#Microbiology

Prescott's MICROBIOLOGY

ELEVENTH EDITION

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Chapter 26

Viruses

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Classification

Virus Classification

Classification based on numerous characteristics.

- Nucleic acid type.
- Presence or absence of envelope.
- Capsid symmetry
- Dimensions of virion and capsid.

Viral mRNA	5′...GAC UCG AGC...3′
Plus-strand RNA	5′...GAC UCG AGC...3′
Negative-strand RNA	3′...CUG AGC UCG...5′
Plus-strand DNA	5′...GAC TCG AGC...3′
Negative-strand DNA	3′...CTG AGC TCG...5′

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Baltimore System of Classification

Focuses on viral genome and process used to synthesize viral mRNA.

7 life cycle groups:

- Double-stranded (ds) DNA viruses.
- Single-stranded (ss) DNA viruses.
- dsRNA viruses.
- Plus-strand ssRNA viruses.
- Negative-strand ssRNA viruses.
- Retroviruses.
- Reverse transcribing DNA viruses.

Some of the Bacterial + Archaeal phages ⇒ Ds DNA.

Double-Stranded DNA Viruses

Largest group of known viruses.

Most bacteriophages and archaeal viruses.

Important vertebrate viruses.

- Herpesviruses, poxviruses.

Insect viruses.

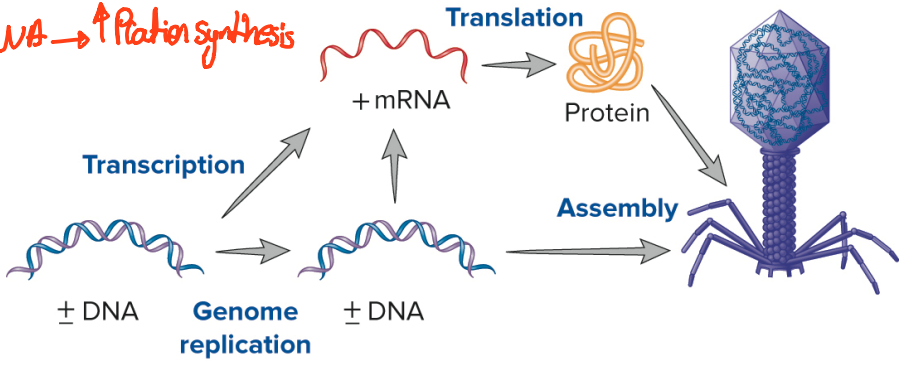
Many can rely on host's DNA/RNA polymerases.

5' ——— 3'

3' ——— 5'

Hijack eukaryotic cells using the enzymes required for the machinery.

↑ Replication → ↑ mRNA → ↑ Protein synthesis



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T4 life cycle:

Bacteriophage T4: A Virulent Bacteriophage

Bacteriophages that infect E.coli

the virus replicate it's Genetic Material and lyse the cell when it goes out.

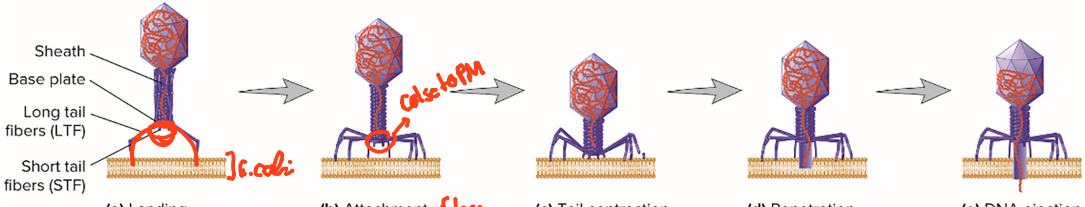
Phage life cycle culminates with host cell bursting, releasing virions.

Steps.

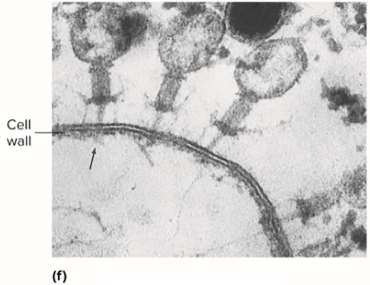
- (1) Adsorption to receptor on *E. coli* outer membrane.
- (2) Baseplate settles down on the surface.
- (3) Baseplate and sheath change shape; tail sheath (4) shortens.
- (5) Central tube pierces the cell wall.
- (6) Viral nucleic acid is injected into host cell through (7) tube.

DNA RNA

T4 Phage Adsorption and DNA Entry



Attachment begins when one or two LTFs contact the cell surface reversibly. This allows the virion to "walk" to locate its preferred surface site. As more LTFs contact the surface, the STFs extend downward. Interaction between STFs and their receptors is irreversible and the virion is now committed to attachment. The baseplate settles onto the cell surface.	After the baseplate is firmly seated, it expands to create a central hole and the tail sheath contracts and shortens. These movements push the central tube through the outer membrane.	Baseplate protein gp5 is released into the periplasm, where its lysozyme activity is needed for further movement through the cell wall. Another protein, gp29, plays two roles. It connects the baseplate to the sheath, and when these structures change shape upon irreversible binding, gp29 travels to the plasma membrane to form a transmembrane channel through which DNA is ejected.



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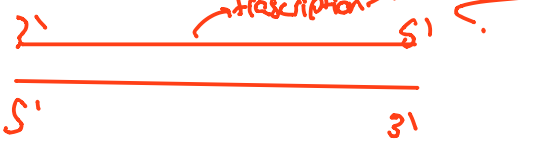
Bacteriophage T4 Life Cycle



Transcription → early mRNA.

- Results in production of viral encoded DNA-dependent DNA polymerase.

Viral DNA bidirectional replication begins at origins.

Transcription → late mRNA.

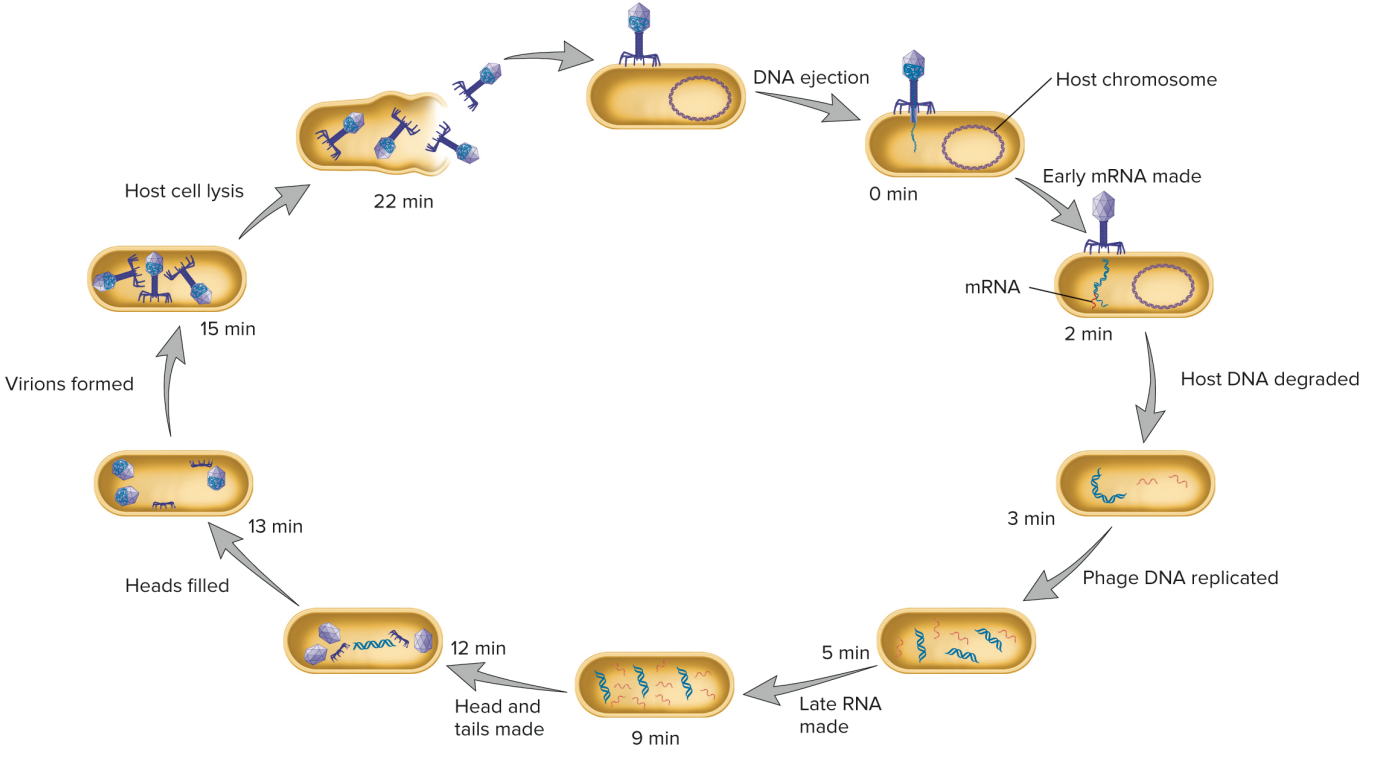
- Translation of capsid and lysis proteins.

Temporal transcription regulated by:

- Alternative *E. coli* polymerase factors induced by virus.
- Early viral gene products stimulate transcription of some late viral genes.
- Genes with related functions are usually separated and clustered together.

double stranded DNA

Life Cycle of Bacteriophage T4



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Regulatory Proteins Determine Lysogeny or the Lytic Cycle

Function as repressors, activators, or both.

- Regulate transcription, termination, and antisense RNA molecules.
- cII activator plays pivotal role in determining if λ will establish lysogeny or the lytic cycle.
  - cII levels high early in infection—lysogeny.
  - cII levels not high early in infection—lytic cycle.

Eukaryotic Viruses—Herpesviruses

1. Herpes simplex virus I and II—cold sores and genital herpes, respectively.
2. Varicella zoster virus—chicken pox, shingles.
3. Epstein–Barr virus—infectious mononucleosis, some cancers.

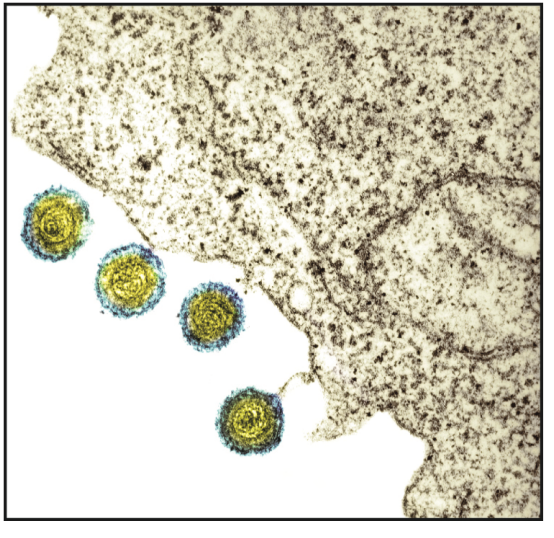
Cytomegalovirus.

HHV 6 and HHV 7—infect children.

HHV 8—Kaposi's sarcoma in AIDS patients.

Herpesvirus Virions

- Icosahedral, 150 to 200 nm, pleomorphic, enveloped, surface spikes.
- Envelope surrounds tegument (layer of proteins) which surrounds nucleocapsid.
- Linear genomes encode 70 to over 200 proteins.
- Targets are epithelial or nerve cells.



Herpesvirus Infections

1. Productive (primary) infections. → Main Symptoms

- Virus multiplies explosively—50,000 to 200,000 virions produced from each infected cell.
- Cell dies due to degraded DNA.

2. Latent infections.

- Infectious virus not detected.
- Can be reactivated in host cells.
- Productive infection.
- Viral genome remains in the host cell after reactivation; recurs.

enters the cell and use their enzymes → DNA depended Polymerase

Herpesvirus Productive Infection

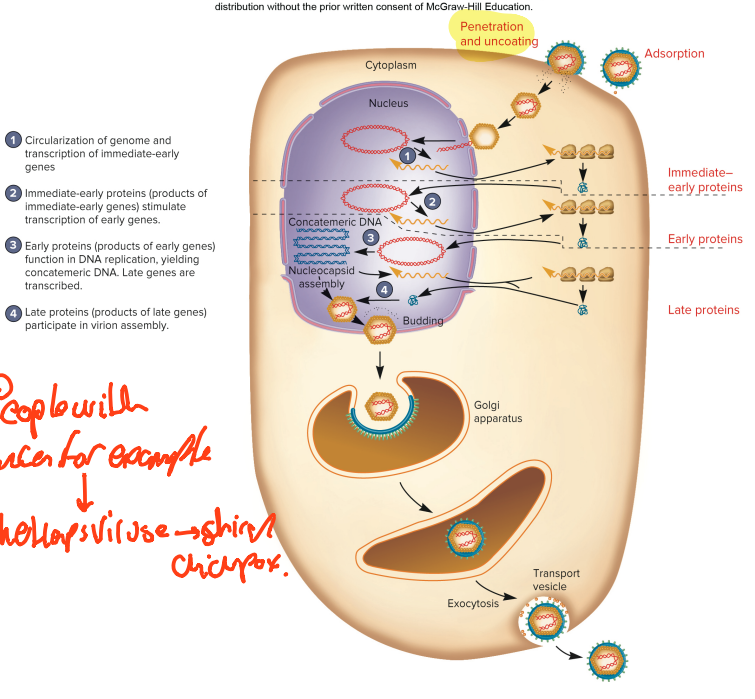
Lelytic infection

Receptor mediated attachment.

Virus envelope fuses with host cell membrane.

Linear dsDNA enters nucleus, circularizes.

- Immediate early and early proteins made—used for viral DNA replication.
- Late gene transcription—viral structural proteins.



People with cancer for example
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Herpesvirus → shingles chickenpox.

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Herpesvirus Productive Infection—Assembly and Release

Nucleocapsid assembles and leaves nucleus.

Tegument proteins associate with nucleocapsid.

Virus envelope is generated by Golgi apparatus or endosomes.

Mature enveloped virion leaves cell.

Herpesvirus Latent Infection

In epithelial cells:

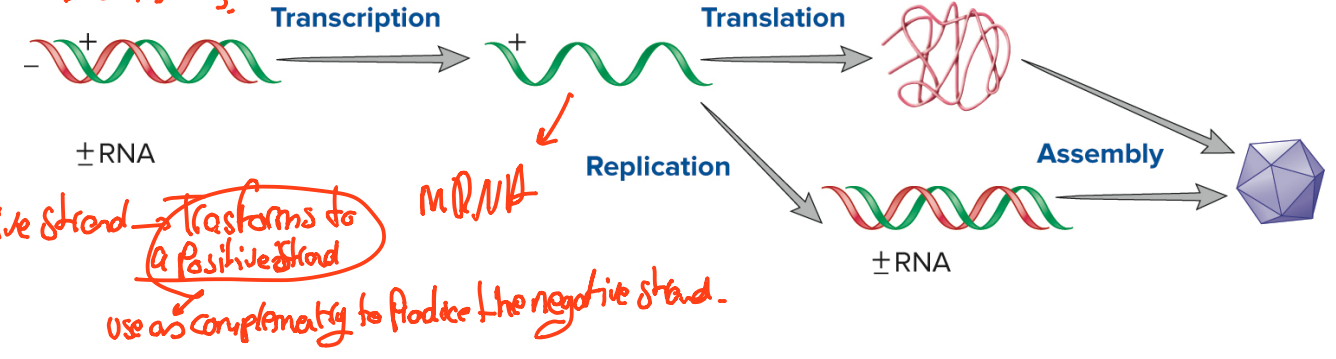
- Viral protein 16 (VP16) and host cell factor 1 (HCF-1) enter nucleus with the viral genome.
- Both required for full expression of immediate early genes and lytic infection.

In neurons, where virus is latent:

- HCF-1 is cytoplasmic.
- Small noncoding RNAs (microRNAs) act to repress the viral lytic cycle.
- Inhibition of early gene expression helps establish latency.
- During reactivation, HCF-1 moves to the nucleus and VP16 is produced.

RNA Viruses → need RNA dependent - RNA Polymerase.

Reproduction of RNA Phages



RNA genomes cannot rely on host cell enzymes for genome replication or mRNA synthesis.

RNA-dependent RNA polymerase completes life cycles.

- Replicase and transcriptase activities.

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Rotavirus

Human rotavirus kills >200,000 children worldwide each year.

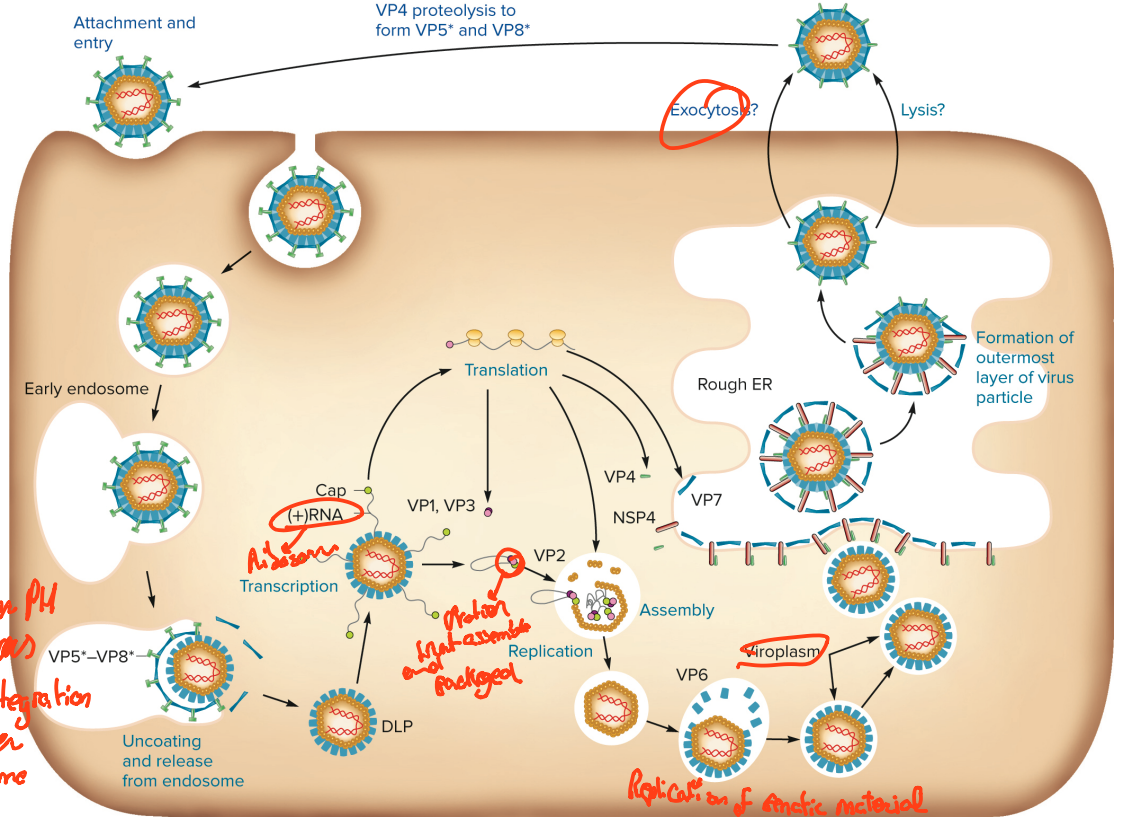
- Causes severe diarrhea resulting in dehydration.

Virion has wheel-like appearance, nonenveloped, segmented genome, dsRNA, three concentric layers of proteins.

Virus loses outer layer of protein when it enters host cell —double-layered particle (DLP).

- mRNA transcription, translation.
- Proteins form inclusion called viroplasm.
- RNA genome replication occurs here.
- Third layer added in ER.

Rotavirus Life Cycle



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Plus-Strand RNA Viruses

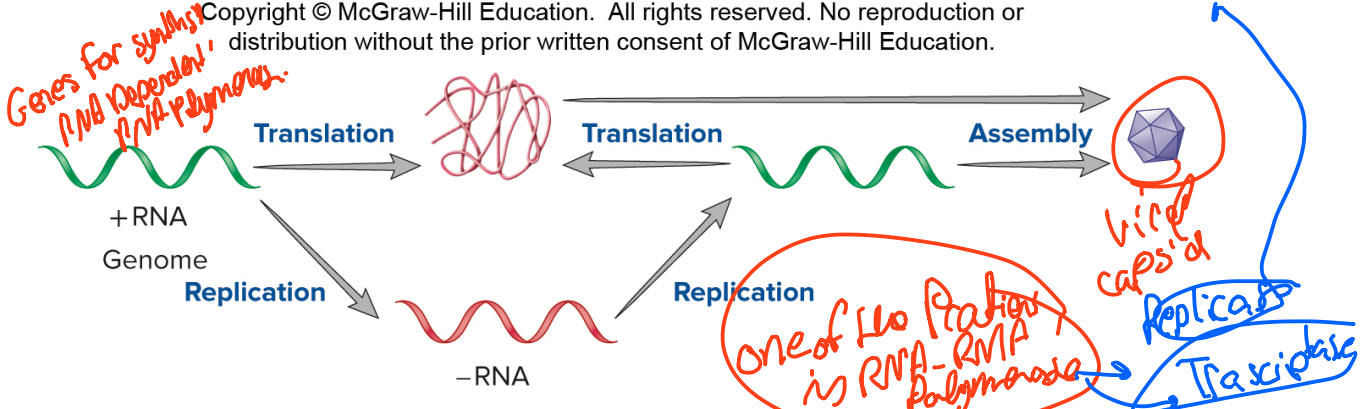
Nonsegmented plus-strand RNA genomes.

Replicate in cytoplasm and synthesize RNA-dependent RNA polymerase.

- Synthesizes negative-strand RNA.

Replication complex for assembly.

- Derived from different cell organelles.



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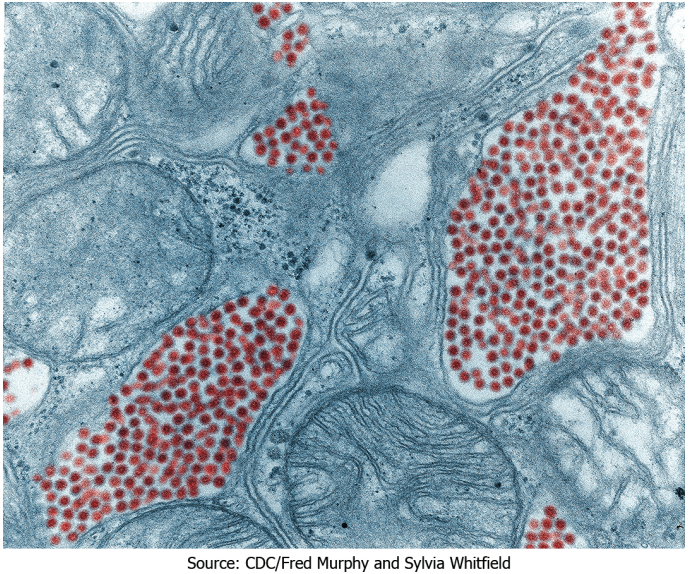
Medically Important Positive-Strand Animal Viruses

Poliovirus.

Zika virus.

Eastern equine encephalitis virus.

Hepatitis A virus.



Source: CDC/Fred Murphy and Sylvia Whitfield

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Poliovirus Life Cycle

Causative agent of poliomyelitis.

- Transmitted by ingestion.
- May cripple and paralyze.
- Vaccine is eradicating the disease.

Virion.

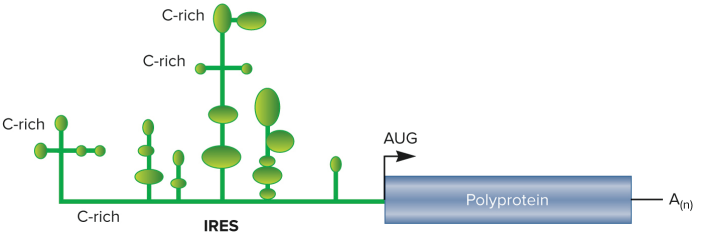
- Nonenveloped.

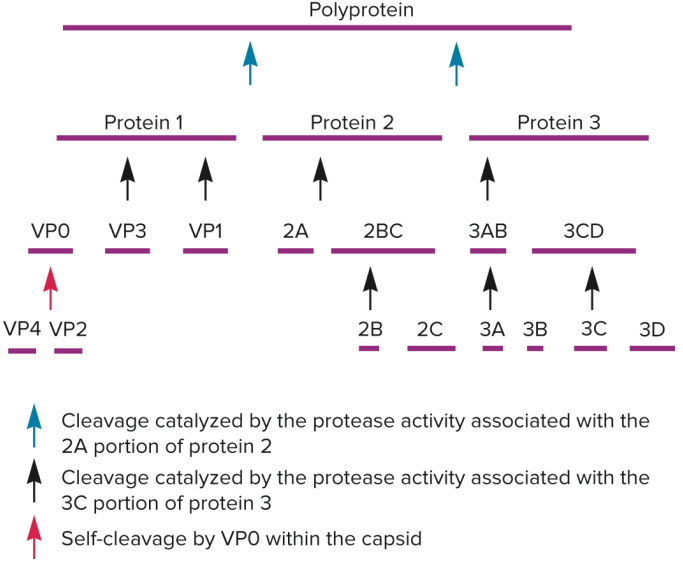
Poliovirus Genome

Attaches to CD155, found on certain white blood cells and neurons of the CNS.

Viral genome acts as mRNA.

- Virus uses internal ribosome entry site (IRES) instead of 5′ cap.
- Polyprotein translated, cleaves itself into small proteins.
- Genomic RNA synthesized.
- Assembly, lysis.





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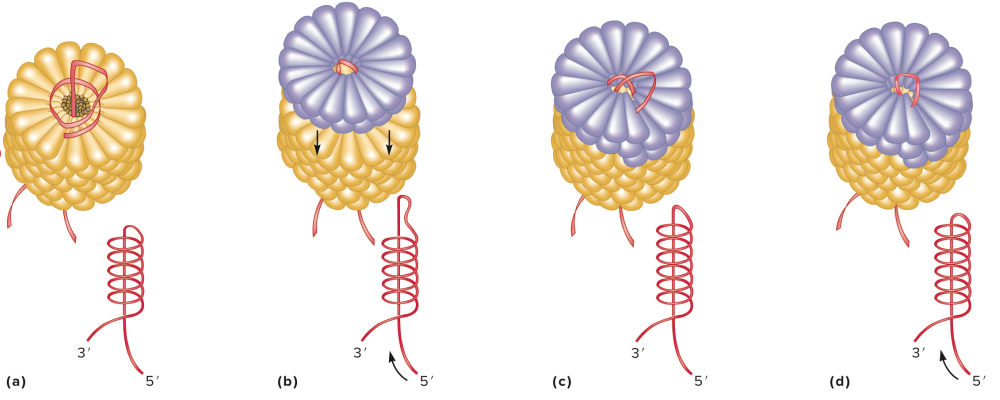
Tobacco Mosaic Virus (TMV)



Most plant viruses are plus-stranded RNA, enter host through abrasion, wound.

TMV.

- Filamentous, helical virion.
- TMV genome translated into two proteins, one with replicase and transcriptase activities.
- Synthesis of coat protein and genome.
- Self-assembly highly organized process.

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Plant Viruses

Movement depends on virus's ability to spread throughout plant.

- Travel in phloem (vasculature).
- Move cell to cell through plasmodesmata.
- Requires viral "movement proteins"—transfer through plasmodesmata.

Minus-Strand RNA Viruses

Enveloped virions.

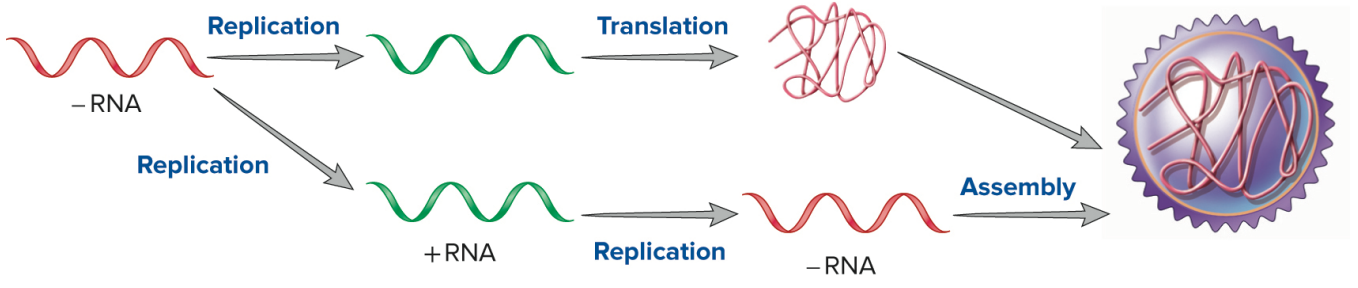
Vary in morphology from spherical, to filamentous, rod-shaped, bullet-shaped, and pleomorphic.

Segmented and nonsegmented genomes.

Minus-sense RNA virus families and examples:

- *Rhabdoviridae*—rabies virus.
- *Filoviridae*—Ebola virus.
- *Paramyxoviridae*—measles and mumps virus.
- *Orthomyxoviridae*—influenza virus.

Negative-Strand Viruses



Cannot serve as mRNA to form viral proteins.

Must bring into cell preformed RNA-dependent RNA polymerase.

- New plus-strand intermediates are synthesized.
- The newly synthesized plus-strand serves as template for genome synthesis and mRNA as well.

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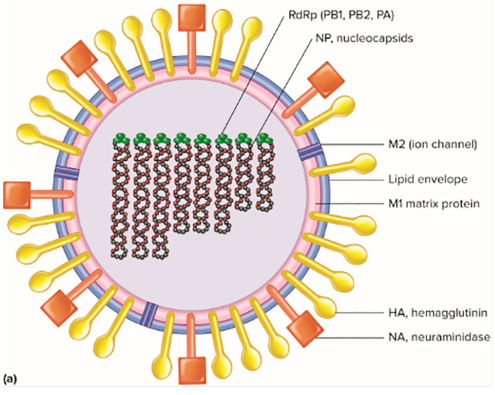
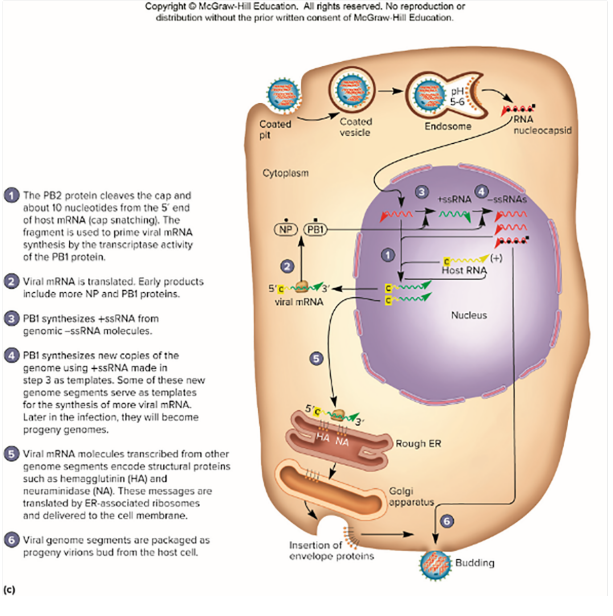
Influenza Virus Life Cycle





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(b) Source: CDC/Fred Murphy, Cynthia Goldsmith, Dr. Erskine

Influenza Virus

Virion contains seven or eight nucleocapsids.

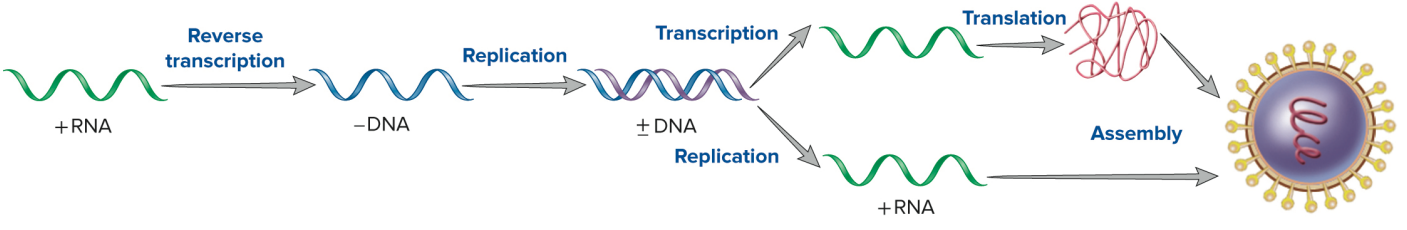
Enters in endosome.

- Low pH causes conformational change in hemagglutinin protein—hydrophobic ends swing outward, membranes fuse; nucleocapsid released.

Genome template for genome synthesis and mRNA synthesis.

Virus buds from host cell acquiring envelope.

Retroviruses



Convert ssRNA into dsDNA using reverse transcriptase.

dsDNA integrates into host cell genome and serves as template for mRNA synthesis and genome synthesis.

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Retroviruses—HIV

Human immunodeficiency virus (HIV).

- Cause of acquired immunodeficiency syndrome (AIDS).
- Globally important pandemic.

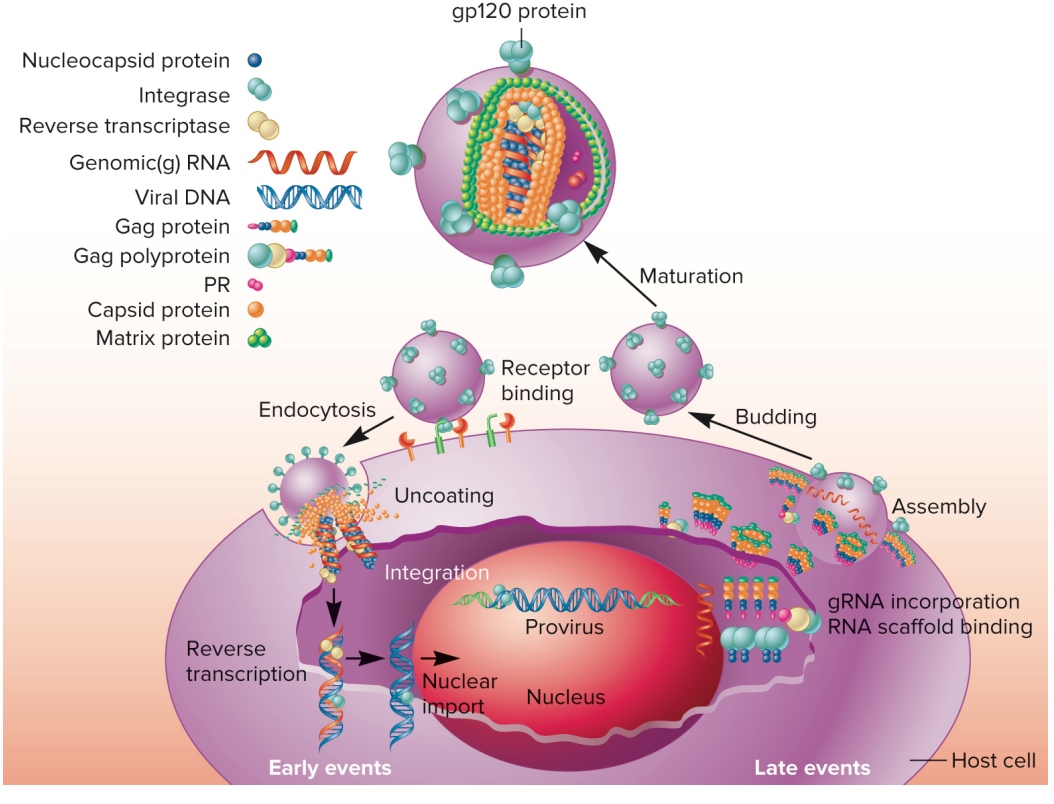
Member of genus *Lentivirus*.

- HIV-1 (most common cause of AIDS in US), HIV-2 (common in developing nations).

HIV-1—enveloped virus.

- Two copies of RNA genome.
- Reverse transcriptase and integrase.

HIV Life Cycle



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HIV—Initial Infection

gp120 binds CD4+ T cells, macrophages, dendritic cells, and monocytes.

- Coreceptor (which can vary) also required to gain entry into cell.
- Virus may enter by viral envelope fusion with the plasma membrane and by endocytosis.

Reverse transcriptase.

- RNA-dependent DNA polymerase.
- DNA-dependent DNA polymerase.
- Ribonuclease.
- Error prone, has no proofreading capability.

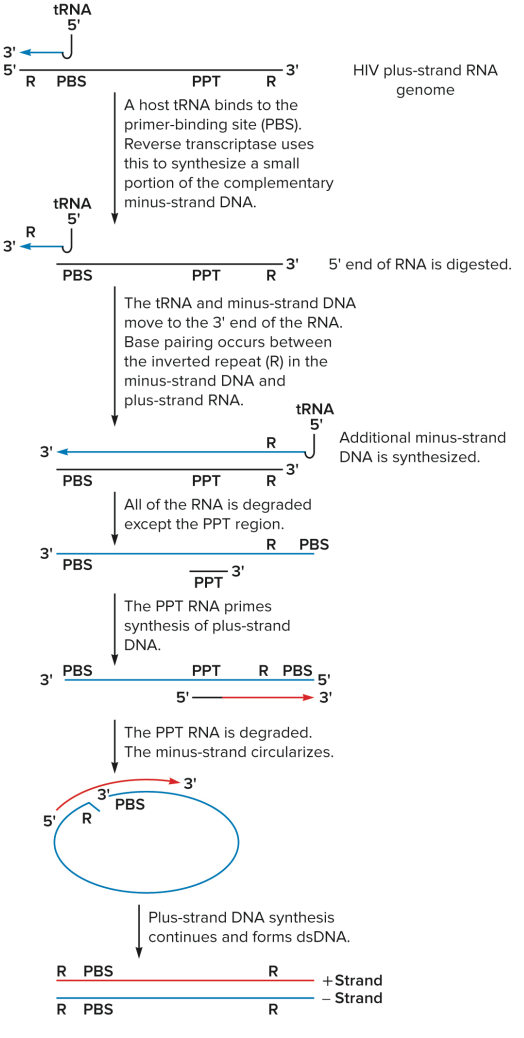
HIV Life Cycle—Middle Steps and Genome Synthesis

Host tRNA molecule is used as a primer.

Small negative-strand DNA molecule is transferred from one end of the RNA template to the other to prime minus-strand synthesis.

Full-length minus-strand circularizes.

dsDNA is formed.



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HIV Life Cycle—Synthesis, Assembly, Release

dsDNA is moved to the nucleus.

- Integrase and other proteins integrate proviral DNA.
- Forces cell to synthesize viral mRNA.
- Splicing forms 10 viral transcripts.

Cleavage forms viral proteins.

Assembly and budding occurs.

Eventually cell dies.

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