Microbiology

Chapter 13

Viruses, Viroids, and Prions

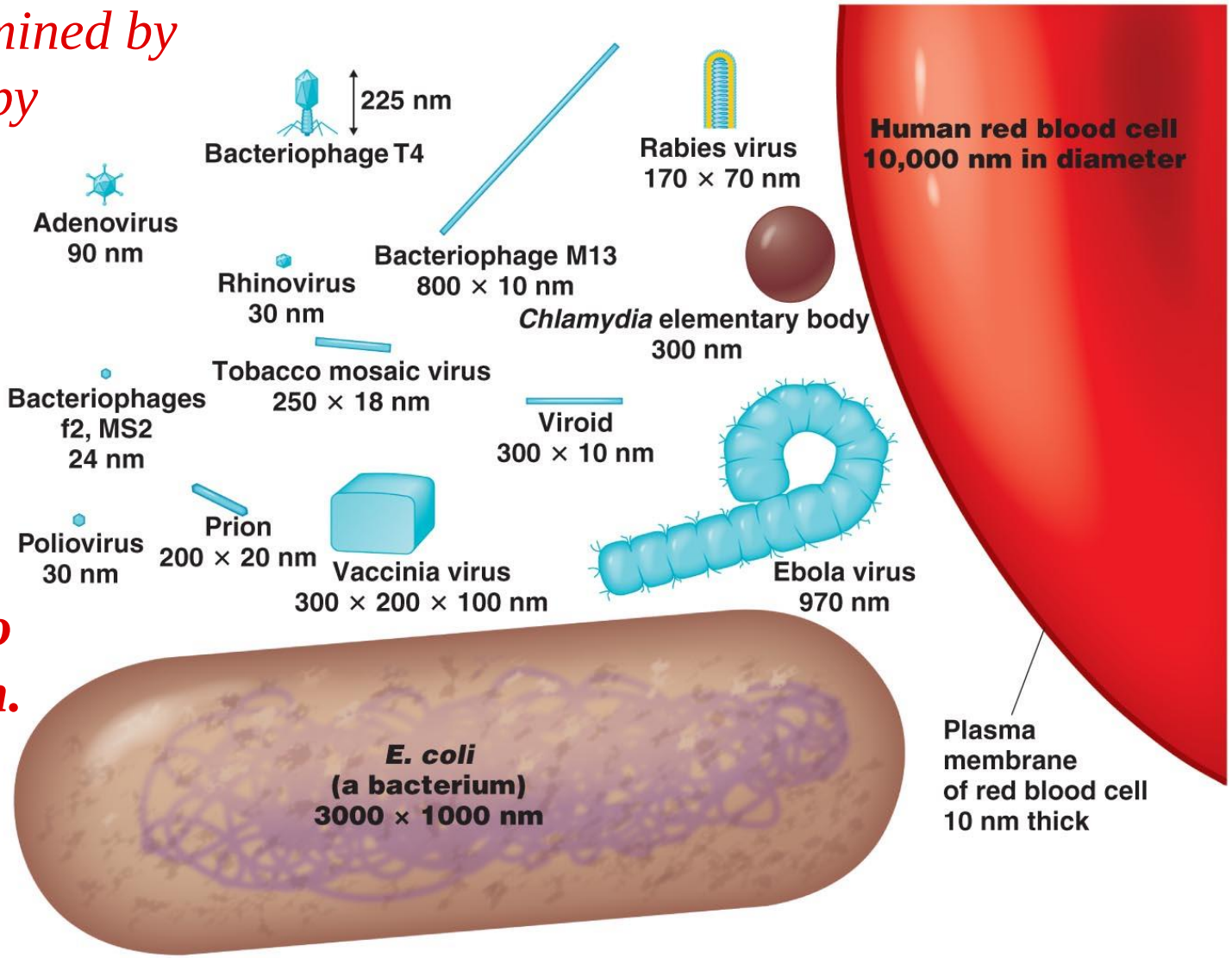
本內容已由授課教師方翠筠修訂

General Characteristics of Viruses

- **Obligatory intracellular parasites** ➔ Multiply inside living cells by using the synthesizing machinery of the cell.
- Contain nucleic acid (DNA or RNA) (single- or double-stranded, linear or circular, or divided into several separate molecules)
- Contain a protein coat
- Some are enclosed by an envelope
- Some viruses have spikes
- Most viruses infect only specific types of cells in one host
- **Host range** is determined by specific host attachment sites and cellular factors

Virus Sizes

Viral size is determined by electron microscopy



Ranges from 20 to 1000 nm in length.

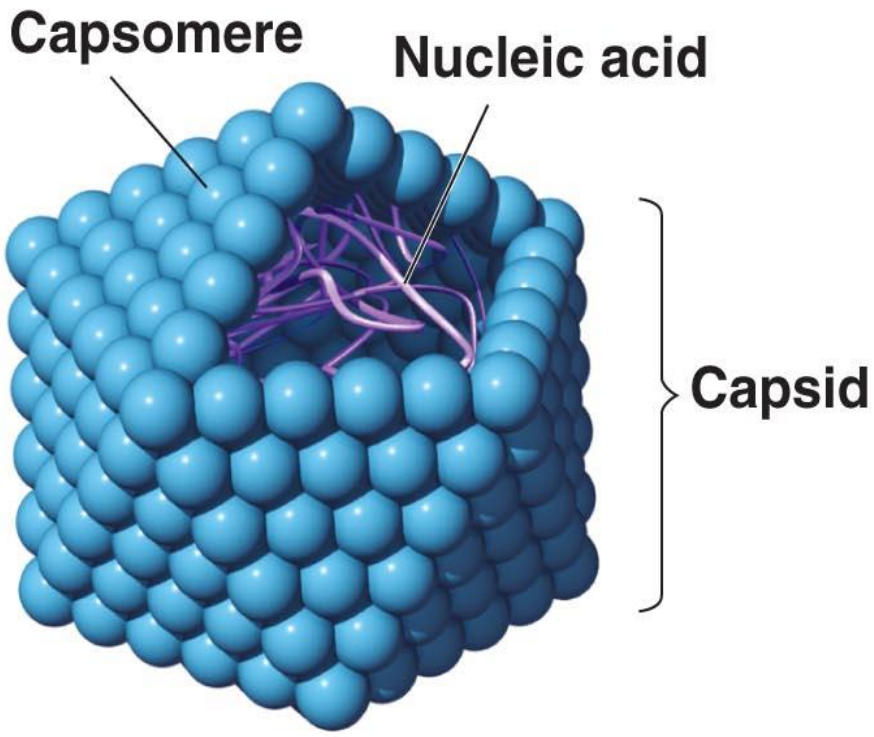
Figure 13.1

Viral Structure

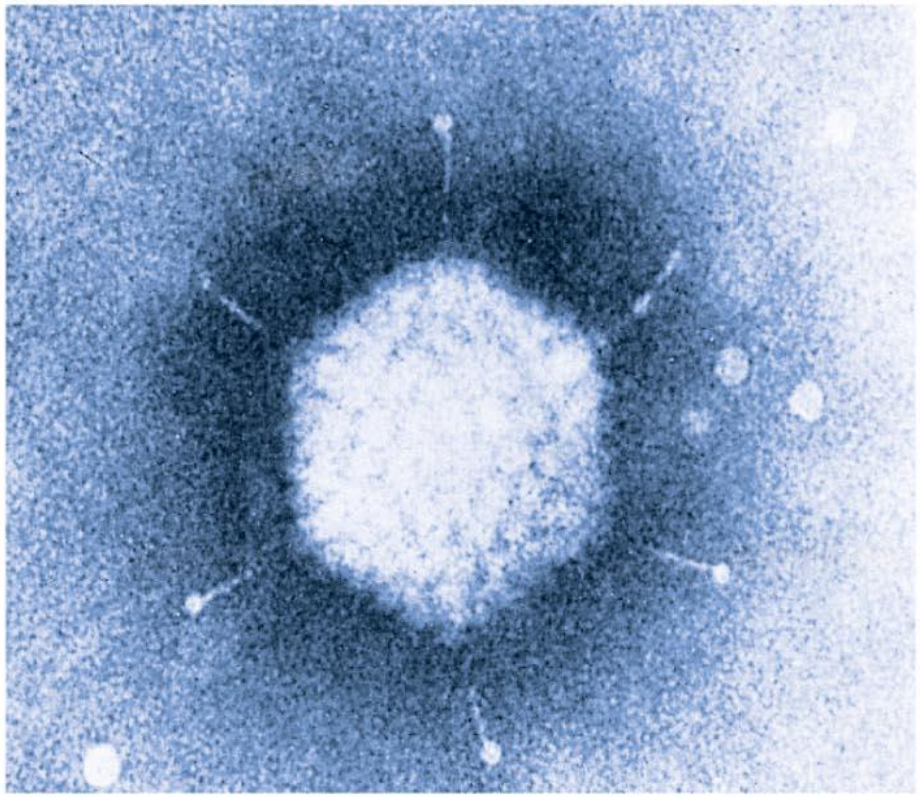
- A **virion** is a complete, fully developed **viral particle** composed of **nucleic acid** (DNA or RNA) surrounded by a coat.
- Viruses are classified by differences in the structures of these coats.
- The protein coat is called the **capsid**.
- The capsid is composed of protein subunits call **capsomeres**. Capsomeres and be a single type of protein or several types.
- The capsid of some virus is enclosed by an **envelope** consisting of lipids, proteins, and carbohydrates.
- Some envelopes are covered with carbohydrate-protein complexes called **spikes** (figure 13.3).

Morphology of a polyhedral virus

Polyhedral viruses (e.g. adenovirus) are many-sided.
Usually the capsid is an icosahedron (二十面體).



(a) A polyhedral virus



(b) *Mastadenovirus*

TEM

30 nm

Figure 13.2a

Polyhedral Viruses

Figure 13.16a

Morphology of an Enveloped Virus

- Enveloped viruses are covered by an envelop and are roughly spherical but highly pleomorphic.
- There are also enveloped helical viruses (e.g. *Influenzavirus,* figure 13.3) and enveloped polyhedral viruses (e.g. *Herpesvirus*).

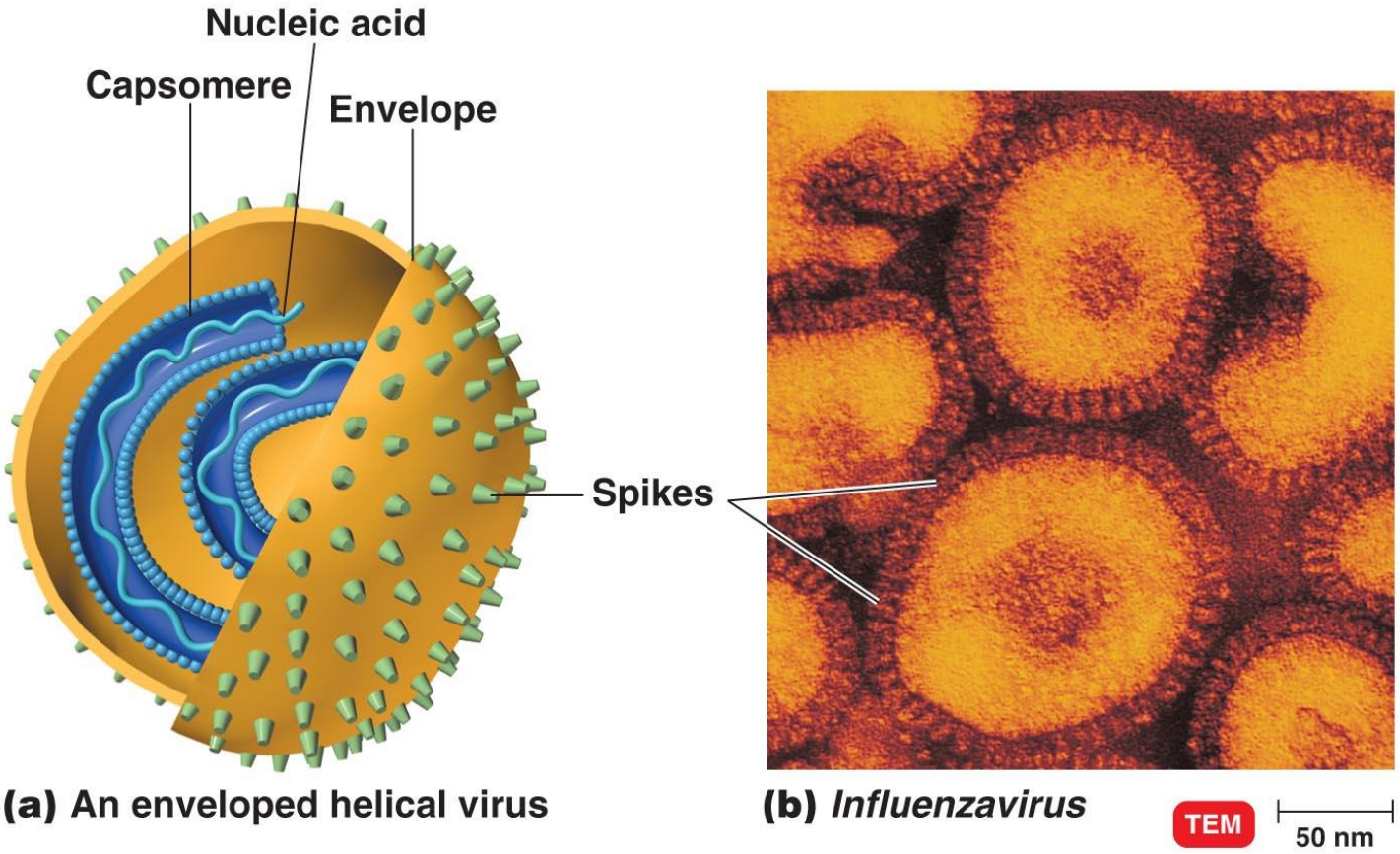


Figure 13.3

Enveloped Viruses

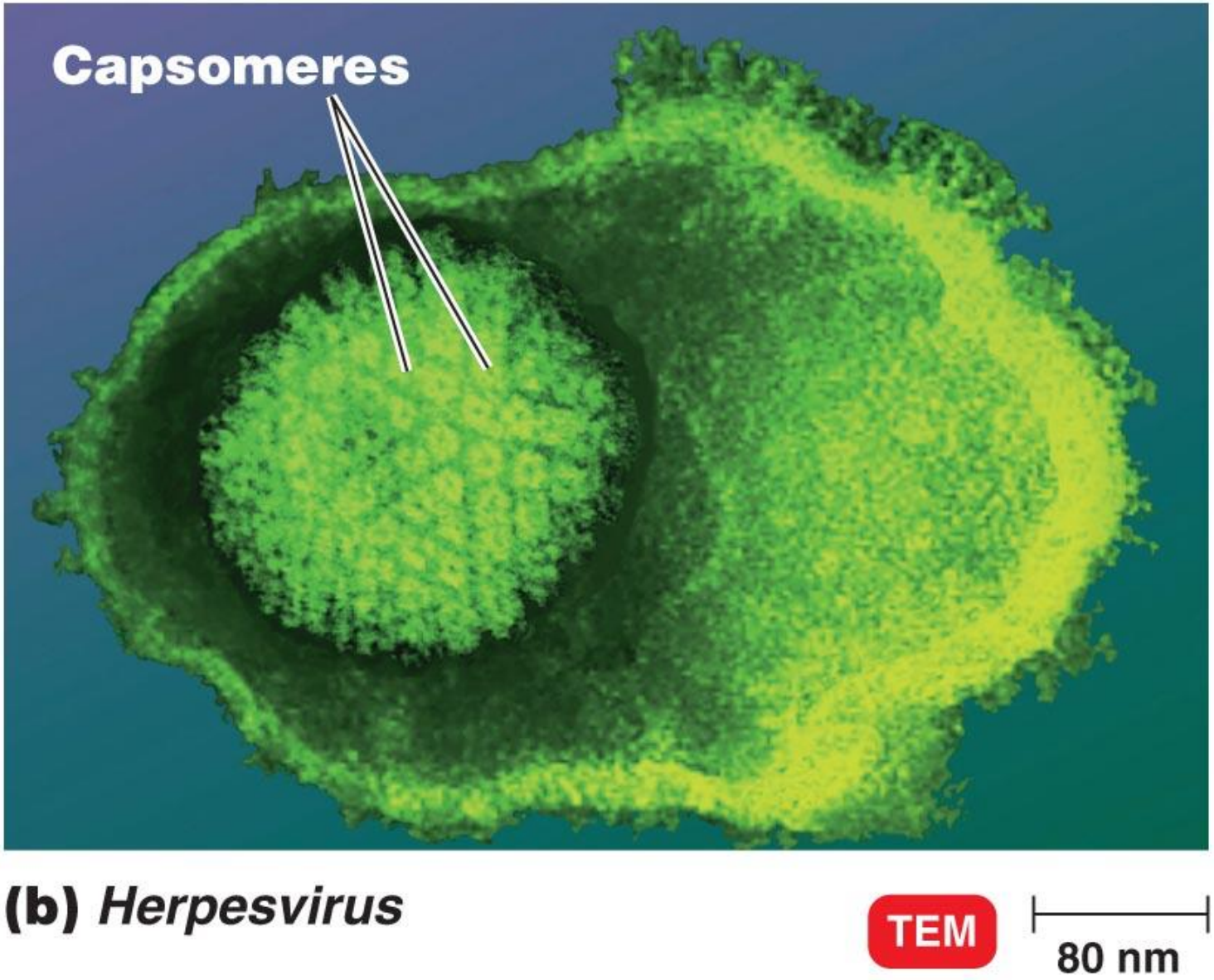
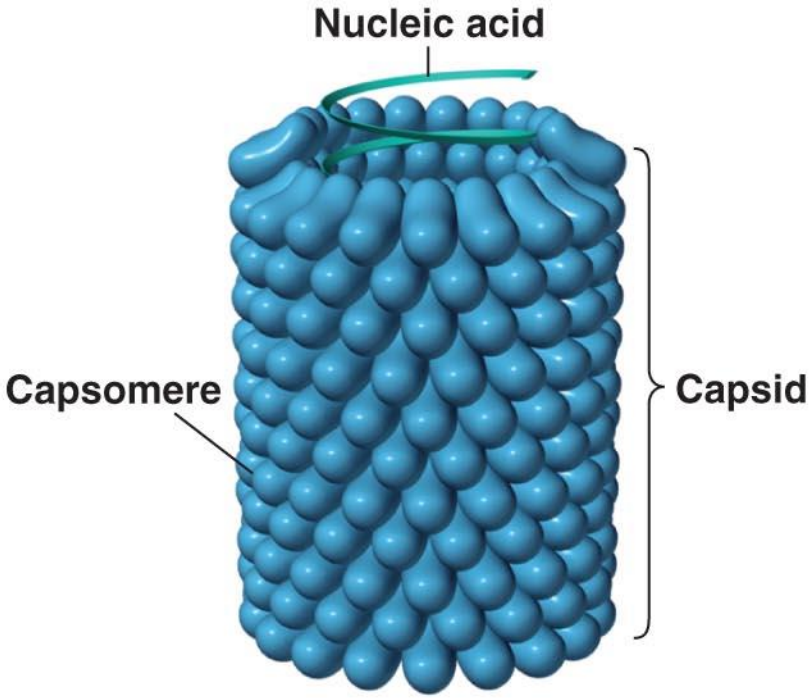


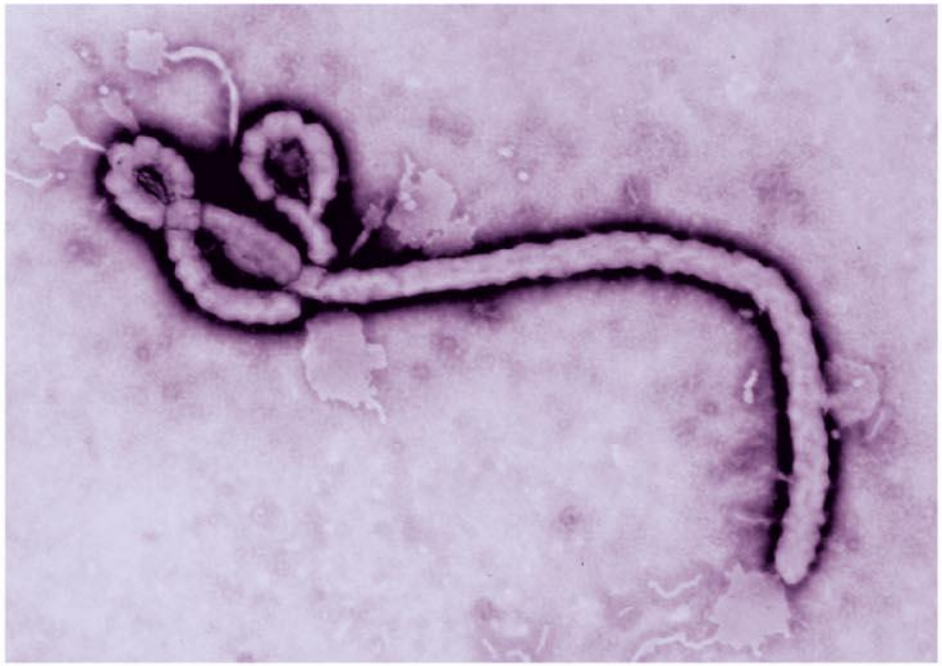
Figure 13.16b

Morphology of a Helical Virus

Helical viruses resemble long rods and their capsids are hollow cylinders surrounding the nucleic acid.



(a) A helical virus



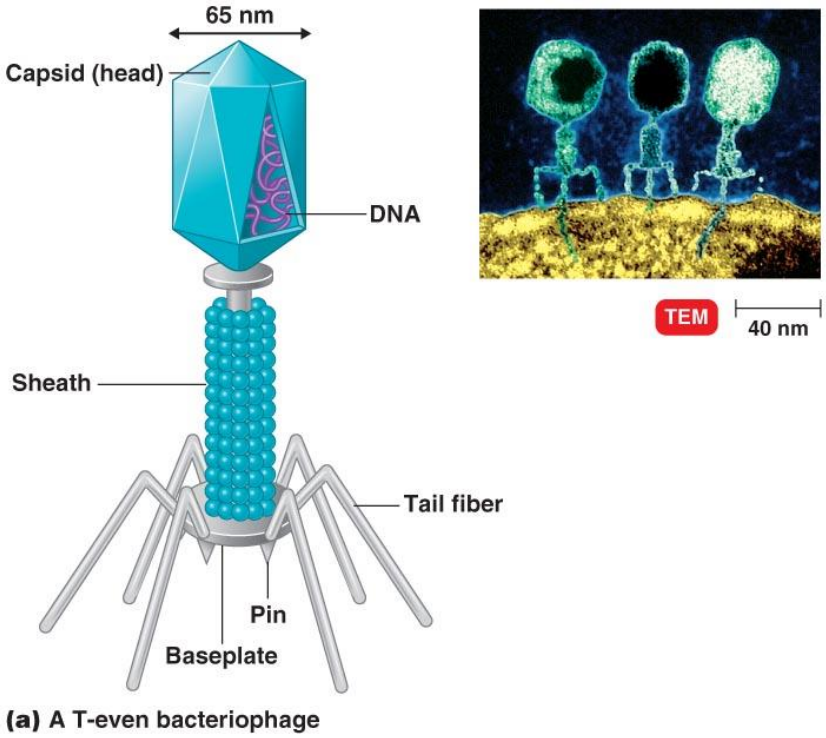
(b) Ebola virus

TEM 100 nm

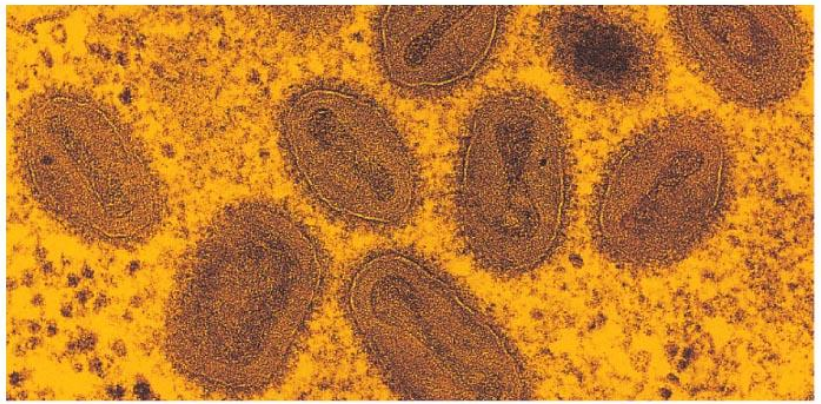
Figure 13.4

Morphology of a Complex Virus

- Complex viruses have complex structures. For example, many bacteriophages have a polyhedral capsid with a helical tail sheath attached.



(a) A T-even bacteriophage



(b) *Orthopoxvirus*

Figure 13.5

Taxonomy of Viruses

- Order names end in -ales
- Family names end in -viridae
- Genus names end in -virus
- Viral species: A group of viruses sharing the same genetic information and **ecological niche** (host range). Common names are used for species
  - Such as human immunodeficiency virus (HIV)
- Subspecies are designated by a number
  - Such as HIV-1

Taxonomy of Viruses

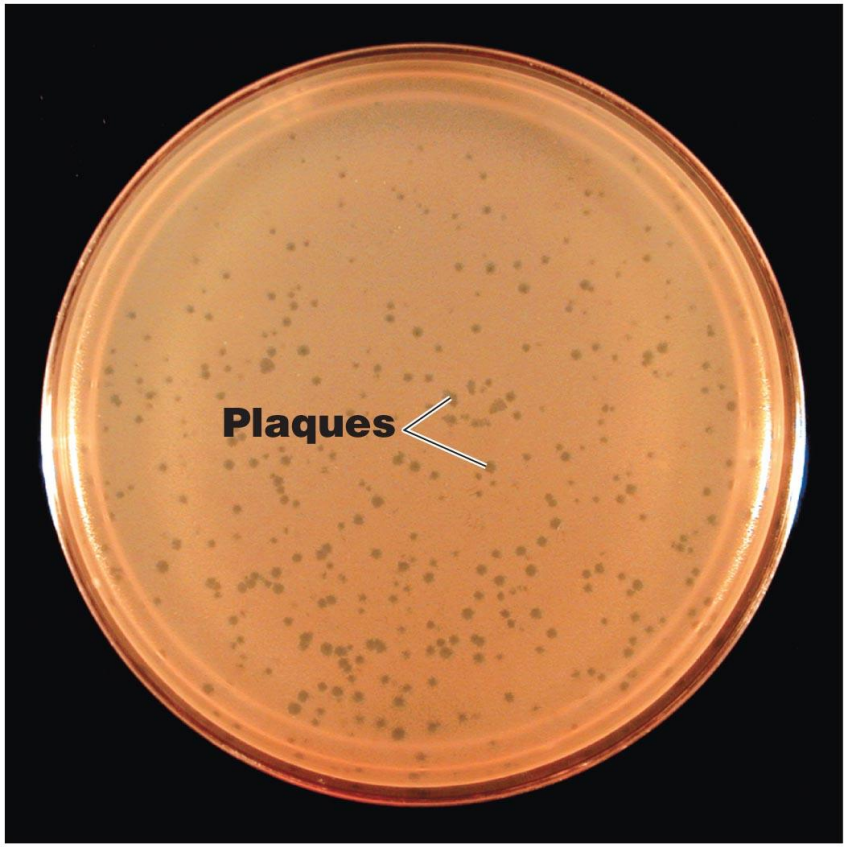
- Herpesviridae
- *Herpesvirus*
- Human herpes virus HHV-1, HHV-2, HHV-3

- Retroviridae
- *Lentivirus*
- Human immunodeficiency virus HIV-1, HIV-2

Isolation, Cultivation, and Identification

Growing Viruses

- Viruses must be grown in living cells.
  - The easiest viruses to grow are **bacteriophages**
  - The **plaque method** mixed bacteriophages with host bacteria and nutrient agar.
  - Bacteriophages form **plaques** on a lawn of bacteria.



- Each plaque originates with a single viral particle; the concentration of viruses is given as **plaque-forming units**.

Figure 13.6

Growing Viruses

- Animal viruses may be grown in living animals or in embryonated eggs
  - Chorioallantoic membrane絨毛尿囊膜
  - Amniotic 羊水
  - Allantoic 尿囊
  - Yolk sac 卵黃囊

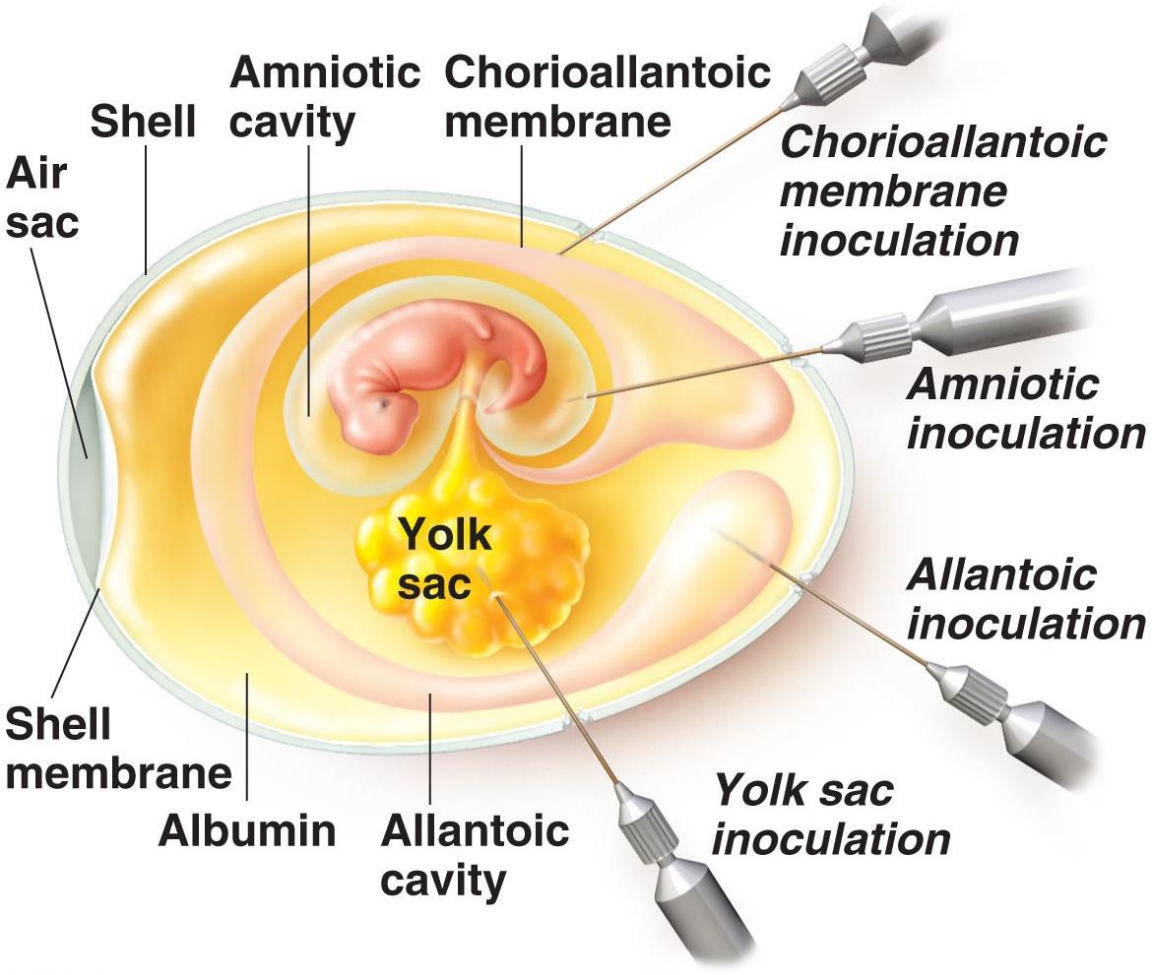


Figure 13.7

Growing Viruses

- Animal and plant viruses may be grown in cell culture.
  - **Primary cell lines (**原代細胞株), derived from tissue slices, tend to die out after only a few generation.
  - Diploid cell lines, derived from human embryos, can be maintained for about 100 generations.
  - **Continuous cell lines** (連續細胞株, transformed and cancerous, immortal cell lines) may be maintained indefinitely.

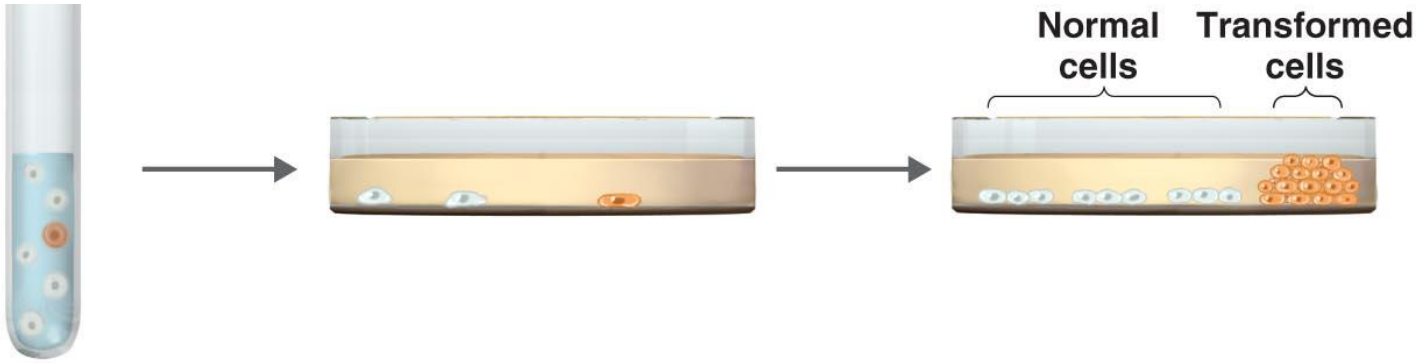
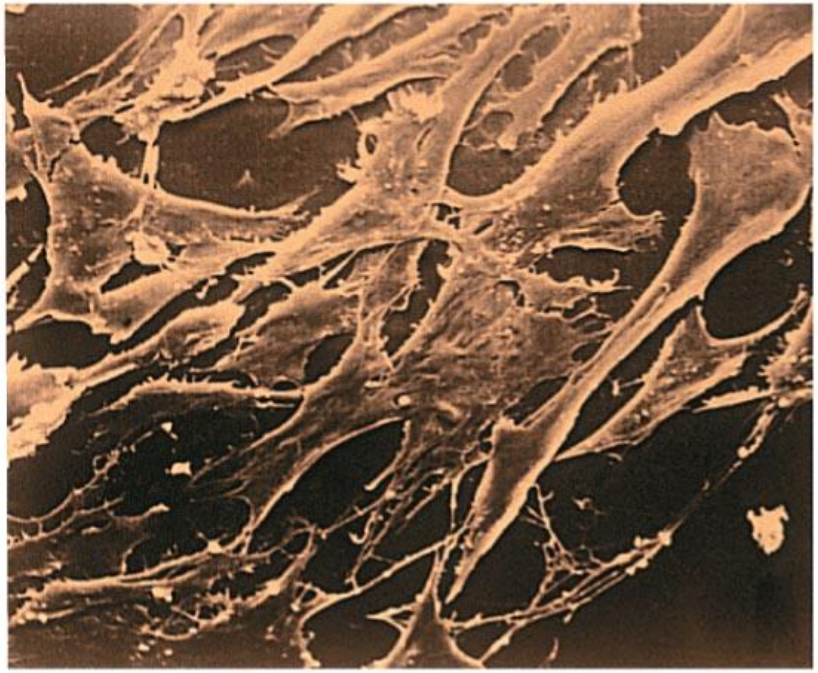


Figure 13.8

Virus Identification

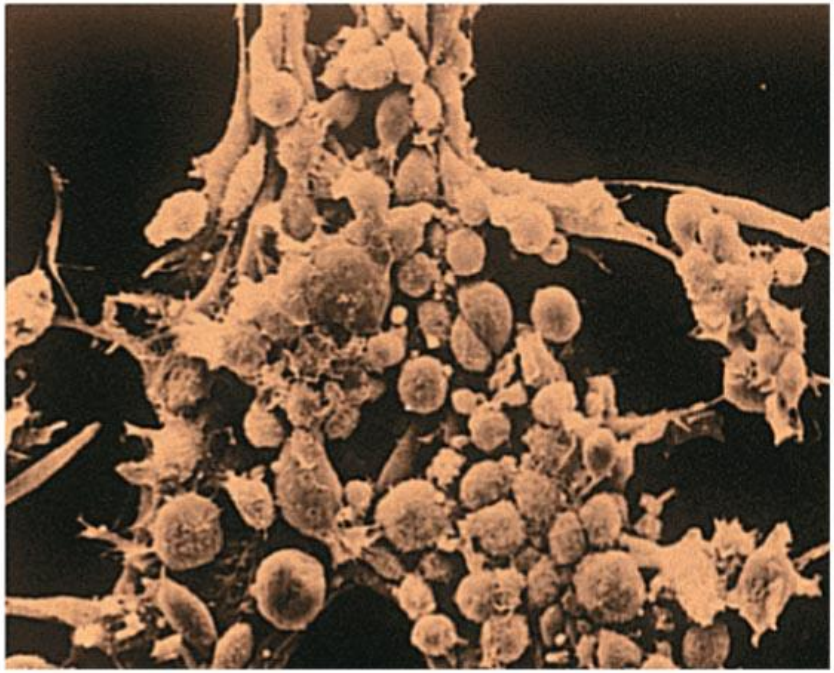
1. Cytopathic effect (CPE) 細胞病變

- When viruses infect host cell, viruses may result in host cell damage or death. This cell damage or death is called cytopathic effect.



(a) *monolayer*

SEM 40μm



(b) *Cells pile up and "round up"*

SEM 20μm

Figure 13.9

Virus Identification

2. **Serological tests**
   - Detect antibodies against viruses in a patient
   - Use antibodies to identify viruses in neutralization tests, viral hemagglutination, and Western blot (Ch17 & 18)

3. **Nucleic acids**
   - **RFLPs** (restriction fragment length polymorphisms; DNA fingerprinting)
   - **PCR** (polymerase chain reaction)

Viral Multiplication

The Lytic Cycle (裂解期): (T-even bacteriophages):

- **Attachment**: Phage attaches by tail fibers to host cell
- **Penetration**: Phage lysozyme opens cell wall; tail sheath contracts to force tail core reaching plasma membrane and injecting DNA into cell
- **Biosynthesis**: Production of phage DNA and proteins
- **Maturation**: Assembly of phage particles
- **Release**: Phage lysozyme breaks cell wall

A Viral One-Step Growth Curve

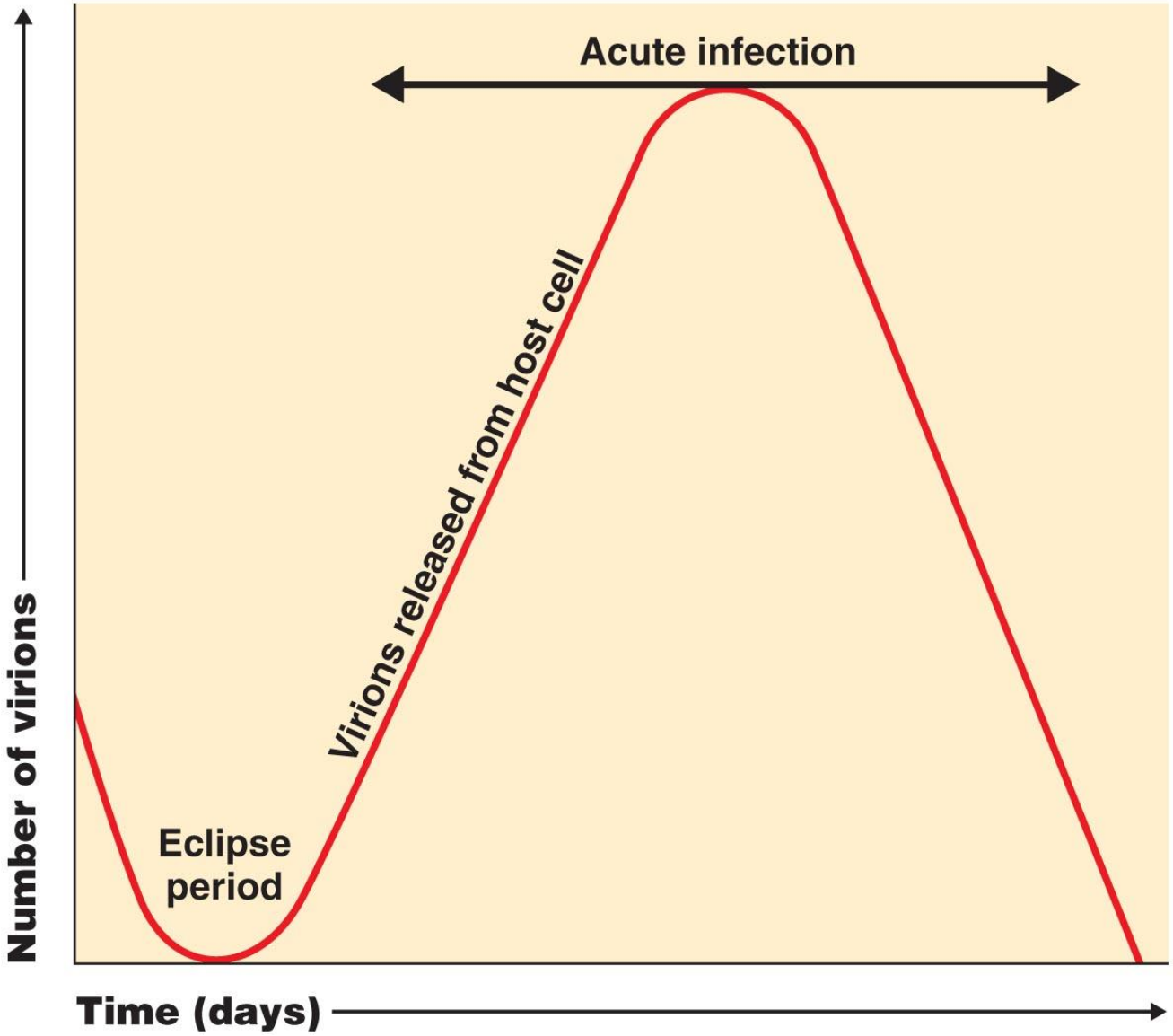


Figure 13.10

Lytic Cycle of a T-Even Bacteriophage

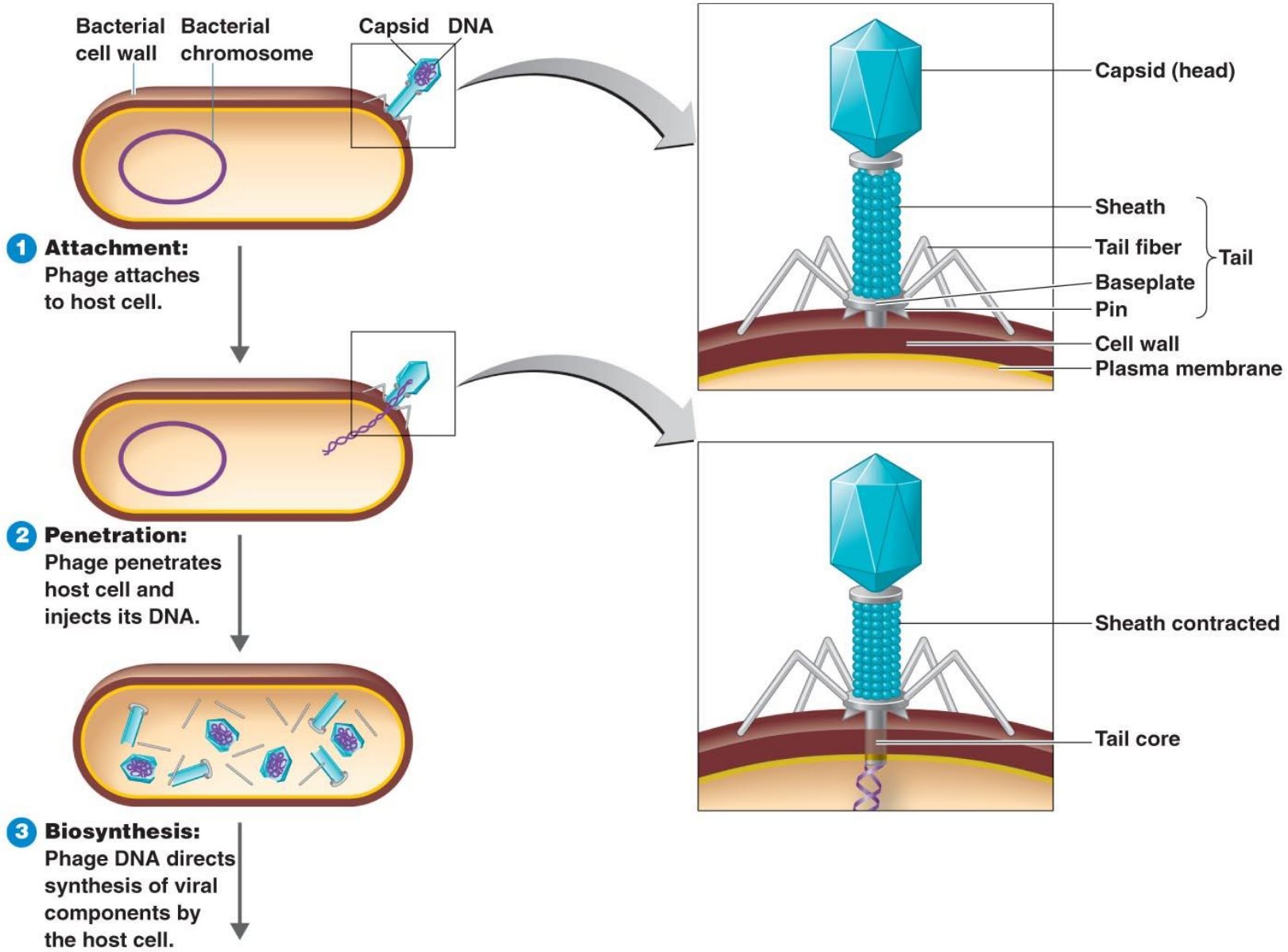


Figure 13.11

Lytic Cycle of a T-Even Bacteriophage

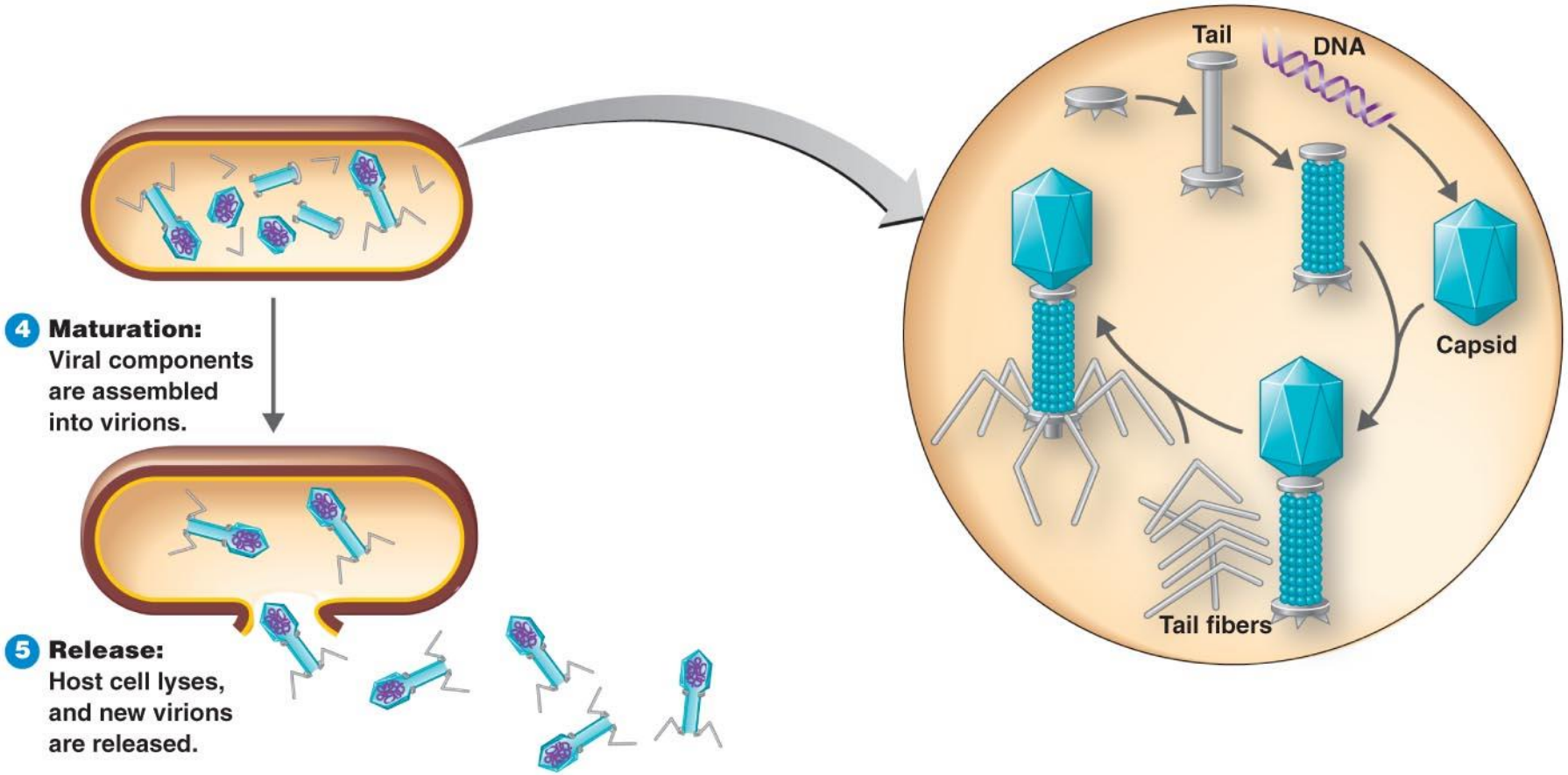


Figure 13.11

Lytic and Lysogenic cycles

- **Lytic cycle (裂解期)**: Phage causes lysis and death of host cell
- **Lysogenic cycle (潜溶期)**: Phage DNA incorporated in host DNA. The host cells are still alive. The inserted phage DNA is now called **prophage**.
- The **lysogenic phages** also called **temperate phages**.
- During the lysogenic cycle, prophage genes are regulated by two repressor proteins coded by the prophage. The prophage is replicated each time when the cell divides.
- The action of UV light or certain mutagens can lead to the excision (popping-out) of the phage DNA, and to initiation of the lytic cycle.

The Lysogenic Cycle

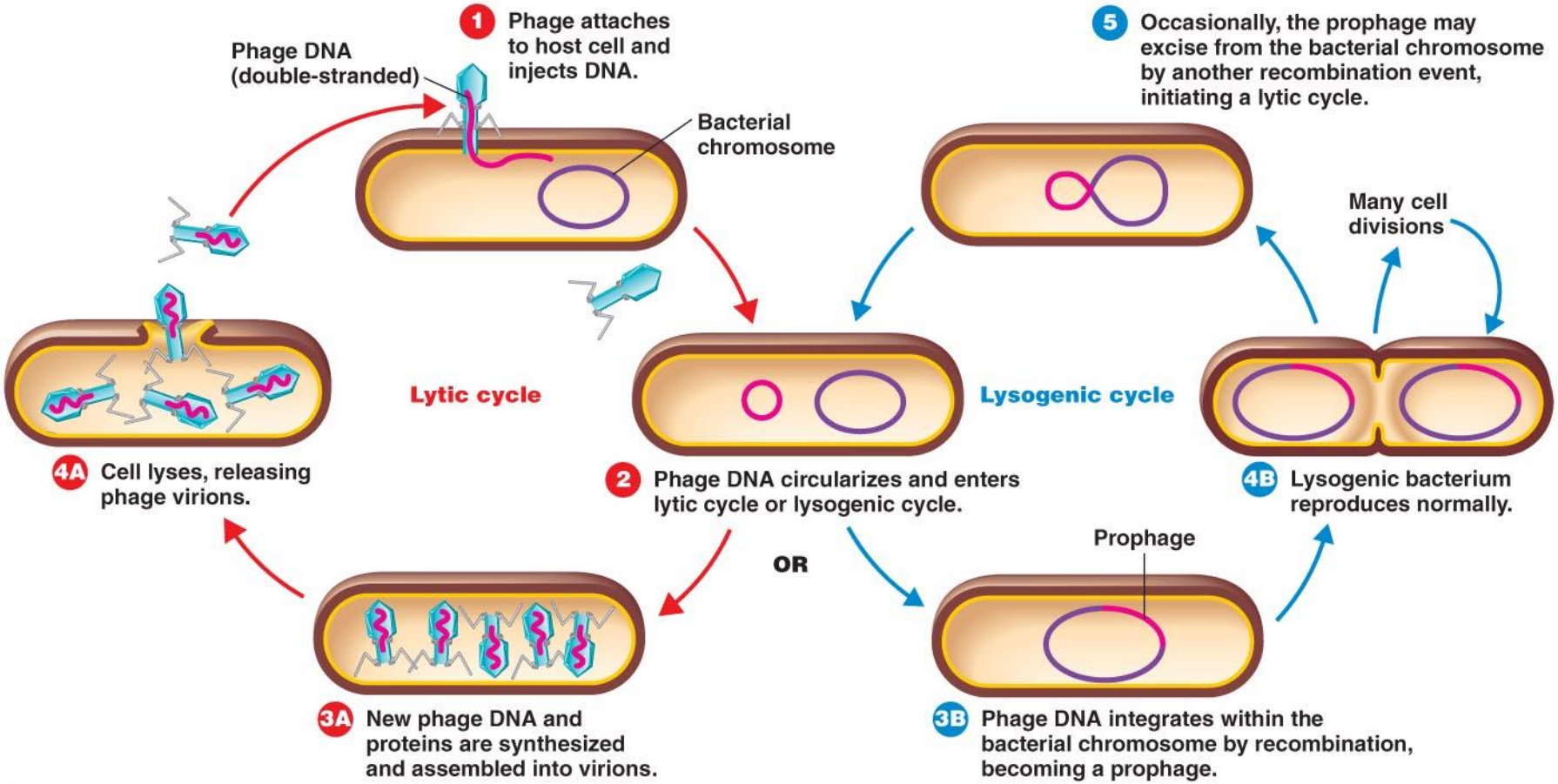


Figure 13.12

Three results of lysogeny

1. The lysogenic cells are immune to reinfection by the same phage. (However, the host cell is not immune to infection by other phage types.)
2. Phage conversion
   - The host cell may exhibit new properties, e.g. a toxin gene carried by a temperate phage
3. Specialized transduction
   - Only certain bacterial genes can be transferred.
   - Lysogenic phage packages **adjacent bacterial DNA** along with its own DNA in the same capsid.
   - Any bacterial genes can be transferred by generalized transduction (Fig. 8.28).

Results of Multiplication of Bacteriophages

- **Lytic cycle**
  - Phage causes lysis and death of host cell
- **Lysogenic cycle**
  - The lysogenic cells are immune to reinfection by the same phage.
  - Phage conversion
  - Specialized transduction

Generalized Transduction

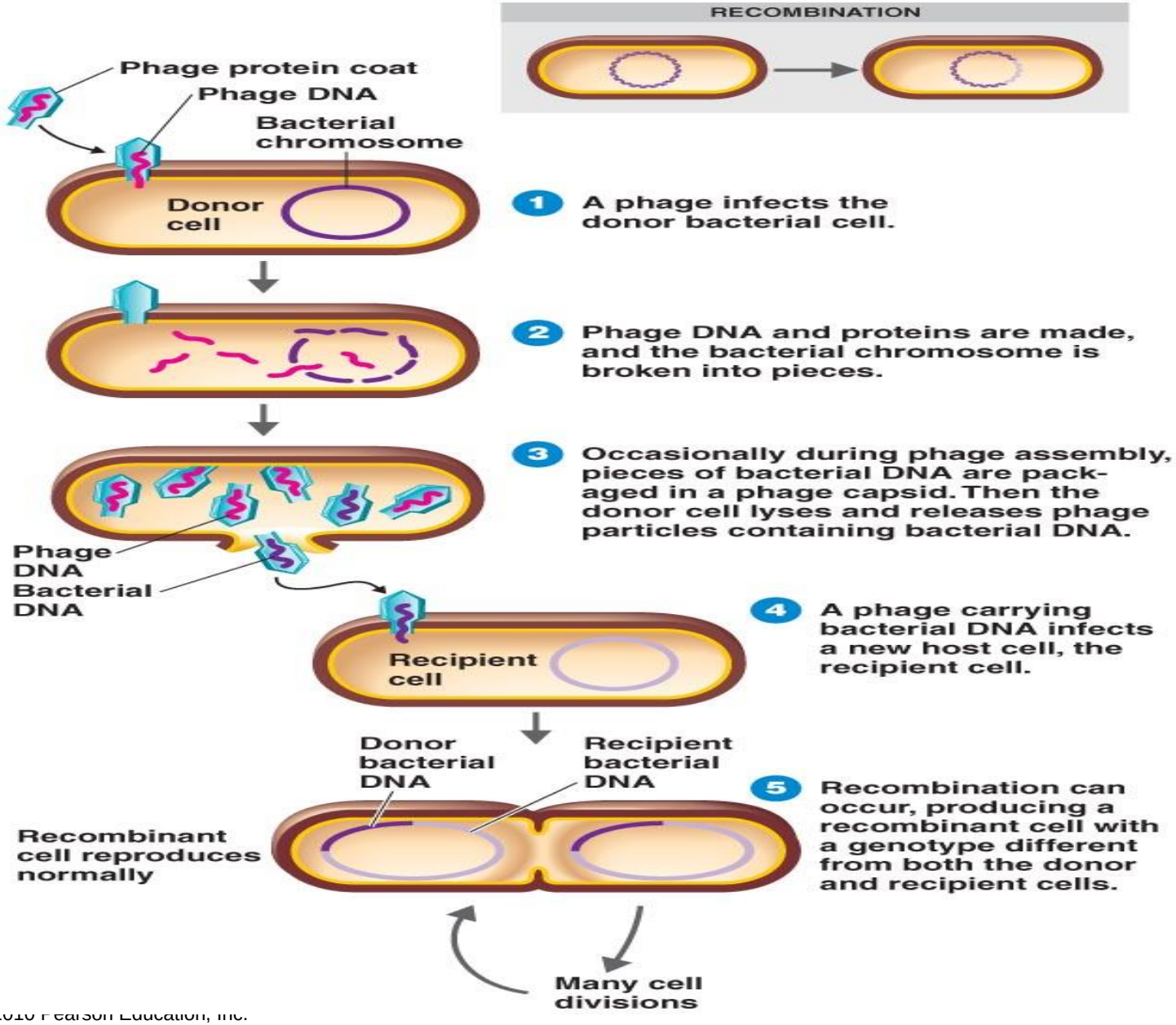
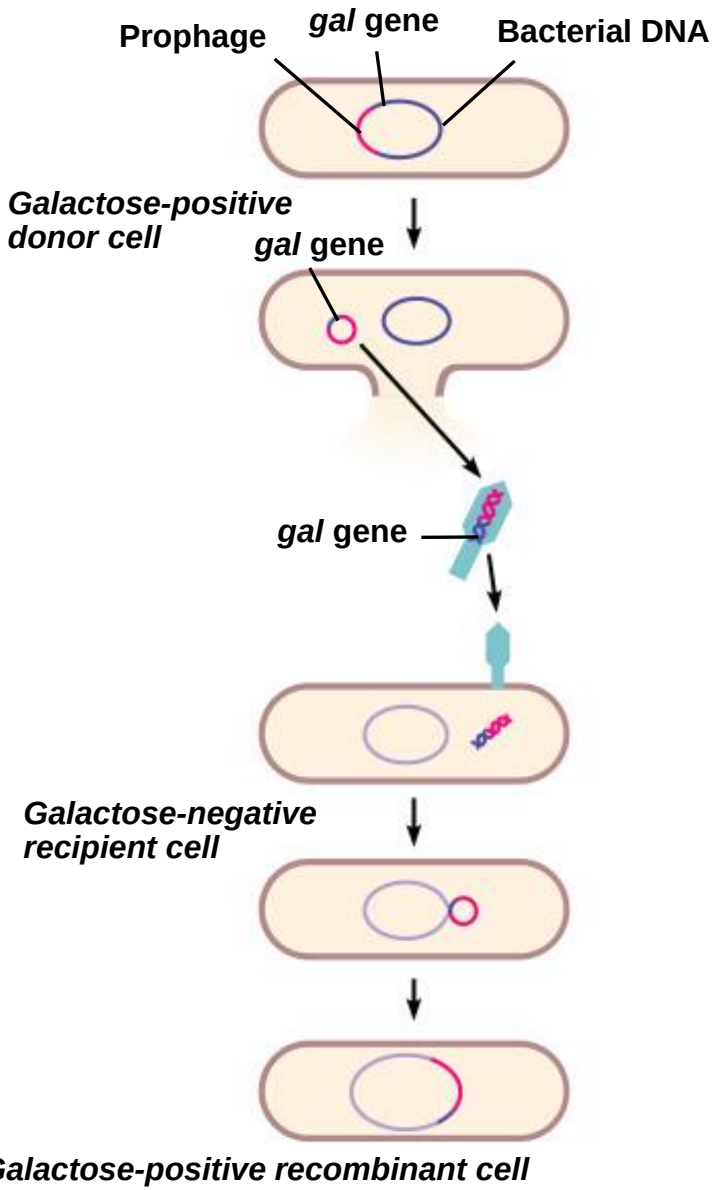


Figure 8.28

Specialized Transduction



1. Prophage exists in galactose-using host (containing the *gal* gene).
2. Phage genome excises, carrying with it the adjacent *gal* gene from the host.
3. Phage matures and cell lyses, releasing phage carrying *gal* gene.
4. Phage infects a cell that cannot utilize galactose (lacking *gal* gene).
5. Along with the prophage, the bacterial *gal* gene becomes integrated into the new host's DNA.
6. Lysogenic cell can now metabolize galactose.

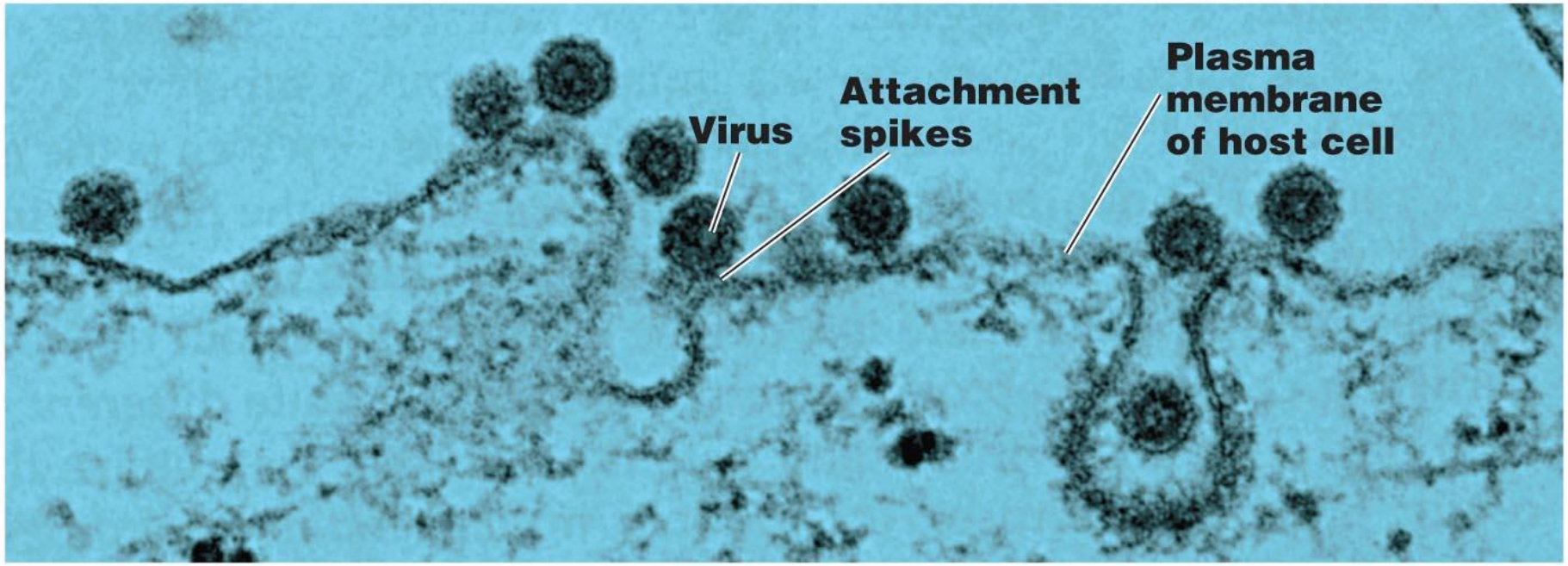
Figure 13.13

Multiplication of Animal Viruses

- **Attachment** Viruses attaches to **cell membrane**
- **Entry** By **pinocytosis** (胞飲作用) or **fusion**
  - (fusion only for enveloped viruses)
- **Uncoating** The separation of the viral nucleic acid from its protein coat by viral or host enzymes
- **Biosynthesis** Production of nucleic acid and proteins
- **Maturation** Nucleic acid and capsid proteins assemble
- **Release** By budding (enveloped viruses) or rupture

Attachment, Penetration, Uncoating

- By pinocytosis

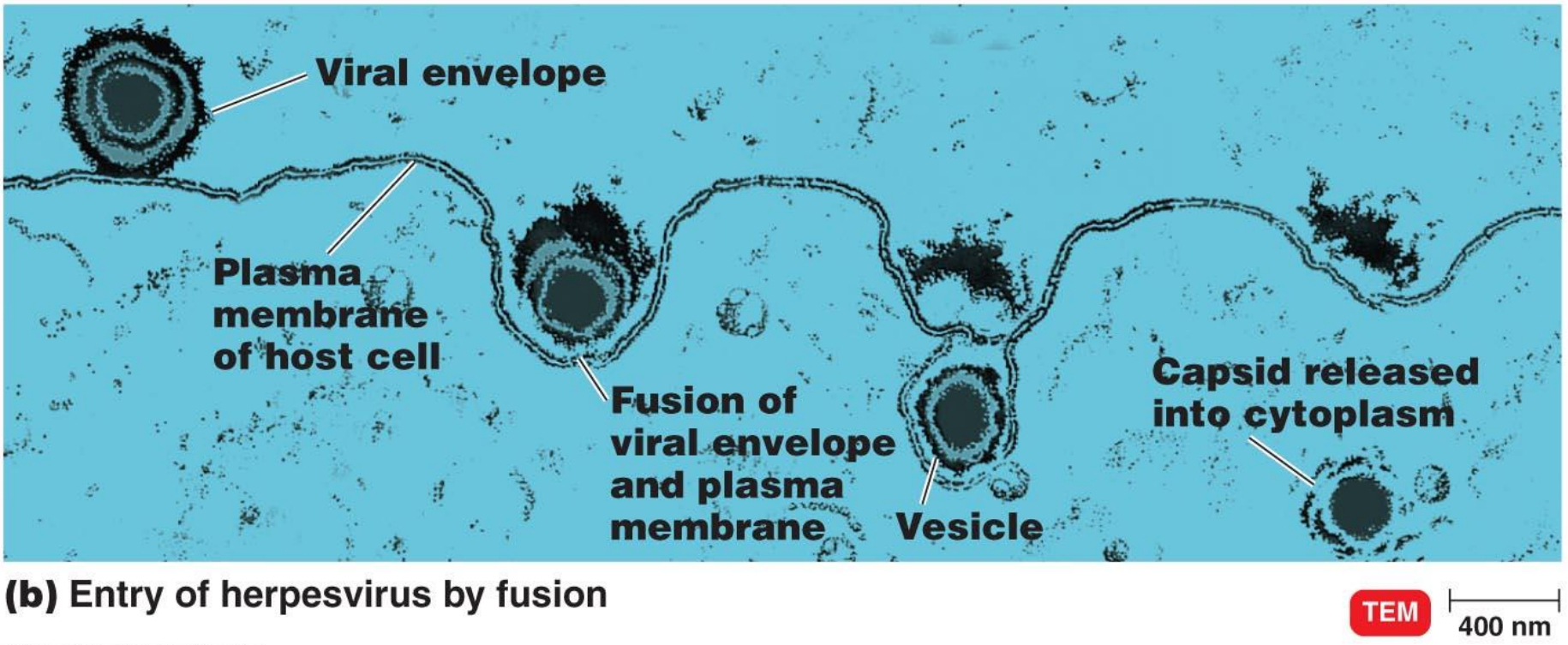


(a) Entry of togavirus by pinocytosis

Figure 13.14a

Attachment, Penetration, Uncoating

- By fusion



(b) Entry of herpesvirus by fusion

Figure 13.14b

Release of an enveloped virus by budding

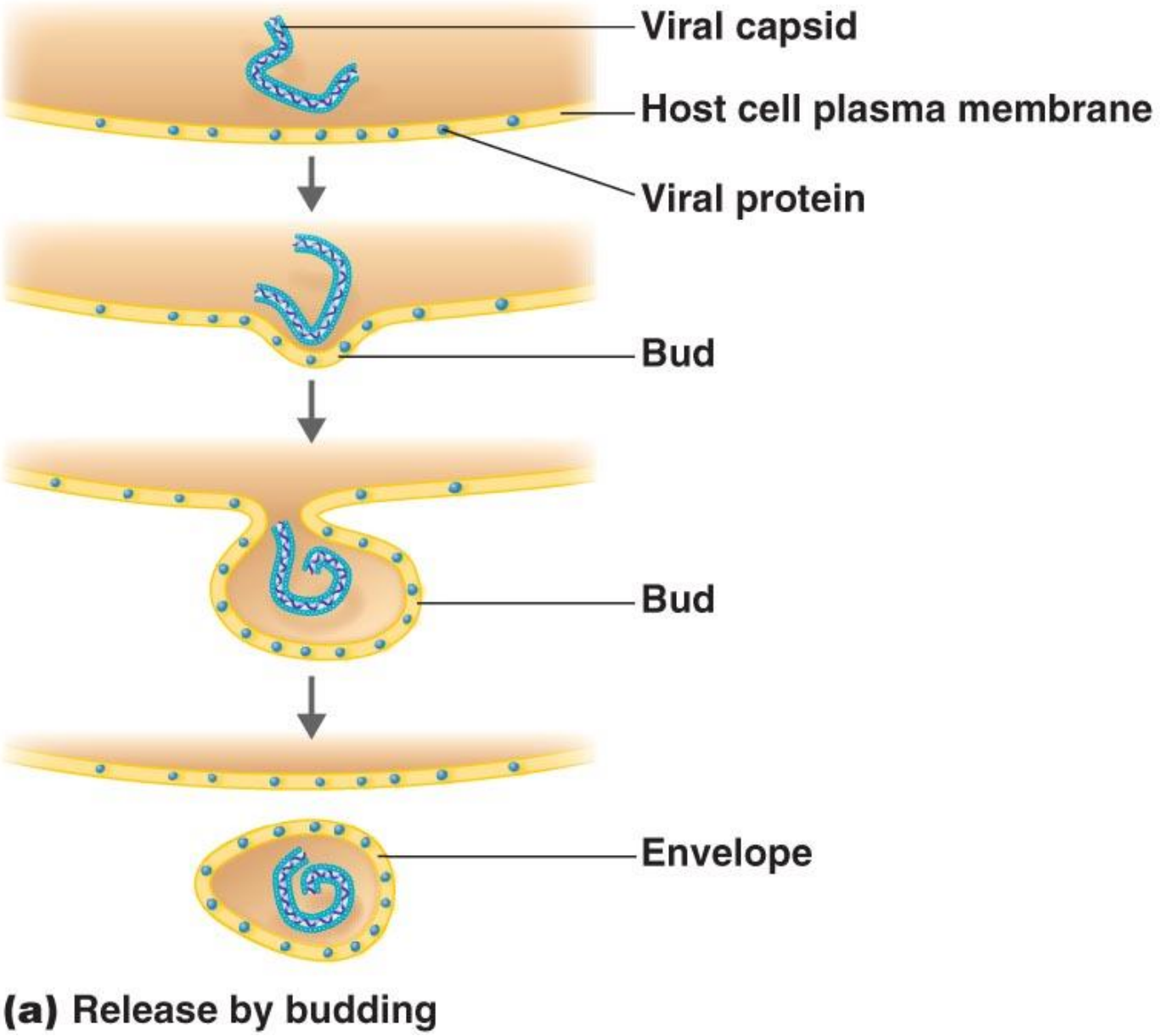


Figure 13.20

Budding of an Enveloped Virus

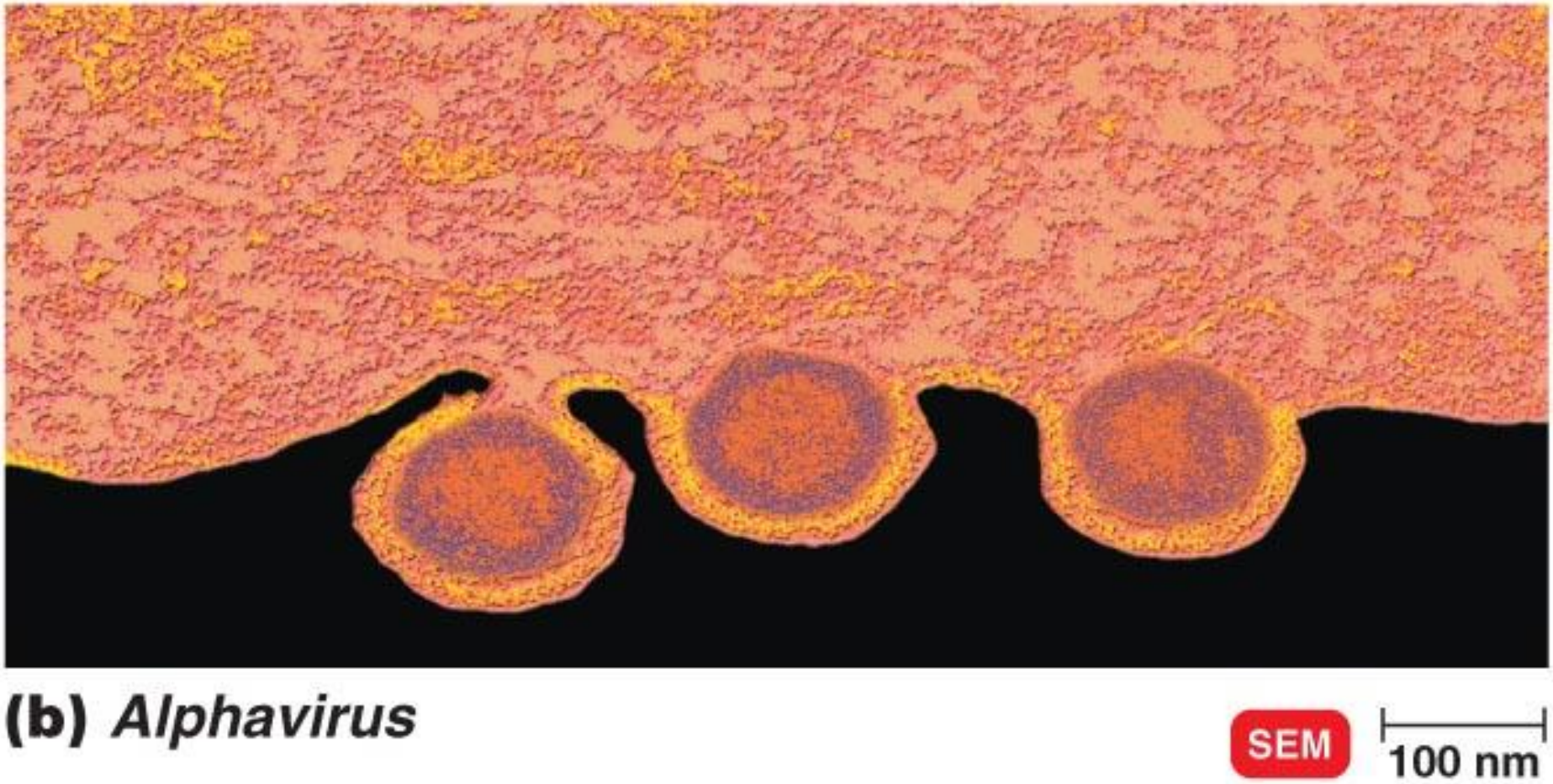


Figure 13.20

Multiplication of DNA Virus

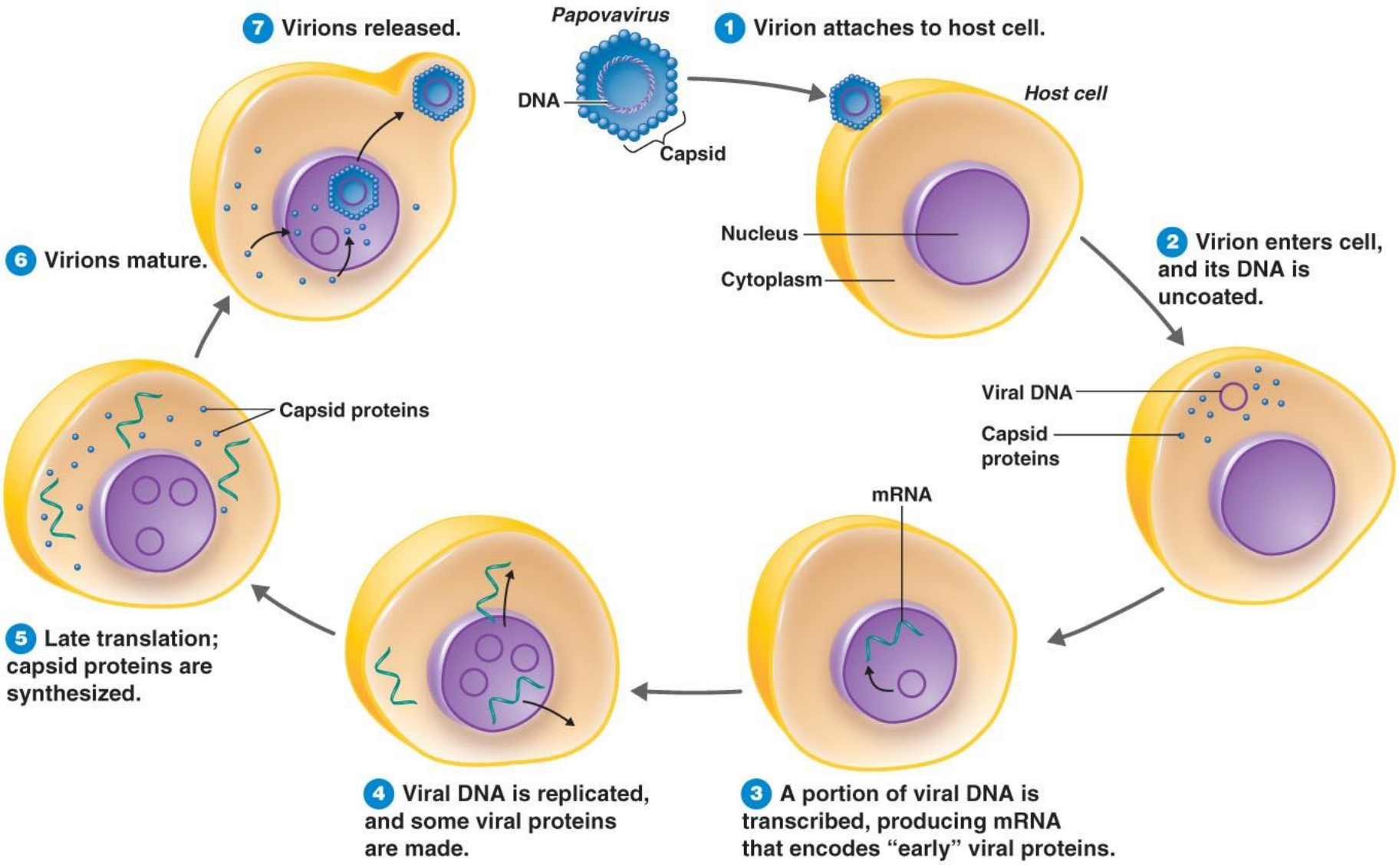


Figure 13.15

Sense Strand (+ Strand) RNA Virus

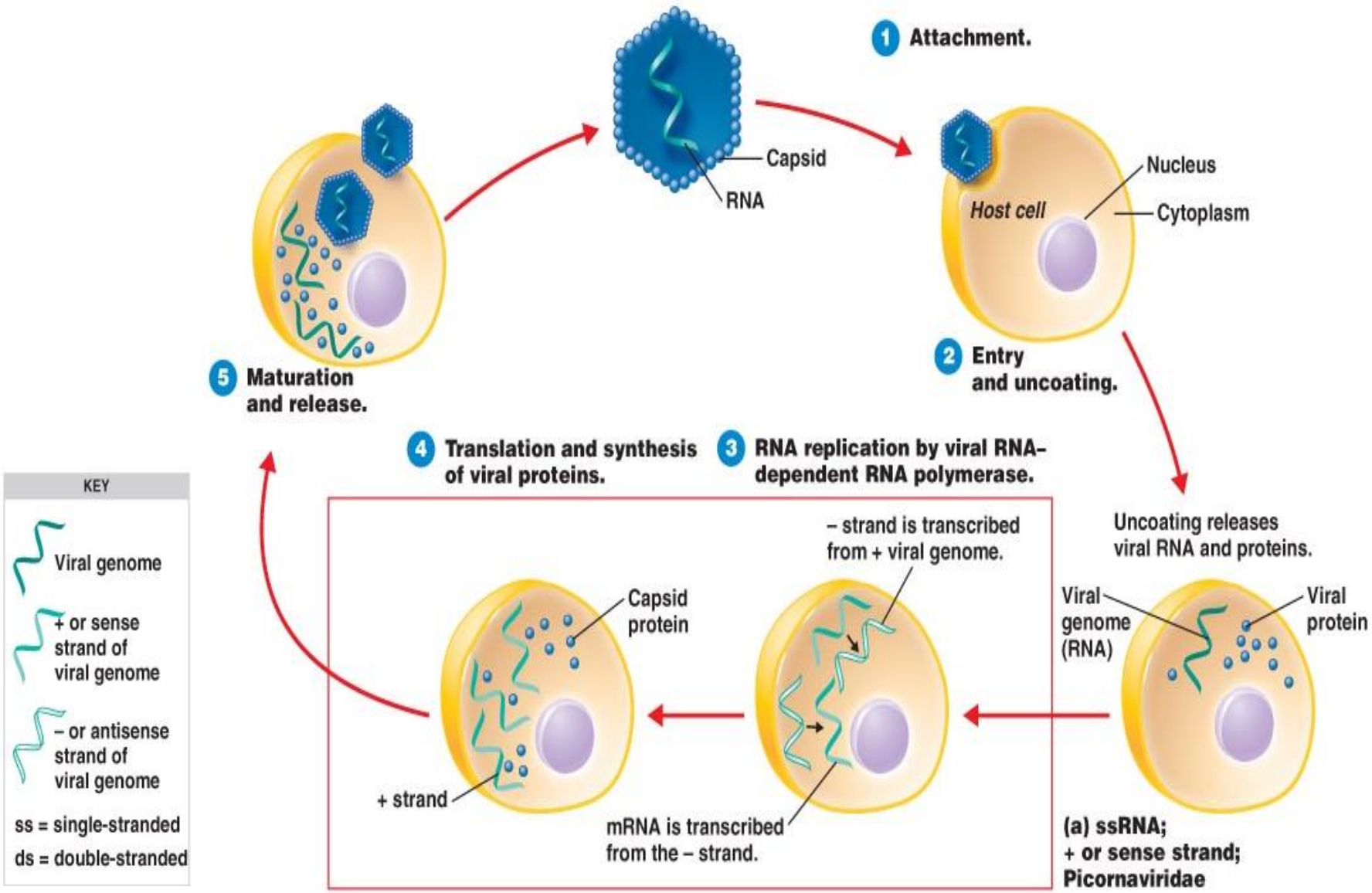


Figure 13.17a

Antisense Strand (– Strand) RNA Virus

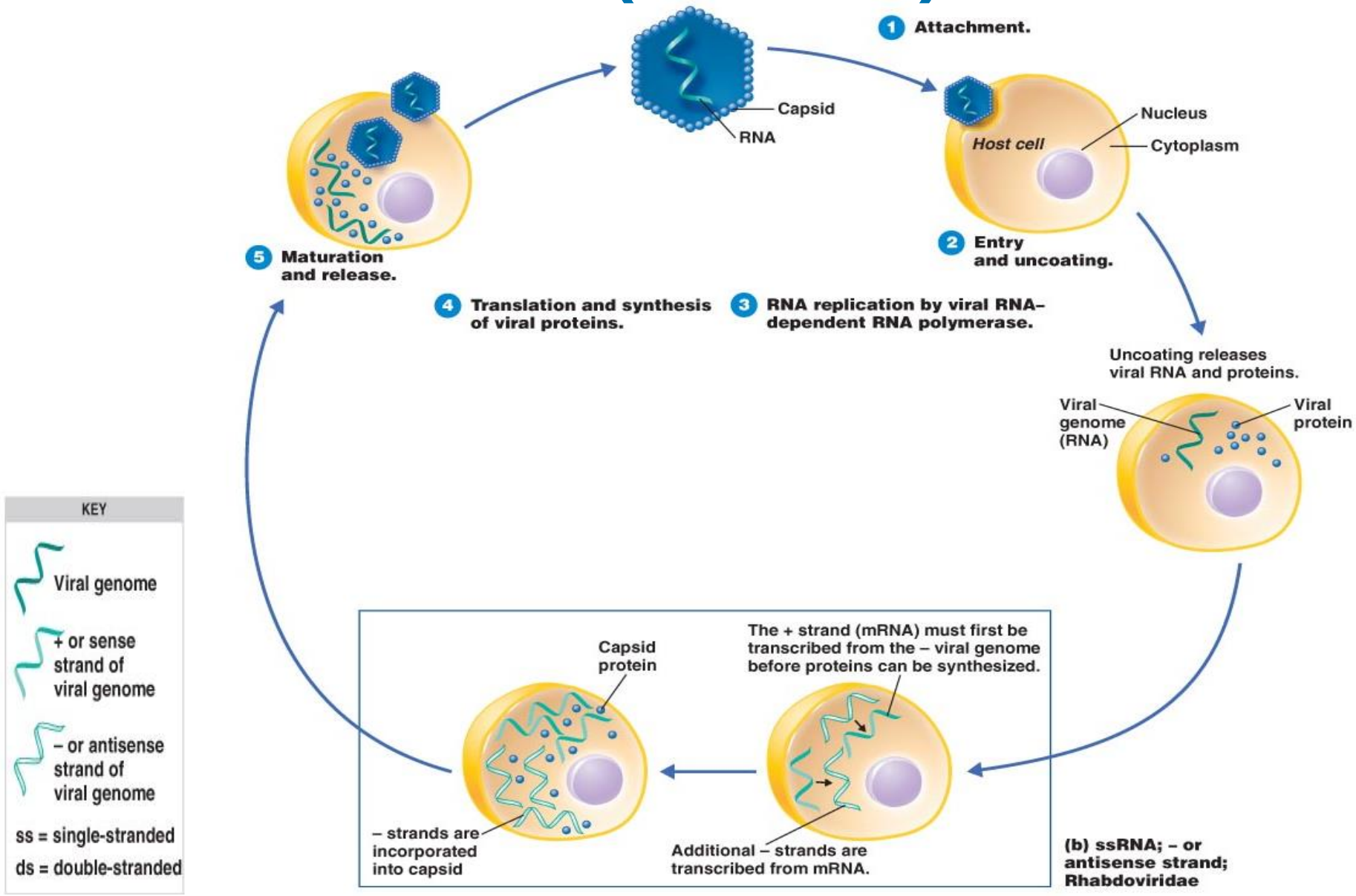


Figure 13.17b

Double-Stranded RNA Virus

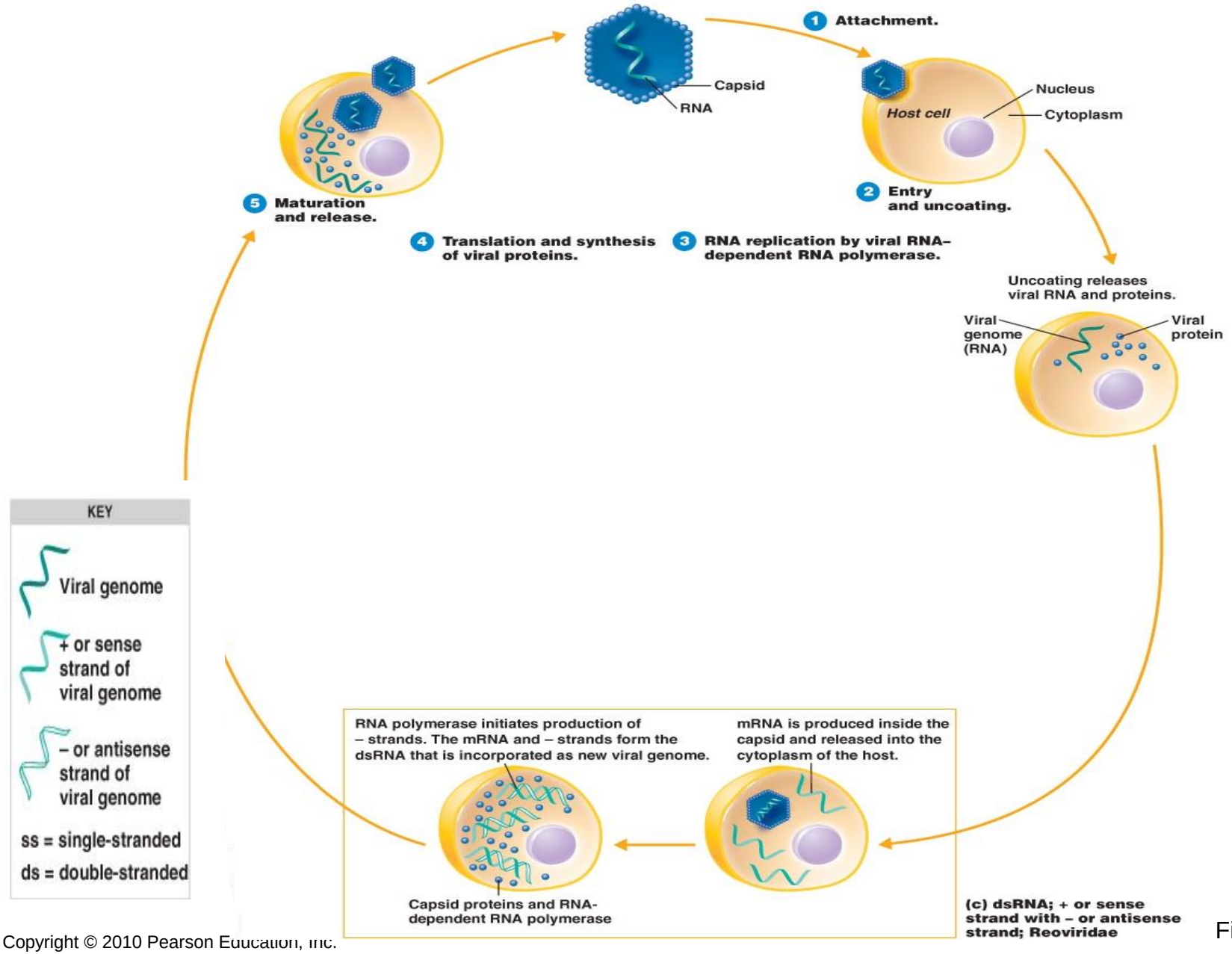


Figure 13.17c

Multiplication of RNA-Containing Viruses

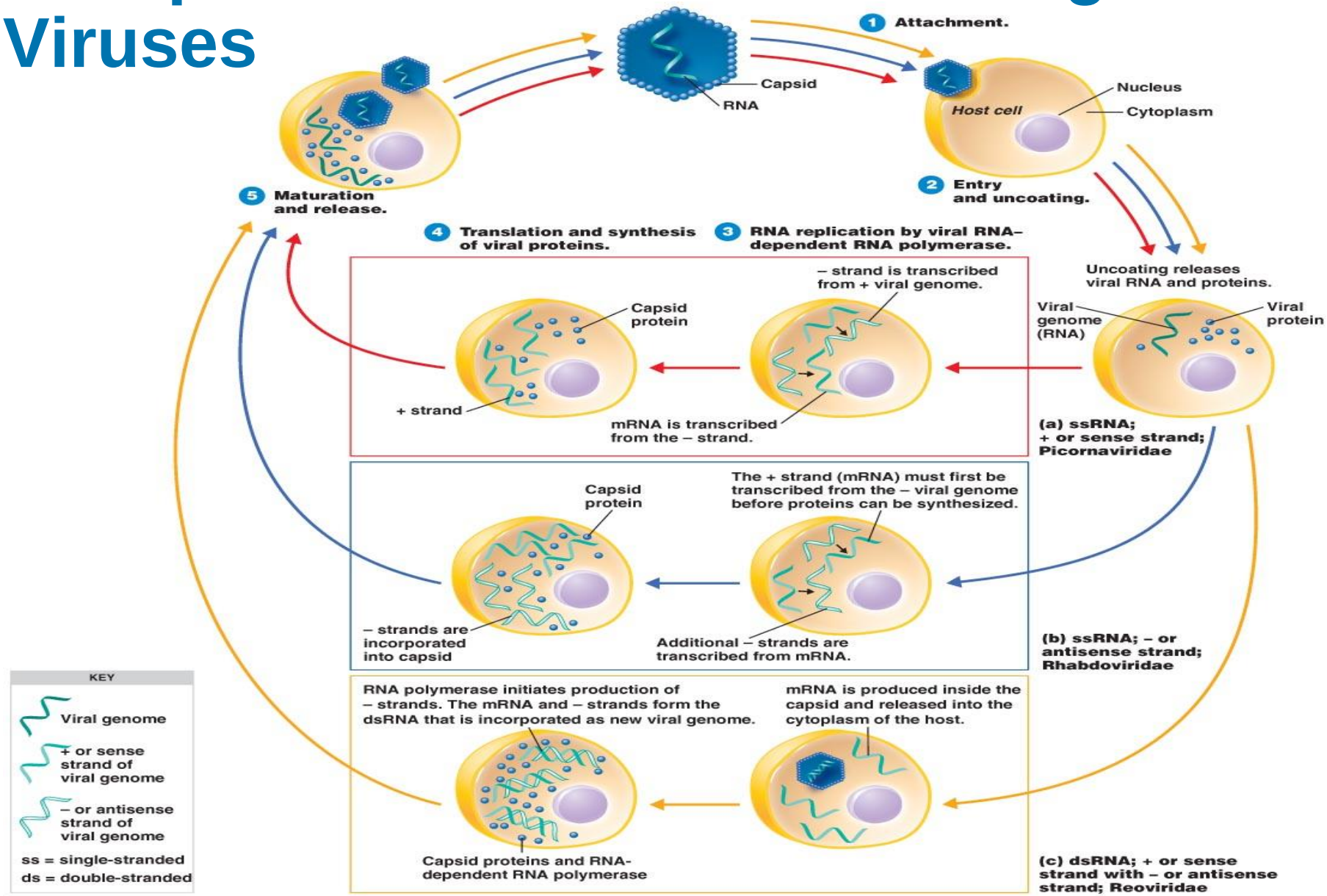


Figure 13.17

Multiplication of a Retrovirus

反轉錄病毒

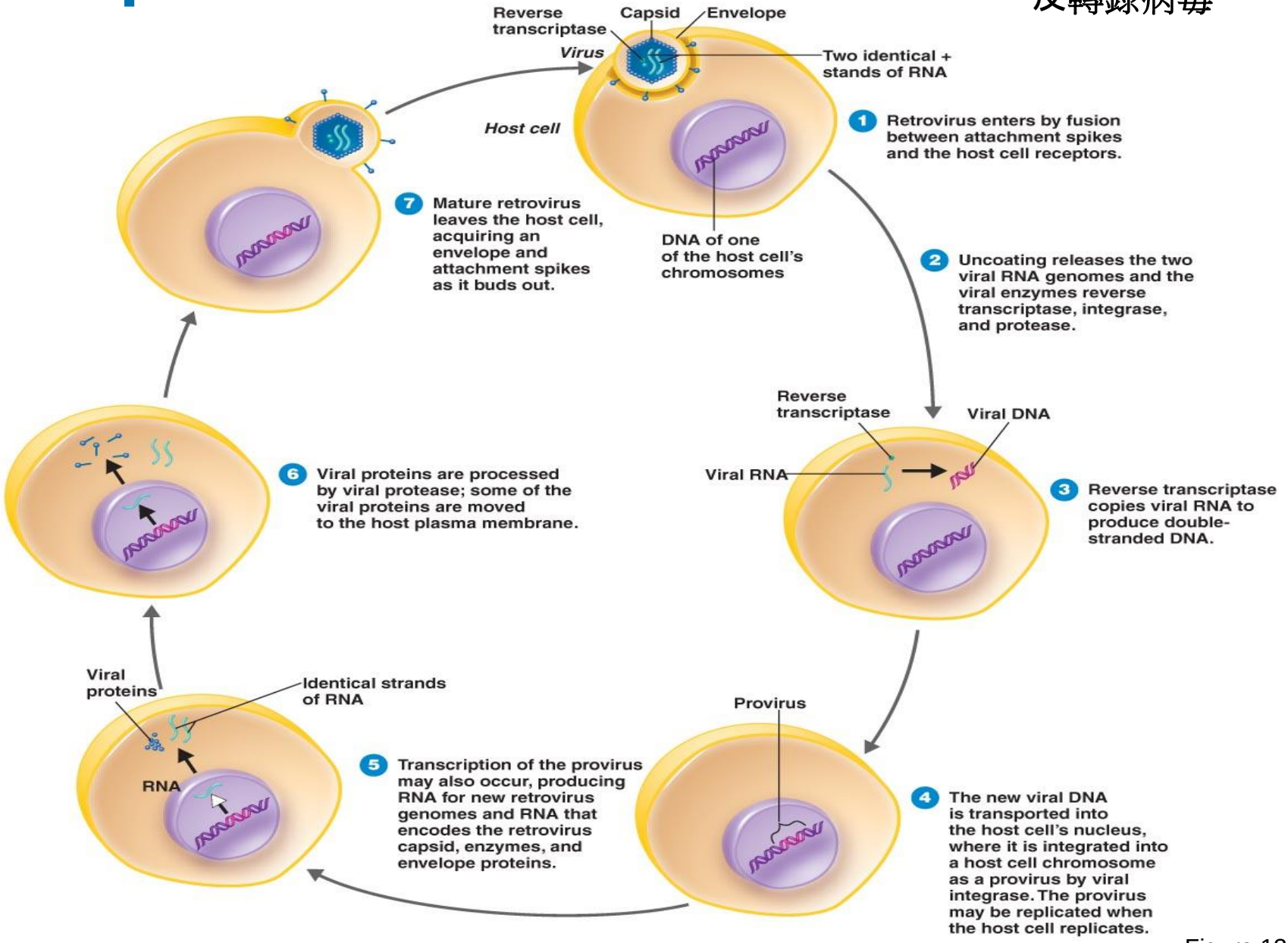


Figure 13.19

Table 13.4 The Biosynthesis of DNA and RNA Viruses Compared

Viral Nucleic Acid	Virus Family	Special Features of Biosynthesis
DNA, single-stranded	Parvoviridae	Cellular enzyme transcribes viral DNA in nucleus
DNA, double-stranded	Herpesviridae Papovaviridae	Cellular enzyme transcribes viral DNA in nucleus
	Poxviridae	Viral enzyme transcribes viral DNA in virion, in cytoplasm
DNA, reverse transcriptase	Hepadnaviridae	Cellular enzyme transcribes viral DNA in nucleus; reverse transcriptase copies mRNA to make viral DNA
RNA, + strand	Picornaviridae Togaviridae	Viral RNA functions as a template for synthesis of RNA polymerase which copies − strand RNA to make mRNA in cytoplasm
RNA, − strand	Rhabdoviridae	Viral enzyme copies viral RNA to make mRNA in cytoplasm
RNA, double-stranded	Reoviridae	Viral enzyme copies − strand RNA to make mRNA in cytoplasm
RNA, reverse transcriptase	Retroviridae	Viral enzyme copies viral RNA to make DNA in cytoplasm; DNA moves to nucleus

Viruses and Cancer

- The earliest relationship between cancer and viruses was demonstrated in the early 1900s, when chicken leukemia and chicken sarcoma were transferred to healthy animals by cell-free filtrates.
- Activated **oncogenes** transform normal cells into cancerous cells.
- Transformed cells have increased growth, loss of contact inhibition, contain virus-specific antigens (tumor specific transplant antigen and T antigen), exhibit chromosomal abnormalities, and can produce tumors when injected into susceptible animals..
- The genetic material of oncogenic viruses becomes integrated into the host cell's DNA.

Oncogenic Viruses

- **Oncogenic DNA viruses**
  - Adenoviridae
  - Herpesviridae
  - Poxviridae
  - Papovaviridae
  - Hepadnaviridae
- **Oncogenic RNA viruses**
  - Retroviridae
  - Viral RNA is transcribed to DNA, which can integrate into host DNA
  - HTLV-1
  - HTLV-2

Latent and Persistent Viral Infections

- Latent Viral Infections
  - Virus can remain in the host cell for long periods without producing disease symptoms.
    - Cold sores (唇皰疹, herpes simplex virus,單純皰疹病毒), shingles (帶狀皰疹, chickenpox virus,水痘病毒)
- Persistent Viral Infections
  - Disease processes occurs over a long period, generally fatal
    - Subacute sclerosing panencephalitis (亞急性硬化性全腦炎,measles virus, 麻疹病毒)

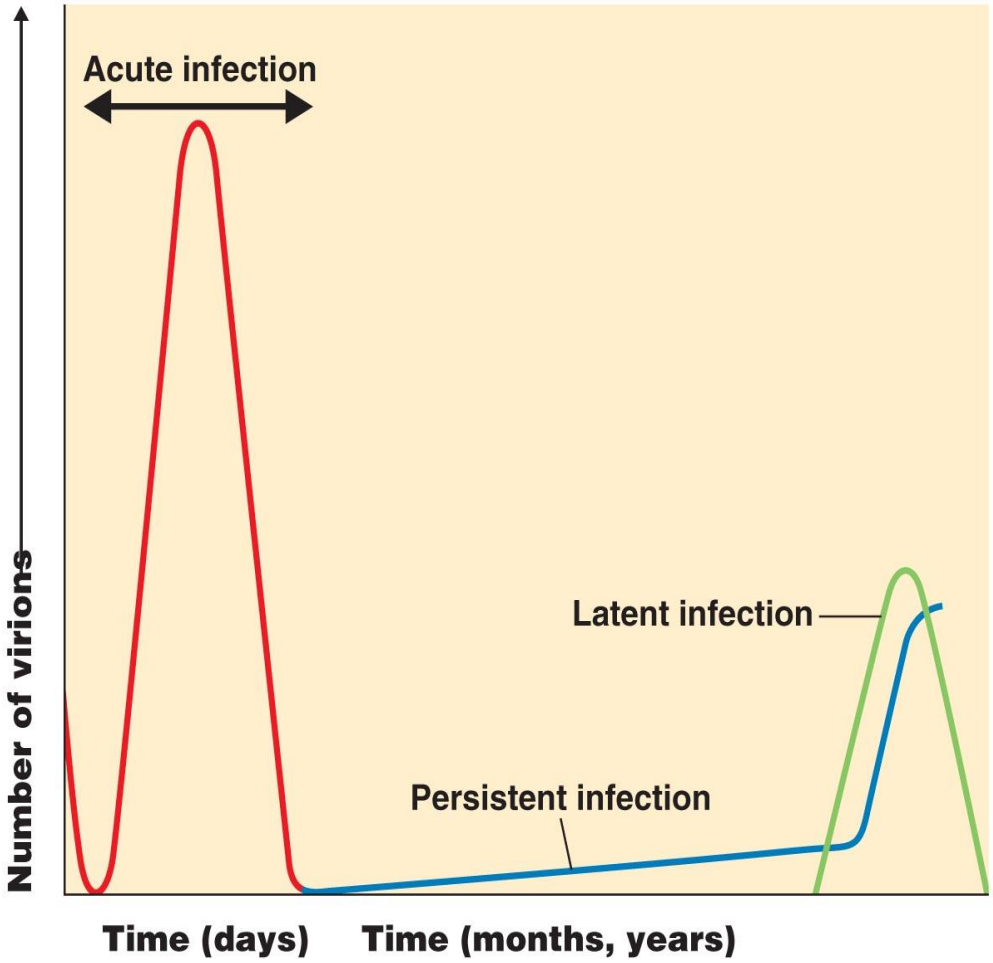


Figure 13.21

Prions, Viroids (類病毒), and Plant Viruses

Prions (傳染性蛋白質):

- **Infectious proteins** discovered in the 1980s
- Inherited and transmissible by ingestion, transplant, & surgical instruments
- Spongiform encephalopathies (海綿樣腦病): Sheep scrapie, **C**reutzfeldt-**J**akob disease (庫賈氏症), **G**erstmann-**S**träussler-**S**cheinker syndrome (GSS氏症), fatal familial insomnia (致死性家族失眠症), mad cow disease
- All involved degeneration of brain tissue.

全家罹罕見「致死性家族失眠症」 已多人死亡 (2016年05月02日, 蘋果日報)

- 澳洲一個家族，被證實罹患遺傳性罕見疾病「致死性家族失眠症」(Fatal Familial Insomnia，FFI)，目前全球經證實罹病者，一千萬人中不到一人，且無藥可醫。FFI患者無法被預測何時發病，患者一般的表現就像是失眠症，難以進入深層睡眠，但與多數失眠症患者是心理或環境因素造成不同，FFI的患者是因為體內的部分蛋白質產生異常結塊，進而引發神經系統受損，在腦部的丘腦產生如海綿般的空洞，而丘腦正是管理睡眠的重要部位。
- 今年30歲的韋伯(Hayley Webb)原本是澳洲《第九頻道》電視台記者，早在青少年時期她就知道自己全家都罹患這種疾病，「十多歲的時候我就知道，我們全家都受到了詛咒」，當時她的祖母率先發病，突然失明，接著出現痴呆症狀，並伴隨長期幻覺，最後連說話功能都喪失，醫生診斷才知道罹患FFI，沒多久就死亡。之後，她的母親、舅舅、阿姨陸續死亡，現在家中就剩下她與28歲弟弟拉克蘭(Lachlan Webb)。目前，兩姐弟已經辭去工作，前往美國加州大學參與一項研究計畫，希望能找出補救措施。（於慶中／綜合外電報導）

Prions

- PrP^{C}: Normal cellular prion protein, on cell surface
- PrP^{Sc}: Scrapie protein; accumulates in brain cells, forming plaques
- Prion diseases are due to an altered protein; the cause can be a mutation in the normal gene for PrP or contact with an altered protein (PrP^{Sc}).

How a Protein Can Be Infectious

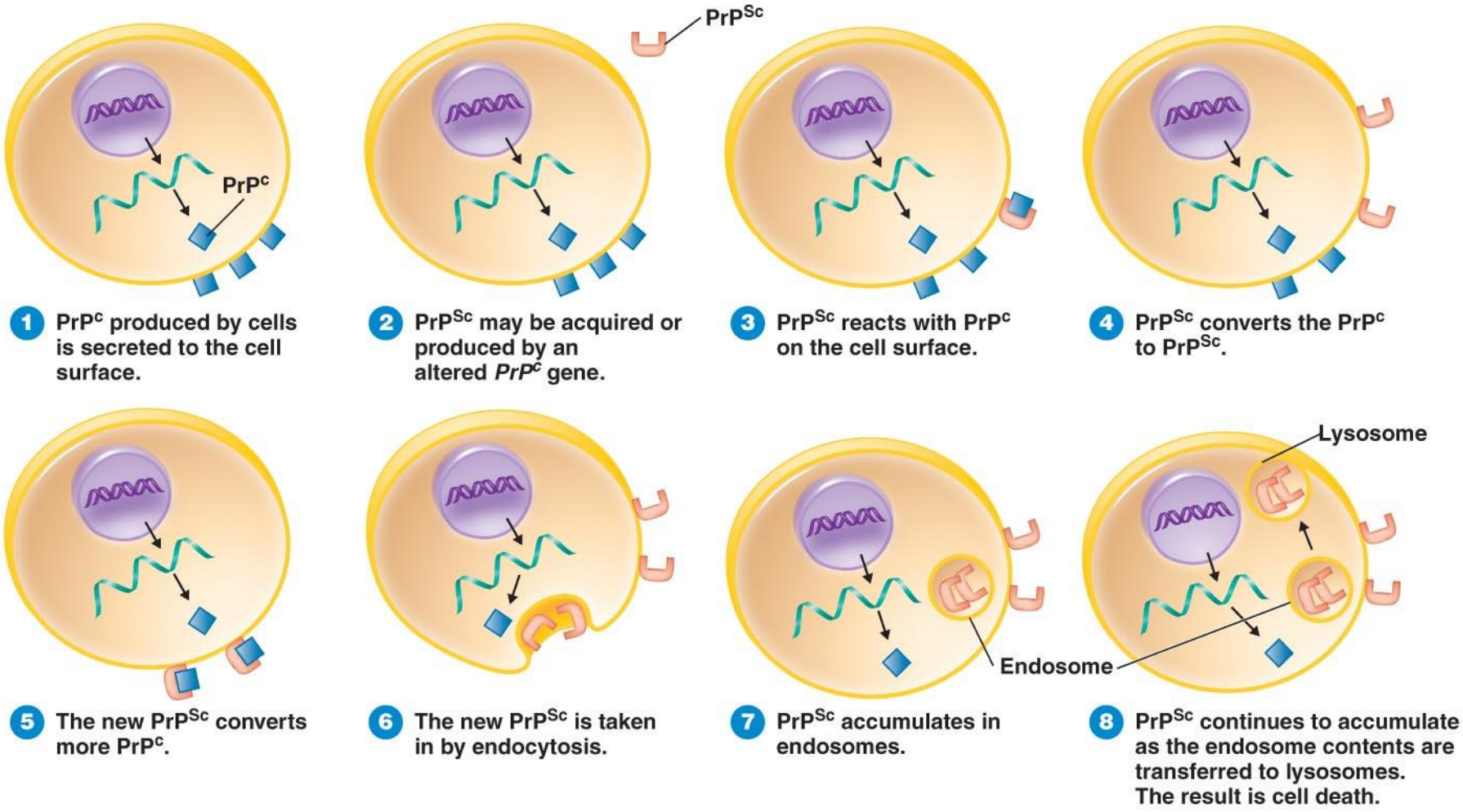


Figure 13.22

Plant Viruses and Viroids

- Plant Viruses
  - Plant viruses enter through wounds or via insects
  - Some plant viruses also multiply in insect (vector) cells.
- Viroids
  - **Viroids are infectious RNA** (short naked RNA, ~300 to 400 nucleotides)
  - potato spindle tuber disease

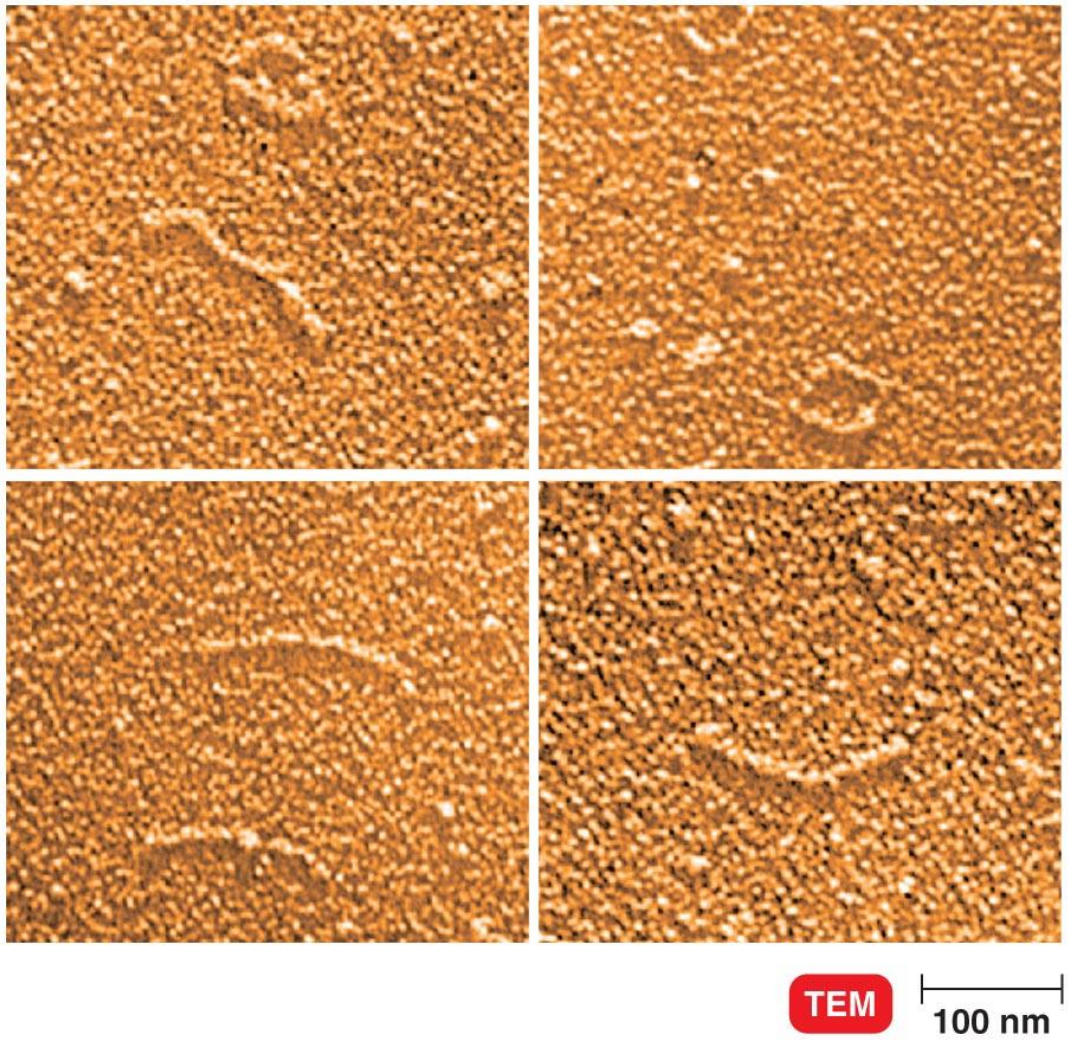
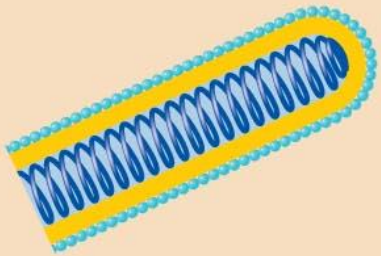


Figure 13.23

Table 13.6 Classification of Some Major Plant Viruses

Characteristic	Viral Family	Viral Genus or Unclassified Members	Morphology	Method of Transmission
Double-stranded DNA, nonenveloped	Papovaviridae	Cauliflower mosaic virus		Aphids
Single-stranded RNA, + strand, nonenveloped	Potyviridae	Watermelon wilt		Whiteflies
	Tetraviridae	*Tobamovirus*		Wounds
Single-stranded RNA, − strand, enveloped	Rhabdoviridae	Potato yellow dwarf virus		Leafhoppers and aphids
Double-stranded RNA, nonenveloped	Reovirus	Wound tumor virus		Leafhoppers