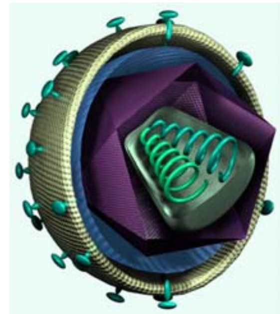
• A **virion** is the extracellular form of a **virus** and contains either an RNA or a DNA genome (**Figure 9.1**). The virus genome is introduced into a new host cell by infection. The virus redirects the host metabolism to support virus replication.

HIV



Why is it difficult to treat viral disease with drugs?

Virus - genes on the move

- Virus - poison or venom (latin)
- acellular entities with genome enclosed in a protein coat (sometimes with membrane)
- reproduce only within living cells
- contain RNA or DNA, not both
- cultured in living host or cell cultures

History

- 1000 - pox vaccine in China
- 1798 - Jenners pox vaccine
- 1892 - filtration of TMV through Chamberland filter
- 1898 - first filterable animal virus
- 1901 - first human virus (yellow fever)
- 1911 - virus causing solid tumor (rous sarcoma)
- 1933 - human influenza
- 1948 - culture of animal cells
- 1950s - polio vaccine

The origin of viruses

- Hypothesis 1:originated from small intracellular parasites? Viruses are radically different from procaryotes, no intermediate forms
- Hypothesis 2: viruses are nucleic acids that are partially independent of cells, retrovirus contain sequences similar to that found in cells, plasmids and transpososns
- Probably originated many times during evolution

Viral habitats

- Plants, Bacteria, Fungi, Eucaryotic cells, soil, fresh and salt water
- Sea water contains 10^9 to 10^{12} viral particles per liter
- This is mostly bacteriophages important for control of bacterial growth (responsible for 1/3 of bacterial death
- Important for flow of genes between bacteria in oceans
- Possible increase of ability to degrade toxic pollutants and antibiotic resistance

Virus cultivation

- Injection in suitable host
- Innoculation of embryonated eggs
- Innoculation of cultured cells
- Virus can be assembled by transfection of cells with the individual viral genes

Virus purification

- Differential centrifugation
- Gradient centrifugation
- Precipitation with ammonium sulfate or polyethylene glycol
- Precipitation of contaminants with organic solvents
- Enzymatic degradation of contaminants

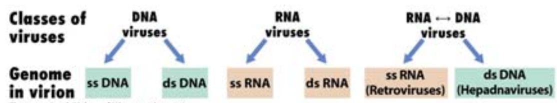


Figure 9-1 Brock Biology of Microorganisms 11/e

- Viruses are classified by replication strategy as well as by type of host (**Table 9.1**).

Table 9.1 Some types of viral genomes[a]

Virus	Host	Viral genome: Type of nucleic acid in virion	Structure	Number of molecules	Size[a]
H-1 parvovirus	Animals	Single-stranded DNA	Linear	1	5,176 bases
φX174	*Bacteria*	Single-stranded DNA	Circular	1	5,386 bases
Simian virus 40 (SV40)	Animals	Double-stranded DNA	Circular	1	5,243 base pairs
Poliovirus	Animals	Single-stranded RNA	Linear	1	7,433 bases
Cauliflower mosaic virus	Plants	Double-stranded DNA	Circular	1	8,025 base pairs
Cowpea mosaic virus	Plants	Single-stranded RNA	Linear	2 different	9,370 bases (total)
Reovirus type 3	Animals	Double-stranded RNA	Linear	10 different	23,549 base pairs (total)
Bacteriophage lambda	*Bacteria*	Double-stranded DNA	Linear	1	48,514 base pairs[b]
Herpes simplex virus type I	Animals	Double-stranded DNA	Linear	1	152,260 base pairs
Bacteriophage T4	*Bacteria*	Double-stranded DNA	Linear	1	168,903 base pairs
Human cytomegalovirus	Animals	Double-stranded DNA	Linear	1	229,351 base pairs

[a] The sizes of the viral genomes chosen for this table are known accurately because they have been sequenced. However, this accuracy can be misleading because only a particular strain or isolate of a virus was sequenced. Therefore, the sequence and exact number of bases for other isolates may be slightly different. No attempt has been made to choose the largest and smallest viruses known, but rather to give a fairly representative sampling of the sizes and structures of the genomes of viruses containing both single- and double-stranded RNA and DNA.

[b] This total includes single-stranded extensions of 12 nucleotides at either end of the linear form of the DNA (see Section 9.11).

Table 9-1 Brock Biology of Microorganisms 11/e

9.2 Nature of the Virion, p. 232

• In the virion of the naked virus, only nucleic acid and protein are present, with the nucleic acid on the inside; the whole unit is called the **nucleocapsid** (**Figure 9.3**).

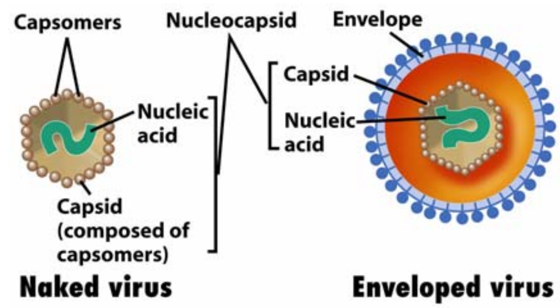


Figure 9-3 Brock Biology of Microorganisms 11/e

• One or more lipoprotein layers surround the nucleocapsid in enveloped viruses. The nucleocapsid is symmetrical, with a precise number and arrangement of structural subunits surrounding the virus nucleic acid (**Figure 9.4**).

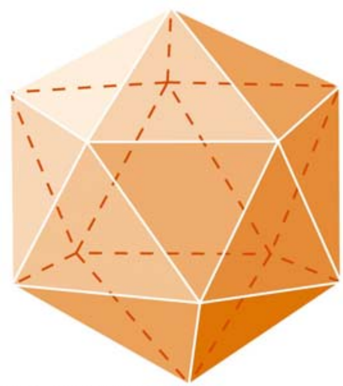
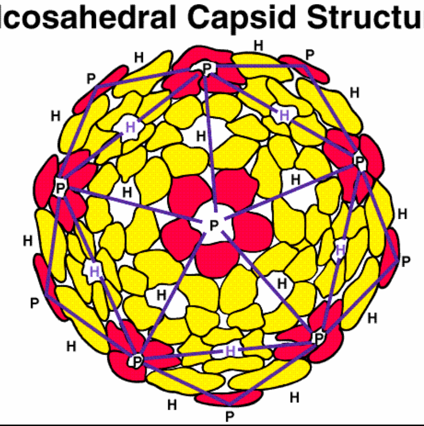


Figure 9-4a Brock Biology of Microorganisms 11/e

Icosahedral Capsid Structure



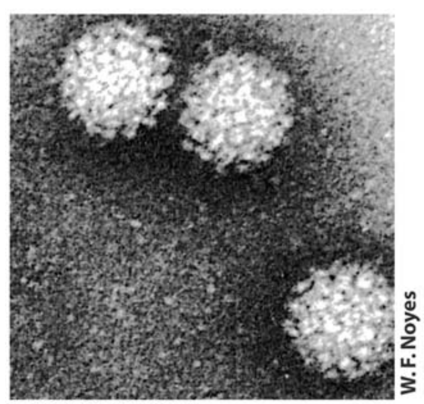
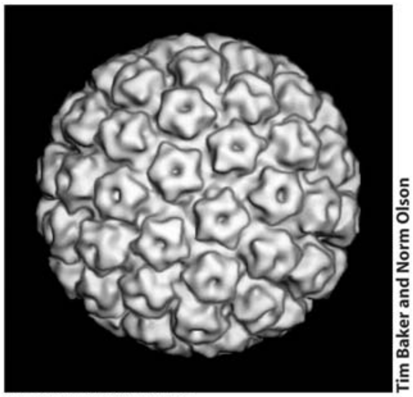


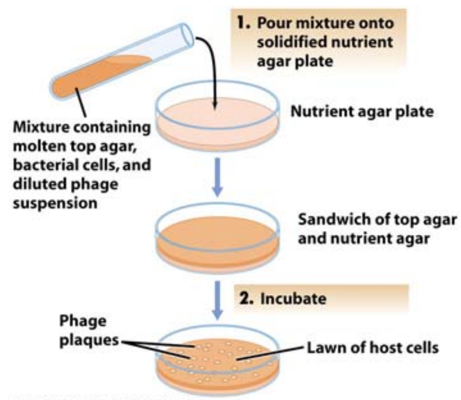
Figure 9-4b Brock Biology of Microorganisms 11/e

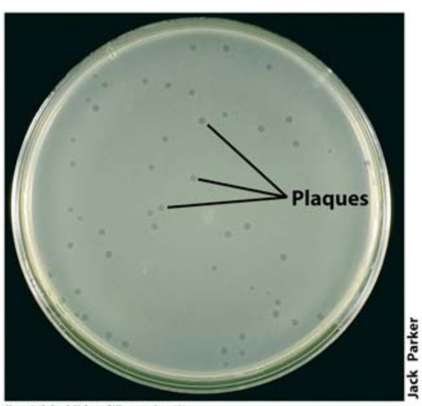


• Viruses can replicate only in certain types of cells or in whole organisms. Bacterial viruses (**bacteriophages**) have proved useful as model systems because the host cells are easy to grow and manipulate in culture. Many animal and plant viruses also can be grown in cultured cells.

9.4 Quantification of Viruses, p. 236

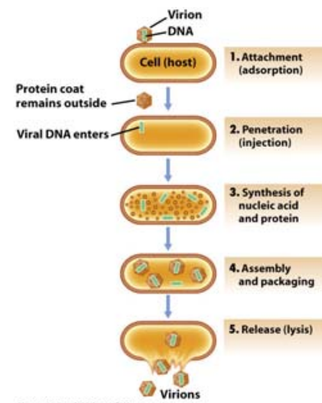
• Although it requires only a single virion to initiate an infectious cycle, not all virions are equally infectious. The plaque assay is one of the most accurate ways to measure virus infectivity (**Figure 9.6**).

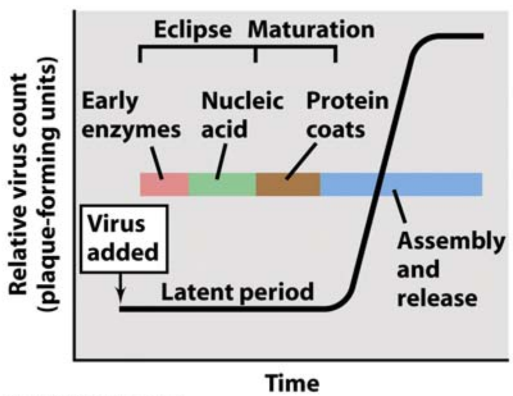




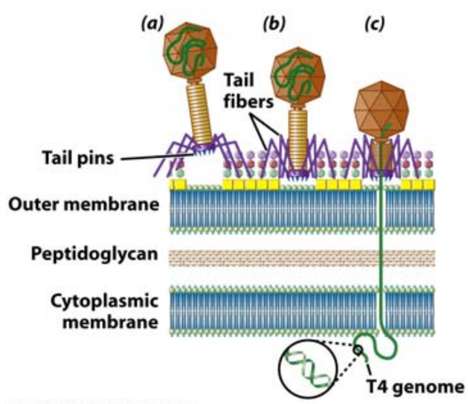
• **Plaques** are clear zones that develop on lawns of host cells. Theoretically, each plaque results from infection by a single virus particle. The virus plaque is analogous to the bacterial colony.

• The virus life cycle can be divided into five stages: attachment (adsorption), penetration (injection), protein and nucleic acid synthesis, assembly and packaging, and virion release (**Figure 9.8**).





• The attachment of a virion to a host cell is a highly specific process involving complementary receptors on the surface of a susceptible host cell and its infecting virus (**Figure 9.10**).



• Resistance of the host to infection by the virus can involve restriction-modification systems that recognize and destroy foreign double-stranded DNA.

• The Baltimore Classification scheme has seven classifications of viruses (**Table 9.2**).

Table 9.2 The Baltimore classification system of viruses

Class	Description of genome and replication strategy	Examples: Bacterial viruses	Examples: Animal viruses
I	Double-stranded DNA genome	Lambda, T4	Herpesvirus, pox virus
II	Single-stranded DNA genome	ϕX174	Chicken anemia virus
III	Double-stranded RNA genome	ϕ6	Reoviruses (Section 16.9)
IV	Single-stranded RNA genome of plus sense	MS2	Poliovirus
V	Single-stranded RNA genome of minus sense		Influenza virus, rabies virus
VI	Single-stranded RNA genome that replicates with DNA intermediate		Retroviruses
VII	Double-stranded DNA genome that replicates with RNA intermediate		Hepatitis B virus

Table 9-2 Brock Biology of Microorganisms 11/e

• Before replication of viral nucleic acid can occur, messenger RNA molecules transcribed from the virus genome encode new virus proteins.

• In some RNA viruses, the viral RNA itself is the mRNA; in others, the virus genome is a template for the formation of viral mRNA. In certain cases, essential transcriptional enzymes are contained in the virion (**Figure 9.11**).

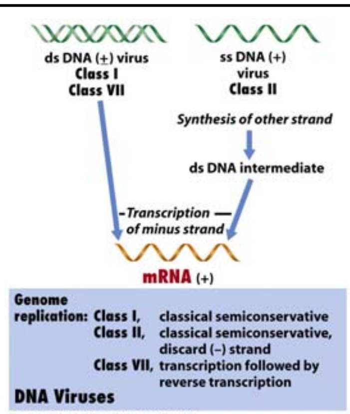


Figure 9-11a Brock Biology of Microorganisms 11/e

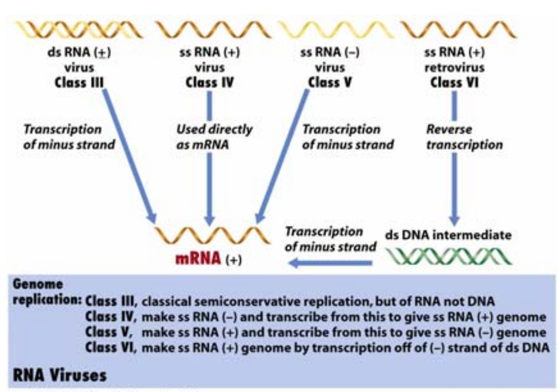
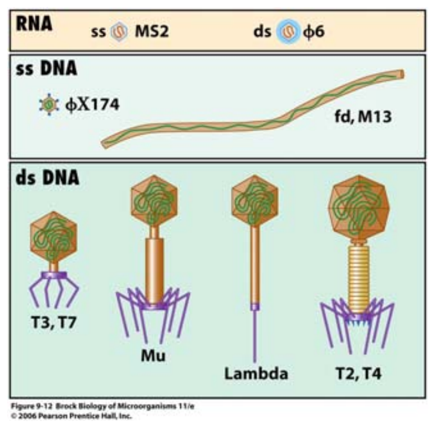


Figure 9-11b Brock Biology of Microorganisms 11/e

• By convention, mRNA is said to be in the plus (+) configuration. Its complement is said to be in the minus (–) configuration. This nomenclature is also used to describe the configuration of the genome of a single-stranded virus, whether its genome contains RNA or DNA.

• For example, a virus that has a single-stranded RNA genome with the same orientation as its mRNA is said to be a **positive-strand** RNA **virus**. A virus whose single-stranded RNA genome is complementary to its mRNA is said to be a **negative-strand** RNA **virus**.

• Bacterial viruses are very diverse (**Figure 9.12**). The best-studied bacteriophages infect enteric bacteria such as *Escherichia coli* and are structurally quite complex, containing heads, tails, and other components.



9.9 Virulent Bacteriophages and T4, p. 243

• After a virion of T4 attaches to a host cell and the DNA penetrates the cytoplasm, the expression of viral genes is regulated to redirect the host synthetic machinery to the reproduction of viral nucleic acid and protein. Lysis then assembles and releases new virions from the cell.

• T4 has a double-stranded DNA genome that is circularly permuted and terminally redundant (**Figure 9.13**).

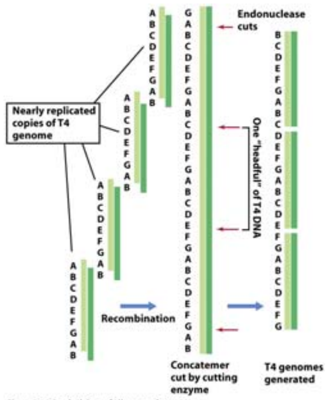


Figure 9-13 Brock Biology of Microorganisms 11/e

• The T4 genome can be divided into three parts, encoding **early proteins**, middle proteins, and **late proteins** (**Figure 9.15**).

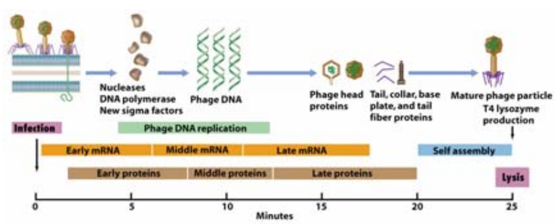


Figure 9-15 Brock Biology of Microorganisms 11/e

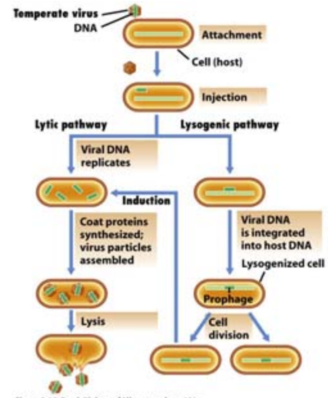
9.10 Temperate Bacteriophages, p. 245

• Bacteriophage T4 is a **virulent virus**. **Temperate viruses**, although also able to kill cells through a lytic cycle, can undergo a different life cycle resulting in a stable genetic relationship with the host.

• These viruses can enter into a state in which most virus genes are not expressed and the virus genome, called a **provirus** (or **prophage)**, is replicated in synchrony with the host chromosome. This is the **lysogenic pathway**.

• Host cells can harbor viral genomes without harm if the expression of the viral genes can be controlled. This is the situation found in **lysogens**.

• If this control is lost, however, the virus enters the **lytic pathway** and produces new virions, eventually lysing the host cell. **Figure 9.16** shows an overall view of the life cycle of a temperate bacteriophage.



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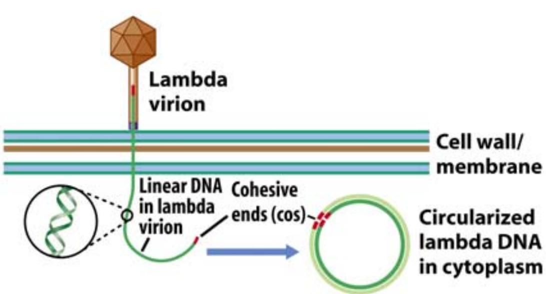
9.11 Bacteriophage Lambda, p. 246

• Lambda is a double-stranded DNA temperate phage. Regulation of lytic versus lysogenic events in lambda is controlled by several promoters and regulatory proteins.

• The cI protein (the lambda repressor) causes repression of lambda lytic events; the Cro protein controls activation of lytic events. Although the genome of lambda is linear, it circularizes inside the cell, where DNA synthesis occurs by a rolling circle mechanism (**Figure 9.18**).



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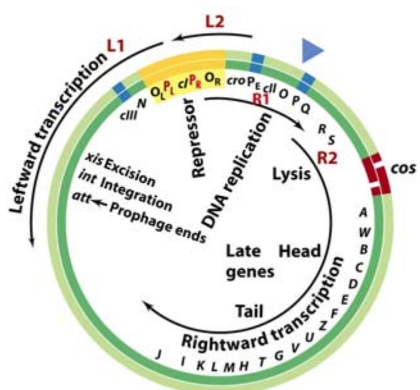

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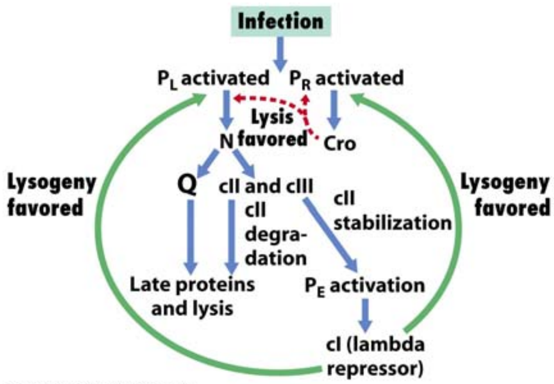

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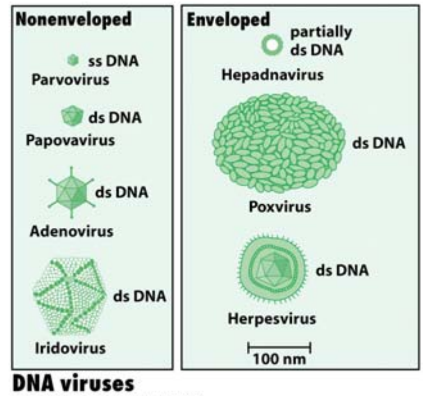

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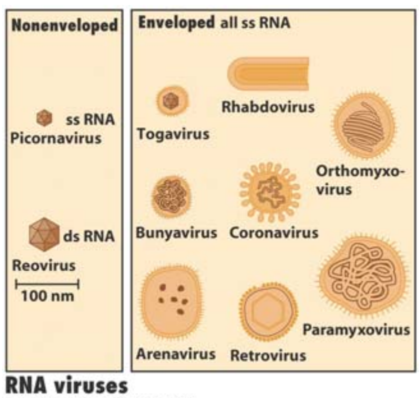

Figure 9-23b Brock Biology of Microorganisms 11/e
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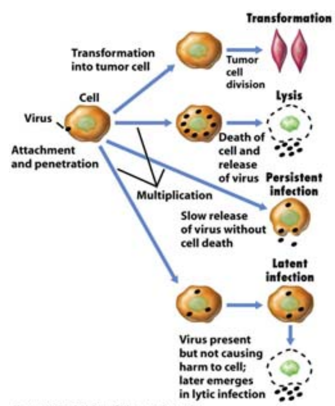
• Many animal viruses are enveloped, picking up portions of the host cytoplasmic membrane as they leave the cell.

• Not all infections of animal host cells result in cell lysis or death; latent or persistent infections are common, and some animal viruses can cause cancer (**Figure 9.24**).



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9.13 Retroviruses, p. 251

• **Retroviruses** are RNA viruses that replicate through a DNA intermediate (**Figure 9.25**). The retrovirus called human immunodeficiency virus (HIV) causes AIDS.

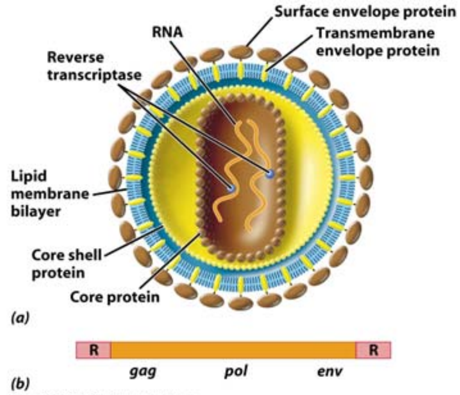


Figure 9-25 Brock Biology of Microorganisms 11/e

• The retrovirus virion contains an enzyme, reverse transcriptase, that copies the information from its RNA genome into DNA, a process called **reverse transcription** (**Figure 9.26**).

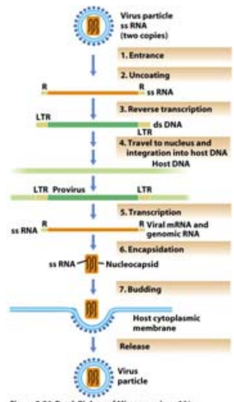
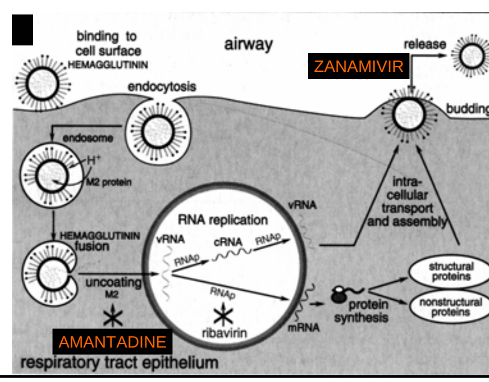


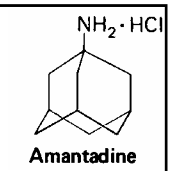
Figure 9-26 Brock Biology of Microorganisms 11/e

• The DNA becomes integrated into the host chromosome in the same way as it does in a temperate virus. The retrovirus DNA can be transcribed to yield mRNA (and new genomic RNA), or it may remain in a latent state.

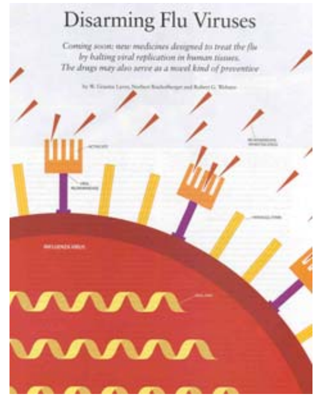
Replication of Influenza Virus



Amantadine



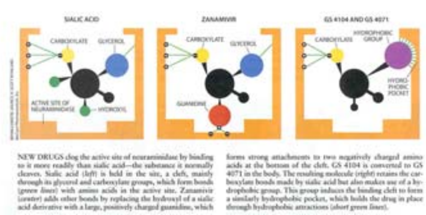
- Mechanisms of Action
  - Inhibits uncoating of viral RNA
  - May also block viral assembly
- Used to prevent spread of influenza A2
- Adverse reactions
  - Dizziness, nervousness, confusion, hallucinations, hypotension
  - CNS: releases dopamine, dopamine agonist



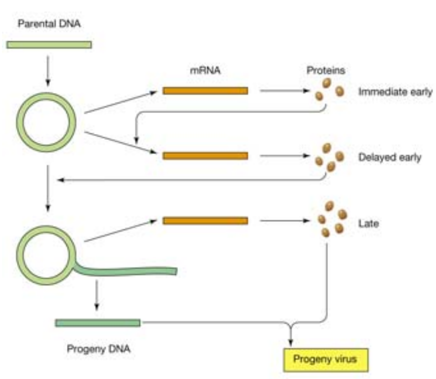
Zanamivir

- Neuraminidase inhibitor
- Inhibits replication of influenza A and B
- Early use reduces severity and duration of influenza symptoms

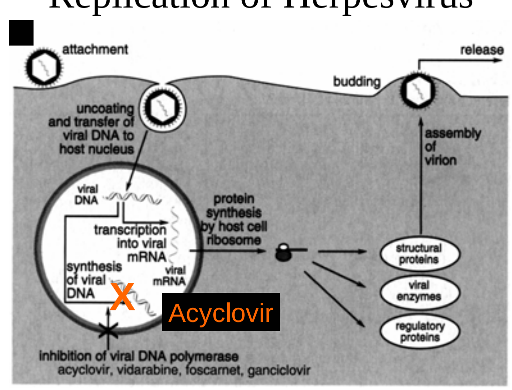
Influenza can be treated with neuraminidase inhibitors

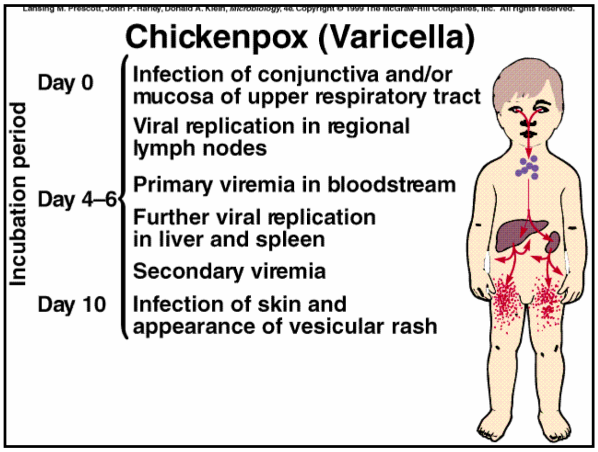


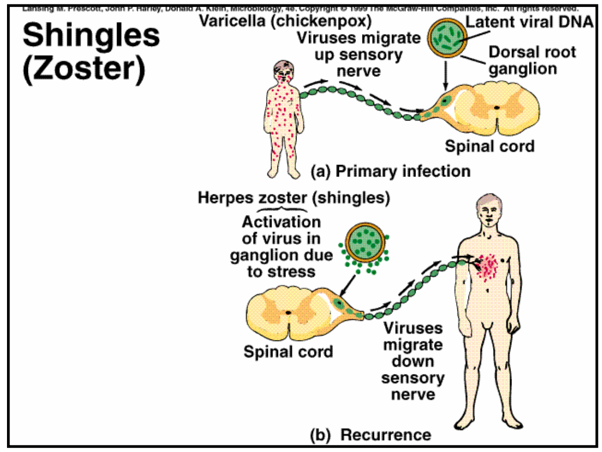
Replication of HSV

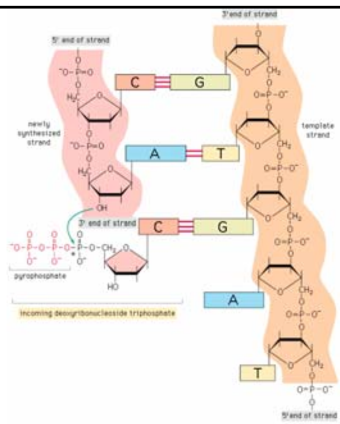


Replication of Herpesvirus

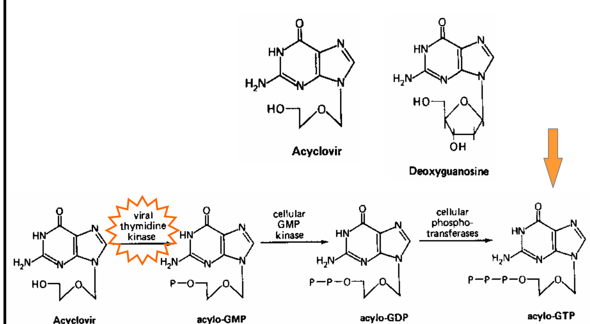


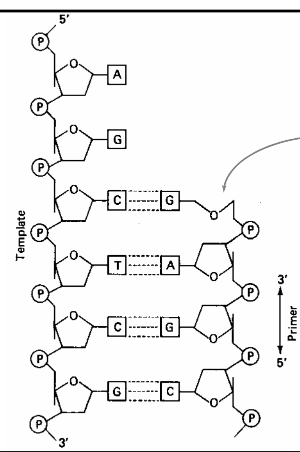






Acyclovir



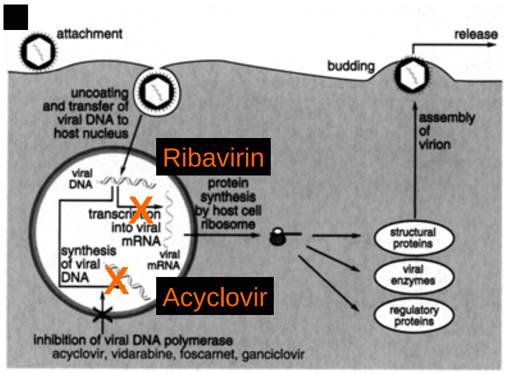


AcycloGTP inhibits DNA polymerase

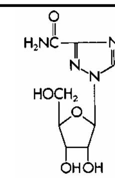
Acyclovir

- Mechanism:
  - Activated by viral thymidine kinase
  - AcycloGTP inhibits viral DNA polymerase
- Uses:
  - Herpes simplex
  - Varicella-Zoster
- Adverse Reactions:
  - IV: local irritation, phlebitis, nephrotoxicity
  - Oral: headache, vertigo, diarrhea, nausea, vomiting, arthalgia

Replication of Herpesvirus



Ribavirin



- Mechanism:
  - Metabolized to a monophosphate which inhibits synthesis of guanine nucleotides - RNA and DNA synthesis is inhibited
- Broad spectrum:
  - Respiratory syncytial virus, influenza
  - Hepatitis C, Myxovirus, paromyxovirus, adenovirus, herpes virus, poxviruses,