Virology II

Lecture 22

Dr. Samer Y. Alqaraleh
PhD. Nanobiotechnology (Microbiology)

Faculty of Dentistry

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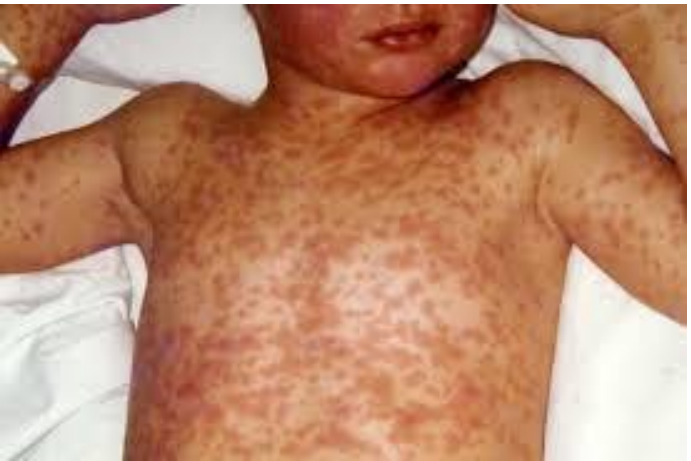
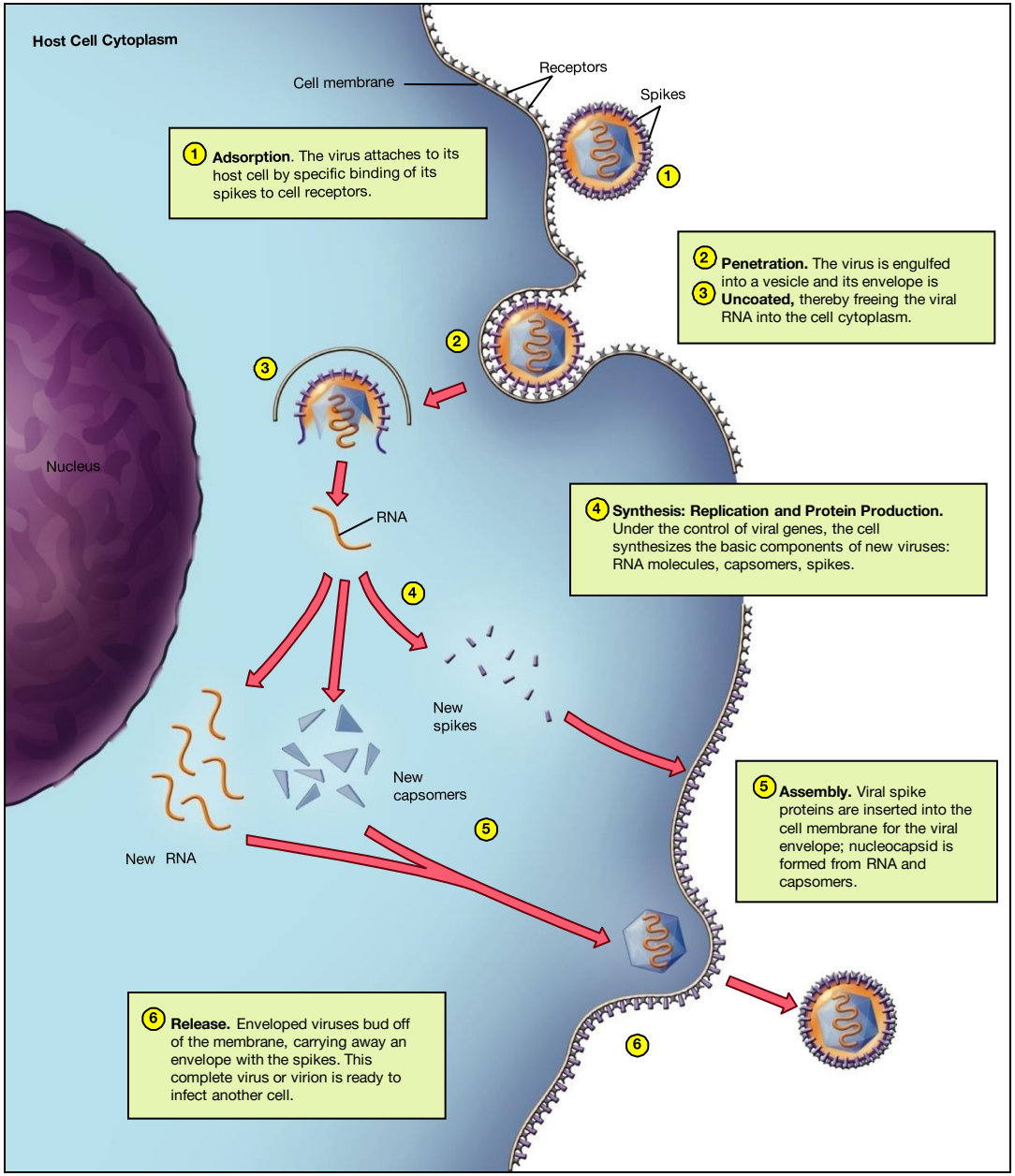


Modes of Viral Multiplication

General phases in animal virus multiplication cycle:

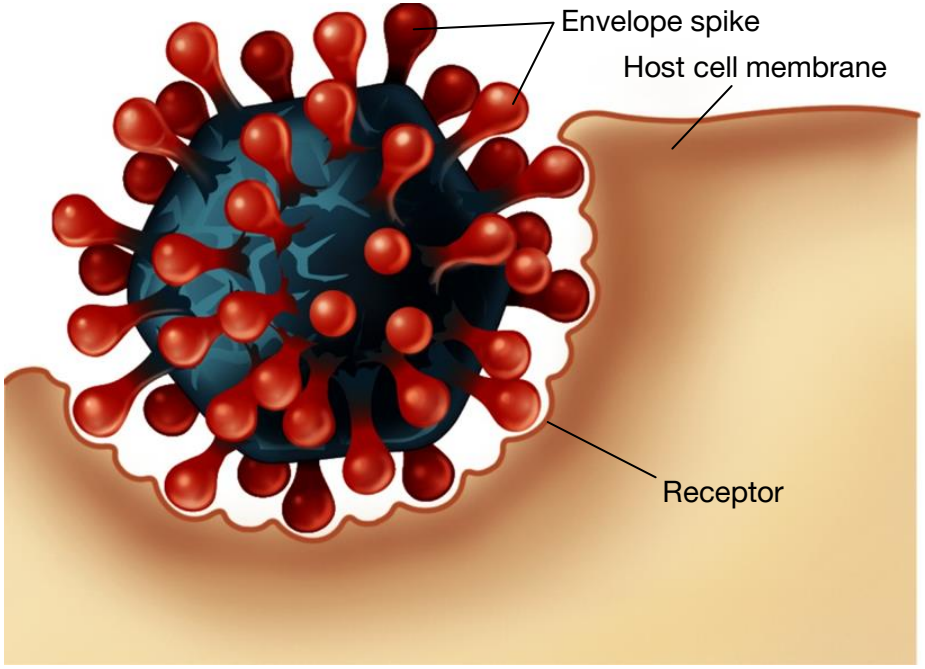
1. **Adsorption** – binding of virus to specific molecules on the host cell.
2. **Penetration** – genome enters the host cell
3. **Uncoating** – the viral nucleic acid is released from the capsid
4. **Eclipse**
5. **Synthesis** – viral components are produced
6. **Assembly** – new viral particles are constructed.
7. **Release** – assembled viruses are released by budding (exocytosis) or cell lysis

Animal Virus Multiplication



Adsorption and Host Range

- Virus coincidentally collides with a susceptible host cell and adsorbs specifically to receptor sites on the membrane (Tropism).
- Spectrum of cells a virus can infect – **host range**
  - Hepatitis B – human liver cells
  - Poliovirus – primate intestinal and nerve cells
  - HIV infecting (CD4+ T cells)
  - Rabies – various cells of many mammals



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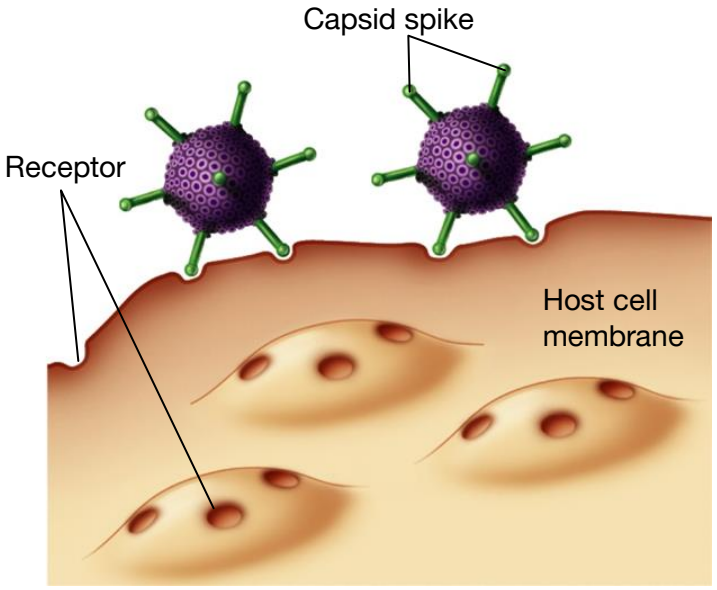

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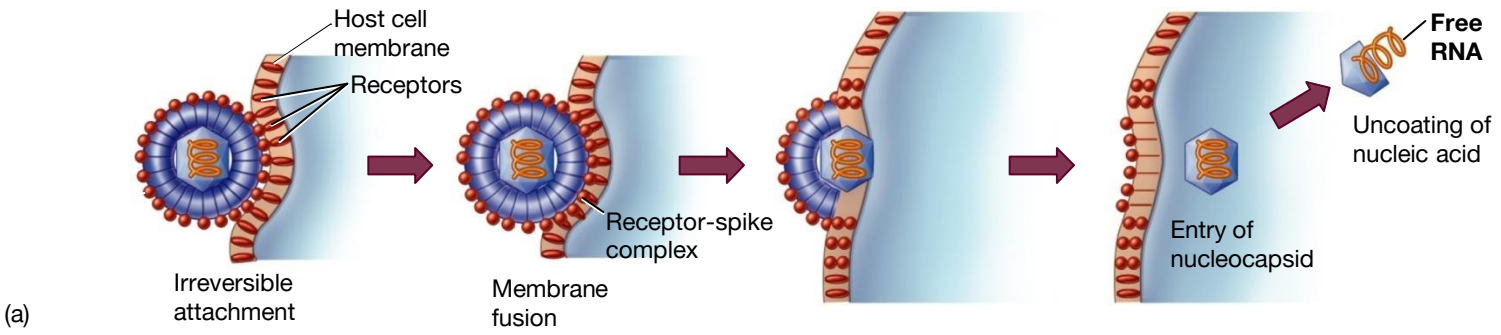
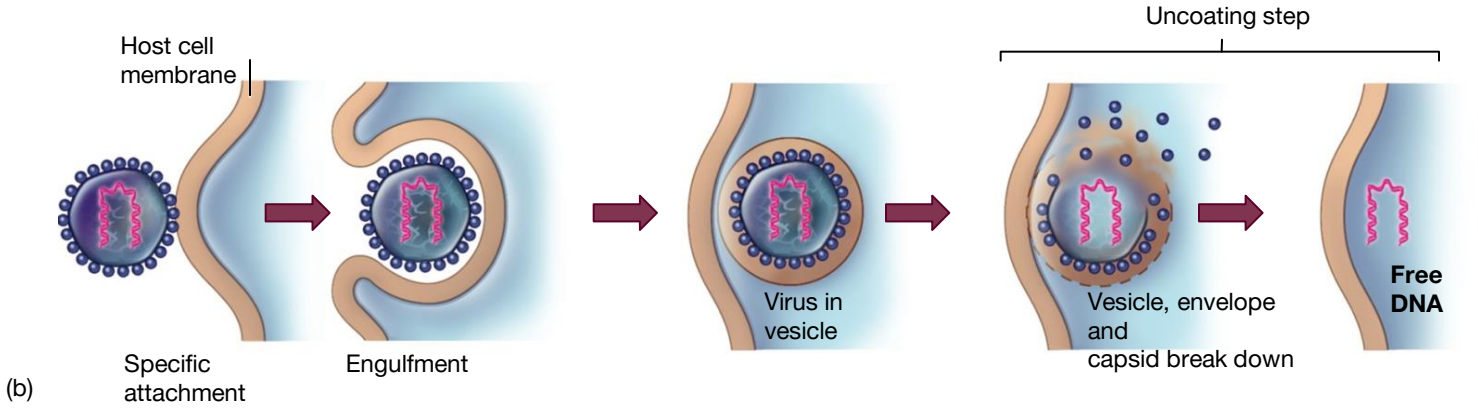
Penetration/Uncoating

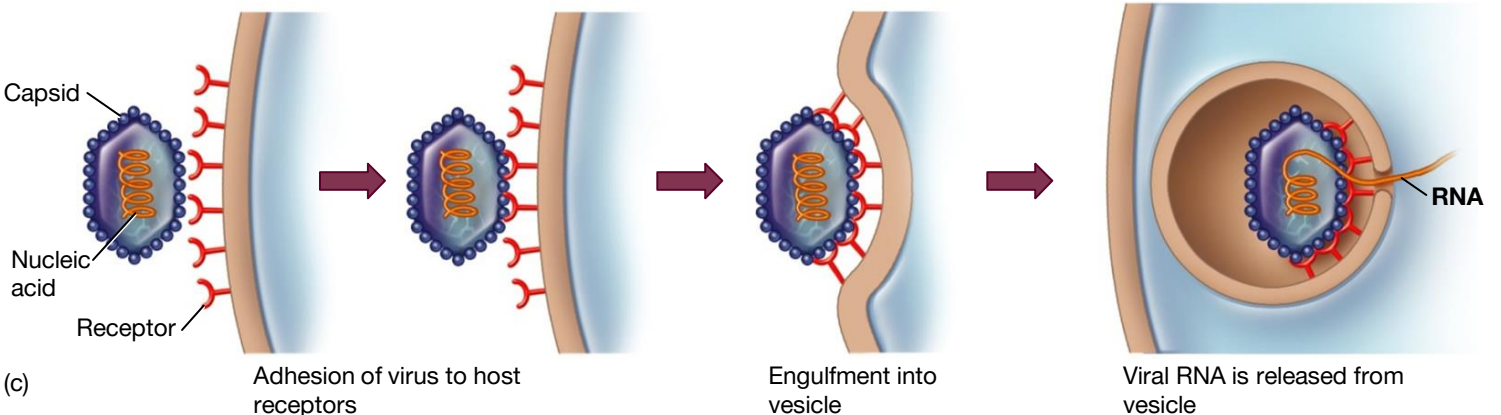
- Animal viruses must penetrate the cell membrane of host cell and this penetration by the whole virus or its nucleic acid .

- Most viruses enter through one of two ways:
  - **Endocytosis** – (envelope or naked) entire virus is engulfed and enclosed in a vacuole or vesicle.
  - **Fusion** – (envelope viruses) viral envelope merges directly with host by arrangement of membrane lipids resulting in nucleocapsid's entry into cytoplasm.

Variety in Penetration and Uncoating

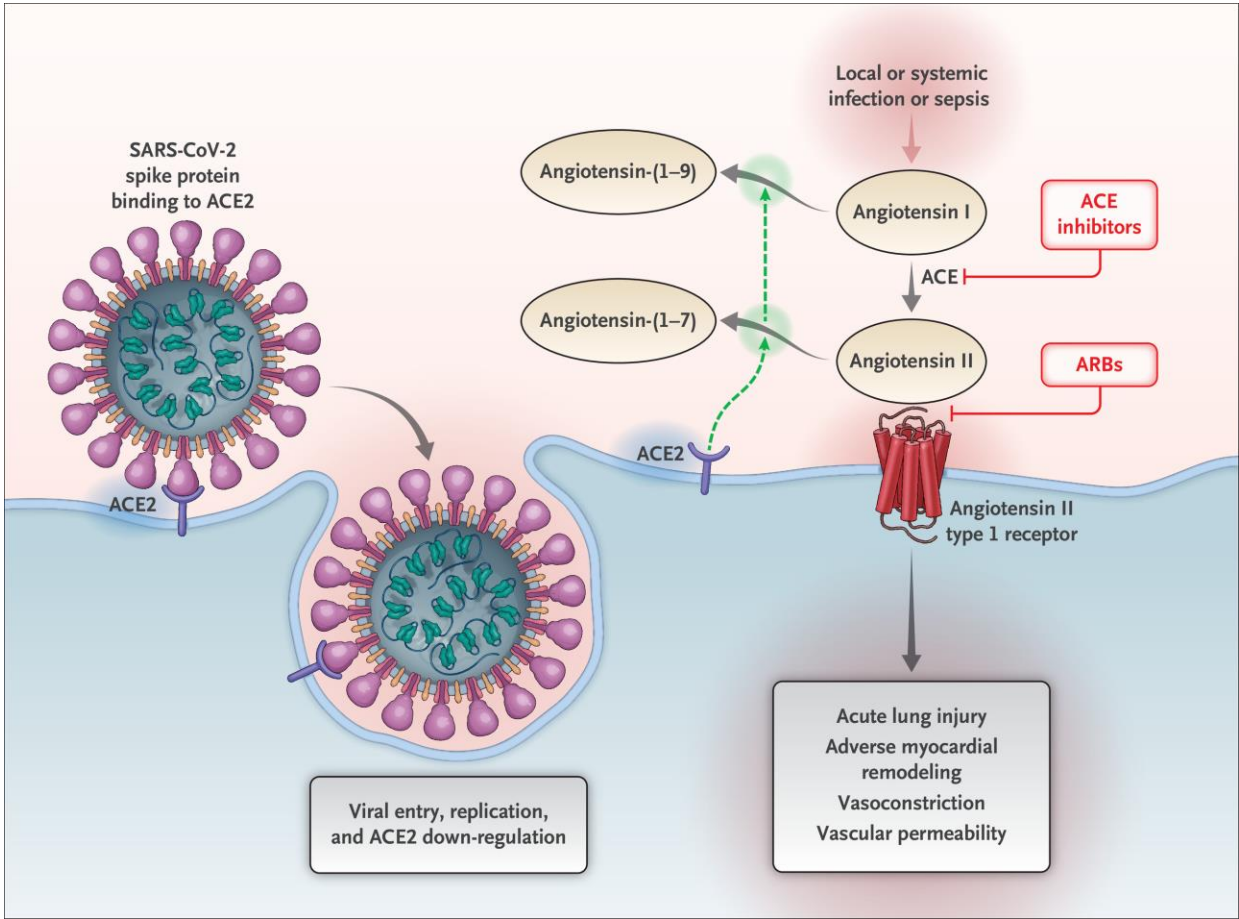






How Coronavirus penetration?

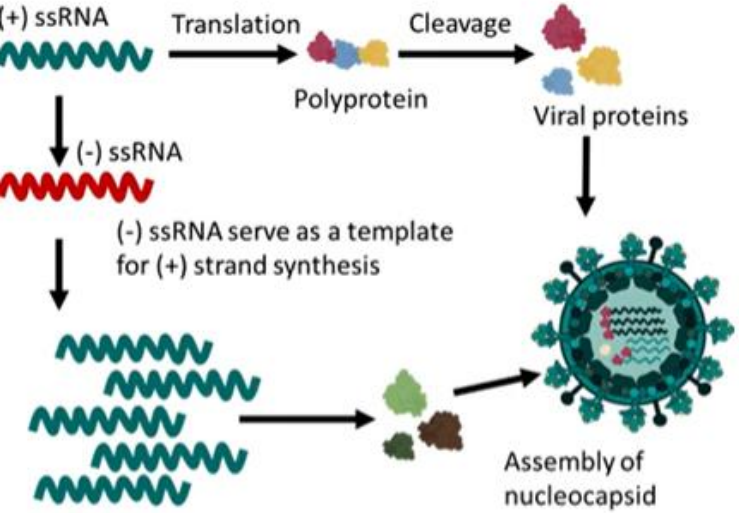
- Angiotensin-converting enzyme 2 (ACE2 receptor) in many our cells.
- Systemic disease, attack many tissues.
- Children above 10years have ACE2 like adult, while below 10years haven't.



Replication and Protein Production

- Once Virus enters cell it has **2 priorities**:
  1. **make viral proteins via + sense mRNA.**
  2. **make copies of viral genome.**
- Varies depending on whether the virus is a DNA or RNA virus
- DNA viruses generally are replicated and assembled in the nucleus
- RNA viruses generally are replicated and assembled in the cytoplasm
  - Positive-sense RNA contain the message for translation
  - Negative-sense RNA must be converted into positive-sense message

Replication of + sense RNA virus



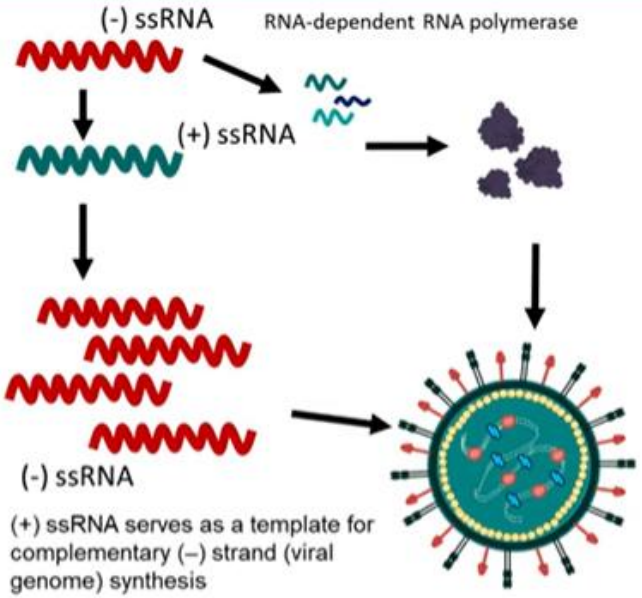
Positive-Sense RNA Viruses

- Genome: Acts directly as mRNA.
- Can be immediately translated into proteins.

Examples:

- Poliovirus (Picornaviridae)
- Hepatitis C virus (Flaviviridae)
- SARS-CoV-2 (Coronaviridae)
- Rubella virus (Togaviridae)

Replication of - sense RNA virus



Negative-Sense RNA Viruses

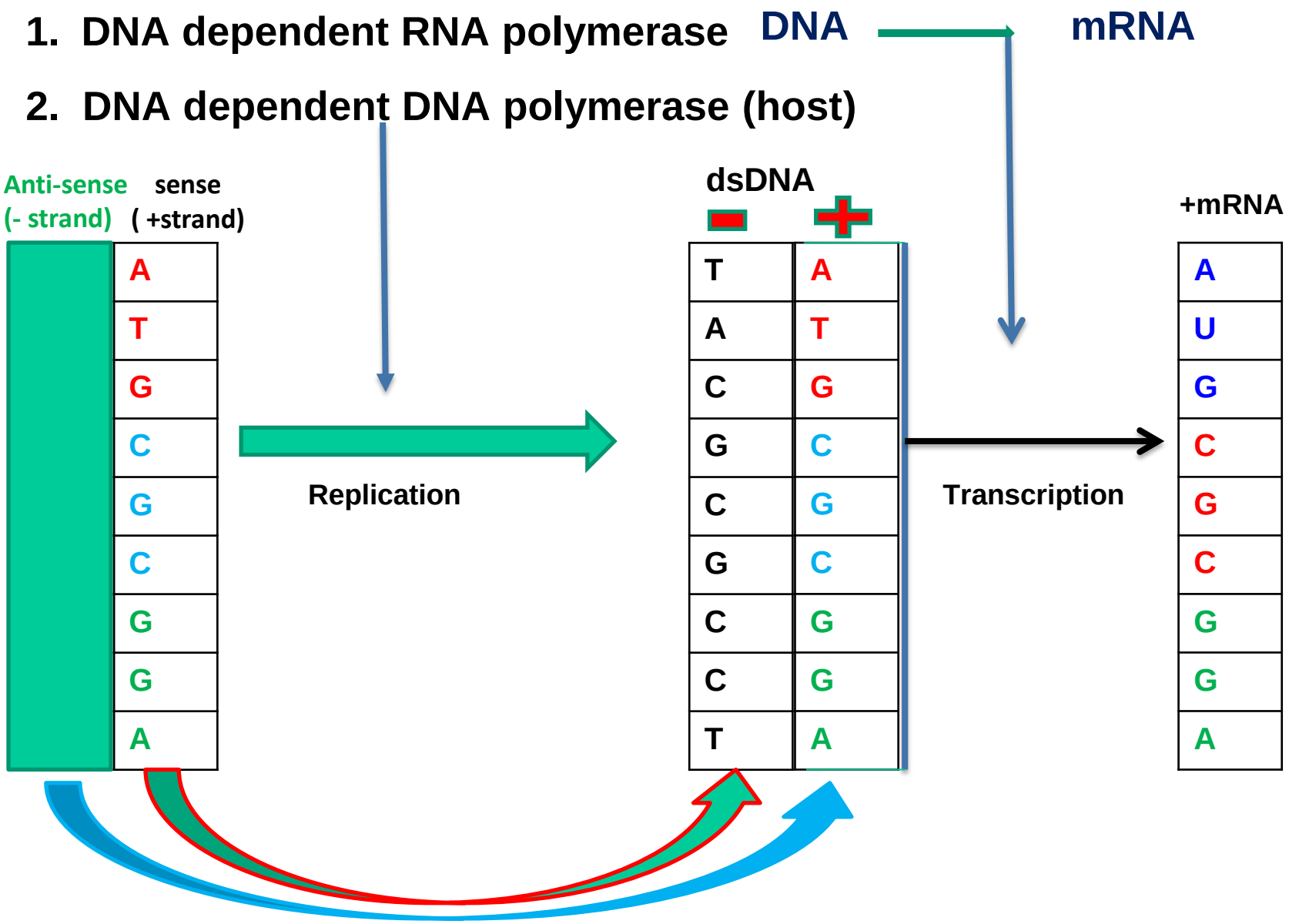
- Genome: Complementary to mRNA.
- Must transcribe into positive-sense RNA.

Examples:

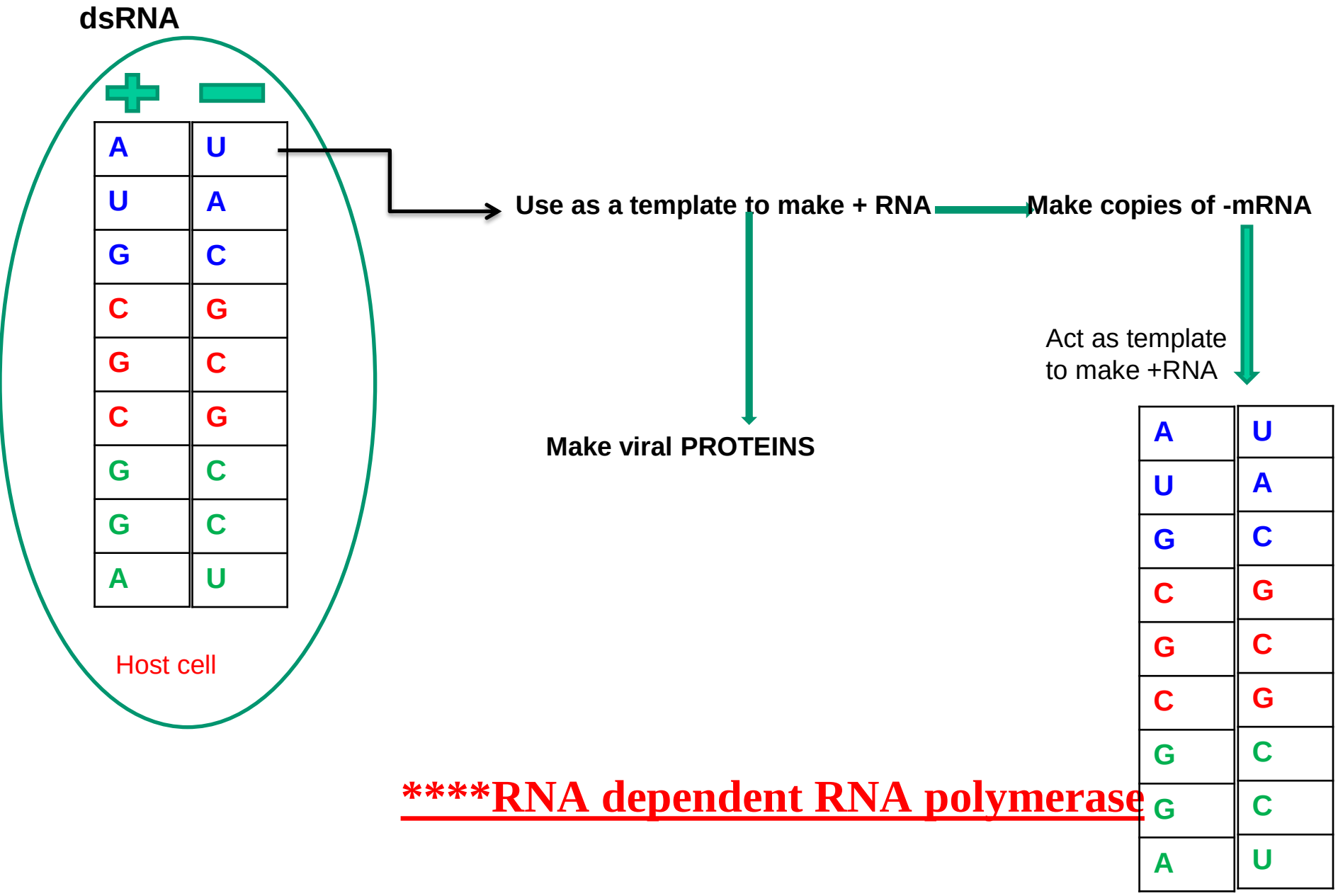
- Influenza virus (Orthomyxoviridae)
- Measles virus (Paramyxoviridae)
- Rabies virus (Rhabdoviridae)
- Ebola virus (Filoviridae)

Synthesis of viral components

1. DNA dependent RNA polymerase
2. DNA dependent DNA polymerase (host)



3. RNA dependent RNA polymerase

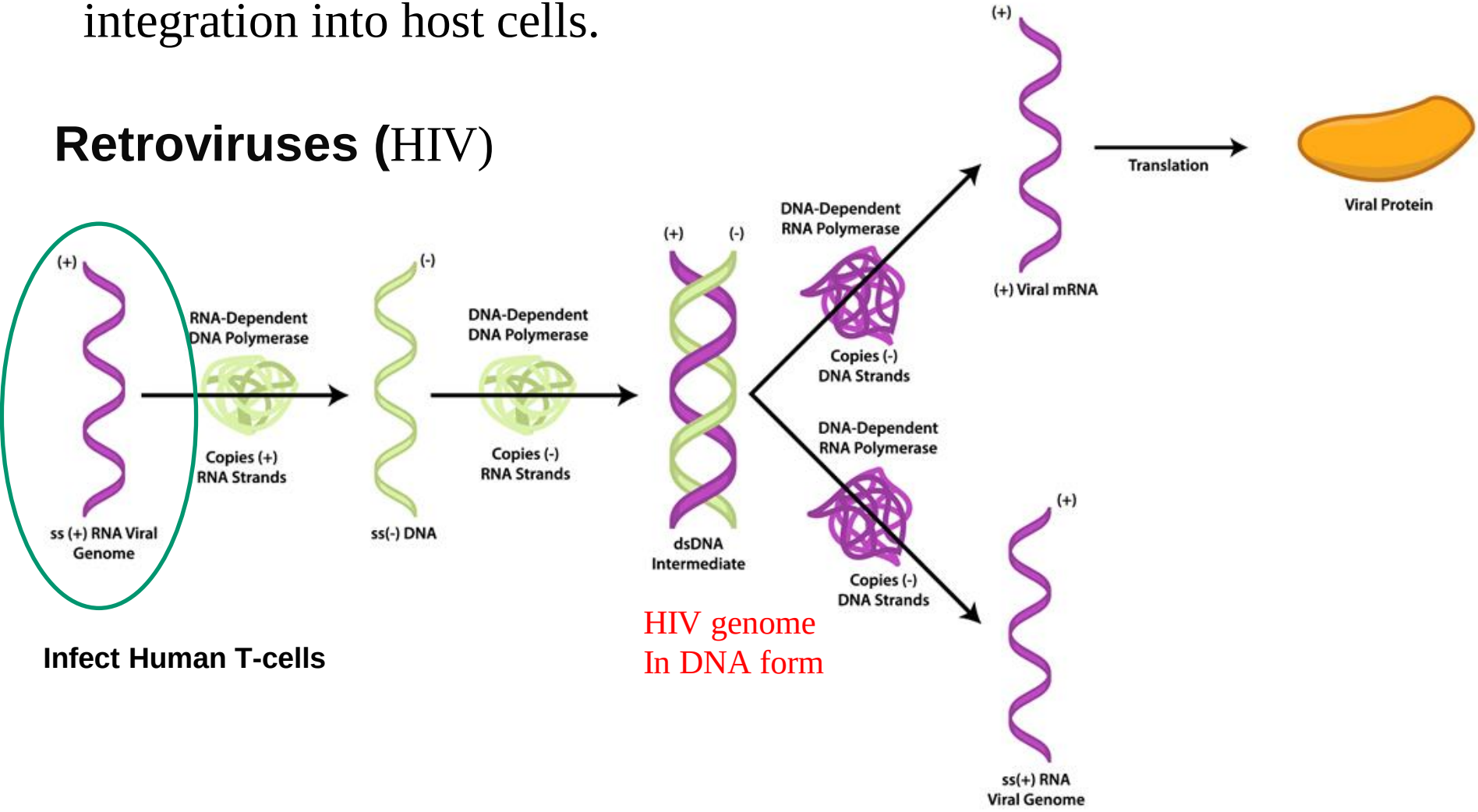


****RNA dependent RNA polymerase

4. Reverse transcriptase (RT) is an RNA-dependent DNA polymerase

- Used by viruses (e.g., HIV, Hepatitis B) to convert their RNA genome into DNA for integration into host cells.

Retroviruses (HIV)

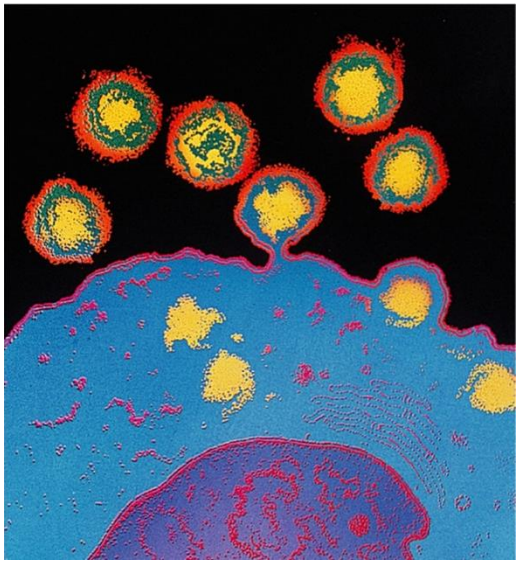


Infect Human T-cells

HIV genome
In DNA form

Release

- Assembled viruses leave the host cell in one of two ways:
  - **Budding** – exocytosis; nucleocapsid binds to membrane which pinches off and sheds the viruses gradually; cell is not immediately destroyed
  - **Lysis** – nonenveloped and complex viruses released when cell dies and ruptures



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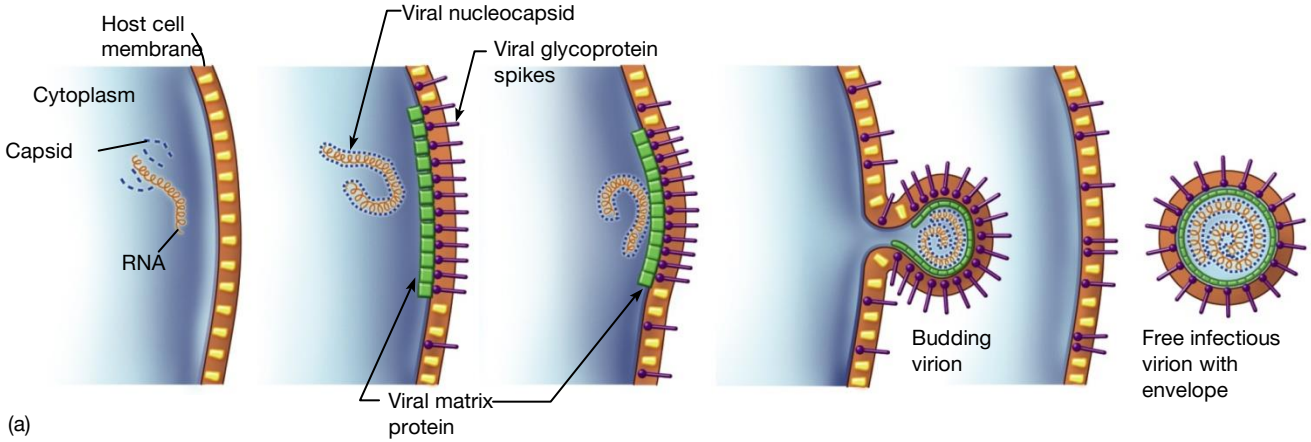
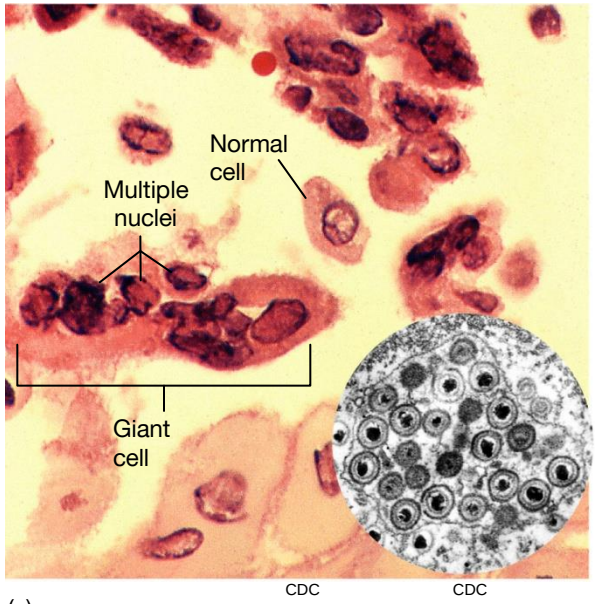


Damage to Host Cell

Cytopathic effects - virus-induced damage to cells

1. Changes in size and shape
2. Cytoplasmic inclusion bodies (Rabies virus)
3. Inclusion bodies in nucleus (Herpesvirus)
4. Cells fuse to form multinucleated cells (syncytium)
5. Cell lysis
6. Alter DNA
7. Transform cells into cancerous cells



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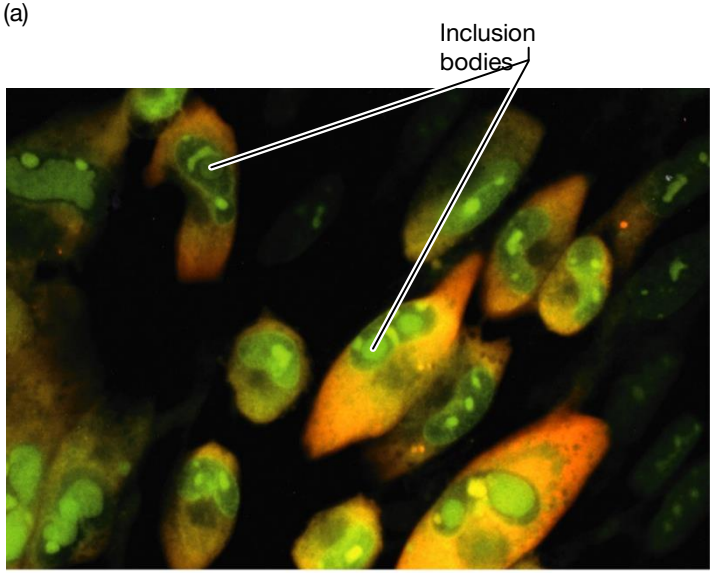
Measles virus



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Varicella- zoster

Persistent Infections

- **Persistent infections** - cell harbors the virus and is not immediately lysed.

- Can last weeks or host's lifetime; several can periodically reactivate – **chronic latent state**
  - Measles virus – may remain hidden in brain cells for many years
  - Herpes simplex virus – cold sores and genital herpes
  - Herpes zoster virus – chickenpox and shingles

Viral Damage

- Some animal viruses enter the host cell and permanently alter its genetic material resulting in cancer – **transformation** of the cell.

- Transformed cells have an increased rate of growth, alterations in chromosomes, and the capacity to divide for indefinite time periods resulting in tumors.

- Mammalian viruses capable of initiating tumors are called **oncoviruses**
  - Papillomavirus – cervical cancer
  - Epstein-Barr virus – Burkitt's lymphoma

Multiplication Cycle in Bacteriophages

- **Bacteriophages** – bacterial viruses (phages)
- Most widely studied are those that infect *Escherichia coli* – complex structure, DNA

- Multiplication goes through similar stages as animal viruses.

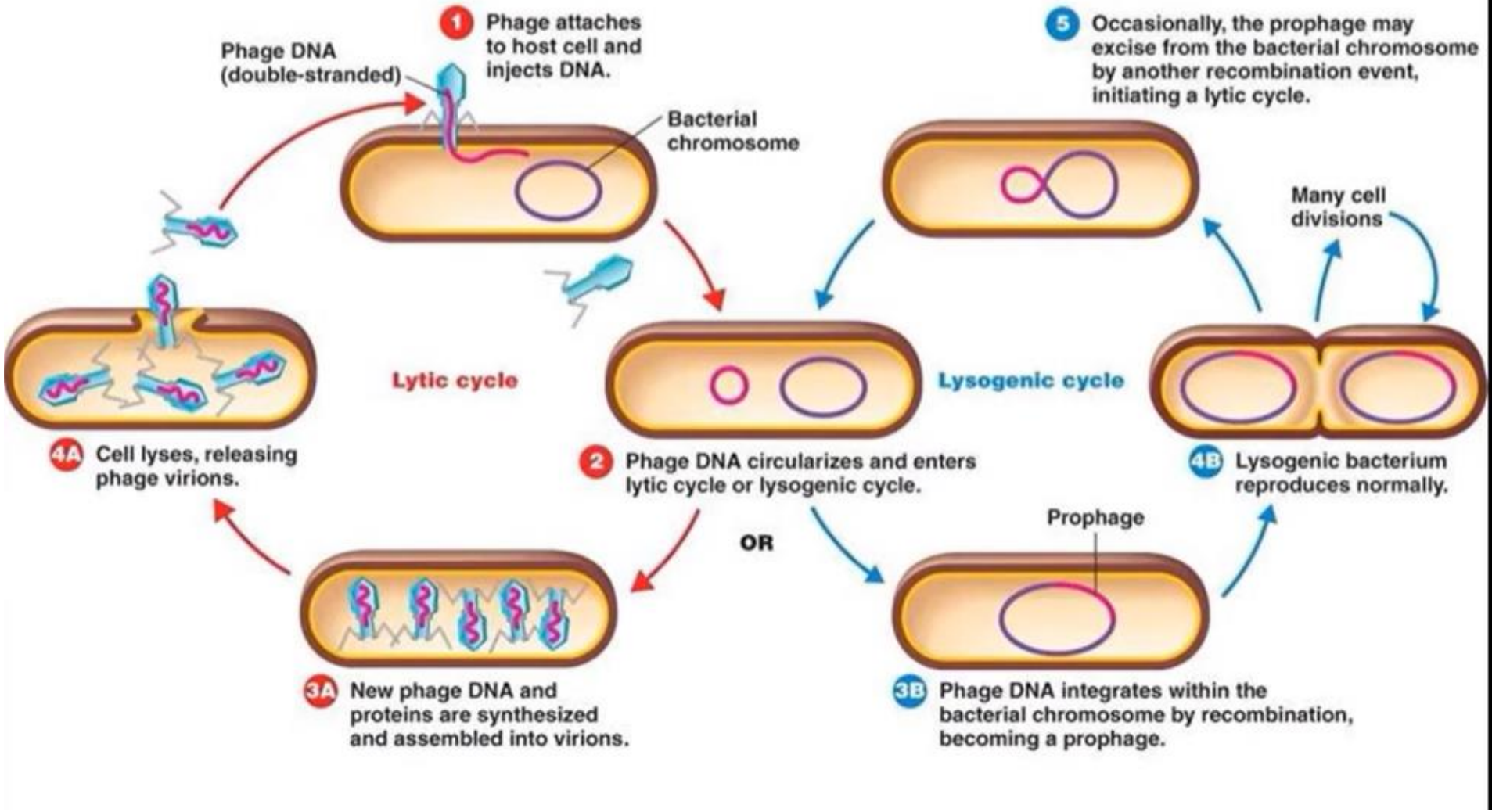
- Only the nucleic acid enters the cytoplasm - uncoating is not necessary

- Release is a result of cell lysis induced by viral enzymes and accumulation of viruses - **lytic cycle**

Steps in Phage Replication

1. **Adsorption** – binding of virus to specific molecules on host cell.
2. **Penetration** – genome enters host cell
3. **Replication** – viral components are produced
4. **Assembly** – viral components are assembled
5. **Maturation** – completion of viral formation
6. **Lysis & Release** – viruses leave the cell to infect other cells, called lytic cycle.

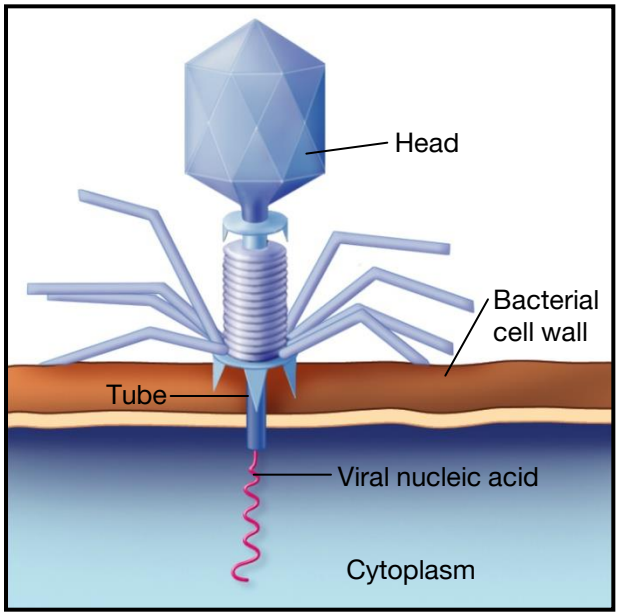
Lytic and Lysogenic Cycles

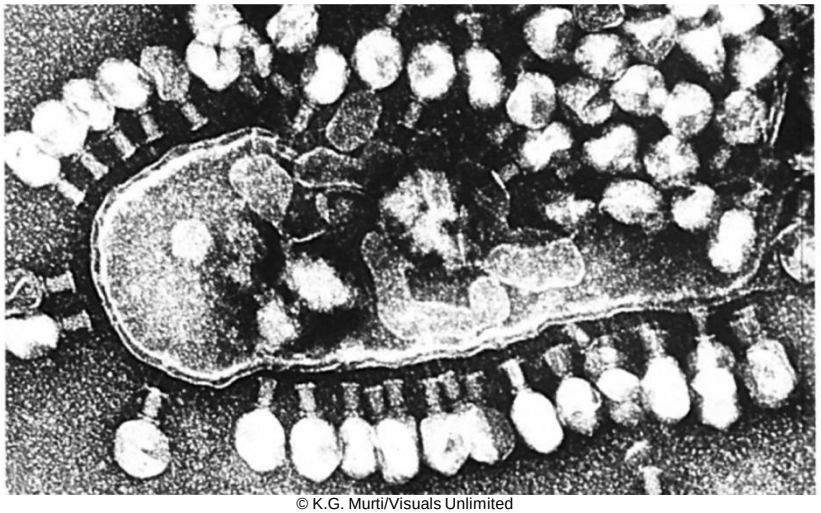


Comparison of Bacteriophage and Animal Virus

TABLE 6.4 Comparison of Bacteriophage and Animal Virus Multiplication

	Bacteriophage	Animal Virus
Adsorption	Precise attachment of special tail fibers to cell wall	Attachment of capsid or envelope to cell surface receptors
Penetration	Injection of nucleic acid through cell wall; no uncoating of nucleic acid	Whole virus is engulfed and uncoated, or virus surface fuses with cell membrane; nucleic acid is released.
Synthesis and Assembly	Occurs in cytoplasm Cessation of host synthesis Viral DNA or RNA replicated Viral components synthesized	Occurs in cytoplasm and nucleus Cessation of host synthesis Viral DNA or RNA replicated Viral components synthesized
Viral Persistence	Lysogeny	Latency, chronic infection, cancer
Release from Host Cell	Cell lyses when viral enzymes weaken it.	Some cells lyse; enveloped viruses bud off host cell membrane.
Cell Destruction	Immediate	Immediate or delayed





Lysogeny: The Silent Virus Infection

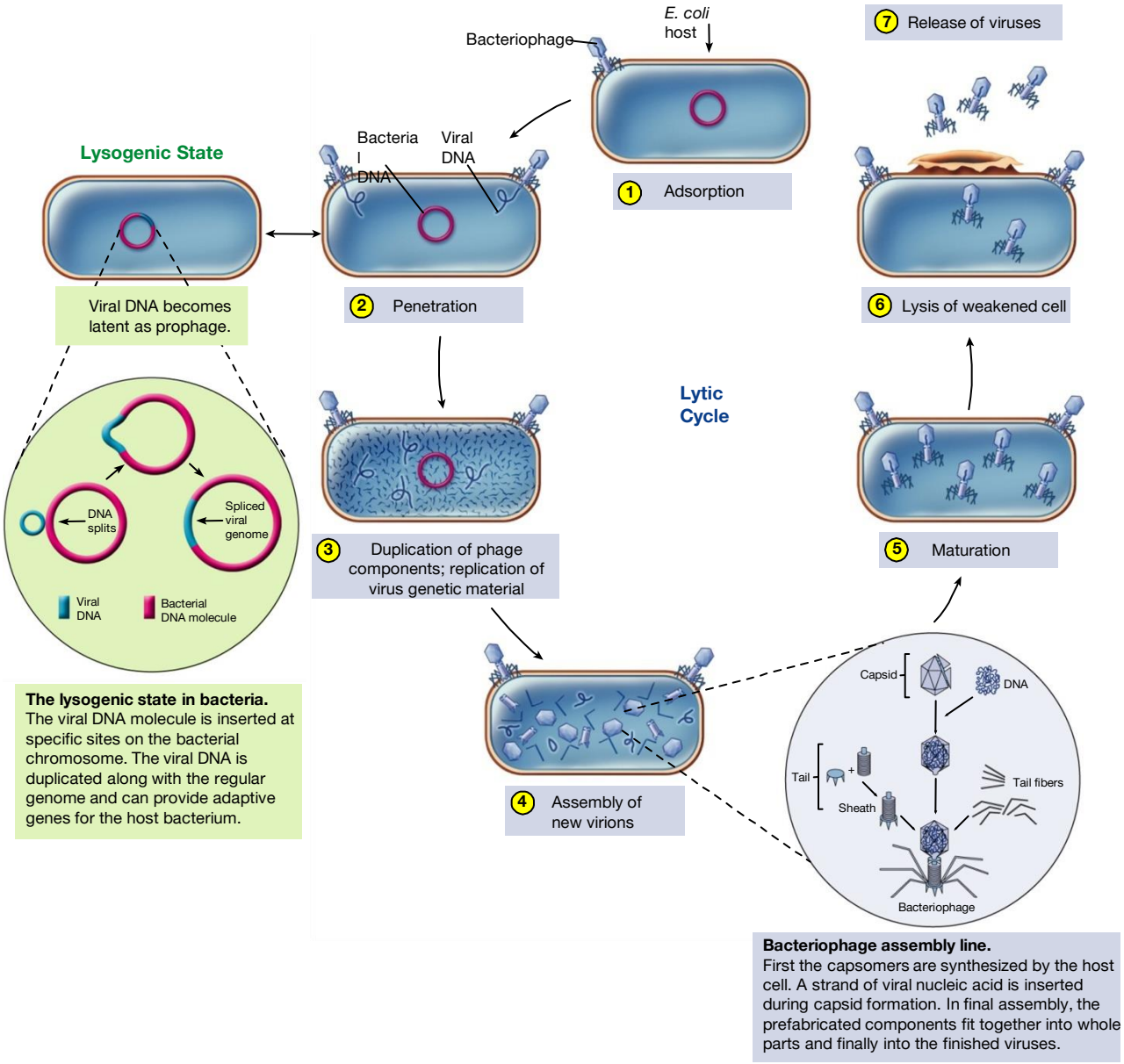
- Not all phages complete the lytic cycle.

- Some DNA phages, called **temperate phages**, undergo adsorption and penetration but don't replicate.
- The viral genome inserts into bacterial genome and becomes an inactive **prophage** – the cell is not lysed.

- Prophage is retained and copied during normal cell division resulting in the transfer of temperate phage genome to all host cell progeny – **lysogeny**

- **Induction** can occur resulting in activation of lysogenic prophage followed by viral replication and cell lysis.

Lytic and Lysogenic Lifecycles



The lysogenic state in bacteria. The viral DNA molecule is inserted at specific sites on the bacterial chromosome. The viral DNA is duplicated along with the regular genome and can provide adaptive genes for the host bacterium.

Bacteriophage assembly line. First the capsomers are synthesized by the host cell. A strand of viral nucleic acid is inserted during capsid formation. In final assembly, the prefabricated components fit together into whole parts and finally into the finished viruses.

Lysogeny

- Lysogeny results in the spread of the virus without killing the host cell

- Phage genes in the bacterial chromosome can cause the production of toxins or enzymes that cause pathology – **lysogenic conversion**
  - *Corynebacterium diphtheriae*
  - *Vibrio cholerae*
  - *Clostridium botulinum*

How do we grow viruses?

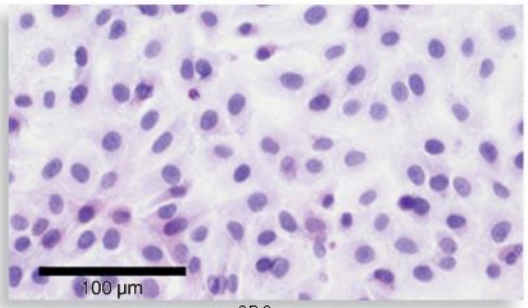
Obligate intracellular parasites – what do they need to grow?

They require appropriate cells to replicate.

Techniques in Cultivating and Identifying Animal Viruses

- Obligate intracellular parasites that require appropriate cells to replicate
- Methods used:
  - Cell (tissue) cultures – cultured cells grow in sheets that support viral replication and permit observation for cytopathic effects
  - Bird embryos – incubating egg is an ideal system; virus is injected through the shell
  - Live animal inoculation – occasionally used when necessary

Methods for Growing Viruses



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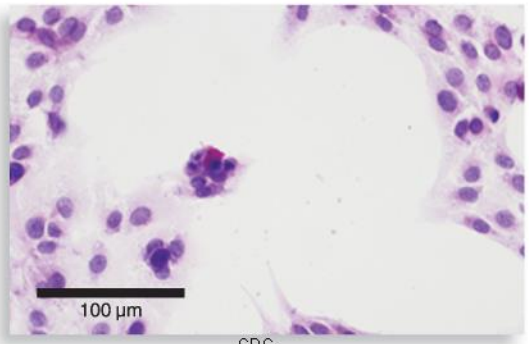

CDC

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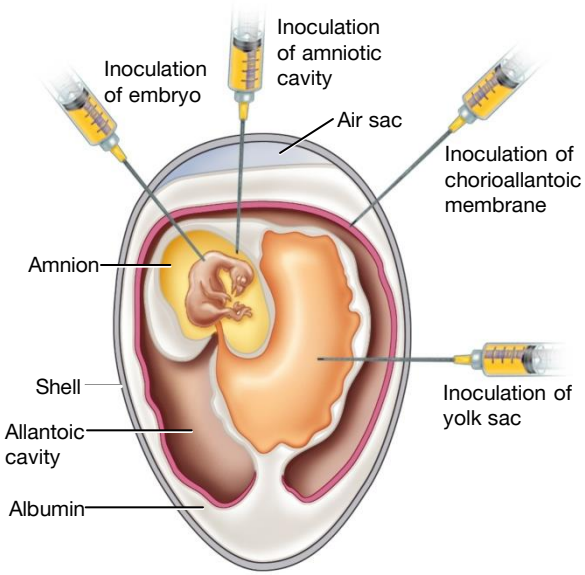

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Prions and Other Infectious Particles

Prions - misfolded proteins, contain no nucleic acid

- Extremely resistant to usual sterilization techniques
- Cause transmissible spongiform encephalopathies – fatal neurodegenerative diseases

Common in animals:

- **Scrapie** in sheep and goats
- **Bovine spongiform encephalopathies** (BSE), mad cow disease
- Humans – **Creutzfeldt-Jakob Syndrome** (CJS), fatal neurodegenerative disorder

Other Noncellular Infectious Agents

- **Satellite viruses** – dependent on other viruses for replication.
  - Have their own genome.
  - Lack essential genes needed for replication.
  - Use proteins or enzymes supplied by the helper virus.
  - Adeno-associated virus (AAV) – replicates only in cells infected with adenovirus.
  - Delta agent (Hepatitis D virus, HDV) – naked ssRNA expressed only in the presence of hepatitis B virus

- **Viroids** – short pieces of RNA, no protein coat; only been identified in plants.

Anti-viral drugs

1) Prevent attachment

2) Prevent Uncoating; Rimantadine

3) Prevent Replication; Acyclovir (Block DNA polymerase), Ribavirin inhibits mRNA translation

4) Prevent release; Tamiflu