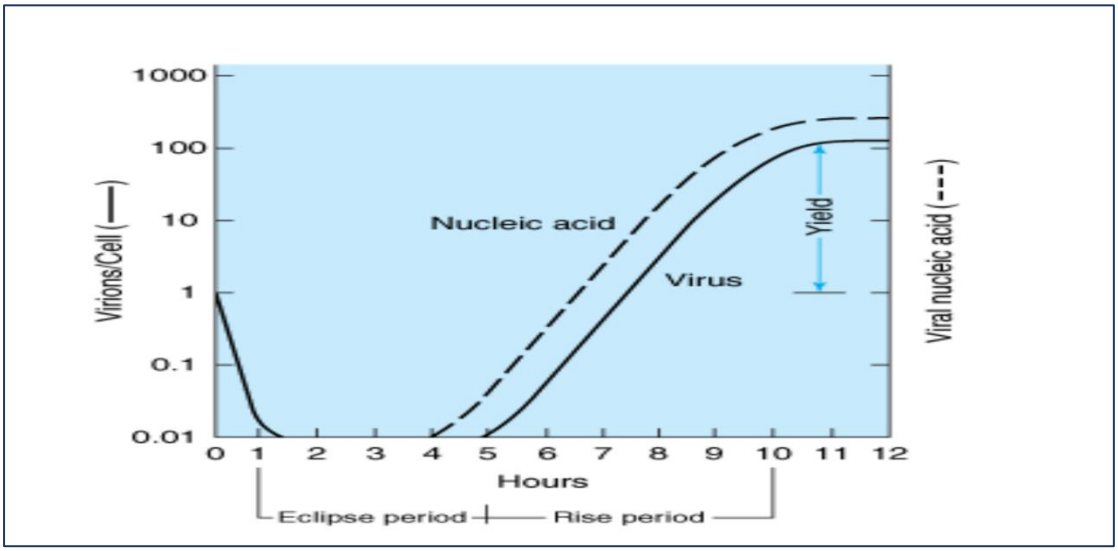
The Essential Requirements for Viral Replication

- **Obligate Intracellular Parasites:** Viruses **multiply only in living cells** .
- **Host Cell Role:** The host cell provides energy**, synthetic machinery, and low-molecular-weight precursors** for synthesizing viral proteins and nucleic acids.
- **Viral Genome Role:** The viral nucleic acid carries the **genetic code** for all virus-specific macromolecules.
- **Protein Synthesis Requirement:** The viral genome must produce a **functional mRNA** to utilize the host's protein-synthesizing machinery. Viral RNAs compete successfully with cellular mRNAs.

The viral replication cycle : . Growth curve, which shows the amount of virus produced at different times after infection.



Viral growth curve. The figure shows that one infectious virus particle (virion) entering a cell at the time of infection results in more than 100 infectious virions 10 hours later, a remarkable increase. Note the eclipse period during which no infectious virus is detectable within the infected cells. In this growth curve, the amount of infecting virus is 1 virion/cell (i.e., 1 infectious unit/cell). (Modified and reproduced with permission from Joklik WK et al. *Zinsser Microbiology*. 20th ed. Originally published by Appleton & Lange. Copyright 1992 by McGraw-Hill.)

Eclipse period The phase of the growth cycle; The eclipse period is actually one of intense synthetic activity as the cell is redirected toward fulfilling the needs of the viral parasite; its duration varies depending on both the particular virus and the host cell, and it is followed by an interval of **rapid accumulation of infectious progeny virus particles.**

Cell Fate and Infection Types

- **Cellular Redirection**: In some cases, cellular metabolism is redirected exclusively toward new virus synthesis, leading to the destruction of the cell 💥 .
- **No Significant** Alteration: In other cases, the cell's metabolic processes are not altered significantly, the cell synthesizes viral components, and is not killed 👍 .
- **Assembly:** After synthesis, viral nucleic acid and proteins assemble to form new infectious virions.
- **Yield and Duration:** The yield of infectious virus per cell and the duration of the cycle vary widely (e.g., picornaviruses: 6-8 hours; some herpesviruses: >40 hours).

Not all infections lead to new progeny virus.

- **Productive infections** occur in **permissive cells** and result in the production of infectious viruses.
- **Abortive infections** fail to produce infectious progeny, either because the cell may be nonpermissive and unable to support the expression of all viral genes or because the infecting virus may be defective, lacking some functional viral gene.
- **A latent infection** may ensue, with the persistence of viral genomes, the expression of no or a few viral genes, and the survival of the infected cell.

General Steps in Viral Replication Cycles

The general steps of a viral replication cycle include

Attachment of the virus to a host cell, **Penetration and entry** into the cell, **Uncoating** to release the viral genome, **Replication** and expression of the viral genome to produce new components, **Assembly** of these new components into new virus particles, and finally **Release** of the new virions from the infected cell.

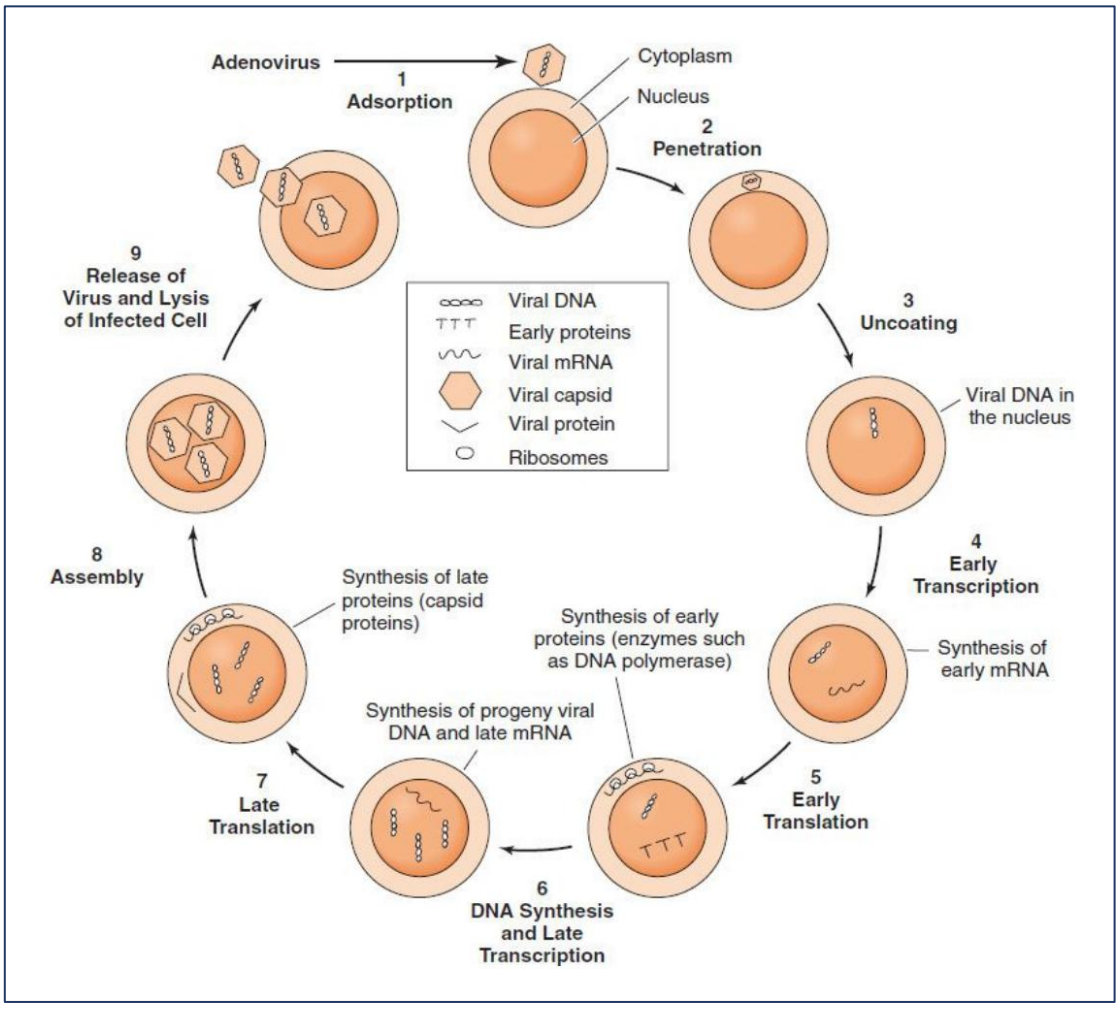


FIGURE Viral growth cycle. The growth cycle of adenovirus, a nonenveloped DNA virus, is shown. (Modified and reproduced with permission from Jawetz E, Melnick JL, Adelberg EA. *Review of Medical Microbiology*. 16th ed. Originally published by Appleton & Lange. Copyright 1984 by McGraw-Hill.)

1. Attachment (Adsorption) 🎯

- This is the initial interaction where a **virion binds to a specific receptor site** on the host cell surface.
- **Receptors** are typically **glycoproteins** (e.g., picornaviruses bind protein sequences; orthomyxoviruses bind oligosaccharides).
- The presence of these receptors is critical for **cell tropism** (determining which cells a virus can infect) and **viral pathogenesis Table 1** .

Table 1 : Examples of Viral Receptors and Their Target Cells

Virus	Target cell	Receptor
Epstein Bar virus	B- cell	CD21
Human Immuno-deficiency virus	Helper T cell	CD4
Rhinovirus	Epithelial cell	ICAM-1 Intracellular adhesion molecule
Rabies cell	Neuron cell	Acetylcholine receptor
Influenza virus	Epithelial cell	Sialic acid
B19 Parvovirus	Erythroid precursor	Erythrocyte P antigen (globoside)

2. Penetration (Engulfment) 📥

- After attachment, the virus particle is **taken up inside the cell**.
- **Mechanisms of Uptake:**
  - **Receptor-mediated endocytosis:** The virus is ingested within **endosomes**.
  - **Direct penetration:** The virus particle passes directly across the plasma membrane.
  - **Fusion:** For enveloped viruses, the viral envelope fuses with the plasma membrane, often involving a **viral fusion protein** and a second cellular coreceptor.

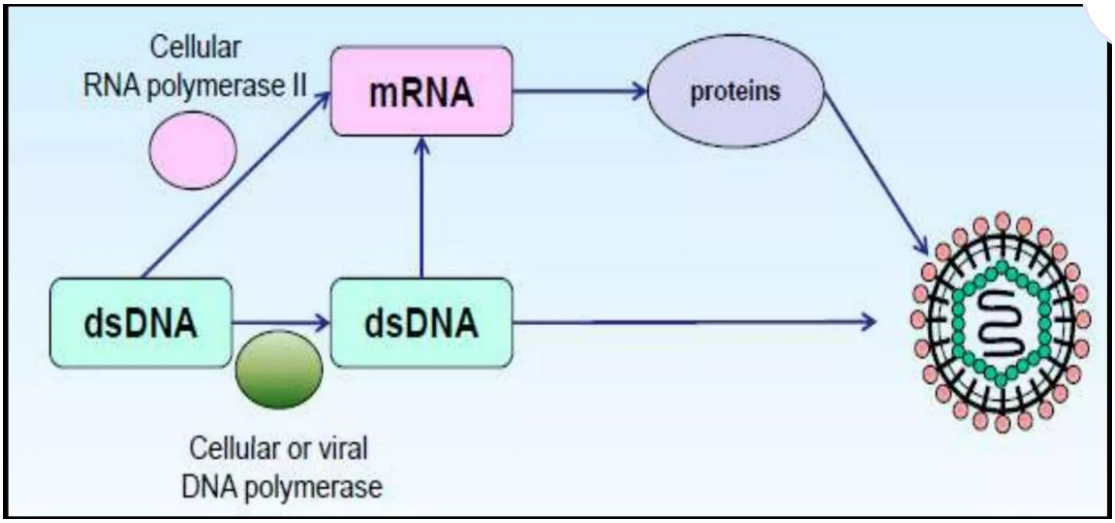
3. Uncoating

- This step occurs concurrently with or shortly after penetration and involves the **physical separation of the viral nucleic acid from the outer structural components** of the virion so that the genome can become active.
- The genome may be released as **free nucleic acid** (e.g., picornaviruses) or as a **nucleocapsid** (e.g., reoviruses).
- Uncoating sometimes requires an **acidic pH** within the endosome.
- The **infectivity of the parental virus is lost** at this stage, making viruses unique infectious agents for which dissolution of the infecting particle is an obligatory part of replication.

4. Expression of Viral Genomes and Synthesis of Viral Components.

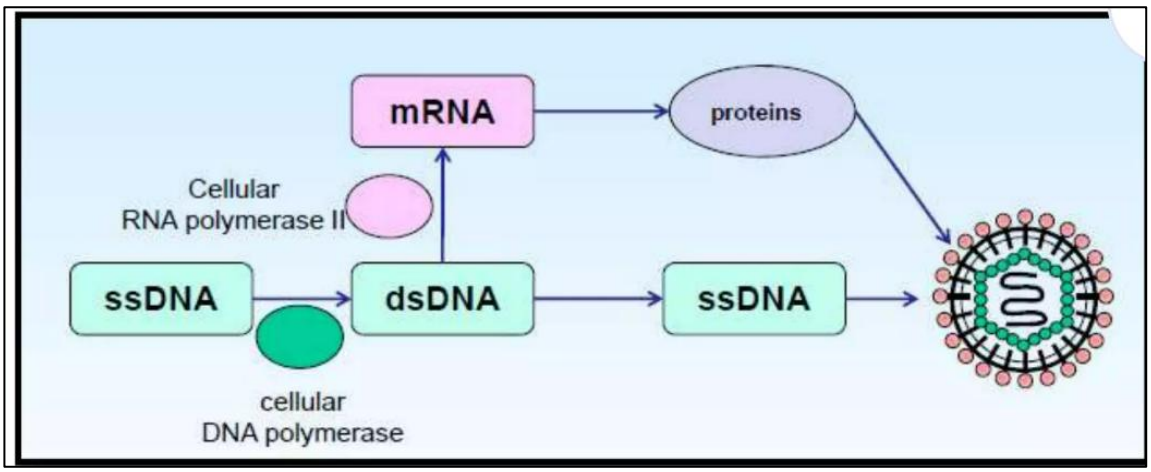
Class I: Double-stranded DNA (dsDNA) viruses

- **Genome:** dsDNA.
- **Replication strategy:** These viruses replicate and transcribe their genes using the host cell's machinery, following the same pathway as the host cell's own DNA. Replication typically occurs in the nucleus, though poxviruses are a notable exception, replicating entirely in the cytoplasm.
- **Examples:** Adenoviruses, herpesviruses, poxviruses.



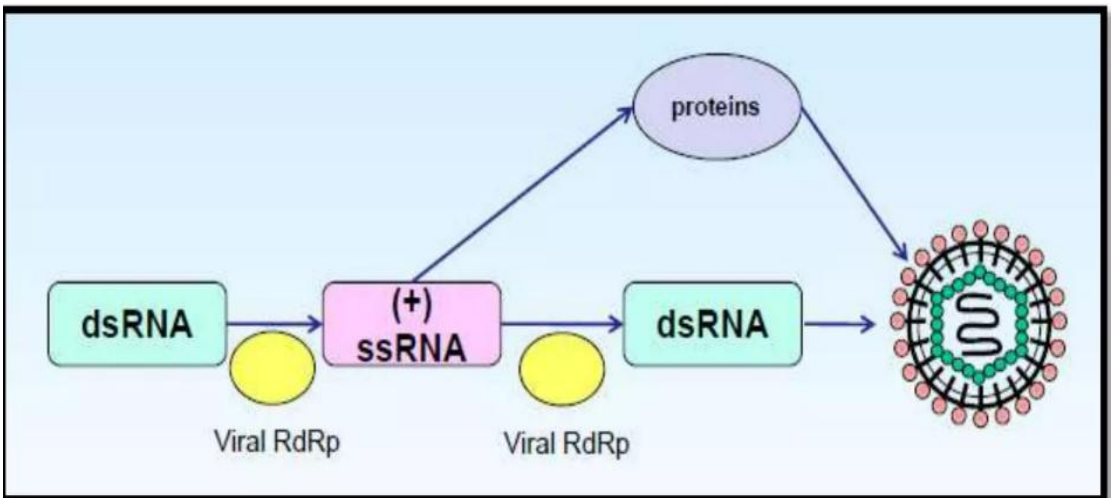
Class II: Single-stranded DNA (ssDNA) viruses

- **Genome:** ssDNA, typically positive-sense (+).
- **Replication strategy:** The ssDNA genome must first be converted into a double-stranded DNA intermediate by the host's enzymes. This intermediate is then transcribed to create viral mRNA.
- **Examples:** Parvoviruses.



Class III: Double-stranded RNA (dsRNA) viruses

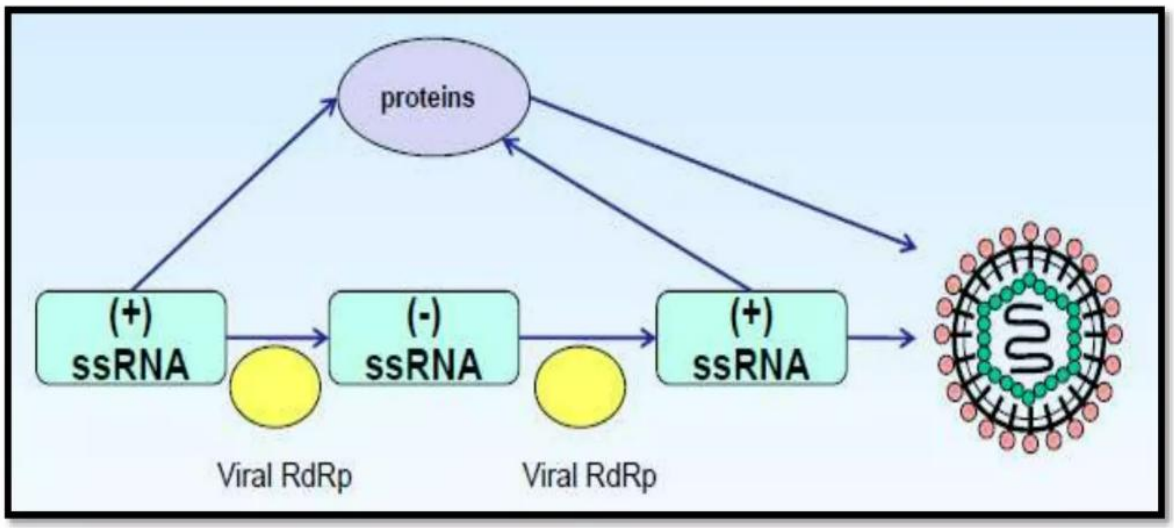
- **Genome:** dsRNA, often segmented.
- **Replication strategy:** Because host cells lack the enzymes to transcribe RNA from an RNA template, these viruses carry their own RNA-dependent RNA polymerase (RdRp). The dsRNA genome is used as a template to make viral mRNA.
- **Examples:** Rotaviruses.



Class IV: Positive-sense single-stranded RNA (+ssRNA) viruses

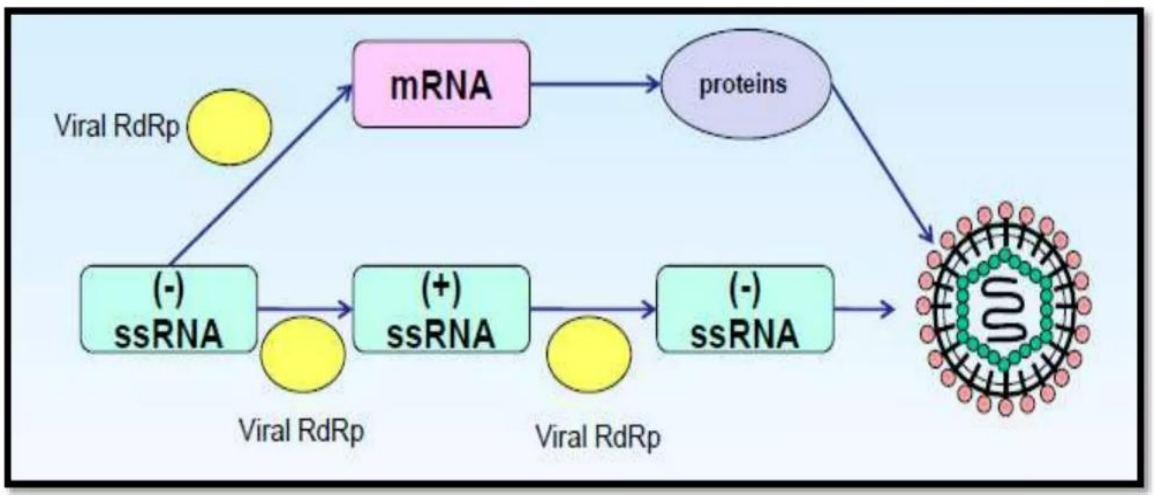
- **Genome:** +ssRNA.
- **Replication strategy:** The viral RNA genome can be directly translated by host ribosomes into proteins, including an RdRp. This new polymerase then creates a negative-sense RNA template, which is used to make more +ssRNA genomes and mRNA.

- **Examples:** Coronaviruses, poliovirus.



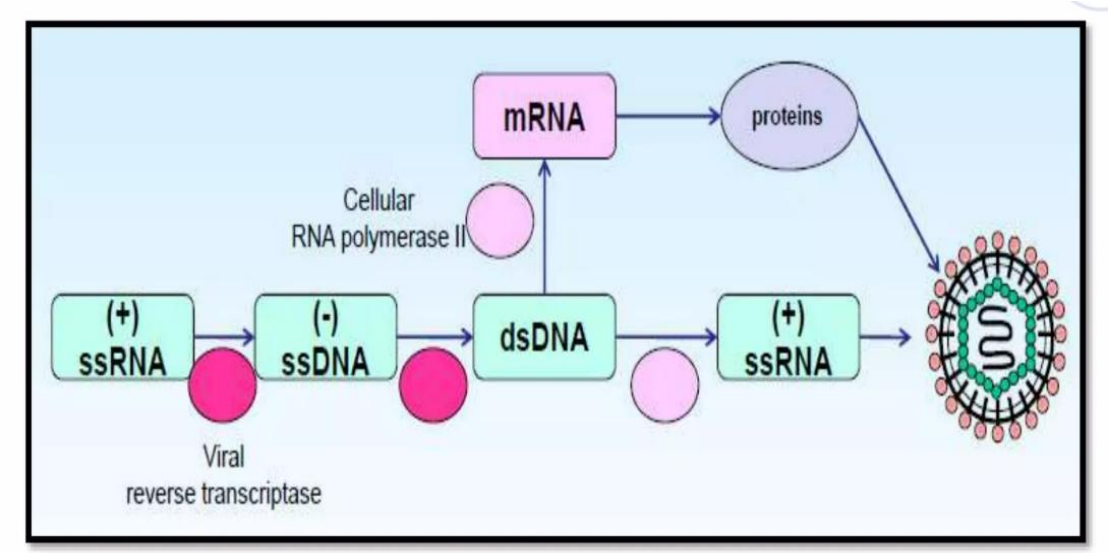
Class V: Negative-sense single-stranded RNA (-ssRNA) viruses

- **Genome:** -ssRNA, which cannot be directly translated.
- **Replication strategy:** These viruses also carry their own RdRp within the virion. The RdRp first transcribes the -ssRNA genome into a complementary +ssRNA strand, which serves as both the mRNA for protein synthesis and the template for creating new -ssRNA genomes.
- **Examples:** Influenza viruses, rabies virus, Ebola virus.



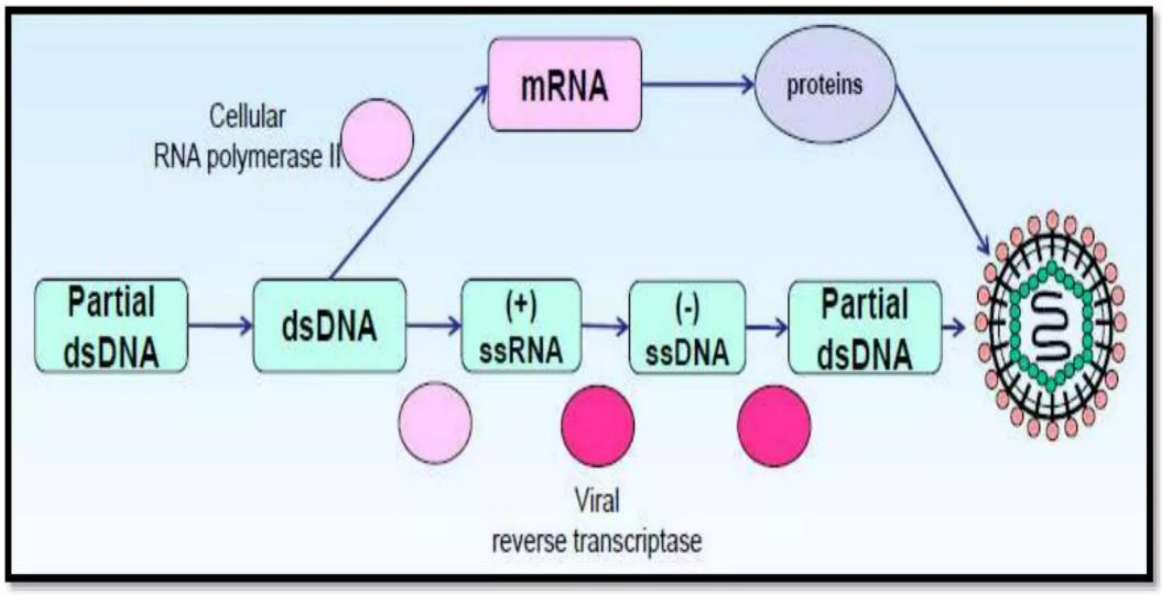
Class VI: Single-stranded RNA reverse-transcribing ((+) ssRNA-RT) viruses

- **Genome:** +ssRNA.
- **Replication strategy:** Using a virion-associated reverse transcriptase enzyme, the viral RNA is reverse-transcribed into dsDNA. This dsDNA is then integrated into the host cell's genome. The host's machinery then transcribes the integrated DNA to produce new viral RNA.
- **Examples:** HIV (a retrovirus)



Class VII: Double-stranded DNA reverse-transcribing (dsDNA-RT) viruses

- **Genome:** Partially double-stranded DNA with a single-stranded gap.
- **Replication strategy:** The viral genome is repaired to become a complete, circular dsDNA molecule. The host's machinery transcribes this DNA into an RNA intermediate, which is then reverse transcribed by a viral enzyme to produce new viral DNA genomes.
- **Examples:** Hepatitis B virus (a Hepadnavirus).



5. Assembly and release: The progeny particles are assembled by packaging the viral nucleic acid within the capsid proteins.

Virus particles are released from the cell by either of two processes:

1. Nonenveloped Viruses

- These viruses tend to **accumulate** inside the infected host cell.
- They are released when the infected cell eventually undergoes **lysis** (breaks open).

2. Enveloped Viruses

- These viruses mature and are released via a process called **budding**.

Maturation Steps:

1. **Glycoprotein Insertion:** Virus-specific envelope glycoproteins are inserted into the host cell's membrane (e.g., plasma membrane or internal membranes).
2. **Budding:** The viral nucleocapsid moves to these modified membrane sites and pushes through (**buds**) the membrane, thereby acquiring an outer **envelope**.

- **Infectivity:** Enveloped viruses are **not infectious** until they have acquired their envelope.
- **Accumulation:** Infectious progeny virions typically **do not accumulate** within the infected cell because they are released immediately upon budding.