VIRUS STRUCTURE

&

REPLICATION

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What are viruses?

- **Small obligate intracellular parasites**
- **Virion**
  - Complete virus particle : nucleic acid + protein coat, which **may** be surrounded by an envelope
  - It is the form in which the virus moves between cells or hosts
- **Viral Genome**
  - EITHER RNA or DNA genome surrounded by a protective virus-coded protein coat (Capsid)
- **Propagation depends on specialized host cells supplying the machinery for replication, metabolism and biosynthesis**

Configuration of Virus

- **The DNA or RNA genome may be :**
  - ss – single stranded or
  - ds – double stranded
- Genomes may be either:
  - (+) sense: Positive-sense viral RNA is identical to viral mRNA and thus can be immediately translated into protein by the host cell.

    OR
  - (-) sense: Negative-sense viral RNA is complementary to mRNA and thus must be converted to positive-sense RNA by an RNA polymerase before translation.

- **Retroviruses?**

Viral Structure - Overview

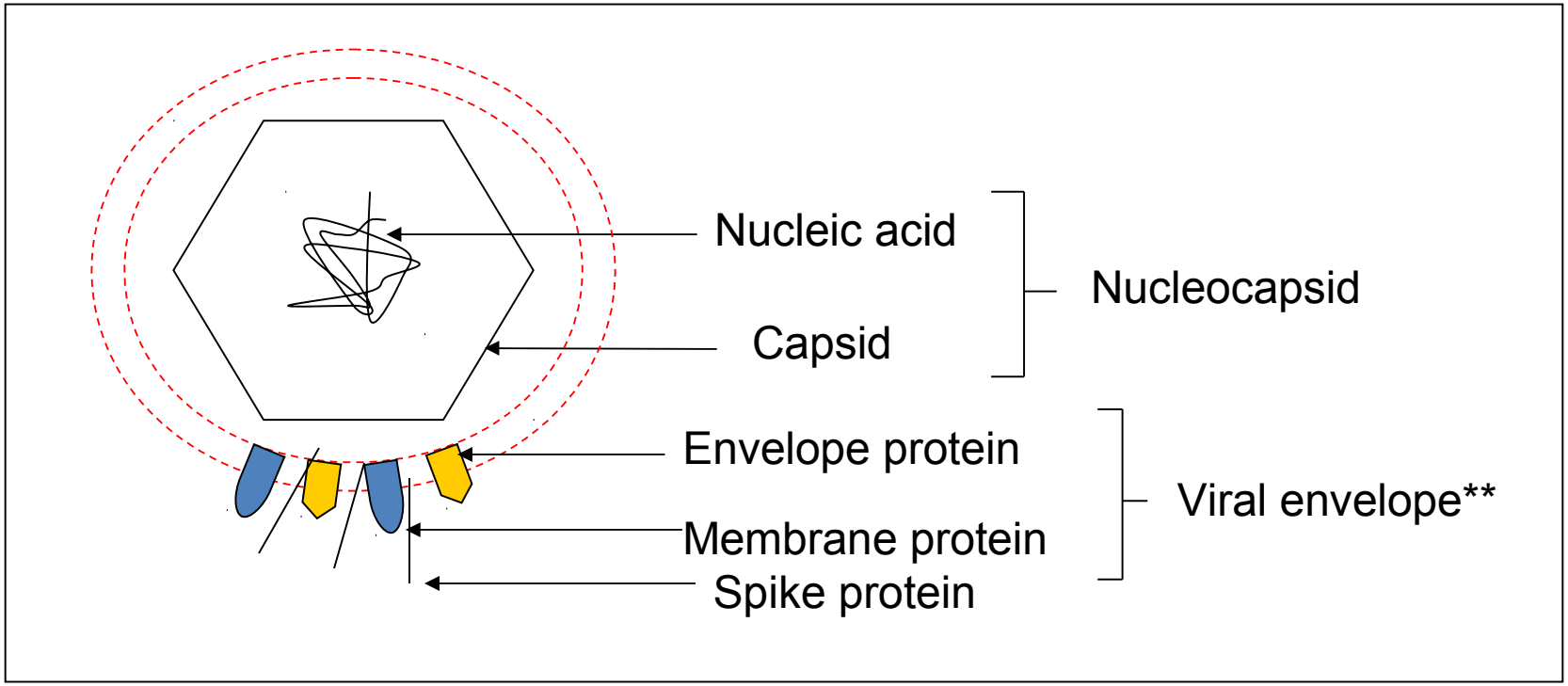
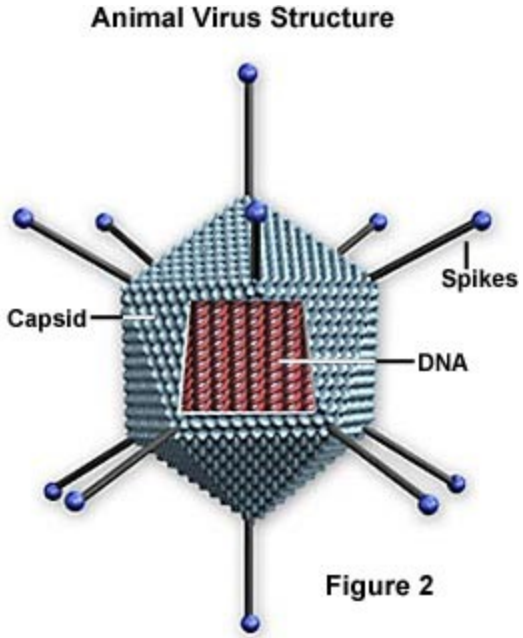
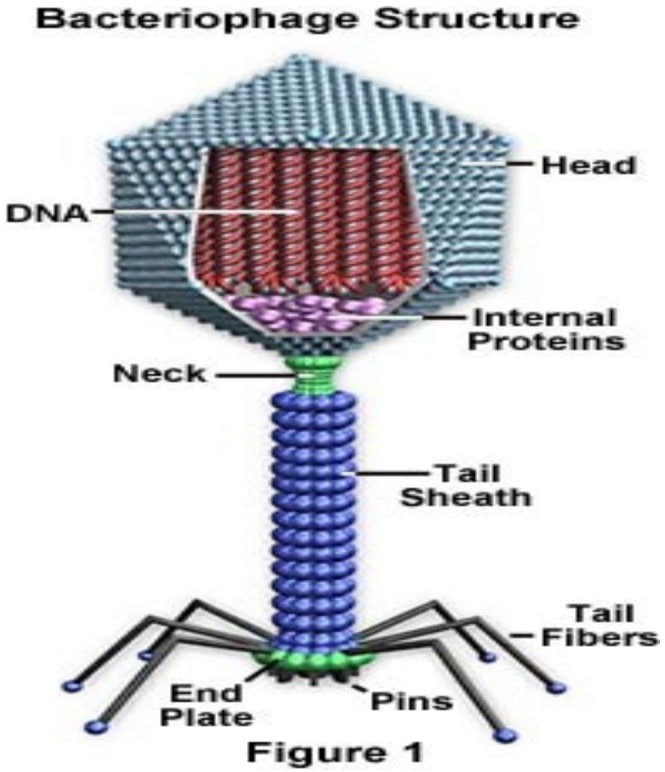


Fig 1. Schematic overview of the structure of animal viruses

** does not exist in all viruses

Bacteriophages





http://micro.magnet.fsu.edu/cells/virus.html

Viroids & Prions

- Viroids
  - ss RNA genome and the smallest known pathogens.
  - Affects plants
- Prions
  - Infectious particles that are entirely protein.
  - No nucleic acid
  - Highly heat resistant
  - Animal disease that affects nervous tissue
  - Affects nervous tissue and results in
    - Bovine spongiform encephalitis (BSE) “mad cow disease”,
    - Scrapie in sheep
    - kuru & Creutzfeldt-Jakob Disease (CJD) in humans

Viral Structure

- Varies in size, shape and symmetry
- VIP for classification
- 3 types of capsid symmetry:
  - Cubic (icosahedral)
    - Has 20 faces, each an equilateral triangle. Eg. adenovirus
  - Helical
    - Protein binds around DNA/RNA in a helical fashion eg. Coronavirus
  - Complex
    - Is neither cubic nor helical eg. poxvirus

Viral Structure

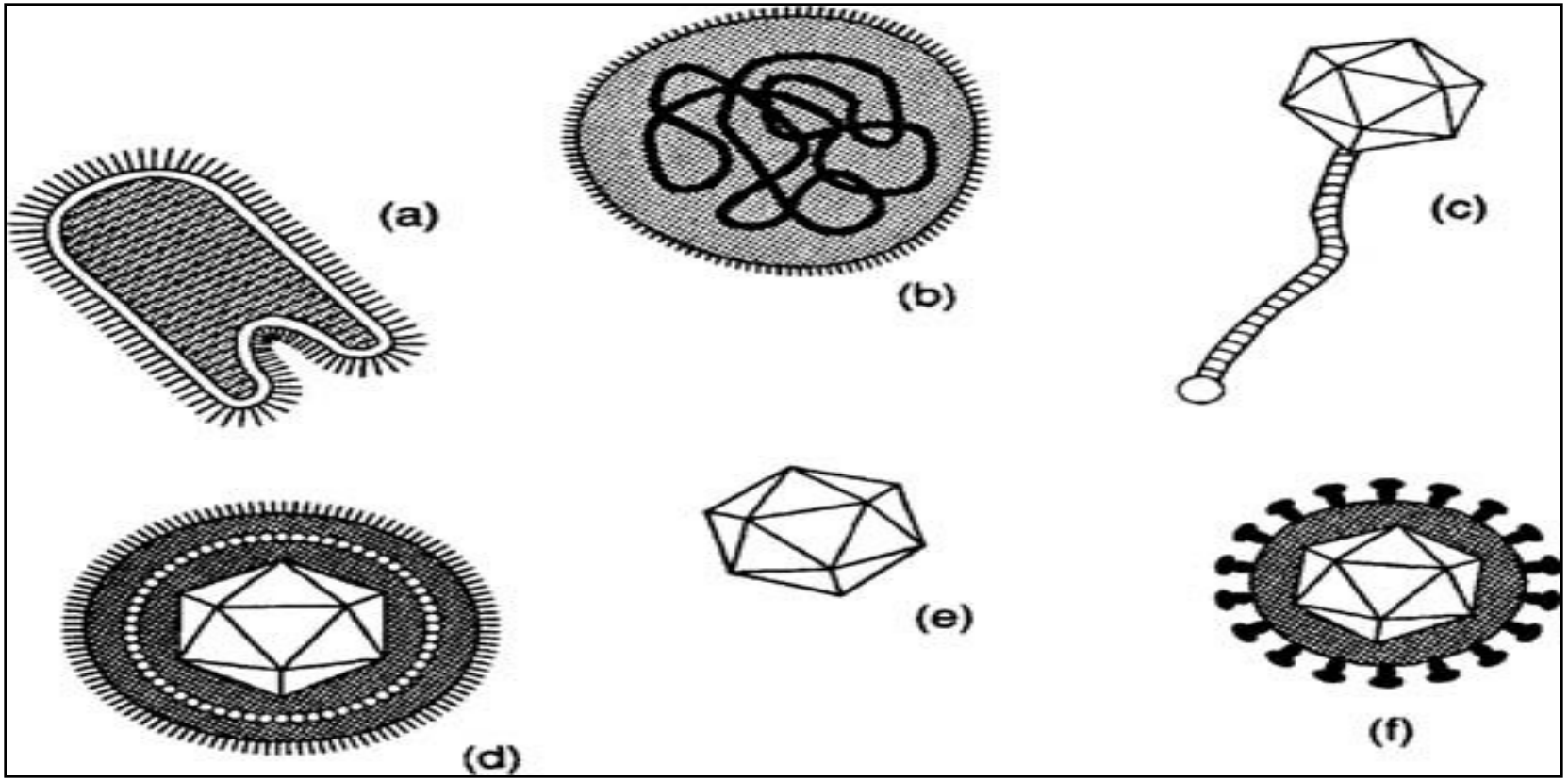
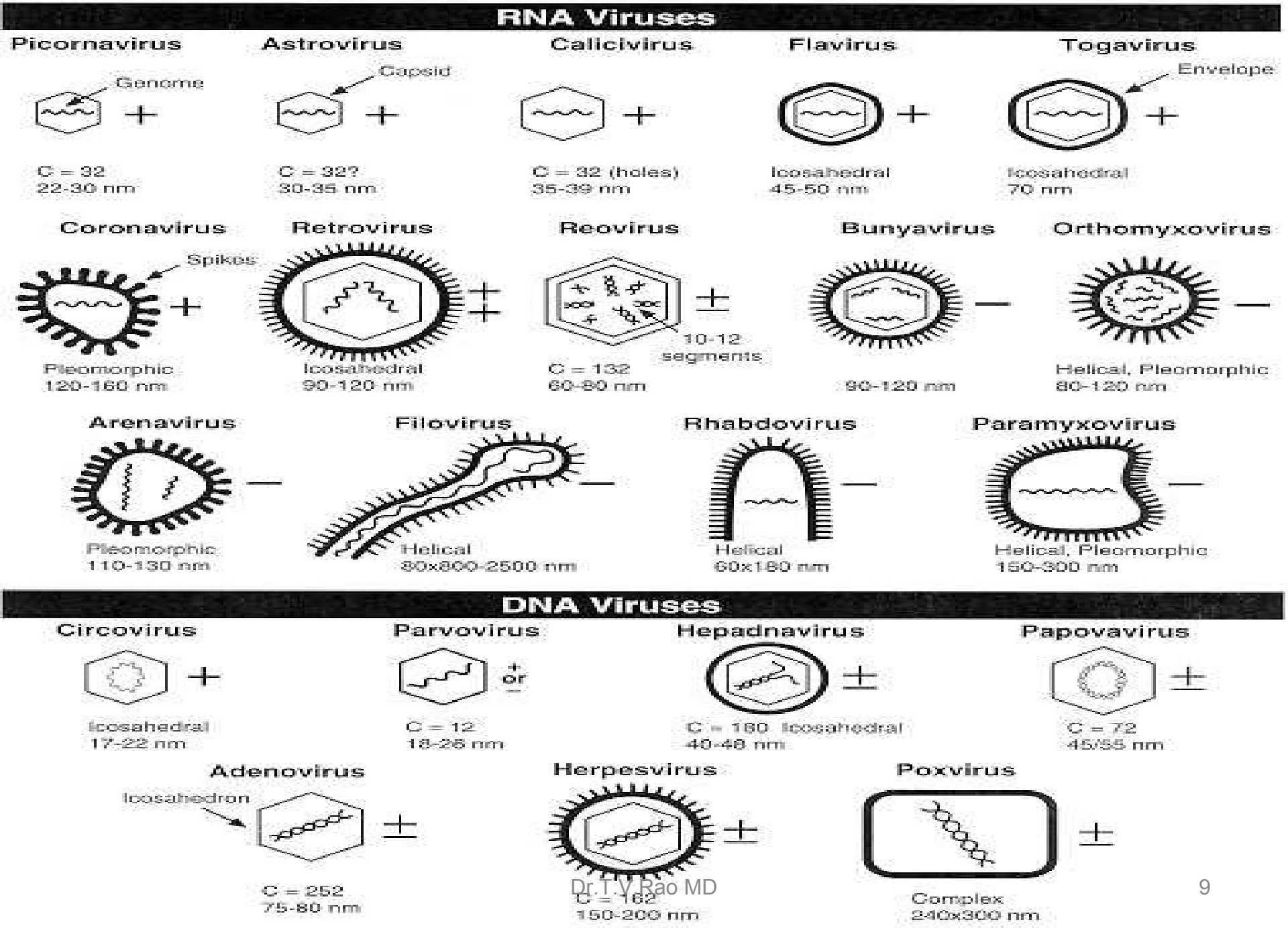


Figure 1 *An array of viruses. (a) The helical virus of rabies. (b) The segmented helical virus of influenza. (c) A bacteriophage with an icosahedral head and helical tail. (d) An enveloped icosahedral herpes simplex virus. (e) The unenveloped polio virus. (f) The icosahedral HIV with spikes on its envelope*.


RNA Viruses
Picornavirus
Genome
+
C = 32
22-30 nm
Astrovirus
Capsid
+
C = 32?
30-35 nm
Calicivirus
+
C = 32 (holes)
35-39 nm
Flavirus
+
Icosahedral
45-50 nm
Togavirus
Envelope
+
Icosahedral
70 nm
Coronavirus
Spikes
+
Pleomorphic
120-160 nm
Retrovirus
++
Icosahedral
90-120 nm
Reovirus
±
10-12 segments
C = 132
60-80 nm
Bunyavirus
—
90-120 nm
Orthomyxovirus
—
Helical, Pleomorphic
80-120 nm
Arenavirus
—
Pleomorphic
110-130 nm
Filovirus
—
Helical
80x800-2500 nm
Rhabdovirus
—
Helical
60x180 nm
Paramyxovirus
—
Helical, Pleomorphic
150-300 nm
DNA Viruses
Circovirus
+
Icosahedral
17-22 nm
Parvovirus
+ or —
C = 12
18-26 nm
Hepadnavirus
±
C = 180 Icosahedral
40-48 nm
Papovavirus
±
C = 72
45/55 nm
Adenovirus
Icosahedron
±
C = 252
75-80 nm
Herpesvirus
±
C = 162
150-200 nm
Poxvirus
±
Complex
240x300 nm

Definitions

- **Bacteriophage**
  - Virus that infects prokaryotic (bacterial) cells.
- **Nucleocapsid:**
  - viral nucleic acid + the protein coat that encloses it.
  - Represents the packaged form of the viral genome.

Viral Replication

- Viruses are **intracellular obligate parasites** which means that they cannot replicate or express their genes without the help of a living cell. A single virus particle (Virion) is in and of itself essentially inert. It lacks needed components that cells have to reproduce. When a virus infects a cell, it marshals the cell's ribosomes, enzymes and much of the cellular machinery to replicate.

Progress of Viral Multiplication

- Once a virus infects its host and the viral progeny components are produced by the host's cellular machinery, the assembly of the viral capsid is a non-enzymatic process. It is usually spontaneous. Viruses typically can only infect a limited number of hosts (also known as host range). The "lock and key" mechanism is the most common explanation for this range. Certain proteins on the virus particle must fit certain receptor sites on the particular host's cell surface.

Viral Replication

- When a virus infects a cell, nucleic acid must be uncoated and gain access to metabolic machinery of cell.
- Virus life cycle is characterized by:
  - **attachment**
  - **penetration**, with entry of nucleic acid into cell
  - **early expression of virus genes** (either directly by translation, if virus contains "+" RNA, or indirectly after transcription and then translation)
  - **replication of virus nucleic acid**
  - **synthesis of new Virion components**
  - **packaging and assembly of new virions**
  - **exit** from cell

Pricipliple of Replication

- Replication of the genome is governed by the principle of complementarity → requires a strand with complementary base sequence be synthesized → serve as template → synthesis of actual viral genome
- Late synthesis → viral structural proteins for the capsid are also synthesized almost simultaneously

IMPORTANT FACTS ABOUT VIRUS REPLICATION

- Viruses multiply only in living cells
- Host cell provides the energy & machinery for the synthesis of viral proteins & nucleic acids
- Viral genome must be able to produce mRNA → host cell protein-synthesizing machinery may be able to synthesize viral proteins

Stages in Multiplication

- Soon after interaction with the host cell → Virion is disrupted → infectivity is lost → ECLIPSE PERIOD
- The yield of infectious virus per cell ranges from moderate numbers to > 100,000 particles
- The duration of replication cycle varies from 6-8 hrs to > 40 hrs

All infections are not Productive

- **PRODUCTIVE INFECTIONS**

  > occur in permissive cells → infectious virus

- **ABORTIVE INFECTIONS**

  > no infectious virus produce because :

  a. cell is non-permissive

  b. virus may be defective

DEFECTIVE VIRUS – lack certain genes for replication & requires the help of another virus (dependo or helper virus)

LATENT INFECTIONS

- **LATENT INFECTIONS**

  a. viral genome persists within the host cell

  b. expression of no or few viral genes

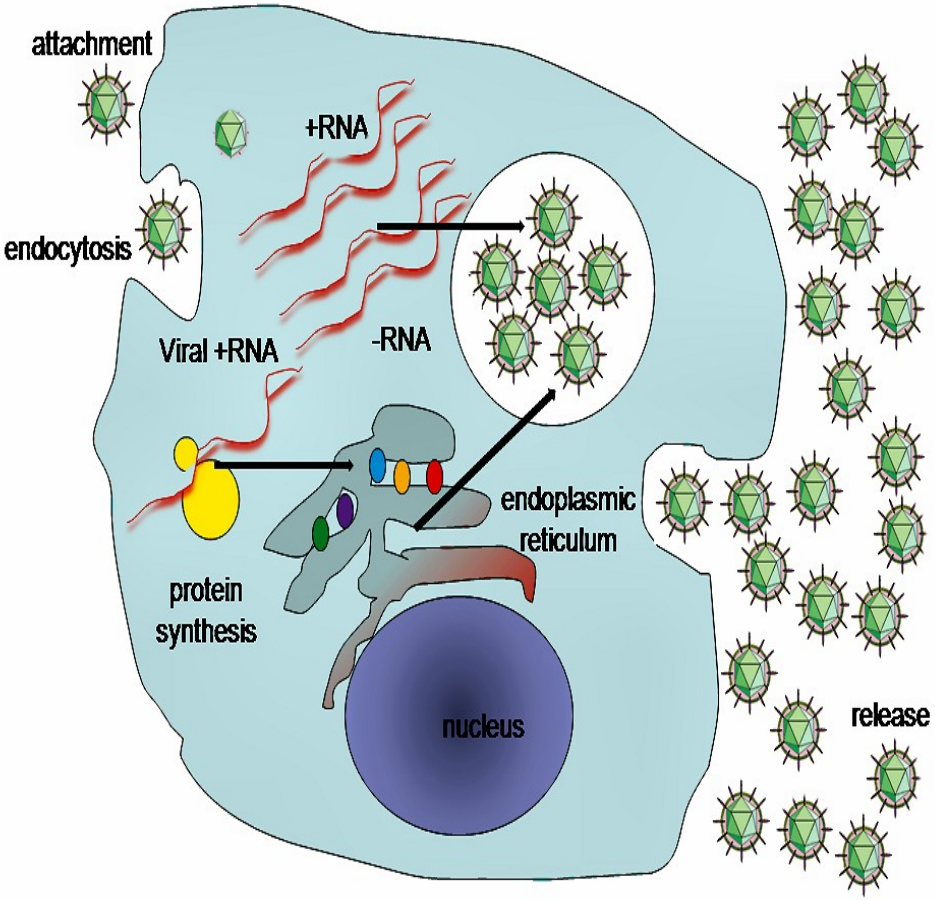
  c. survival of the infected cell

Pricipliple of Replication

- Replication of the genome is governed by the principle of complementarity → requires a strand with complementary base sequence be synthesized → serve as template → synthesis of actual viral genome
- Late synthesis → viral structural proteins for the capsid are also synthesized almost simultaneously

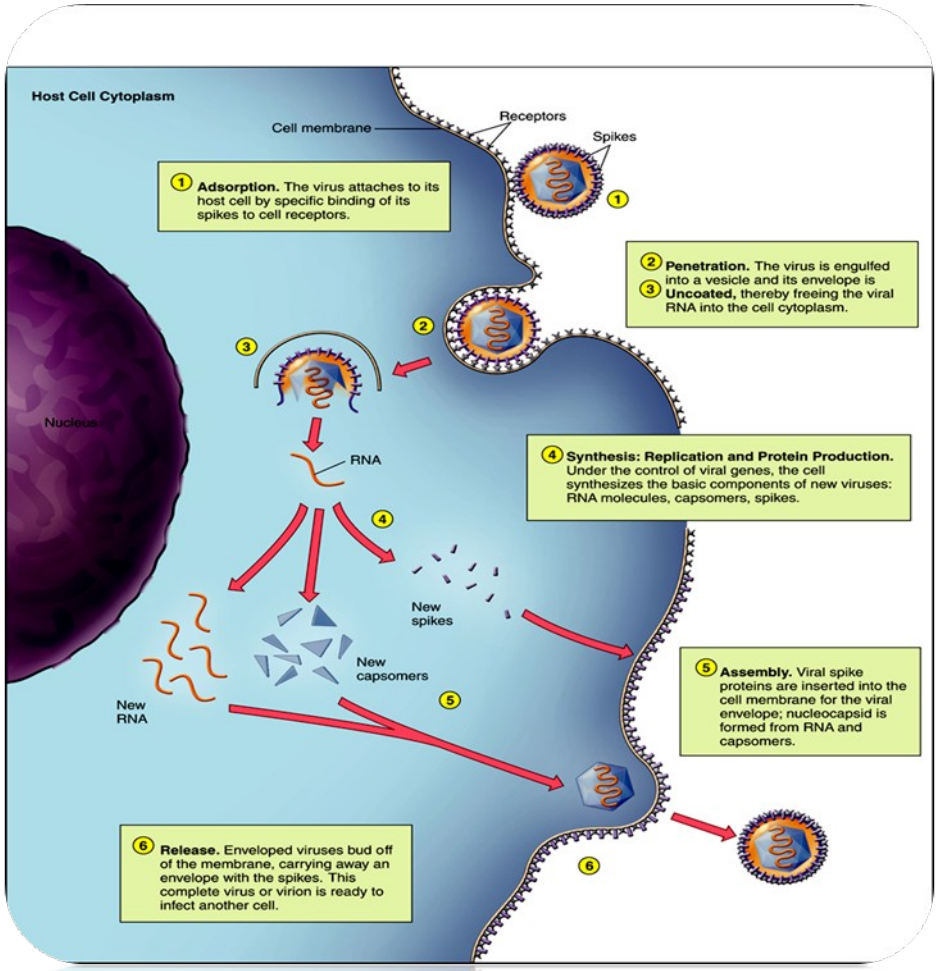
STEPS IN VIRAL REPLICATION

1. Attachment & adsorption
2. Penetration
3. Uncoating
4. Early viral mRNA synthesis
5. Early viral protein synthesis



STEPS IN VIRAL REPLICATION

6. Viral genome replication
7. Late viral mRNA synthesis
8. Late viral protein synthesis
9. Assembly
10. Release



Early steps in Multiplication

- **Attachment**
  - specific binding of a Virion protein (the anti-receptor) to a constituent of the cell surface (the receptor)
    - *e.g*. hemagglutinin of influenza virus
    - some complex viruses (HSV) may have more than one species of anti-receptor molecule
- **Penetration**
  - energy-dependent step
  - occurs almost instantaneously after attachment

ASSEMBLY & RELEASE

- It is thru budding that the virus acquire its envelope
- Budding process begin when virus-specific proteins enter the cell membrane at specific sites
- Herpesviruses → nuclear membrane

  Poxviruses → inclusion bodies

  Coronaviruses → endoplasmic reticulum

ASSEMBLY & RELEASE

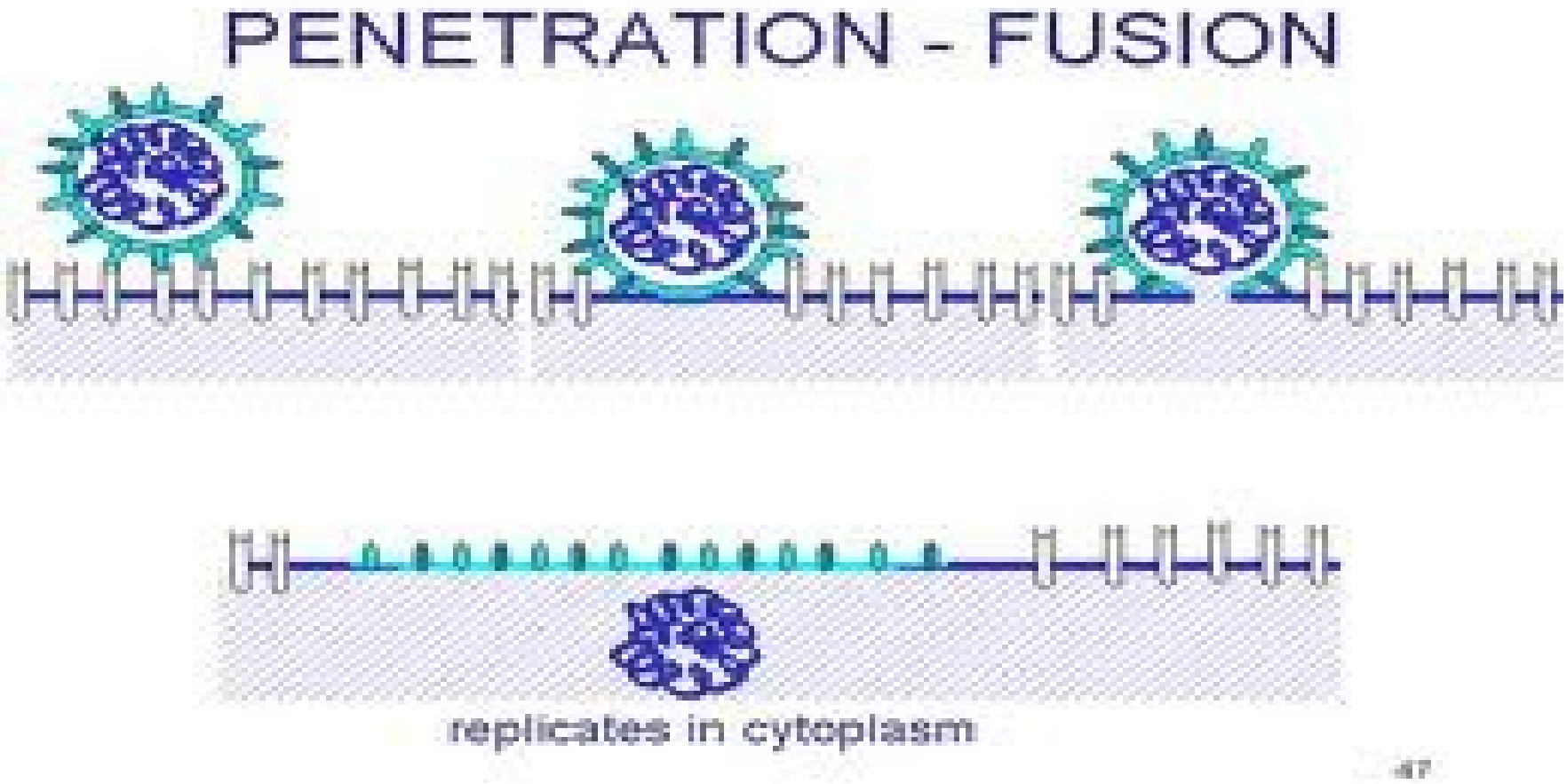
- Viral nucleocapsid then interacts with the specific membrane site mediated by matrix protein
- Cell membrane evaginates at that site → an enveloped particle bud off from the membrane

ATTACHMENT & ADSORPTION

- Reversible step
- Does not require energy
- 2 requirements:

  1. recognition & attachment to specific host receptor → determines the host range of the virus

Penetration and Fusion



Mechanism differ the various types

> Rhinovirus – ICAM-1

> HIV – CD4 + T cells

> Rabies virus – acetylcholine receptors

> HSV-1 – fibroblast growth factor receptor

2. appropriate ph & ionic concentration →

both the host cell & viral particle are negatively charged at ph 7 → require counter-ion → Magnesium ion

PENETRATION

- Refers to the entry of the viral particle into the cytoplasm of the host cell
- Temperature-dependent step (37 C)
- Carried out through:

  a. receptor-mediated endocytosis

  b. direct penetration (viropexis)

  c. cell fusion

UNCOATING

- Refers to the physical separation of the viral capsid from the viral genome
- Considered an obligatory step in viral replication → makes the viral genome accessible for transcription
- Favored by low pH

Assembly and Release

- Components of capsid synthesis directed by late genes
- Assembly of enveloped viruses needs interaction with plasma membrane which has been modified
- Final stage of infection
- Enveloped viruses released gradually by budding or exocytosis
- Naked viruses accumulate in cytoplasm and released

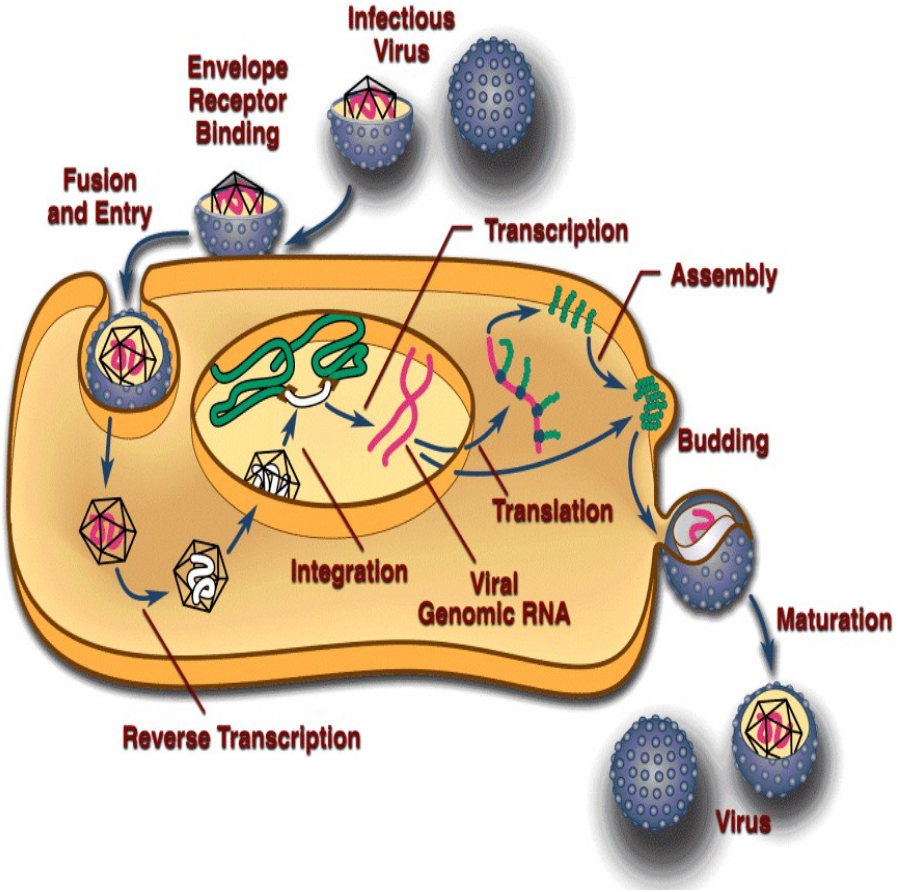
INFECTIOUS NUCLEIC ACID

- Purified viral nucleic acid (without any protein) that can carry out the entire viral growth cycle → complete viral particles
- Can bypass the host range specificity provided by the viral protein-host cell receptor interaction

  e.g. Poliovirus

GENE EXPRESSION & GENOME REPLICATION

- 1st step in gene expression → mRNA synthesis
- DNA viruses Except Poxviruses replicate in the nucleus → use host cell DNA-dependent RNA polymerase → synthesize mRNA



Multiply in

- Poxviruses replicate in the cytoplasm→ no access to host cell RNA polymerase → carry their own RNA polymerase
- RNA viruses replicate in the cytoplasm EXCEPT Influenza virus & Retrovirus

ASSEMBLY & RELEASE

- Progeny particles assembled by packaging the viral nucleic acid within the capsid proteins
- 2 processes of Release:

  1. Rupture or lysis of cell membrane

  2. Budding through the outer membrane

Differences in Single Stranded and Double Stranded Virus

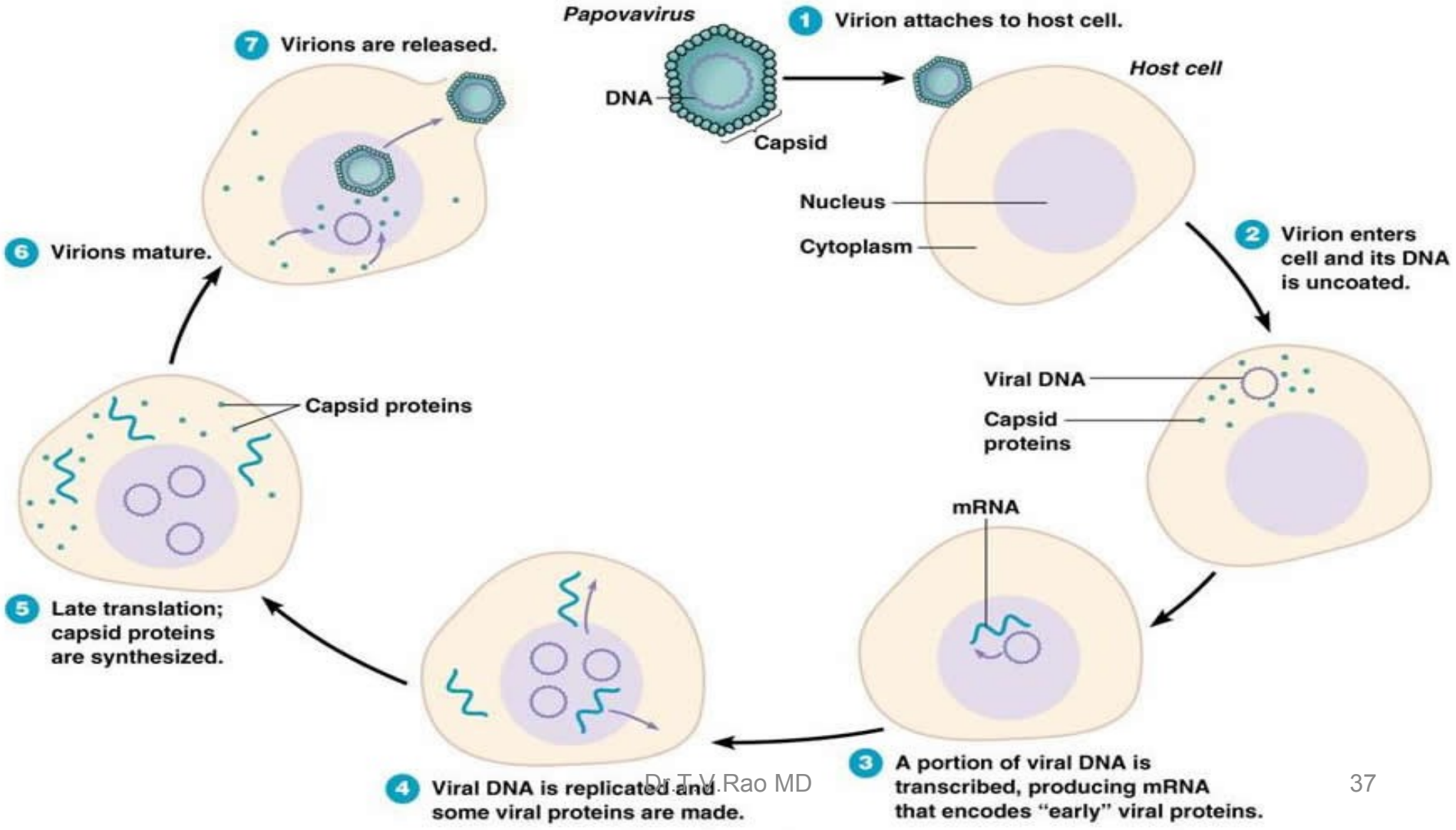
Double-stranded RNA → cell has no enzyme to transcribe RNA into mRNA → virus carries its own polymerase

Single-stranded RNA (+ polarity) e.g. Retrovirus → carries RNA-dependent DNA polymerase → ds DNA → transcribed to mRNA by host cell polymerase

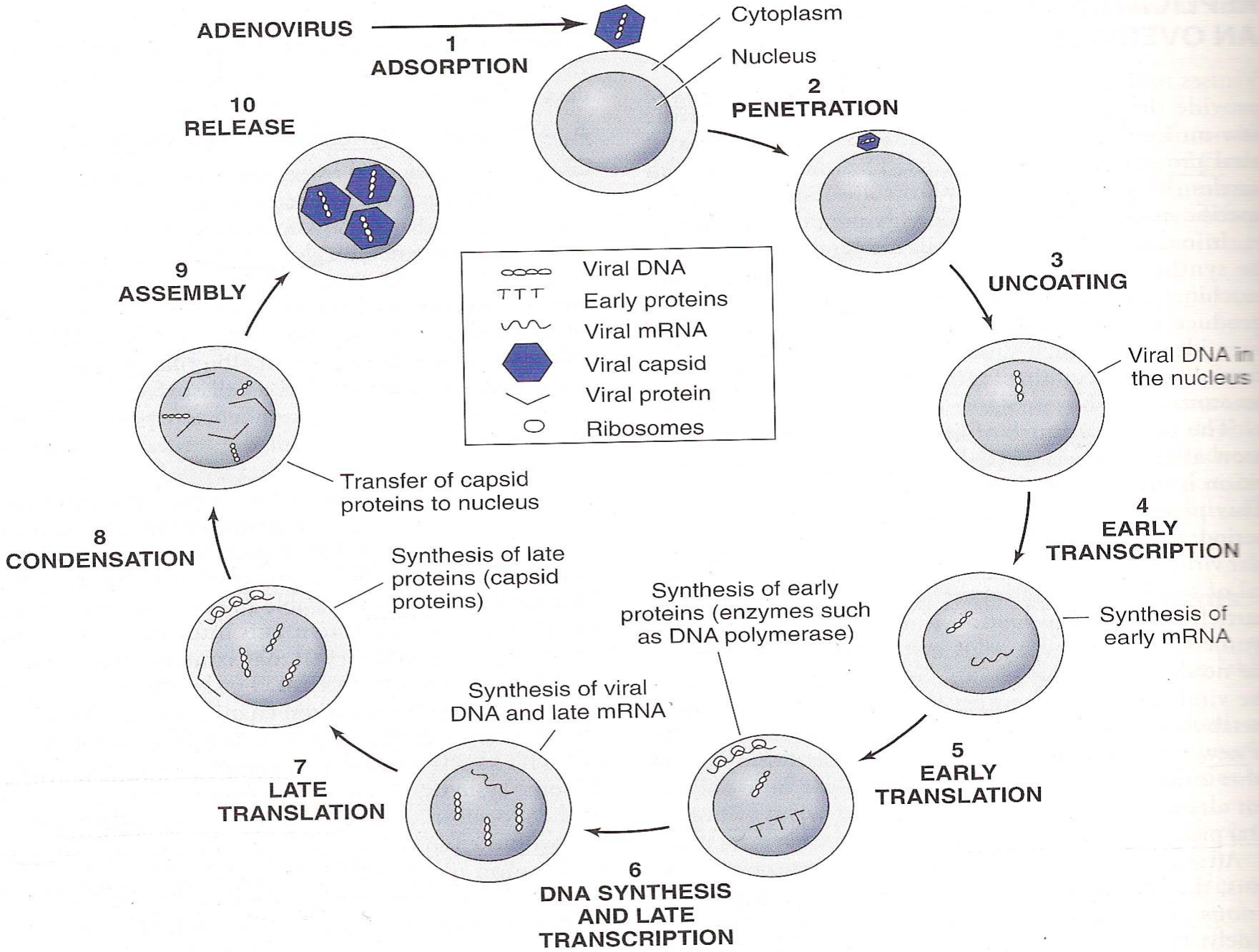
Synthesis of RNA

- Once m RNA is synthesized → translated into viral proteins (enzymes & early proteins for the genome) by host ribosomes
- The most important of the early proteins is the *Polymerase* → synthesize many copies of viral genetic material for the progeny virus particle

Synthesis of PapovaVirus



RNA Genome	Polarity	Virion Polyme-rase	Source Of mRNA	Infectivity Of Genome	Prototype
SS, non segmented	+	No	Genome	Yes	Poliovirus
SS					
Nonseg-mented	-	Yes	Transcrip-tion	No	Measles Rabies
segmented	-	Yes	Transcrip-tion	No	Influenza
DS segmented	+/-	Yes	Transcrip-tion	No	Reovirus
SS diploid	+	Yes	Transcrip-tion	No	HLTV HIV


ADENOVIRUS
1
ADSORPTION
Cytoplasm
Nucleus
2
PENETRATION
3
UNCOATING
Viral DNA in the nucleus
4
EARLY
TRANSCRIPTION
Synthesis of early mRNA
5
EARLY
TRANSLATION
Synthesis of early proteins (enzymes such as DNA polymerase)
6
DNA SYNTHESIS
AND LATE
TRANSCRIPTION
Synthesis of viral DNA and late mRNA
7
LATE
TRANSLATION
Synthesis of late proteins (capsid proteins)
8
CONDENSATION
Transfer of capsid proteins to nucleus
9
ASSEMBLY
10
RELEASE
Viral DNA
Early proteins
Viral mRNA
Viral capsid
Viral protein
Ribosomes

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