Chapter 13
Viruses, Viroids, and Prions
General Characteristics of Viruses

Learning Objective

13-1 Differentiate a virus from a bacterium.
General Characteristics of Viruses

- Obligatory intracellular parasites
- Contain DNA or RNA
- No ribosomes
- No ATP-generating mechanism
- Contain a protein coat
General Characteristics of Viruses

- Some viruses 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
Figure 13.1 Virus sizes.

- Adenovirus: 90 nm
- Bacteriophage T4: 225 nm
- Bacteriophage f2, MS2: 24 nm
- Rhinovirus: 30 nm
- Rabies virus: 225 nm
- Bacteriophage M13: 800 × 10 nm
- Tobacco mosaic virus: 250 × 18 nm
- Prion: 200 × 20 nm
- Chlamydia elementary body: 300 nm
- Viroid: 300 × 10 nm
- Vaccinia virus: 300 × 200 × 100 nm
- Ebola virus: 970 nm
- E. coli: 3000 × 1000 nm
- Human red blood cell: 10,000 nm in diameter
- Plasma membrane of red blood cell: 10 nm thick
Check Your Understanding

✓ How could the small size of viruses have helped researchers detect viruses before the invention of the electron microscope? 13-1
13-2 Describe the chemical and physical structure of both an enveloped and a nonenveloped virus.
Virion Structure

- Nucleic acid
  - DNA or RNA
- Capsid
  - Capsomeres
- Envelope
- Spikes
Figure 13.2 Morphology of a nonenveloped polyhedral virus.

(a) A polyhedral virus

(b) Mastadenovirus

TEM
35 nm
Figure 13.16a DNA-containing animal viruses.

(a) *Mastadenovirus*
Figure 13.3 Morphology of an enveloped helical virus.

(a) An enveloped helical virus

(b) Influenzavirus

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Figure 13.16b DNA-containing animal viruses.

(b) Herpesvirus

Capsomeres
Figure 13.4 Morphology of a helical virus.

(a) A helical virus

(b) Ebola virus
Figure 13.5 Morphology of complex viruses.

(a) A T-even bacteriophage

(b) Orthopoxvirus
Check Your Understanding

✓ Diagram a nonenveloped polyhedral virus that has spikes. 13-2
Taxonomy of Viruses

Learning Objectives

13-3 Define \textit{viral species}.
13-4 Give an example of a family, genus, and common name for a virus.
Taxonomy of Viruses

- 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)
  - Common names are used for species
  - Subspecies are designated by a number
Taxonomy of Viruses

- Herpesviridae
  - *Herpesvirus*
  - Human herpesvirus
    - HHV-1, HHV-2, HHV-3

- Retroviridae
  - *Lentivirus*
  - Human immunodeficiency virus
    - HIV-1, HIV-2
Check Your Understanding

✓ How does a virus species differ from a bacterial species? 13-3

✓ Attach the proper endings to *Papilloma-* to show the family and genus that includes HPV, the cause of cervical cancer. 13-4
Isolation, Cultivation, and Identification

Learning Objectives

13-5 Describe how bacteriophages are cultured.
13-6 Describe how animal viruses are cultured.
13-7 List three techniques used to identify viruses.
Growing Viruses

- Viruses must be grown in living cells
  - Bacteriophages form plaques on a lawn of bacteria
  - Animal viruses may be grown in living animals or in embryonated eggs or in cell cultures
    - Continuous cell lines
Figure 13.6 Viral plaques formed by bacteriophages.
Figure 13.7 Inoculation of an embryonated egg.

- Shell
- Amniotic cavity
- Chlorioallantoic membrane

- Air sac
- Yolk sac
- Shell membrane
- Albumin
- Allantoic cavity
- Yolk sac

Inoculations:
- Chlorioallantoic membrane inoculation
- Amniotic inoculation
- Allantoic inoculation

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Figure 13.8 Cell cultures.

1. A tissue is treated with enzymes to separate the cells.
2. Cells are suspended in culture medium.
3. Normal cells or primary cells grow in a monolayer across the glass or plastic container. Transformed cells or continuous cell cultures do not grow in a monolayer.
Virus Identification

- Cytopathic effects
- Serological tests
  - Detect antibodies against viruses in a patient
  - Use antibodies to identify viruses in neutralization tests, viral hemagglutination, and Western blot
- Nucleic acids
  - RFLPs
  - PCR
Figure 13.9 The cytopathic effect of viruses.
Check Your Understanding

✓ What is the plaque method? 13-5
✓ Why are continuous cell lines of more practical use than primary cell lines for culturing viruses? 13-6
✓ What tests could you use to identify influenza virus in a patient? 13-7
Viral Multiplication

Learning Objectives

13-8 Describe the lytic cycle of T-even bacteriophages.

13-9 Describe the lysogenic cycle of bacteriophage lambda.
The Lytic Cycle

- **Attachment**: phage attaches by tail fibers to host cell
- **Penetration**: phage lysozyme opens cell wall; tail sheath contracts to force tail core and DNA into cell
- **Biosynthesis**: production of phage DNA and proteins
- **Maturation**: assembly of phage particles
- **Release**: phage lysozyme breaks cell wall
Figure 13.10 A viral one-step growth curve.

- **Acute infection**
- **Eclipse period**
- Virions released from host cell
Figure 13.11 The lytic cycle of a T-even bacteriophage.

1. **Attachment:** Phage attaches to host cell.
2. **Penetration:** Phage penetrates host cell and injects its DNA.
3. **Biosynthesis:** Phage DNA directs synthesis of viral components by the host cell.
4. **Maturation:** Viral components are assembled into virions.
5. **Release:** Host cell lyses, and new virions are released.
Results of Multiplication of Bacteriophages

- **Lytic cycle**
  - Phage causes lysis and death of host cell

- **Lysogenic cycle**
  - Prophage DNA incorporated in host DNA
  - Phage conversion
  - Specialized transduction

**ANIMATION** Viral Replication: Virulent Bacteriophages

**ANIMATION** Viral Replication: Temperate Bacteriophages

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Figure 13.12 The lysogenic cycle of bacteriophage λ in *E. coli*.

1. Phage attaches to host cell and injects DNA.

2. Phage DNA circularizes and enters lytic cycle or lysogenic cycle.

3A. New phage DNA and proteins are synthesized and assembled into virions.

3B. Phage DNA integrates within the bacterial chromosome by recombination, becoming a prophage.

4A. Cell lyses, releasing phage virions.

4B. Lysogenic bacterium reproduces normally.

5. Occasionally, the prophage may excise from the bacterial chromosome by another recombination event, initiating a lytic cycle.

OR
Figure 8.29 Transduction by a bacteriophage.

1. A phage infects the donor bacterial cell.
2. Phage DNA and proteins are made, and the bacterial chromosome is broken into pieces.
3. Occasionally during phage assembly, pieces of bacterial DNA are packaged in a phage capsid. Then the donor cell lyses and releases phage particles containing bacterial DNA.
4. A phage carrying bacterial DNA infects a new host cell, the recipient cell.
5. Recombination can occur, producing a recombinant cell with a genotype different from both the donor and recipient cells.

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Prophage exists in galactose-using host (containing the gal gene).

Phage genome excises, carrying with it the adjacent gal gene from the host.

Phage matures and cell lyses, releasing phage carrying gal gene.

Phage infects a cell that cannot utilize galactose (lacking gal gene).

Along with the prophage, the bacterial gal gene becomes integrated into the new host’s DNA.

Lysogenic cell can now metabolize galactose.
Specialized Transduction

ANIMATION Transduction: Generalized Transduction

ANIMATION Transduction: Specialized Transduction
Check Your Understanding

 ✓ How do bacteriophages get nucleotides and amino acids if they don’t have any metabolic enzymes? 13-8

 ✓ *Vibrio cholerae* produces toxin and is capable of causing cholera only when it is lysogenic. What does this mean? 13-9
Viral Multiplication

Learning Objective

13-10 Compare and contrast the multiplication cycle of DNA- and RNA-containing animal viruses.
Multiplication of Animal Viruses

- **Attachment**: viruses attach to cell membrane
- **Penetration** by endocytosis or fusion
- **Uncoating** 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
Figure 13.14a The entry of viruses into host cells.

(a) Entry of togavirus by receptor-mediated endocytosis
Figure 13.14b The entry of viruses into host cells.

(b) Entry of herpesvirus by fusion

Viral envelope

Plasma membrane of host cell

Fusion of viral envelope and plasma membrane

Vesicle

Capsid released into cytoplasm

TEM 200 nm
Figure 13.20a Budding of an enveloped virus.

(a) Release by budding
Figure 13.20b Budding of an enveloped virus.

(b) *Lentivirus*
Figure 13.15 Replication of a DNA-Containing Animal Virus.

1. **ATTACHMENT**
   - Virion attaches to host cell.

2. **ENTRY and UNCOATING**
   - Virion enters cell, and its DNA is uncoated.

3. **A portion of viral DNA is transcribed, producing mRNA that encodes “early” viral proteins.**

4. **BIOSYNTHESIS**
   - Viral DNA is replicated, and some viral proteins are made.

5. **Late translation; capsid proteins are synthesized.**

6. **MATURATION**
   - Virions mature.

7. **RELEASE**
   - Virions are released.

A papovavirus is a typical DNA-containing virus that attacks animal cells.
Attachment

Entry and uncoating

Uncoating releases viral RNA and proteins.

Viral genome (RNA)

Translation and synthesis of viral proteins

RNA replication by viral RNA–dependent RNA polymerase

Maturation and release

(a) ssRNA; + or sense strand; Picornaviridae

Viral protein

Viral genome

+ or sense strand of viral genome

– or antisense strand of viral genome

ss = single stranded

ds = double-stranded

Host cell

Cytoplasm

Nucleus

Capsid

RNA

+ strand

mRNA is transcribed from the – strand.

Viral protein

Capsid protein

Figure 13.17a Key Pathways of multiplication used by various RNA-containing viruses.
Figure 13.17b Key Pathways of multiplication used by various RNA-containing viruses.

1. **Attachment**
   - Capsid
   - RNA

2. **Entry and uncoating**
   - Nucleus
   - Cytoplasm
   - Viral genome
   - + or sense strand of viral genome
   - – or antisense strand of viral genome

3. **RNA replication by viral RNA-dependent RNA polymerase**
   - Uncoating releases viral RNA and proteins.

4. **Translation and synthesis of viral proteins**
   - Capsid

5. **Maturation and release**
   - Host cell
   - Capsid protein

(b) ssRNA; – or antisense strand; Rhabdoviridae
Entry and uncoating
Uncoating releases viral RNA and proteins.

Maturation and release
Capsid RNA
Translation and synthesis of viral proteins
RNA replication by viral RNA-dependent RNA polymerase

Viral genome (RNA)
Capsid proteins and RNA-dependent RNA polymerase

Figure 13.17c Key Pathways of multiplication used by various RNA-containing viruses.
Figure 13.17 Key Pathways of multiplication used by various RNA-containing viruses.

1. **Attachment**
   - Capsid binds to the host cell.
   - Virus enters the cell.

2. **Entry and uncoating**
   - Capsid is uncoated.
   - Viral RNA and proteins are released.

3. **RNA replication by viral RNA–dependent RNA polymerase**
   - Viral genome (RNA) is replicated.
   - mRNA is synthesized.

4. **Translation and synthesis of viral proteins**
   - Capsid protein is produced.
   - + strand mRNA is transcribed from the – strand.
   - – strands are incorporated into capsid.
   - Additional – strands are transcribed from mRNA.

5. **Maturation and release**
   - Capsid proteins and RNA-dependent RNA polymerase are produced.
   - mRNA is produced inside the capsid and released into the cytoplasm.
   - Viral genome (RNA) and viral protein are produced.

**Key**
- **Viral genome**
  - + or sense strand of viral genome
  - – or antisense strand of viral genome
- **ss** = single stranded
- **ds** = double-stranded
- **RNA polymerase initiates production of – strands. The mRNA and – strands form the dsRNA that is incorporated as new viral genome.**
Retrovirus enters by fusion between attachment spikes and the host cell receptors. Uncoating releases the two viral RNA genomes and the viral enzymes reverse transcriptase, integrase, and protease. Reverse transcriptase copies viral RNA to produce double-stranded DNA. The new viral DNA is transported into the host cell's nucleus, where it is integrated into a host cell chromosome as a provirus by viral integrase. The provirus may be replicated when the host cell replicates.

Viral proteins are processed by viral protease; some of the viral proteins are moved to the host plasma membrane. Transcription of the provirus may also occur, producing RNA for new retrovirus genomes and RNA that encodes the retrovirus capsid, enzymes, and envelope proteins.

Mature retrovirus leaves the host cell, acquiring an envelope and attachment spikes as it buds out.
Animal Viruses

ANIMATION Viral Replication: Overview

ANIMATION Viral Replication: Animal Viruses
Table 13.3 Bacteriophage and animal viral multiplication compared.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Bacteriophages</th>
<th>Animal Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attachment</td>
<td>Tail fibers attach to cell wall proteins.</td>
<td>Attachment sites are plasma membrane proteins and glycoproteins.</td>
</tr>
<tr>
<td>Entry</td>
<td>Viral DNA is injected into host cell.</td>
<td>Capsid enters by receptor-mediated endocytosis or fusion.</td>
</tr>
<tr>
<td>Uncoating</td>
<td>Not required</td>
<td>Enzymatic removal of capsid proteins</td>
</tr>
<tr>
<td>Biosynthesis</td>
<td>In cytoplasm</td>
<td>In nucleus (DNA viruses) or cytoplasm (RNA viruses)</td>
</tr>
<tr>
<td>Chronic infection</td>
<td>Lysogeny</td>
<td>Latency; slow viral infections; cancer</td>
</tr>
<tr>
<td>Release</td>
<td>Host cell is lysed.</td>
<td>Enveloped viruses bud out; nonenveloped viruses rupture plasma membrane.</td>
</tr>
</tbody>
</table>
Check Your Understanding

✓ Describe the principal events of attachment, entry, uncoating, biosynthesis, maturation, and release of an enveloped DNA-containing virus. 13-10
Viruses and Cancer

Learning Objectives

13-11 Define *oncogene* and *transformed cell*.
13-12 Discuss the relationship between DNA- and RNA-containing viruses and cancer.
Cancer

- Activated oncogenes transform normal cells into cancerous cells.

- **Transformed cells** have increased growth, loss of contact inhibition, **tumor-specific transplant antigens**, and **T antigens**.

- 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
Check Your Understanding

✓ What is a provirus? 13-11
✓ How can an RNA virus cause cancer if it doesn’t have DNA to insert into a cell’s genome? 13-12
Latent and Persistent Viral Infections

Learning Objectives

13-13 Provide an example of a latent viral infection.
13-14 Differentiate persistent viral infections from latent viral infections.
Figure 13.21 Latent and persistent viral infections.

- Acute infection
- Latent infection
- Persistent infection
Latent and Persistent Viral Infections

- Virus remains in asymptomatic host cell for long periods
  - Cold sores, shingles
- Disease process occurs over a long period; generally is fatal
  - Subacute sclerosing panencephalitis (measles virus)
Check Your Understanding

✓ Is shingles a persistent or latent infection?  
13-13, 13-14
Prions, Viroids, and Plant Viruses

Learning Objectives

13-15 Discuss how a protein can be infectious.
13-16 Differentiate virus, viroid, and prion.
13-17 Describe the lytic cycle for a plant virus.
Prions

- Proteinaceous infectious particle
- Inherited and transmissible by ingestion, transplant, and surgical instruments
  - Spongiform encephalopathies: sheep scrapie, Creutzfeldt-Jakob disease, Gerstmann-Sträussler-Scheinker syndrome, fatal familial insomnia, mad cow disease
Prions

- PrP^C: normal cellular prion protein, on cell surface
- PrP^Sc: scrapie protein; accumulates in brain cells, forming plaques
1. PrP<sub>c</sub> produced by cells is secreted to the cell surface.

2. PrP<sub>Sc</sub> may be acquired or produced by an altered PrP<sub>c</sub> gene.

3. PrP<sub>Sc</sub> reacts with PrP<sub>c</sub> on the cell surface.

4. PrP<sub>Sc</sub> converts the PrP<sub>c</sub> to PrP<sub>Sc</sub>.

5. The new PrP<sub>Sc</sub> converts more PrP<sub>c</sub>.

6. The new PrP<sub>Sc</sub> is taken in, possibly by receptor-mediated endocytosis.

7. PrP<sub>Sc</sub> accumulates in endosomes.

8. PrP<sub>Sc</sub> continues to accumulate as the endosome contents are transferred to lysosomes. The result is cell death.
Plant Viruses and Viroids

- **Plant viruses**: enter through wounds or via insects
- **Viroids**: infectious RNA; e.g., potato spindle tuber disease
Figure 13.23 Linear and circular potato spindle tuber viroid (PSTV).
Table 13.6 Classification of some major plant viruses.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Viral Family</th>
<th>Viral Genus or Unclassified Members</th>
<th>Morphology</th>
<th>Method of Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double-stranded DNA, nonenveloped</td>
<td>Papoviridae</td>
<td>Cauliflower mosaic virus</td>
<td>[Image]</td>
<td>Aphids</td>
</tr>
<tr>
<td></td>
<td>Tetraviridae</td>
<td><em>Tobamovirus</em></td>
<td>[Image]</td>
<td>Wounds</td>
</tr>
<tr>
<td>Single-stranded RNA, - strand, enveloped</td>
<td>Rhabdoviridae</td>
<td>Potato yellow dwarf virus</td>
<td>[Image]</td>
<td>Leafhoppers and aphids</td>
</tr>
<tr>
<td>Double-stranded RNA, nonenveloped</td>
<td>Reoviridae</td>
<td>Wound tumor virus</td>
<td>[Image]</td>
<td>Leafhoppers</td>
</tr>
</tbody>
</table>
Check Your Understanding

✓ Contrast viroids and prions, and for each name a disease it causes. 13-15, 13-16

✓ How do plant viruses enter host cells? 13-17
Virus Families That Affect Humans

Learning Objective

13-10 Compare and contrast the multiplication cycle of DNA and RNA containing animal viruses.
Parvoviridae

- Single-stranded DNA, nonenveloped viruses
  - Fifth disease
  - Anemia in immunocompromised patients
Parvoviridae
Adenoviridae

- Double-stranded DNA, nonenveloped viruses
  - Respiratory infections in humans
  - Tumors in animals
Adenoviridae
Papovaviridae

- Double-stranded DNA, nonenveloped viruses
  - *Papillomavirus*
    - Human wart virus
  - *Polyomavirus*
    - Cause tumors; some cause cancer
Papovaviridae
Poxviridae

- Double-stranded DNA, enveloped viruses
  - *Orthopoxvirus* (vaccinia and smallpox viruses)
  - *Molluscipoxvirus*
  - Smallpox
  - Molluscum contagiosum
  - Cowpox
Poxviridae
Herpesviridae

- Double-stranded DNA, enveloped viruses
  - Simplexvirus (HHV-1 and HHV-2)
  - Varicellovirus (HHV-3)
  - Lymphocryptovirus (HHV-4)
  - Cytomegalovirus (HHV-5)
  - Roseolovirus (HHV-6 and HHV-7)
  - Kaposi’s sarcoma (HHV-8)

- Some herpesviruses can remain latent in host cells
Herpesviridae
Hepadnaviridae

- Double-stranded DNA, enveloped viruses
  - Hepatitis B virus
  - Use reverse transcriptase
Hepadnaviridae
Picornaviridae

- Single-stranded RNA, + strand, nonenveloped
  - *Enterovirus*
    - Poliovirus and coxsackievirus
  - *Rhinovirus*
  - Hepatitis A virus
Picornaviridae
Caliciviridae

- Single-stranded RNA, + strand, nonenveloped
  - Hepatitis E virus
  - *Norovirus* causes gastroenteritis
Caliciviridae
Togaviridae

- Single-stranded RNA, + strand, enveloped
  - *Alphavirus*
    - Transmitted by arthropods; includes EEE and WEE
  - *Rubivirus* (rubella virus)
Togaviridae
Flaviviridae

- Single-stranded RNA, + strand, enveloped
  - Arboviruses can replicate in arthropods; include yellow fever, dengue, SLE, and West Nile viruses
  - Hepatitis C virus
Flaviviridae
Coronaviridae

- Single-stranded RNA, + strand, enveloped
  - Upper respiratory infections
  - Coronavirus
  - SARS
Coronaviridae
Rhabdoviridae

- Single-stranded RNA, − strand, one RNA strand
  - *Vesiculovirus*
  - *Lyssavirus* (rabies virus)
  - Cause numerous animal diseases
Rhabdoviridae
Filoviridae

- Single-stranded RNA, – strand, one RNA strand
  - *Filovirus*
  - Enveloped, helical viruses
  - Ebola and Marburg viruses
Filoviridae
Paramyxoviridae

- Single-stranded RNA, − strand, one RNA strand
  - *Paramyxovirus*
  - *Morbillivirus*
  - Parainfluenza
  - Mumps
  - Newcastle disease (chickens)
Paramyxoviridae
Deltaviridae

- Single-stranded RNA, − strand, one RNA strand
  - Hepatitis D virus
  - Depends on coinfection with hepadnavirus
Deltaviridae
Orthomyxoviridae

- Single-stranded RNA, − strand, multiple RNA strands
  - Envelope spikes can agglutinate RBCs
  - *Influenzavirus* (influenza viruses A and B)
  - Influenza C virus
Orthomyxoviridae
Model for antigenic shift in influenza virus.

- 1918 H1N1
- North American swine
- Avian gene pool
- Human H3N2
- Eurasian swine H1N1
- 2009 H1N1 pandemic
- Triple reassortment H1N2
Bunyaviridae

- Single-stranded RNA, − strand, multiple RNA strands
  - *Bunyavirus* (CE virus)
  - *Hantavirus*
Bunyaviridae
Arenaviridae

- Single-stranded RNA, − strand, multiple RNA strands
  - Helical capsids contain RNA-containing granules
  - Lymphocytic choriomeningitis
  - VEE and Lassa fever
Arenaviridae
Retroviridae

- Single-stranded RNA, two RNA strands, produce DNA
  - Use reverse transcriptase to produce DNA from viral genome
  - *Lentivirus* (HIV)
- Oncogenic viruses
  - Includes all RNA tumor viruses
Reoviridae

- Double-stranded RNA, nonenveloped
  - *Reovirus* (respiratory enteric orphan)
  - *Rotavirus* (mild respiratory infections and gastroenteritis)
  - Colorado tick fever
Reoviridae