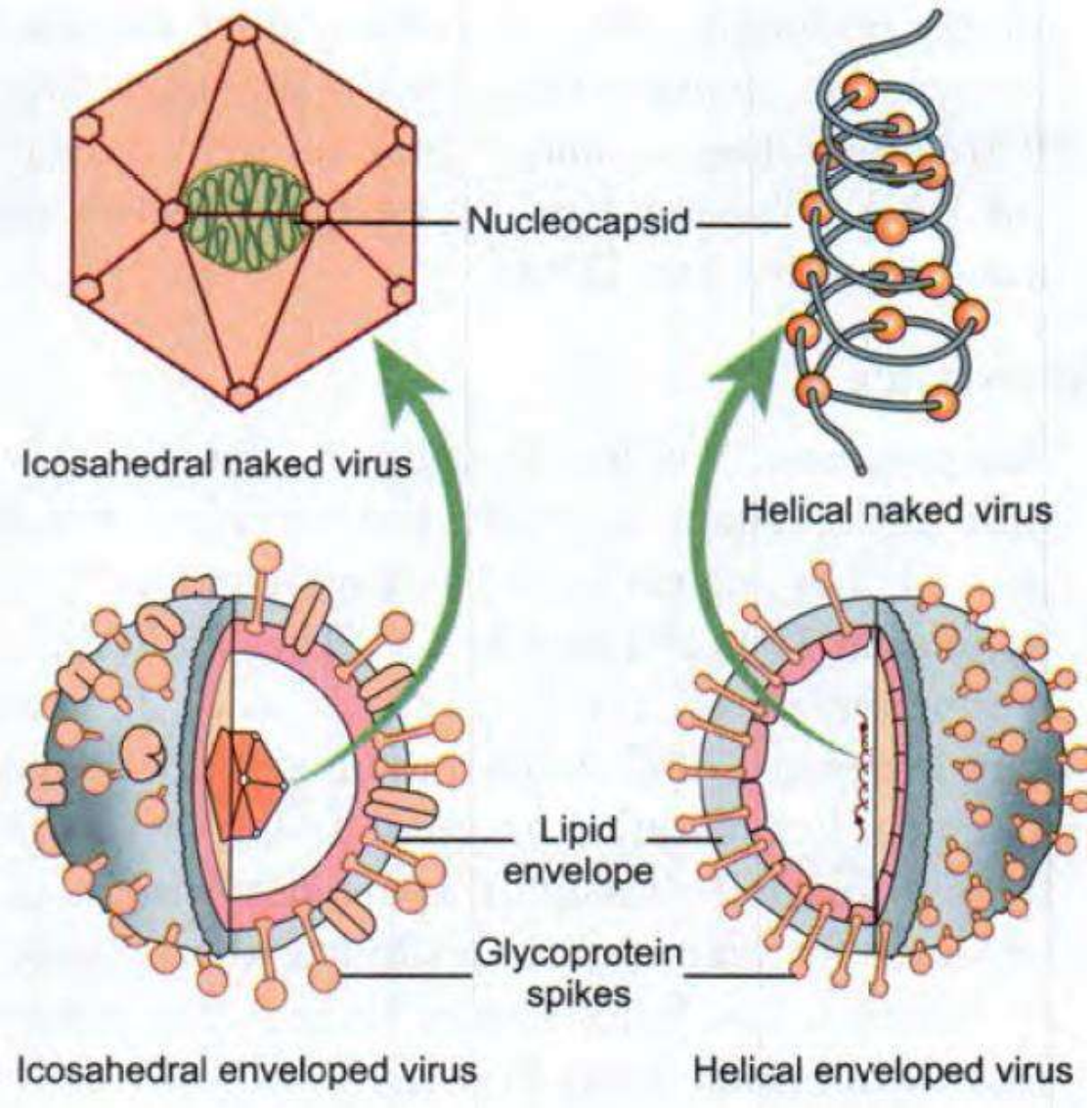
Outer envelope derived from the membrane of the host cell where they were assembled.



Genome

- The type of nucleic acid found in the virus particle 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.
- Single-stranded viral RNA genomes are further subdivided into those of “positive polarity” (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 (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


single-stranded RNA from virus particle
–
SYNTHESIZE COMPLEMENTARY (+) STRAND
–
+
USE – STRAND AS TEMPLATE
USE + STRAND AS TEMPLATE
–
+
+
–
MANUFACTURE OF + STRANDS
MANUFACTURE OF – STRANDS
+
+
+
–
–
–
mRNA to code for proteins
Virus genome to pack in virus particles



B. Capsid symmetry

- Three kinds of symmetry are encountered in the capsid:
- Icosahedral (cubical): An icosahedron is a polygon with 12 vertices or corners and 20 facets or sides. Each facet is in the shape of an equilateral triangle.
- Helical: In nucleocapsids with helical symmetry, the capsomers and nucleic acid are wound together to form a helical or spiral tube.
- Complex: Some, like the poxviruses, exhibit complex symmetry

Classification of virus

Family	Classification of Viruses		
	Nature	Envelope	Members causing human disease
DNA Viruses			
1. Poxviridae	ds	±	Variola virus, vaccinia virus, cowpox, monkeypox
2. Herpersviridae	ds	Yes	Herpes simplex 1 and 2, EBV, CMV, varicella zoster, HSV 6,7,8
3. Adenovirus	ds	No	Human adenoviruses A-F
4. Papovaviridae	ds	No	Papilloma virus, polyomavirus
5. Hepadenoviridae	ds	Yes	Hepatitis B virus
6. Parvoviridae	ss	No	Parvovirus
RNA Viruses			
1. Picornaviridae	ss	No	Enteroviruses – poliovirus, coxsackie, echo viruses
2. Orthomyxoviridae	ss	Yes	Influenza virus A–C
3. Paramyxoviridae	ss	Yes	Paramyxovirues – mumps and parainfluenza viruses Morbillivirus – measles virus, Pneumoviruses – RSV
4. Togaviridae	ss	Yes	Alpha (group A) – Chikungunya virus Rubiviruses – rubella virus
5. Flaviviruridae	ss	Yes	Flaviviruses – yellow fever, dengue viruses Japanese encephalitis virus, Hepatitis C virus
6. Bunyaviridae	ss	Yes	Sandfly fever, hantaviruses
7. Arenaviruses	ss	Yes	LCM, Lassa fever
8. Rhabdoviridae	ss	Yes	Vesiculovirus – Chandipura virus, Lyssavirus – Rabies virus
9. Reoviridae	ds	No	Human rotavirus
10. Coronaviridae	ss	Yes	Human coronaviruses, SARS virus
11. Retroviridae	ss	Yes	HIV 1 -2, HTLV1-2
12. Calciviridae	ss	No	Norwalk virus, hepatitis E virus
13. Filoviridae	ss	Yes	Marburg, Ebola viruses
14. Astroviridae	ss	No	Human astroviruses
15. Deltaviruses	ss	Yes	Hepatitis deltavirus

C. Envelope

Virions may be enveloped or non-enveloped (naked).

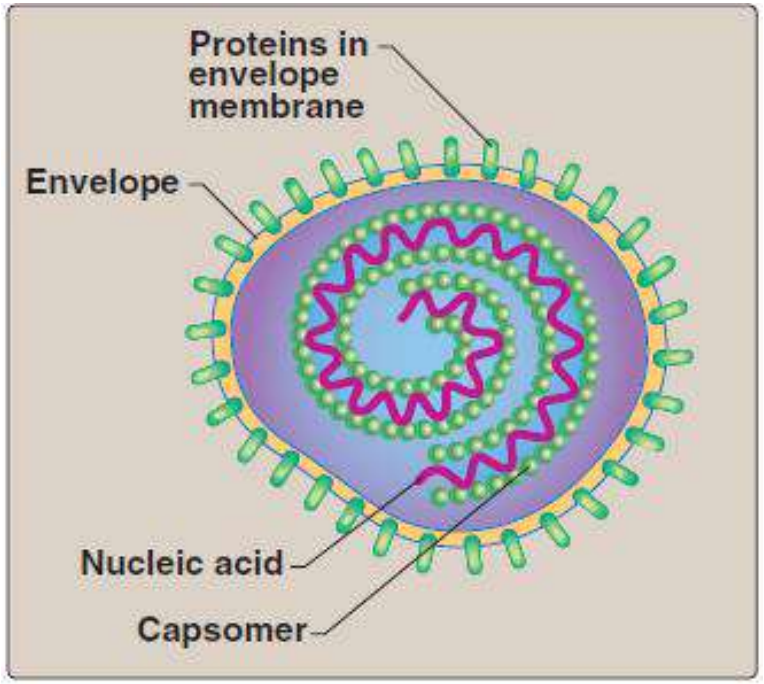
The envelope or outer covering is derived from the host cell membrane when the progeny virus is released by budding.

The envelope is made of lipoprotein

The lipid is largely of host cell origin while the protein is virus coded.

Protein subunits may be seen as projecting spikes on the surface of the envelope.

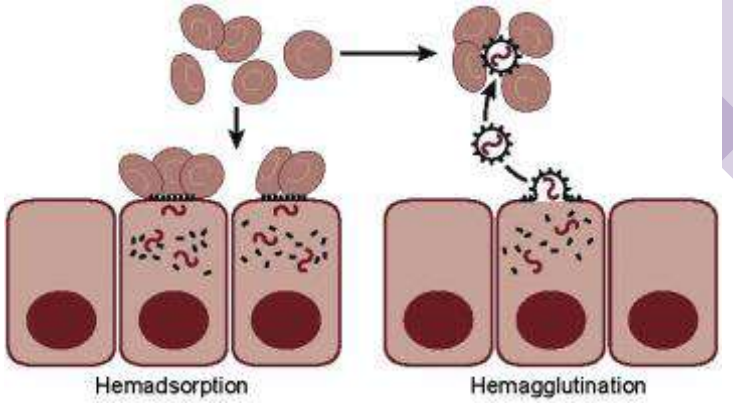
These structures are called peplomers (from peplos, meaning envelope). A virus may have more than one type of peplomer. The influenza virus carries two kinds of peplomers: the hemagglutinin which is a triangular spike and the neuraminidase which is a mushroom-shaped structure.



Structure of an enveloped helical virus.

VIRAL HAEMAGGLUTININ

- A large number of viruses contain haemagglutinin spikes (peplomers) on the capsid or envelope which can agglutinate erythrocytes of different species.
- Haemagglutination of influenza virus has been studied extensively. The viral haemagglutinin (glycoprotein) has special affinity for a different glycoprotein located in the 'receptor areas' on the surface of erythrocyte.
- When erythrocytes are added to serial dilutions of viral suspension, the virus and ertythrocytes collide in the suspension and adhere to each other resulting in haemagglutination. This test provides a simple and rapid method for detection of viruses in egg or tissue culture fluid.
- The haemagglutination reaction is specifically inhibited by the antibody to the virus → The haemagglutination inhibition test (HI) is routinely used for detecting antiviral antibody in diagnosis
- Some viruses, particularly influenza and parainfluenza viruses also carry on their surface another peplomer, the enzyme neuraminidase which acts on the receptors on erythrocytes and destroys them. It is known as receptor destroying enzyme (RIDE). (It is also produced by many other bacteria including Vibrio cholerae)
- Destruction of surface receptors results in the reversal of haemagglutination and the release of viruses from the surface of erythrocyte. This process is known as elution.
- After elution, the receptors are irreversibly damaged and erythrocytes are no longer agglutinable by that particular virus. The free viruses are, however, unharmed.



Hemadsorption and hemagglutination. Viral envelope proteins may bind glycoproteins expressed on the surface of erythrocytes from a species other than the natural host of the virus. Diagnostic tests have been developed that exploit this phenomenon. Erythrocytes may bind to infected cells that express these viral envelope proteins on their surface (hemadsorption) or cell free viruses may cross-link erythrocytes to form aggregates (hemagglutination), indicating the presence of virus infection.

REPLICATION OF VIRUSES

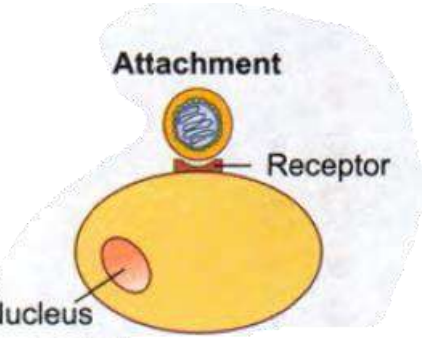
Due to lack of biosynthetic enzymes, viruses replicate by taking over the biochemical machinery of the host cell to synthesise virus specific macromolecules required for the production of virus progeny.

The genetic information necessary for viral replication is contained in the viral nucleic acid.

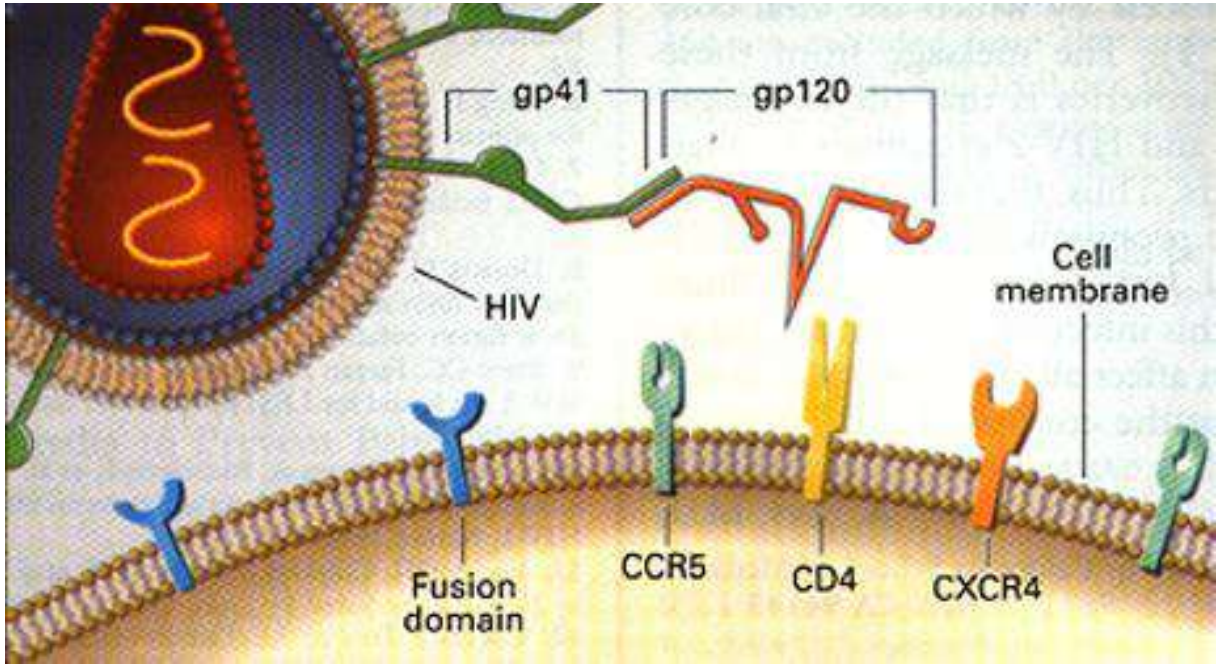
The replicative cycle can be divided into six sequential phases.

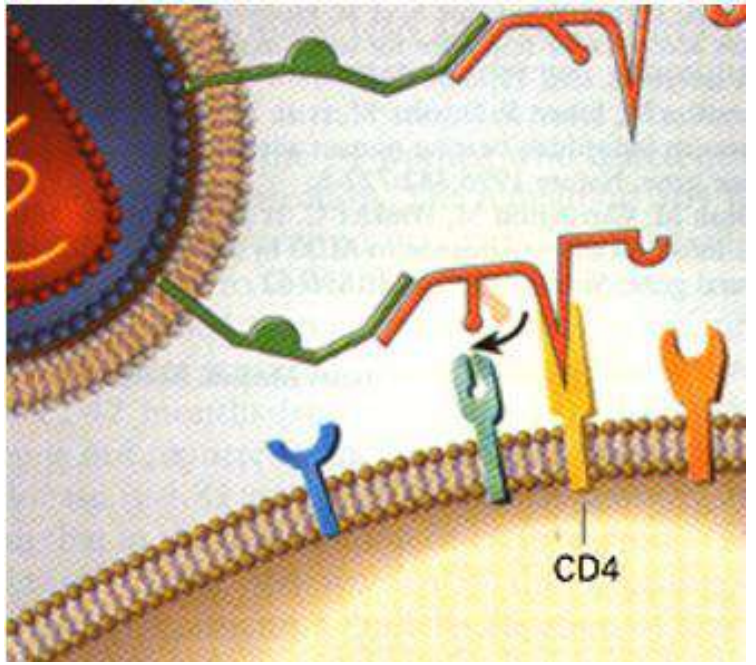
- Adsorption
- Penetration
- Uncoating
- Biosynthesis
- Maturation and
- Release

1. ADSORPTION OR ATTACHMENT

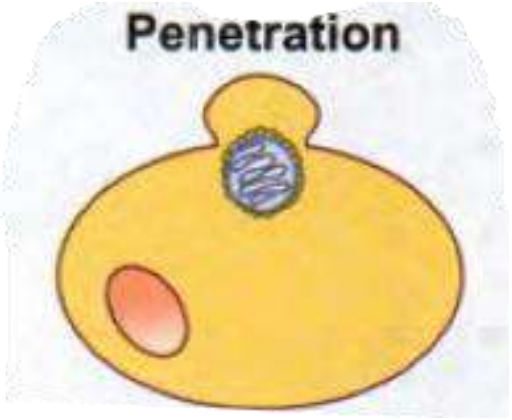


- The viruses come in contact with the cells by random collision, but adsorption or attachment is mediated by the binding of virus surface structures, known as ligands, to the receptors on cell surface.
- In case of influenza virus, the haemagglutinin (a surface glycoprotein) binds specifically to sialic acid residue of glycoprotein receptor sites on the surface of respiratory epithelium.
- With the human Immunodeficiency virus (HIV), attachment is between the viral surface glycoprotein gp 120 and the CD4 receptor on host cells.



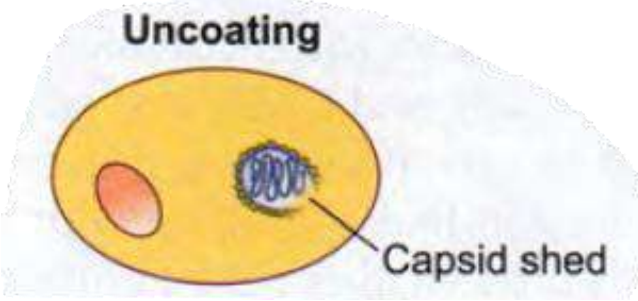


2. Penetration



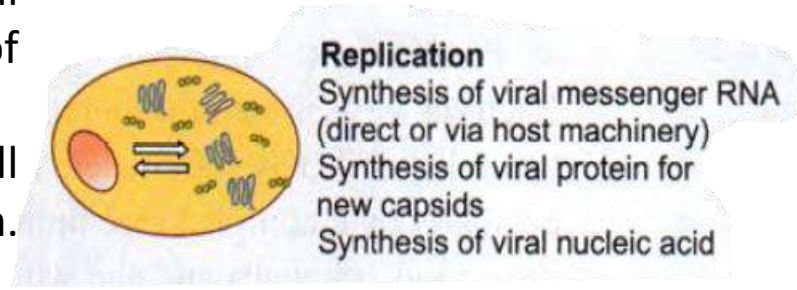
- After attachment, the virus particles may be engulfed by a mechanism resembling phagocytosis, a process known as viropexis.
- Alternatively, in case of the enveloped viruses, the envelope may fuse with the plasma membrane of the host cell releasing the nucleocapsid into the cytoplasm.

3. Uncoating



- This is the process of stripping the virus of its outer layers and capsid to release the nucleic acid into the cell.
- With most viruses, uncoating is affected by the action of lysosomal enzymes of the host cells.

4. Biosynthesis/Replication



- After uncoating, the viral genome directs the biosynthetic machinery of the host cell to shut down the normal cellular metabolism and direct the sequential production of viral components.
- In general, the nucleic acid genome of most DNA viruses is synthesised in the host cell nucleus. However, the poxviruses synthesise all their components in the cytoplasm. Nucleic acid genome of most RNA viruses is synthesised in the cytoplasm.
- The exceptions are orthomyxoviruses, some paramyxoviruses and retroviruses which are synthesised partly in the nucleus of the host

Biosynthesis consists of the following steps:

(i) Transcription of messenger RNA (mRNA) from viral nucleic acid,
(ii) Translation of the mRNA into 'early proteins' or 'nonstructural proteins'.
These are enzymes which initiate and maintain synthesis of virus components.
They may also induce shutdown of host protein and nucleic acid synthesis.
(iii) Replication of viral nucleic acid.
(iv) Synthesis of 'late proteins' or 'structural proteins' which constitute daughter virion capsids.
The mechanisms of nucleic acid synthesis differ in the different type of viruses.

Replication of single stranded DNA viruses

In case of these viruses (for example parvovirus), a complementary strand is first synthesised, producing double stranded 'replicative forms'.

This double stranded viral DNA acts as a template for its replication, and also for transcribing into mRNA which are translated into viral proteins.

Replication of double stranded DNA viruses

- Initially only a part of the viral DNA is transcribed into early mRNA.
- This encodes for synthesis of early proteins which are required for DNA replication. Late proteins are synthesised after viral DNA replication has commenced.

Replication of RNA viruses

• In many single stranded RNA viruses (e.g. poliovirus), the viral RNA can act directly as mRNA. These are named as positive strand (plus strand, positive sense) RNA viruses. The single stranded parental RNA (positive strand) acts as the template for the production of a complementary strand (negative strand), which acts as the template for progeny viral RNA.

• In some other single stranded RNA viruses (e.g. influenza and parainfluenza viruses), they carry their own RNA polymerases for mRNA transcription. These are named as negative strand (minus sense) RNA viruses. Parental RNA produces complementary positive strands which act both as mRNA and as template for the synthesis of progeny viral RNA.

• In the double stranded RNA viruses (e.g. reoviruses), the viral RNA is transcribed to mRNA by viral polymerases.

• Retroviruses exhibits a unique replicative cycle. Virus genome (single stranded RNA) is converted into an RNA : DNA hybrid by the viral enzyme, RNA directed DNA polymerase (reverse transcriptase).
Double stranded DNA is synthesised from the hybrid (RNA : DNA). The double stranded DNA form of the virus (provirus) integrates into the host cell genome. The provirus acts as the template for the synthesis of progeny viral RNA. The integration of the provirus into the host cell genome may lead to transformation of the cell and development of neoplasia.

Maturation

- The viral nucleic acid and capsid polypeptide assemble together to form the daughter virions. The assembly takes place in either the nucleus(herpes and adenoviruses) or cytoplasm (picorna and pox viruses).
- In case of enveloped viruses, the envelope is derived from the nuclear membrane (herpes virus) and from plasma membrane when the assembly occurs in the cytoplasm of host cell (orthomyxoviruses and paramyxoviruses).

Release

- Enveloped viruses are released by a process of budding from the cell membrane over a period of time.
- The host cell is usually not affected but there are exceptions e.g. polioviruses not only damage host cell but may also be released by the lysis of the host cell.
- In case of bacterial viruses (e.g. bacteriophages), they are usually released by lysis of the infected bacterium.

ECLIPSE PHASE

- From the stage of penetration of virus into the host cell till the appearance of first infectious virus progeny particle, the virus cannot be demonstrated inside the host cell.
- This period is known as eclipse phase.
- The duration of eclipse phase is about 15 to 30 minutes for bacteriophages and 15—30 hours for animal viruses.

CULTIVATION OF VIRUSES

As viruses multiply only in living cells, they cannot be grown on any of the inanimate culture medium. Three methods are employed for the cultivation of viruses:

A. Animal inoculation

B. Embryonated egg inoculation

C. Tissue culture

Detection of virus growth in cell cultures

- Cytopathic effect
- Metabolic inhibition
- Hemadsorption
- Interference
- Transformation
- Immunofluorescence