Introduction to Viruses

A virus is a submicroscopic infectious agent (small parasite) that cannot reproduce by itself. All viruses are obligatory replicates only inside the living cells of an organism. Also viruses can infect all types of life forms, from animals and plants to microorganisms, including bacteria and archaea. When infected by a virus, a host cell is forced to produce many thousands of identical copies of the original virus.

A **virus** Viruses may be defined as **acellular organisms** whose **genomes** consist of **nucleic acid**, and which obligatory **replicate inside host cells** using **host metabolic machinery** and **ribosomes** to form a **pool of components** which assemble into particles called **VIRIONS**, which serve to **protect the genome** and to **transfer it to other cells**. When infected by a virus, a host cell is forced to produce many thousands of identical copies of the original virus. Unlike most living things, viruses do not have cells that divide; new viruses are assembled in the infected host cell. But unlike still simpler infectious agents, viruses contain genes, which gives them the ability to mutate and evolve. Over 5,000 species of viruses have been discovered yet.

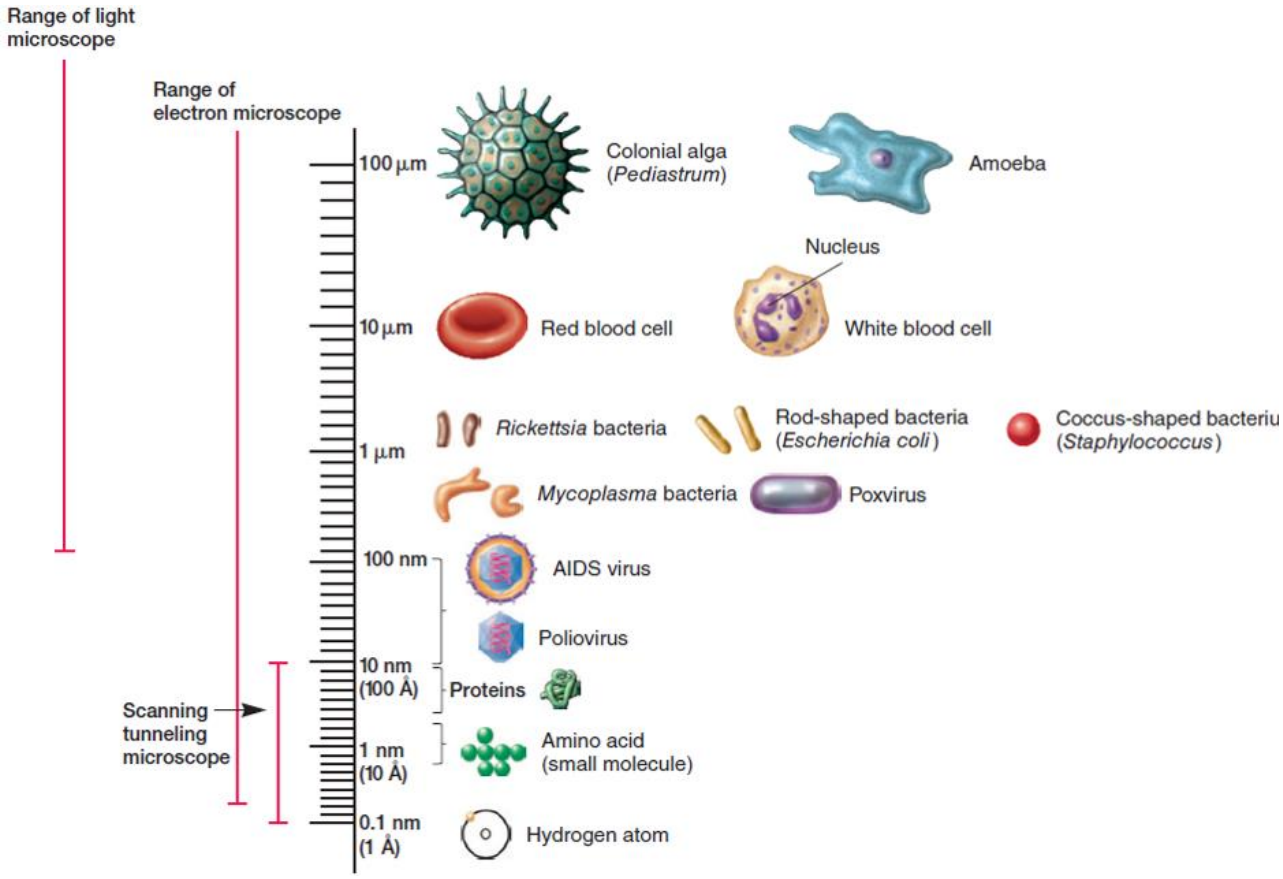
Most viruses have either RNA or DNA as their genetic material. The nucleic acid may be single- or double-stranded of genetic material. The entire infectious virus particle, called a virion, consists of the nucleic acid and an outer shell of protein. The simplest viruses contain only enough RNA or DNA to encode four proteins. The most complex can encode 100 – 200 proteins.

Viral infections can cause disease in humans, animals and even plants. Antibiotics have no effect on viruses, but antiviral drugs have been developed to treat life-threatening infections. Vaccines that produce lifelong immunity can prevent some viral infections.

Viruses reproduce rapidly because they have only a few genes compared to humans who have 20,000–25,000. For example, influenza virus has only eight genes and rotavirus has eleven. These genes encode structural proteins that form the virus particle, or non-structural proteins, that are only found in cells infected by the virus.

Size of Viruses

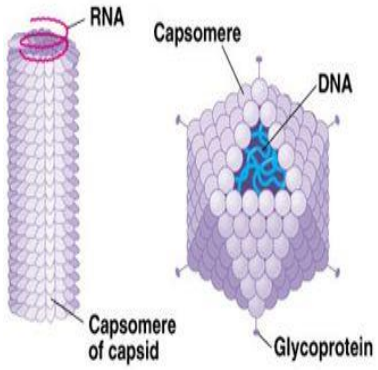
A small virus has a diameter of about 20 nm. ***Parvovirus***. A large virus has a diameter of up to 400 nm. ***Poxviruses***. Viruses are among the smallest infectious agents, and most of them can only be seen by electron microscopy. Most viruses cannot be seen by light microscopy, their sizes range from 20 to 300 nm.



Shape of Viruses: -

Viruses vary in shape from the simple helical and icosahedral to more complex structures. A virus consists of two or three parts: genome and capsid or genome, capsid and envelope

Viral Shapes



- The shape of the virus is determined by either its capsid or its nucleic acid.

- Icosahedron has 20 trianglular faces
  ex: herpes simplex, chicken pox and polio

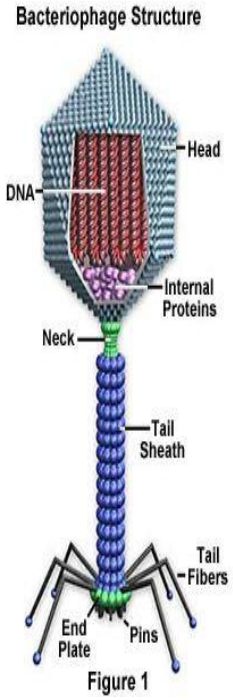


Figure 1

- Helix is a spiral shape (like DNA)
  ex: rabies, measles and tobacco mosaic virus

- Complex is a combination of two other shapes
  ex: bacteriophages

Structure of virus

A virus particle, also known as a virion, (infectious unit) consists of genes made from DNA or RNA which are surrounded by a protective coat of protein called a capsid (nucleic **acid genome and protein capsid called nucleocapsid**). Some viruses are surrounded by a bubble of lipid (fat) called an envelope.

1-Genome: - Most viruses have either RNA or DNA as their genetic material. The nucleic acid may be single- or double-stranded. David Baltimore proposed that viruses be classified according to the nature of their genome and the relationship between the genome and the viral mRNA.

The Baltimore classification of viruses is based on the mechanism of mRNA production. Viruses must generate mRNAs from their genomes to produce proteins and replicate themselves, but different mechanisms are used to achieve this in each virus family. Viral genomes may be single-stranded (ss) or double-stranded (ds), RNA or DNA, and may or may not use reverse transcriptase (RT). In addition, ssRNA viruses may be either sense (+) or antisense (−). This classification places viruses into seven groups:

I: dsDNA viruses (e.g. Adenoviruses, Herpesviruses, Poxviruses)

II: ssDNA viruses (+ strand or "sense") DNA (e.g. Parvoviruses)

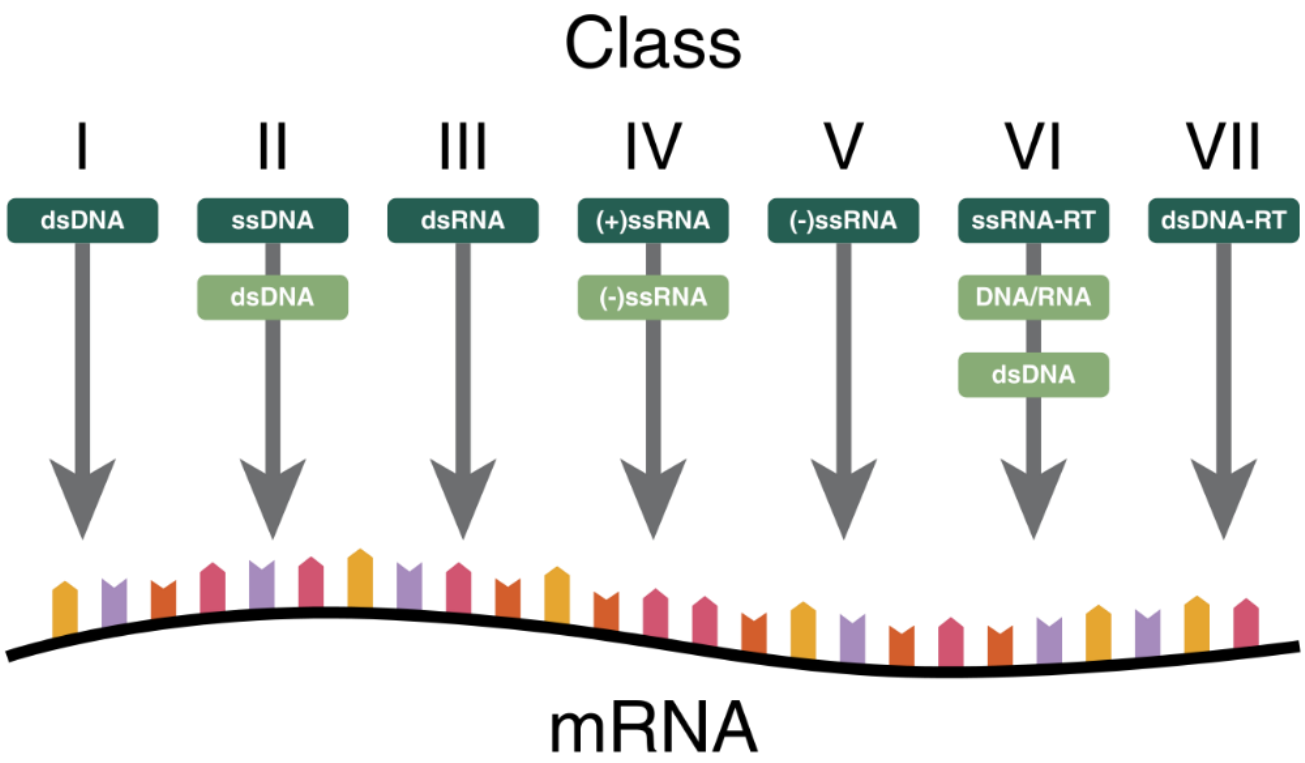
III: dsRNA viruses (e.g. Reoviruses)

IV: (+) ssRNA viruses (+ strand or sense) RNA (Coronaviruses, Picoronaviruses, Togavrises)

V: (−) ssRNA viruses (− strand or antisense) RNA (e.g. Orthomyxoviruses, Rhabdoviruses)

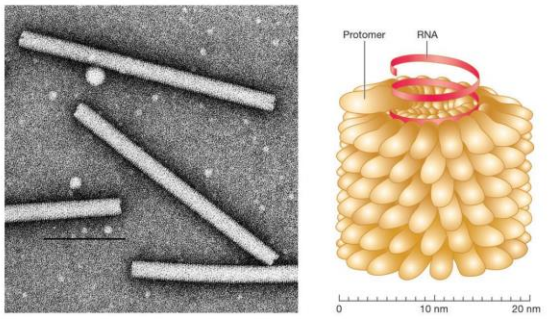
VI: ssRNA-RT viruses (+ strand or sense) RNA with DNA intermediate in life-cycle (e.g. Retroviruses)

VII: dsDNA-RT viruses DNA with RNA intermediate in life cycle (e.g. Hepadnaviruses)

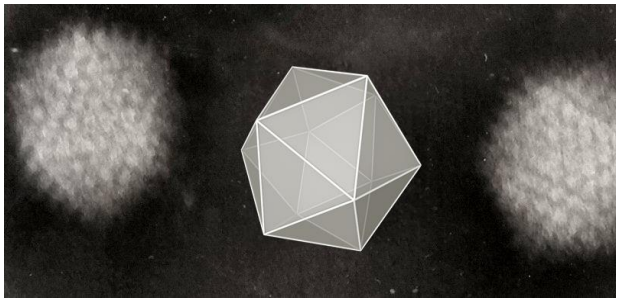


2- Protein capsid (**nucleocapsid**) :-The protein shell, or coat, that encloses the nucleic acid genome. A capsid is almost always made up of repeating structural subunits that are arranged in one of two symmetrical structures, a **helix** or an **icosahedron.** The functions of protein capsid are **a-** Protect the viral nucleic acid, **b-** Participate in the viral infection, and **c-** Share the antigenicity.

A



B

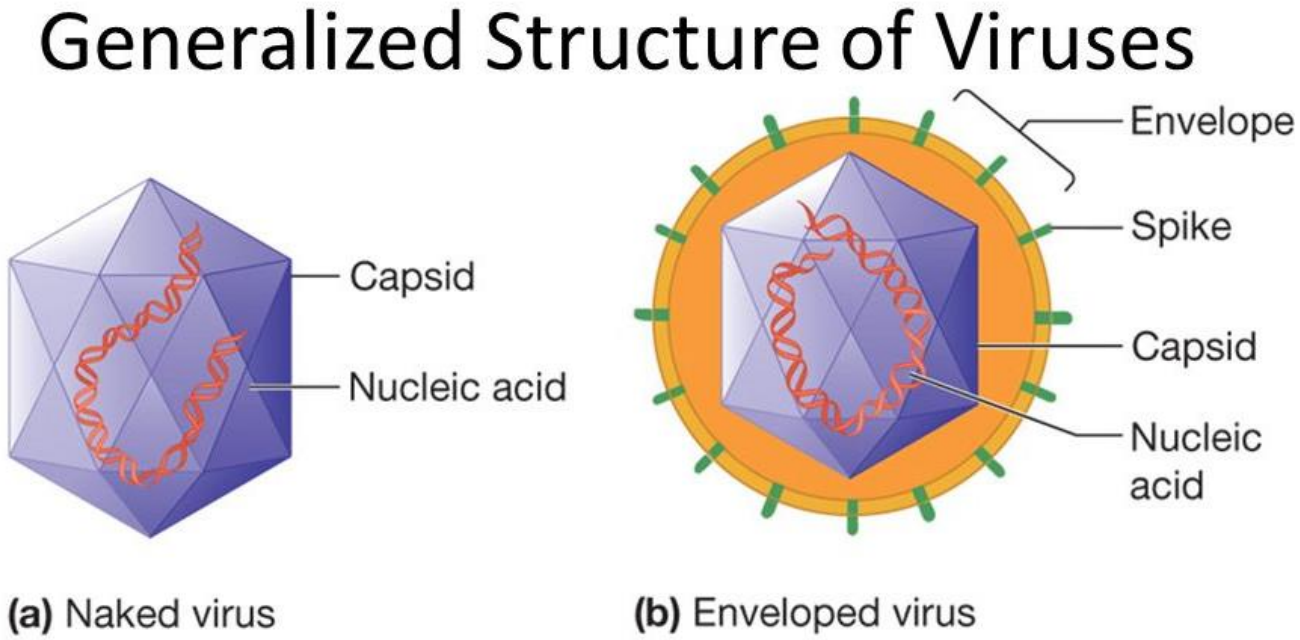


A- The helical structure of the virus rod.

B- Structure of icosahedral adenovirus. Electron micrograph with an illustration to show shape

3-Viral Envelope: In some animal viruses, the nucleocapsid is surrounded by a membrane, called an envelope, made up of a lipid bilayer, and is **comprised of host-cell lipids.** It also contains **virally encoded proteins**, often **glycoproteins** which are trans-membrane proteins. These viral proteins serve many purposes, such as *binding to receptors on the host cell, *playing a role in membrane fusion and cell entry, etc.

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. 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.



Viruses spread in many ways.

1-Viruses influenza are spread through the ***air*** by droplets of moisture when people cough or sneeze.

2- Viruses such as Hepatitis A virus are transmitted by the ***fecal–oral route***, which involves the contamination of hands, food and water.

3- Rotavirus is often spread by ***direct contact*** with infected children.

4-The human immunodeficiency virus, HIV, is transmitted by bodily fluids transferred ***during sex***.

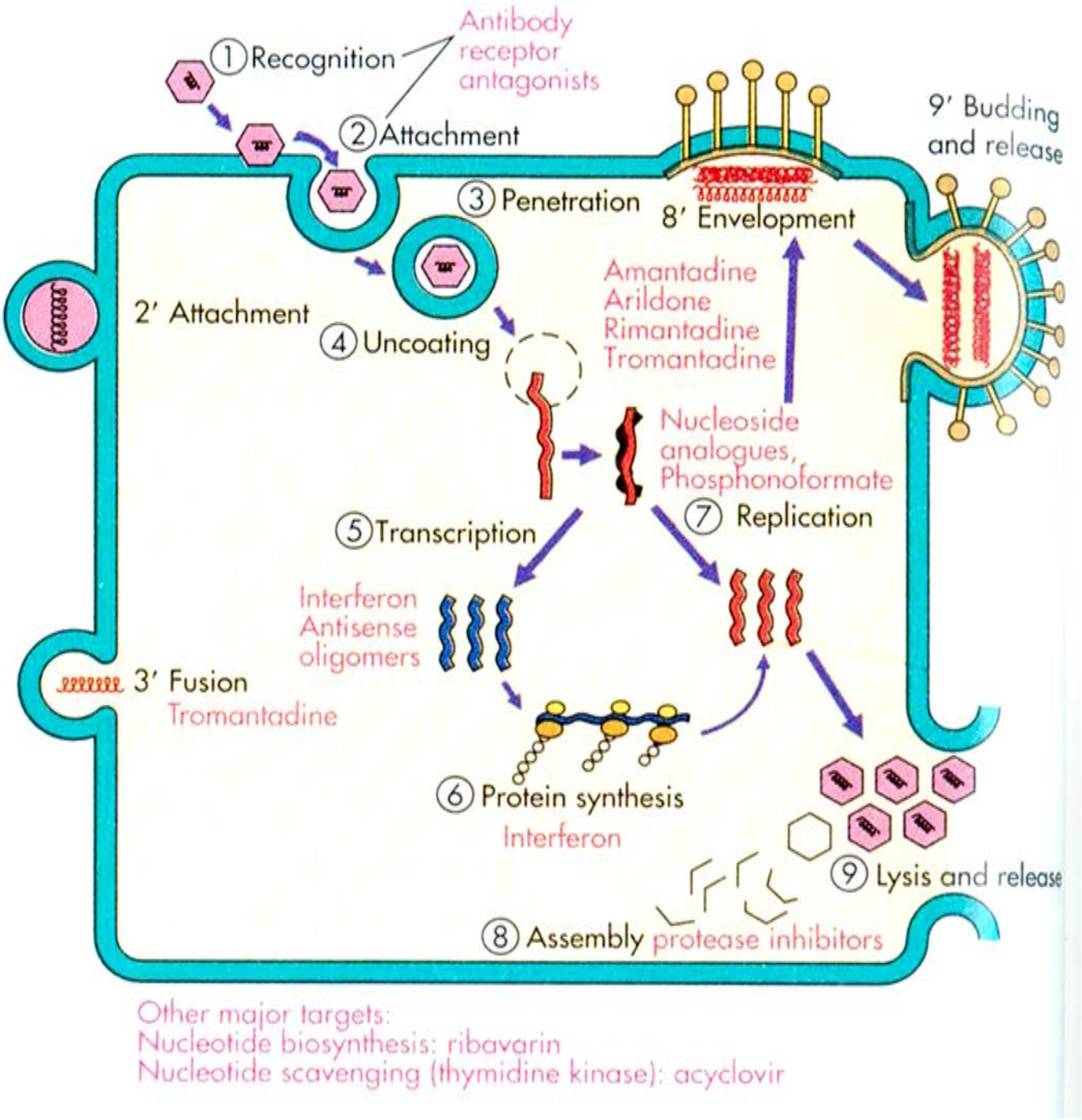
5- Dengue virus, are spread by ***blood-sucking insects***.

- ## Lifecycle of Viruses

As obligate intracellular parasites, Virus must enter and replicate in living cells in order to "reproduce" themselves. This "growth cycle" involves specific attachment of virus, penetration and un-coating, nucleic acid transcription, protein synthesis, maturation and assembly of the virions and their subsequent release from the cell by budding or lysis

There are six basics, overlapping stages in the life cycle of viruses in living cell.

- **Attachment** is the binding of the virus to specific molecules on the surface of the cell.
- **Penetration** follows attachment; viruses penetrate the host cell by endocytosis or by fusion with the cell. Virions are either engulfed into vacuoles by "endocytosis" or the virus envelope fuses with the plasma membrane to facilitate entry
- **Uncoating** happens inside the cell when the viral capsid is removed and destroyed by viral enzymes or host enzymes, thereby exposing the viral nucleic acid.
- **Replication** of virus particles is the stage where a cell uses viral messenger RNA in its protein synthesis systems to produce viral proteins. The RNA or DNA synthesis abilities of the cell produce the virus's DNA or RNA.
- **Assembly** takes place in the cell when the newly created viral proteins and nucleic acid combine to form hundreds of new virus particles.
- **Release** occurs when the new viruses escape or are released from the cell. Most viruses achieve this by making the cells burst, a process called lysis. Other viruses such as HIV are released more gently by a process called budding.


Antibody receptor antagonists
1 Recognition
2 Attachment
3 Penetration
8′ Envelopment
9′ Budding and release
2′ Attachment
4 Uncoating
Amantadine
Arildone
Rimantadine
Tromantadine
Nucleoside analogues, Phosphonoformate
7 Replication
5 Transcription
Interferon
Antisense oligomers
3′ Fusion
Tromantadine
6 Protein synthesis
Interferon
9 Lysis and release
8 Assembly
protease inhibitors
Other major targets:
Nucleotide biosynthesis: ribavarin
Nucleotide scavenging (thymidine kinase): acyclovir

- **Anti-viral targeting**

Antiviral drugs are medicines that decrease the ability of flu viruses to reproduce. The general idea behind modern antiviral drug design is to identify viral proteins, or parts of proteins, that can be disabled. For example, a researcher might target a critical enzyme synthesized by the virus, but not by the patient, that is common across strains, and see what can be done to interfere with its operation.

1- Inhibitors of attachment fusion and uncoating:

Fusion inhibitor: A class of antiretroviral drugs that work on the outside of the host CD4 cell to prevent Human Immunodeficiency Virus (HIV) from fusing with and infecting it. Fusion inhibitors act by binding to an envelope protein and blocking the structural changes necessary for the virus to fuse with the host CD4 cell.

This stage of viral replication can be inhibited in two ways:

1. Using agents which mimic the virus-associated protein (VAP) and bind to the cellular receptors. This may include VAP anti-idiotypic antibodies, natural ligands of the receptor and anti-receptor antibodies.
2. Using agents which mimic the cellular receptor and bind to the VAP. This includes anti-VAP antibodies, receptor anti-idiotypic antibodies, extraneous receptor and synthetic receptor mimics.

2. Inhibitors of nucleic acid synthesis:

Ribavirin is an analog of the nucleoside guanosine; its action varies for different viruses. This drug alters cellular nucleotide pools, inhibits viral RNA synthesis, and may cause

lethal RNA mutations.

3. Protease inhibitors:

They inhibit the action of viruses protease; used in combination with AZT and a second nucleoside analog as “cocktail” therapy for HIV.

4. Neuraminidase inhibitors:

a. These drugs include oseltamivir and zanamivir.

b. They inhibit the neuraminidase of influenza A and B viruses; they may be used for prophylaxis as well as treatment.

5. mRNA inhibitors:

a. Fomivirsen is a synthetic oligonucleotide complementary to a sequence in CMV RNA (an antisense compound). It prevents transcription of early CMV genes.

b. It is approved for intravitreal therapy of CMV retinitis after other therapies have failed.