RNA Viruses

- Diverse group of microbes
- Assigned to one of 12 families based on envelope, capsid, and nature of RNA genome
TABLE 25.1

RNA Viruses with Examples of Diseases

RNA Viruses

- Enveloped
  - Single-stranded genome
    - Segmented genome
      - Orthomyxoviruses
        - Influenza
      - Bunyaviruses
        - Hantavirus
    - Non-segmented genome
      - Paramyxoviruses
        - Measles
      - Rhabdoviruses
        - Rabies
  - Single-stranded genome encodes reverse transcriptase
    - Retroviruses
      - AIDS
    - Togaviruses
      - Rubella
  - Flaviviruses
    - Dengue fever
  - Filoviruses
    - Ebola fever

- Nonenveloped
  - Single-stranded genome
    - Picornaviruses
      - Polio
      - Hepatitis A
    - Calciviruses
      - Norwalk enteritis
  - Double-stranded genome
    - Reoviruses
      - Rotavirus
      - Diarrhea
25.1 Enveloped Segmented Single-Stranded RNA Viruses
The Biology of Orthomyxoviruses: Influenza

- 3 distinct influenza virus types: A, B, C; Type A causes most infections
- Viral infection
  - Virus attaches to, and multiplies in, the cells of the respiratory tract
  - Segments of RNA genome enter the nucleus (transcribed/translated)
  - Finished viruses are assembled and budded off the cell with an envelope
Figure 25.1 Influenza virus cycle

1. Virus (structure shown in a cutaway view) adsors to a respiratory epithelial cell by hemagglutinin spikes and fuses with the membrane.

2. The virus is endocyted into a vacuole and uncoated to release its 8 nucleocapsid segments into the cytoplasm.

3. The nucleocapsids are transported into the nucleus. There the \((-\) sense RNA strand (black) is transcribed into a \((+)\) sense strand (red) that will be translated into viral proteins that make up the capsid and spikes.

4. \((+)\) Sense RNA is used to synthesize glycoprotein spikes inserted into the host membrane.

5. The \((+)\) sense RNA strands are used to synthesize new \((-\) sense RNA strands. These are assembled into nucleocapsids and transported out of the nucleus to the cell membrane.

6. Release of mature virus occurs when viral parts gather at the cell membrane and are budded off with an envelope containing spikes.
Key to influenza are glycoprotein spikes –
- **Hemagglutinin** (H) – 15 different subtypes; most important virulence factor; binds to host cells
- **Neuraminidase** (N) – 9 subtypes – hydrolyzes mucus and assists viral budding and release
<table>
<thead>
<tr>
<th>Type</th>
<th>H/N Subtype</th>
<th>Strain/History</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>H1N1</td>
<td>Spanish flu pandemic of 1918</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/New Jersey/76* (swine flu outbreak)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/USSR/90/77</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/Texas/36/91</td>
</tr>
<tr>
<td>H2N2</td>
<td></td>
<td>A/Singapore/57 (Asian flu pandemic)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/Japan/62</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/Taiwan/64</td>
</tr>
<tr>
<td>H3N2</td>
<td></td>
<td>A/Hong Kong/68 (Hong Kong flu pandemic)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/Johannesburg/33/94</td>
</tr>
<tr>
<td>B</td>
<td>None</td>
<td>B/Harbin/07/94</td>
</tr>
<tr>
<td>C</td>
<td>None</td>
<td>C/JHB/2/66</td>
</tr>
</tbody>
</table>

*The last number is the year the virus appeared.*
• Both glycoproteins frequently undergo genetic changes decreasing the effectiveness of the host immune response

• Constant mutation is called **antigenic drift** – gradually change their amino acid composition

• **Antigenic shift** – one of the genes or RNA strands is substituted with a gene or strand from another influenza virus from a different animal host
  – Genome of virus consists of 10 genes encoded on 8 separate RNA strands
Figure 25.2 Hemagglutinin (HA)

Binding sites used to anchor virus to host cell receptors (low rate of mutation)

Site for antibody binding (high rate of mutation)

Viral envelope
Figure 25.3
Antigenic shift event
Influenza B
• Only undergo antigenic drift
• Not known to undergo antigenic shift

Influenza C
• Known to cause only minor respiratory disease; probably not involved in epidemics
Influenza A

- Acute, highly contagious respiratory illness
- Seasonal, pandemics; among top 10 causes of death in U.S. – most commonly among elderly and small children
- Binds to ciliated cells of respiratory mucosa
- Causes rapid shedding of cells, stripping the respiratory epithelium; severe inflammation
- Fever, headache, myalgia, pharyngeal pain, shortness of breath, coughing
- Weakened host defenses predispose patients to secondary bacterial infections, especially pneumonia
Diagnosis, Treatment, Prevention

• Rapid immunofluorescence tests to detect antigens in a pharyngeal specimen; serological testing to screen for antibody titer
• Treatment: control symptoms; amantadine, rimantadine, zanamivir (Relenza), and oseltamivir (Tamiflu)
• Flu virus has developed high rate of resistance to amantadine and rimantadine
• Annual trivalent vaccine recommended
Bunyaviruses and Arenaviruses

- Transmitted zoonotically; cause periodic epidemics; extremely dangerous; biosafety level 4 viruses

Bunyaviruses – transmitted by insects and ticks
  - California encephalitis, Rift Valley fever, Korean hemorrhagic fever
  - American bunyavirus is a hantavirus, Sin Nombre – emerging disease; high fever, lung, edema, and pulmonary failure; 33% mortality rate
    - Carried by deer and harvest mice; transmitted via airborne dried animal waste

Arenaviruses
- Lassa fever, Argentine hemorrhagic fever, Bolivian hemorrhagic fever, and Lymphocytic choriomeningitis
- Closely associated with rodent host
- Transmission through aerosols and contact
Figure 25.4 Hantavirus pulmonary syndrome cases
25.2 Enveloped Nonsegmented ssRNA Viruses
Paramyxoviruses

Paramyxoviruses (parainfluenza, mumps virus)
Morbiliviruses (measles virus)
Pneumoviruses (respiratory syncytia virus)

- Respiratory transmission
- Envelope has glycoprotein and F spikes that initiate cell-to-cell fusion
- Fusion with neighboring cells – syncytium or multinucleate giant cells form
Figure 25.5 The effects of paramyxoviruses
Parainfluenza

- Widespread as influenza but more benign
- Respiratory transmission
- Seen mostly in children
- Minor cold, bronchitis, bronchopneumonia, croup
- No specific treatment available; supportive therapy
Mumps

- Epidemic parotitis; self-limited, associated with painful swelling of parotid salivary glands
- Humans are the only reservoir
- 40% of infections are subclinical; long-term immunity
- 300 cases in U.S./year
- Incubation 2-3 weeks fever, muscle pain and malaise, classic swelling of one or both cheeks
- Usually uncomplicated invasion of other organs; in 20-30% of infected adult males, epididymis and testes become infected; sterility is rare
- Symptomatic treatment
- Live attenuated vaccine MMR
Figure 25.6 Mumps
Measles

- Caused by Morbillivirus
- Also known as red measles and rubeola
- Different from German measles
- Very contagious; transmitted by respiratory aerosols
- Humans are the only reservoir
- Less than 100 cases/yr in U.S.; frequent cause of death worldwide
- Virus invades respiratory tract
- Sore throat, dry cough, headache, conjunctivitis, lymphadenitis, fever, Koplik spots – oral lesions
- Exanthem
<table>
<thead>
<tr>
<th></th>
<th>Synonyms</th>
<th>Etiology</th>
<th>Primary Patient</th>
<th>Complications</th>
<th>Skin Rash</th>
<th>Koplik’s Spots</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Measles</strong></td>
<td>Rubeola, red measles</td>
<td>Paramyxovirus: <em>Morbillivirus</em></td>
<td>Child</td>
<td>SSPE,* pneumonia</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td><strong>German Measles</strong></td>
<td>Rubella, 3-day measles</td>
<td>Togavirus: <em>Rubivirus</em></td>
<td>Child/fetus</td>
<td>Congenital defects**</td>
<td>Present</td>
<td>Absent</td>
</tr>
</tbody>
</table>

*Subacute sclerosing panencephalitis.
**When transmitted in utero.
Figure 25.7
Signs and symptoms of measles

(a) Koplik’s spots

(b) Rash
Measles

- Most serious complication is subacute sclerosing panencephalitis (SSPE), a progressive neurological degeneration of the cerebral cortex, white matter, and brain stem
  - 1 case in a million infections
  - Involves a defective virus spreading through the brain by cell fusion and destroys cells
  - Leads to coma and death in months or years

- Attenuated viral vaccine MMR
Respiratory Syncytial Virus (RSV)

- Also called Pneumovirus
- Infects upper respiratory tract and produces giant multinucleate cells
- Most prevalent cause of respiratory infection in children 6 months or younger; most susceptible to serious disease
- Epithelia of nose and eye portal of entry; replicates in nasopharynx
- Fever, rhinitis, pharyngitis, otitis, croup
- Treatment: synagis, a monoclonal antibody that blocks attachment, ribavirin
Rabies

- Rhabdovirus family; genus Lyssavirus
- Enveloped, bullet-shaped virions
- Slow, progressive zoonotic disease
- Primary reservoirs are wild mammals; it can be spread by both wild and domestic mammals by bites, scratches, and inhalation of droplets
Figure 25.8 Structure of the rabies virus
Figure 25.9 Rabies in the United States
Rabies

- Virus enters through bite, grows at trauma site for a week and multiplies, then enters nerve endings and advances toward the ganglia, spinal cord and brain
- Infection cycle completed when virus replicates in the salivary glands

Clinical phases of rabies:

- Prodromal phase – fever, nausea, vomiting, headache, fatigue; some experience pain, burning, tingling sensations at site of wound
- Furious phase – agitation, disorientation, seizures, twitching, hydrophobia
- Dumb phase – paralyzed, disoriented, stuporous
- Progress to coma phase, resulting in death
Figure 25.10 Pathologic pictures of rabies
• Often diagnosed at autopsy – intracellular inclusions (Negri bodies) in nervous tissue

• Bite from wild or stray animals demands assessment of the animal, meticulous wound care, and specific treatment

• Preventive therapy initiated if signs of rabies appear

• Treatment – passive and active postexposure immunization
  – Infuse the wound with human rabies immune globulin (HRIG) and globulin; vaccination with human diploid cell vaccine (HDCV), an inactivated vaccine given in 6 doses with 2 boosters

• Control – vaccination of domestic animals, elimination of strays, and strict quarantine practices
  – Live oral vaccine incorporated into bait for wild animals
25.3 Other Enveloped RNA Viruses: Coronaviruses, Togaviruses, and Flaviviruses
Coronaviruses

- Relatively large RNA viruses with distinctively spaced spikes on their envelopes
- Common in domesticated animals
- 3 types of human coronaviruses have been characterized:
  - HCV causes a cold
  - An enteric virus
  - Severe Acute Respiratory Syndrome (SARS)
    - Airborne transmission
    - 9% of cases fatal
Severe Acute Respiratory Syndrome-Associated Coronavirus (SARS)

- Newly emerging disease – 2002
- Transmitted through droplet or direct contact
- Fever, body aches, and malaise
- May or may not experience respiratory symptoms with breathing problems; severe cases can result in respiratory distress and death
- Diagnosis relies on exclusion of other likely agents
- Treatment is supportive
Rubella

• Caused by Rubivirus, a Togavirus
• ssRNA with a loose envelope
• German measles
• Endemic disease
• Most cases reported are adolescents and young adults
• Transmitted through contact with respiratory secretions
Rubella

Two clinical forms:

• Postnatal rubella – malaise, fever, sore throat, lymphadenopathy, rash, generally mild, lasting about 3 days

• Congenital rubella – infection during 1st trimester most likely to induce miscarriage or multiple defects such as cardiac abnormalities, ocular lesions, deafness, mental and physical retardation

• Diagnosis based on serological testing

• No specific treatment available

• Attenuated viral vaccine MMR
Figure 25.11 Congenital rubella
Hepatitis C Virus (HCV)

• Flavivirus
• Acquired through blood contact – blood transfusions, needle sharing by drug abusers
• Infections with varying characteristics – 75-85% will remain infected indefinitely; possible to have severe symptoms without permanent liver damage; more common to have chronic liver disease, without overt symptoms
• Cancer may also result from chronic HCV infection
• Treatment with interferon and ribavirin to lessen liver damage; no cure
• No vaccine
25.4 Arboviruses: Viruses Spread by Arthropod Vectors

- Mosquitoes, ticks, flies, and gnats
- 400 viruses
- Togaviruses, flaviviruses, some bunyaviruses and reoviruses
- Most illnesses caused by these viruses are mild fevers; some may cause severe encephalitis, and life-threatening hemorrhagic fever
Figure 25.12 Worldwide distribution of major arboviral diseases
The Influence of the Vector

• Vectors and viruses tend to be clustered in the tropics and subtropics; many temperate zones have periodic epidemics

• Arbovirus life cycles are closely tied to the ecology of the vectors

• Infections show a peak incidence when the arthropod is actively feeding and reproducing

• Humans can serve as dead-end, accidental hosts or they can be a maintenance reservoir

• Controlling the vector controls the disease
Figure 25.12 Distribution of major arboviral diseases
General Characteristics of Arbovirus Infections

- Acute arbovirus infection may result in undifferentiated mild fever with rash; no long-term effects; prominent symptoms are fever, headache, myalgia, joint stiffness, rash

- Viral encephalitis – brain, meninges, and spinal cord are involved; convulsions, tremor, paralysis, loss of coordination, memory deficits, changes in speech and personality, coma; survivors may experience permanent brain damage
• Colorado tick fever (CTF) – most common tick-borne viral fever in U.S.; Rocky Mountain states
• Western equine encephalitis (WEE) – western U.S. and Canada; extremely dangerous to infants and small children
• Eastern equine encephalitis (EEE) – eastern U.S. and Canada
• California encephalitis – 2 different strains:
  – California strain – western states; little human impact
  – LaCrosse strain – eastern U.S. and Canada; prevalent cause of viral encephalitis
• St. Louis encephalitis (SLE) – most common of all in America; epidemics in midwestern and southern states; inapparent infections are very common
• West Nile encephalitis
Hemorrhagic Fevers

Yellow fever – eliminated in U.S.
• Two patterns of transmission:
  – Urban cycle – humans and mosquitoes, *Aedes aegypti*
  – *Sylvan cycle* – forest monkeys and mosquitoes; South America
• Acute fever, headache, muscle pain; may progress to oral hemorrhage, nosebleed, vomiting, jaundice, and liver and kidney damage; significant mortality rate

Dengue fever – flavivirus carried by *Aedes* mosquito; not in U.S.; usually mild infection
  – Dengue hemorrhagic shock syndrome, breakbone fever – extreme muscle and joint pain; can be fatal
25.5 HIV Infections and AIDS

- Human immunodeficiency virus
- Acquired immunodeficiency syndrome
- First emerged in early 1980s
- HIV-1 may have originated from a chimpanzee virus
- 1959 first documented case of AIDS
Causative Agent

- Retrovirus, genus Lentivirus
- Encode reverse transcriptase enzyme which makes a double stranded DNA from the single-stranded RNA genome
- Viral genes permanently integrated into host DNA
- Human Immunodeficiency Virus (HIV) – the cause of Acquired Immunodeficiency Syndrome (AIDS)
- HIV-1 and HIV-2
- T-cell lymphotropic viruses I and II – leukemia and lymphoma
- HIV can only infect host cells that have the required CD4 marker plus a coreceptor
Figure 25.13
The general structure of HIV
Epidemiology of HIV Infections

• Transmission occurs by direct and specific routes: mainly through sexual intercourse and transfer of blood or blood products; babies can be infected before or during birth, and from breast feeding

• HIV does not survive long outside of the body
Figure 25.14 Infection by HIV

- Blood exposure through needles
- Direct blood exposure, during sexual intercourse or other intimate contact
- Semen, vaginal fluid exposure during sexual intercourse
- Infected macrophage
- Epithelial cell
- Lacerations
- Membrane or skin portal of entry

- Dendritic cells underlying skin shelter and amplify virus
- Spread of virus to lymphatic organs, bone marrow, circulation

Legend:
- Infected blood
- Infected sexual secretions
- HIV
- Infected white blood cells
• First nationally notifiable in 1984
• 6th most common cause of death among people aged 25-44 years in the U.S.
• Men account for 70% of new infections
• Anal sex provides an entrance for the virus
• IV drug abusers can be HIV carriers; significant factor in spread to heterosexual population
• In 2006, the number of infected individuals worldwide is estimated to be 33 million with ~1 million in the U.S.
Figure 25.15
Patterns of HIV infection
Pathogenesis and Virulence Factors of HIV

- HIV enters through mucous membrane or skin and travels to dendritic phagocytes beneath the epithelium, multiplies, and is shed
- Virus is taken up and amplified by macrophages in the skin, lymph organs, bone marrow, and blood
- HIV attaches to CD4 and coreceptor; HIV fuses with cell membrane
- Reverse transcriptase makes a DNA copy of RNA
- Viral DNA is integrated into host chromosome
- Can produce a lytic infection or remain latent
Figure 25.16
Multiplication cycle of HIV

The virus is adsorbed and fuses with the cell. The twin RNAs are uncoated. Reverse transcriptase catalyzes the synthesis of a single complementary strand of DNA (ssDNA). This single strand serves as a template for synthesis of a double strand (ds) of DNA. In latency, dsDNA is inserted into the host chromosome as a provirus.

After a latent period, various immune activators stimulate the infected cell, causing reactivation of the provirus genes and production of viral mRNA.

HIV mRNA is translated by the cell's synthetic machinery into virus components (capsid, reverse transcriptase, spikes), and the viruses are assembled. Budding of mature viruses lyses the infected cell.
Primary effects of HIV infection:

– Extreme leukopenia – lymphocytes in particular
– Formation of giant T cells and other syncytia allowing the virus to spread directly from cell to cell
– Infected macrophages release the virus in central nervous system, with toxic effect, inflammation

Secondary effects of HIV:

– Destruction on CD4 lymphocytes allows for opportunistic infections and malignancies
Signs and Symptoms of HIV Infections and AIDS

- Symptoms of HIV are directly related to viral blood level and level of T cells
- Initial infection – mononucleosis-like symptoms that soon disappear
- Asymptomatic phase 2-15 years (avg. 10)
- HIV destroys the immune system
- When T4 cell levels fall below 200/μL, AIDS symptoms appear including fever, swollen lymph nodes, diarrhea, weight loss, neurological symptoms, opportunistic infections, and cancers
Figure 25.17 Timeline in HIV infection

- **Antibody (-)**
  - Acute symptoms of HIV infection
  - Antibody appears in serum
  - 2 weeks

- **Antibody (+)**
  - Exposure
  - Incubation period
  - Symptoms occur

(I) Infection with virus.
(II) Appearance of antibodies in standard HIV tests.
(III) Asymptomatic HIV disease, which can encompass an extensive time period.
(IV) Overt symptoms of AIDS include some combination of opportunistic infections, cancers, and general loss of immune function.
Figure 25.18 Changes in virus, antibody levels, and T cells

- Virus levels are high during the initial acute infection and decrease until the later phases of HIV disease and AIDS.
- Antibody levels gradually rise and remain relatively high throughout phases III and IV.
- T-cell numbers remain relatively normal until the later phases of HIV disease and full-blown AIDS.
Diagnosis of HIV Infection

- Testing based on detection of antibodies specific to the virus in serum or other fluids; done at 2 levels
- Initial screening
  - ELISA, latex agglutination, and rapid antibody tests
  - Rapid results but may result in false positives
- Follow up with Western blot analysis to rule out false positives
- False negatives can also occur; persons who may have been exposed should be tested a second time 3-6 months later
Diagnosis of AIDS is made when a person meets the criteria:

1. Positive for the virus, and

2. They fulfill one of the additional criteria:
   - They have a CD4 count of fewer than 200 cells/ml of blood
   - Their CD4 cells account for fewer than 14% of all lymphocytes
   - They experience one or more of a CDC-provided list of AIDS-defining illnesses
### TABLE 25.A

**AIDS-Defining Illnesses**

<table>
<thead>
<tr>
<th>Skin and/or Mucous Membranes (includes eyes)</th>
<th>Nervous System</th>
<th>Cardiovascular and Lymphatic System or Multiple Organ Systems</th>
<th>Respiratory Tract</th>
<th>Gastrointestinal Tract</th>
<th>Genitourinary and/or Reproductive Tract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytomegalovirus retinitis (with loss of vision)</td>
<td>Cryptococcosis, extrapulmonary</td>
<td>Coccidiomycosis, disseminated or extrapulmonary</td>
<td>Candidiasis of trachea, bronchi, or lungs</td>
<td>Candidiasis of esophagus, GI tract</td>
<td>Invasive cervical carcinoma</td>
</tr>
<tr>
<td>Herpes simplex chronic ulcers (&gt;1 month duration)</td>
<td>HIV encephalopathy</td>
<td>Cytomegalovirus (other than liver, spleen, nodes)</td>
<td>Herpes simplex bronchitis or pneumonitis</td>
<td>Herpes simplex chronic ulcers (&gt;1 month duration)</td>
<td>Herpes simplex chronic ulcers (&gt;1 month duration)</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>Lymphoma, primarily in brain</td>
<td>Histoplasmosis, disseminated or extrapulmonary</td>
<td>Mycobacterium avium complex</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Progressive multifocal leukoencephalopathy</td>
<td>Burkitt lymphoma</td>
<td>Tuberculosis (Mycobacterium tuberculosis)</td>
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<tr>
<td></td>
<td></td>
<td>Immunoblastic lymphoma</td>
<td>Pneumocystis (carinii) jiroveci pneumonia</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Mycobacterium kansasii, disseminated or extrapulmonary</td>
<td>Pneumonia, recurrent in 12-month period</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Mycobacterium tuberculosis, disseminated or extrapulmonary</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Salmonella septicemia, recurrent Wasting syndrome</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Preventing and Treating HIV

• No vaccine available
  – Monogamous sexual relationships
  – Condoms
  – Universal precautions

• No cure; therapies slow down the progress of the disease or diminish the symptoms
  – Inhibit viral enzymes: reverse transcriptase, protease, integrase
  – Inhibit fusion
  – Inhibit viral integration
  – Highly active anti-retroviral therapy
Figure 25.19 “Trojan horse”, technique for making AIDS vaccine
Figure 25.20 Mechanisms of action of anti-HIV drugs

(a) **Reverse transcriptase blockers.**
A prominent group of drugs (AZT, ddI, 3TC) act as nucleoside analogs to inhibit reverse transcriptase. They are inserted in place of the natural nucleotide by reverse transcriptase but block further action of the enzyme and synthesis of viral DNA.

(b) **Protease inhibitors that cause abnormal viruses to be released.**
Protease inhibitors plug into the active sites on HIV protease. This enzyme is necessary to cut elongate HIV protein strands and produce smaller protein units. During budding viruses incorporate this uncut nonfunctioning protein. The resultant viruses are unable to mount an infection.
25.6 Other Retroviruses: Human T-Cell Lymphototropic Viruses
Adult T-Cell Leukemia and Hairy-Cell Leukemia

Leukemia is a malignant disease of the white blood cell forming elements in bone marrow

• 2 leukemias are thought to be viral:
  – Adult T-Cell leukemia – HTLV-I; signs include cutaneous T-cell lymphoma with lymphadenopathy and dissemination of the tumors to other organs
  – HTLV II – may be a factor in certain neurodegenerative conditions
25.7 Nonenveloped Nonsegmented ssRNA Viruses: Picornaviruses and Caliciviruses

• Picornaviruses
  – *Enterovirus* – poliovirus, HAV
  – *Rhinovirus* – rhinovirus
  – *Cardiovirus* – infects heart and brain
<table>
<thead>
<tr>
<th>Genus</th>
<th>Representative</th>
<th>Primary Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enterovirus</strong></td>
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<td></td>
<td>Poliovirus</td>
<td>Poliomyelitis</td>
</tr>
<tr>
<td></td>
<td>Coxsackievirus A</td>
<td>Focal necrosis, myositis</td>
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<tr>
<td></td>
<td>Coxsackievirus B</td>
<td>Myocarditis of newborn</td>
</tr>
<tr>
<td></td>
<td>Echovirus</td>
<td>Aseptic meningitis, enteritis, others</td>
</tr>
<tr>
<td></td>
<td>Enterovirus 72</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td><strong>Rhinovirus</strong></td>
<td>Rhinovirus</td>
<td>Common cold</td>
</tr>
<tr>
<td><strong>Cardiovirus</strong></td>
<td>Cardiovirus</td>
<td>Encephalomyocarditis</td>
</tr>
<tr>
<td><strong>Aphthovirus</strong></td>
<td>Aphthovirus</td>
<td>Foot-and-mouth disease (in cloven-foot animals)</td>
</tr>
</tbody>
</table>
Poliovirus and Poliomyelitis

Poliomyelitis (polio) – acute enteroviral infection of the spinal cord that can cause neuromuscular paralysis

• Poliovirus – naked capsid; resistant to acid, bile, and detergents; can survive stomach acids when ingested

• Worldwide vaccination programs have reduced the number of cases; eradication is expected
Figure 25.21 Typical structure of a picornavirus
Figure 25.22 The stages of infection and pathogenesis of poliomyelitis
• Transmitted by fecal-oral route
• Polioviruses adhere to receptors of mucosal cells in oropharynx and intestine, multiply in number and shed in throat and feces, some leak into blood
• Most infections are short-term, mild viremia
• Some develop mild nonspecific symptoms of fever, headache, nausea, sore throat, and myalgia
• If viremia persists, virus spreads to spinal cord and brain
• If nervous tissue is infected but not destroyed – muscle pain and spasm, meningeal inflammation, and vague hypersensitivity
• Invasion of motor neurons causes flaccid paralysis
• Decades later post-polio syndrome (PPS) – progressive muscle deterioration; occurs in 25-50% of patients infected with polioviruses in childhood
Treatment and Prevention

• Treatment is largely supportive for pain and suffering; respiratory failure may require artificial ventilation; physical therapy may be needed

• Prevention is vaccination
  • Inactivated polio vaccine (IPV) Salk vaccine
  • Oral polio vaccine (OPV) Sabin vaccine, attenuated virus – no longer recommended in the U.S.

• Worldwide eradication anticipated by 2010
Figure 25.23 Targets of poliovirus
Figure 25.24 Possible outcomes of poliovirus infection
Nonpolio Enteroviruses

- Most common
  - Coxsackieviruses A and B
  - Echoviruses
  - Nonpolioenteroviruses

- Similar to poliovirus in epidemiological and infectious characteristics but less virulent

- Responsible for respiratory infections, conjunctivitis, and hand-foot-mouth disease

- Rare cases of coxsackievirus and echovirus paralysis, aseptic meningitis, and encephalitis
Hepatitis A Virus and Infectious Hepatitis

- Cubical picornavirus relatively resistant to heat and acid
- Not carried chronically, principal reservoirs are asymptomatic, short-term carriers or people with clinical disease
- Fecal-oral transmission; multiplies in small intestine and enters the blood and is carried to the liver
- Most infections subclinical or vague, flu-like symptoms occur; jaundice is seldom present
- No specific treatment once the symptoms begin
- Inactivated viral vaccine
- Attenuated viral vaccine
- Pooled immune serum globulin for those entering into endemic areas
Human Rhinovirus (HRV)

- More than 110 serotypes associated with the common cold
- Sensitive to acidic environments; optimum temperature is 33°C
- Unique molecular surface makes development of a vaccine unlikely
- Many strains circulating in the population at one time; acquired from contaminated hands and fomites
• Headache, chills, fatigue, sore throat, cough, nasal drainage
• Treat the symptoms
• Handwashing and care in handling nasal secretions
Figure 25.26
Antigen structure of a rhinovirus
Caliciviruses

- Norwalk agent best known; believed to cause 1/3rd of all viral gastroenteritis cases
- Transmitted by fecal-oral route
- Infection in all ages at any time of year
- Acute onset, nausea, vomiting, cramps, diarrhea, chills
- Rapid and complete recovery
25.8 Nonenveloped Segmented dsRNA Viruses: Reoviruses

Unusual double-stranded RNA genome

Two best known:

• Rotavirus – oral-fecal transmission; primary viral cause of mortality and morbidity resulting from diarrhea in infants and children
  – Treatment with rehydration and electrolyte replacement
• Reovirus – cold-like upper respiratory infection, enteritis
25.9 Prions and Spongiform Encephalopathies

Prions – proteinaceous infectious particles; highly resistant to chemicals, radiation, and heat

• Cause transmissible spongiform encephalopathies (TSEs) in humans and animals
  – Neurodegenerative diseases with long incubation periods
| TABLE 25.5 | Properties of the Agents of Spongiform Encephalopathies |

- Very resistant to chemicals, radiation, and heat (can withstand autoclaving)
- Do not present virus morphology in electron microscopy of infected brain tissue
- Not integrated into nucleic acid of infected host cells
- Proteinaceous
- Do not elicit inflammatory reaction or cytopathic effects in host
- Do not elicit antibody formation in host
- Responsible for vacuoles and abnormal fibers forming in brain of host
- Transmitted only by close, direct contact with infected tissues and secretions
Human TSE:

• Creutzfeldt-Jakob Disease (CJD) – alteration in the structure of normal PrP protein found in the brain
  – Abnormal PrP converts normal PrP into abnormal form

• Abnormal PrP results in nerve cell death, spongiform damage, and severe loss of brain function

• Transmission is through direct or indirect contact with infected brain tissue or CSF
• Variant CJD became apparent in the late 1990s after eating meat from cattle afflicted with bovine spongiform encephalopathy
• Difficult to diagnose; requires examination of biopsied brain or nervous tissue
• Prevention relies on avoidance of contaminated tissue
• Treatment focuses on easing symptoms
Figure 25.28 The microscopic effects of spongiform encephalopathy