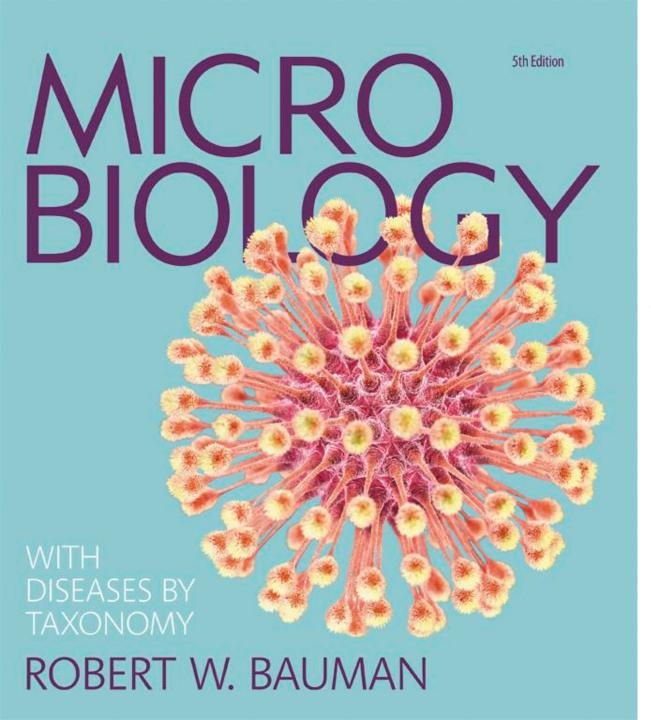
# **Chapter 25 – Pathogenic RNA Viruses**

NIMESH PATEL| HLSC 2400 NOVEMBER 23, 2017



PowerPoint® Lecture
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CHAPTER 24

## Pathogenic DNA Viruses



Communicable Disease Control Chapter I - Management of Specific Diseases Hepatitis B September 2009 Page 14

#### 14.0 INTERPRETATION OF TESTING RESULTS

Factor to be tested	Term	Use
HBsAg	Hepatitis B surface antigen	Detection of acutely or chronically infected person
Anti-HBs	Antibody to HBsAg	Identification of resolved infection with HBV; determination of immunity after hepatitis B vaccination
Anti-HBc	Antibody to core antigen (HBcAg)	Identification of individuals with prior infection with HBV (not present after immunization).
Anti-HBc IgM	IgM class antibody to HBcAg	Indicates acute or recent infection with HBV; detectable for 4-6 months after infection.
HBeAg	Hepatitis B e Antigen	Identification of infected individuals at increased risk of transmitting HBV.
Anti-HBe	Antibody to HBeAg	Identification of infected individuals at lower risk for transmitting HBV.

## Interpretation of test results

		<del>-</del>
HBsAg anti-HBc anti-HBs	negative negative negative	susceptible
HBsAg anti-HBc anti-HBs	negative negative positive ( ≥ 10 IU/L)	immune due to vaccination
HBsAg anti-HBc anti-HBs	negative positive positive ( ≥ 10 IU/L)	immune due to natural infection
HBsAg anti-HBc IgM anti-HBs	positive positive negative	acute infection
HBsAg anti-HBc anti-HBs	positive positive negative	chronic infection
HBsAg anti-HBc anti-HBs	negative positive negative	"isolated anti-core positive" four interpretations possible Interpretation unclear; four possibilities:

- 1. Resolved infection (most common)
- 2. False-positive anti-HBc, thus susceptible
- 3. "Low level" chronic infection
- 4. Resolving acute infection

 $http://www.bccdc.ca/resource-gallery/Documents/Guidelines\%20 and \%20 Forms/Guidelines\%20 and \%20 Manuals/Epid/CD\%20 Manual/Chapter\%201\%20-\%20 CDC/HepatitisB\_Sept\_2009.pdf$ 

https://www.cdc.gov/hepatitis/HBV/PDFs/SerologicChartv8.pdf

## Hepadnaviridae

## The Role of Hepatitis B Virus in Hepatic Cancer

- Evidence shows HBV associated with hepatic cancer
  - Hepatic cancer occurs in areas with high prevalence of HBV
  - HBV genome integrated into hepatic cancer cells
  - Hepatic cancer cells express HBV antigen
  - Chronic HBV carriers more likely to develop hepatic cancer
- Hepatic cancer may be the first cancer eliminated by vaccination

## Parvoviridae

- Only human pathogen with a ssDNA genome
- Have icosahedral capsid
- Smallest of the DNA viruses
- Cause a number of diseases in animals
- B19 virus is the primary parvovirus of humans
  - Causes erythema infectiosum
    - Also called fifth disease
  - Infection results in a reddening of the skin
  - Sunlight aggravates the condition

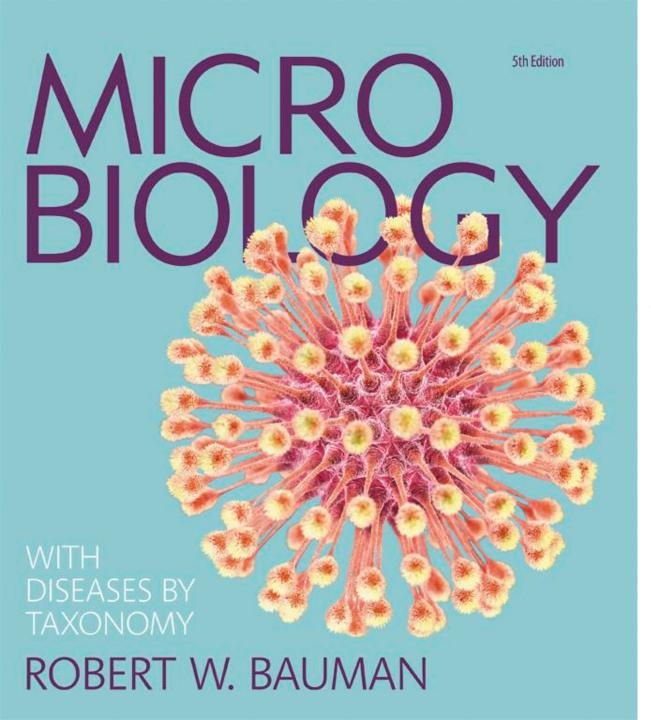
Figure 24.22 A case of erythema infectiosum (fifth disease).



Table 24.2 Taxonomy and Characteristics of DNA Viruses of Humans

#### TABLE **24.2** Taxonomy and Characteristics of DNA Viruses of Humans

Family	Strand Type	Enveloped or Naked	Capsid Symmetry	Size (diameter, nm)	Representative Genera (disease)	
Poxviridae	Double	Enveloped	Complex	200–300	Orthopoxvirus (smallpox, cowpox), Molluscipoxvirus (molluscum contagiosum)	
Herpesviridae	Double	Enveloped	Icosahedral	150–200	Simplexvirus—type 1 herpes (fever blisters, respiratory infections, encephalitis), type 2 herpes (genital infections), Varicellovirus (chickenpox), Lymphocryptovirus Epstein-Barr virus (infectious mononucleosis, Burkitt's lymphoma), Cytomegalovirus (birth defects), Roseolovirus (roseola)	
Papillomaviridae	Double	Naked	Icosahedral	45–55	Papillomavirus (benign tumors, warts, cervical and penile cancers)	
Polyomaviridae	Double	Naked	Icosahedral	45–55	Polyomavirus (progressive multifocal leukoencephalopathy)	
Adenoviridae	Double	Naked	Icosahedral	60–90	Mastadenovirus (conjunctivitis, respiratory infections)	
Hepadnaviridae	Partial single and partial double	Enveloped	Icosahedral	42	Orthohepadnavirus (hepatitis B)	
Parvoviridae	Single	Naked	Icosahedral	18–26	Erythrovirus (fifth disease)	



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CHAPTER 25

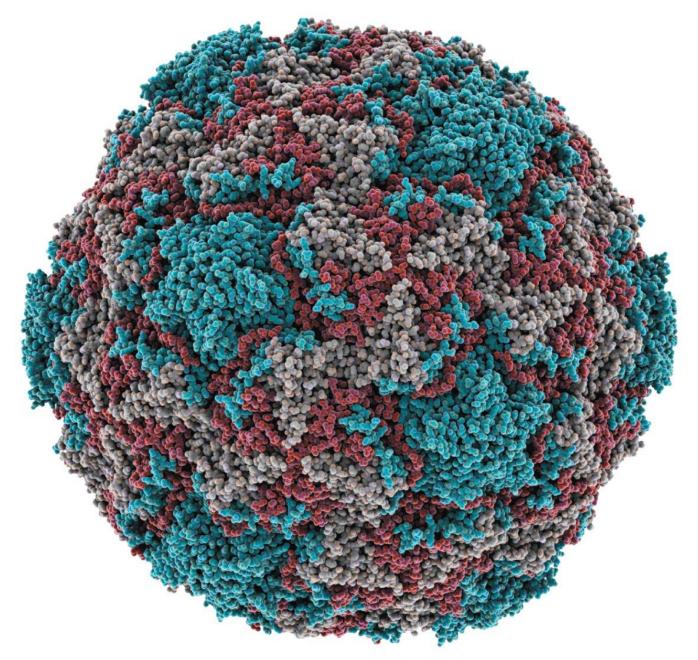
## Pathogenic RNA Viruses

### RNA Viruses

- Only agents that store genetic information in RNA molecules
- RNA viruses are categorized by several factors
  - Their genomic structure
  - Presence of an envelope
  - Size and shape of their capsid
- Four types of RNA viruses
  - Positive single-stranded RNA (+ssRNA)
  - Retroviruses (+ssRNA viruses that convert their genome to DNA)
  - Negative single-stranded RNA (–ssRNA)
  - Double-stranded RNA (dsRNA)
- Positive RNA can be used by a ribosome to translate protein
  - Negative RNA transcribed as mRNA to be processed by a ribosome

- Picornaviridae
  - Smallest of the animal viruses
  - Large family that contains many human pathogens
    - Picornaviruses that cause human disease are in several genera
      - Rhinovirus, Enterovirus, and Hepatovirus
- Caliciviridae, Astroviridae, and Hepeviridae
  - Larger than picornaviruses
  - Cause gastrointestinal disease

Figure 25.1 Artist's rendition of rhinovirus 14.



#### TABLE **25.1**

## Manifestations of Respiratory Infections

Ailment	Manifestations
Common Cold (viral)	Sneezing, rhinorrhea, congestion, sore throat, headache, malaise, cough
Influenza (viral)	Fever, rhinorrhea, headache, body aches, fatigue, dry cough, pharyngitis, congestion
"Strep" Throat (bacterial)	Fever, red and sore throat, swollen lymph nodes in neck
Viral Pneumonia	Fever, chills, mucus-producing cough, headache, body aches, fatigue
Bacterial Pneumonia	Fever, chills, congestion, cough, chest pain, rapid breathing, and possible nausea and vomiting
Bronchitis (viral or bacterial)	Mucus-producing cough, wheezing
Inhalation Anthrax (bacterial)	Fever, malaise, cough, chest discomfort, vomiting
Severe Acute Respiratory Syndrome (SARS)	High <u>fever</u> (>38°C), chills, shaking, headache, malaise, myalgia
Middle East Respiratory Syndrome (MERS)	Fever, cough, shortness of breath

## Common Colds Caused by Rhinoviruses

- Epidemiology
  - Rhinoviruses cause most cases of the cold
  - Infections limited to the upper respiratory tract
  - A single virus is often sufficient to cause a cold
  - Virus transmitted by aerosols, fomites, or hand-to-hand contact – highly infective
    - Most commonly transmitted by direct person-toperson contact
  - People acquire some immunity against serotypes that have infected them
    - The number of infections tends to decrease with age
    - Very common in newborns and infants
    - Herd immunity

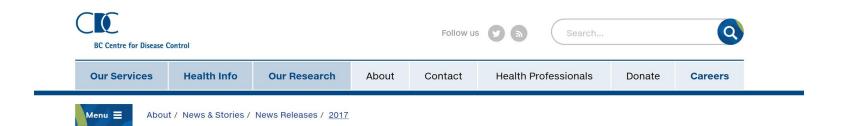
## Common Colds Caused by Rhinoviruses

- Diagnosis, Treatment, and Prevention
  - Diagnosis
    - Manifestations of rhinoviruses are usually diagnostic
  - Treatment
    - Rest & fluids helps mount a more effective immune response
    - Pleconaril (anti-viral medication) can reduce the severity and duration of colds
      - Must be taken at the onset of symptoms
    - Other medications can help relieve the symptoms (antihistamines, decongestants and pain relievers)
      - Does not reduce the duration

- Common Colds Caused by Rhinoviruses
  - Diagnosis, Treatment, and Prevention
    - Prevention
      - Handwashing is the most important preventive measure
      - Zinc and vitamin C have not been demonstrated to prevent colds

## Hepatitis A

- Hepatitis A virus is the causative agent
  - Survives on various surfaces for months and is resistant to common household disinfectants
  - "High temperatures such as boiling or cooking food or liquids for at least 1 minute at 185° F (85° C), kill the virus, although freezing temperatures do not" - CDC
- Transmitted through the fecal-oral route
  - Contamination of food or water sources
  - May spread from close personal contact with an infected person such as through sex or caring for someone who is ill (Centers for Disease Control and Prevention)



#### **UPDATE:** Hepatitis A in pineapple chunks

September 05, 2017



**UPDATE:** The ongoing investigation into hepatitis A virus in pineapple chunks has identified additional products that may be affected.



## Hepatitis A

- Signs and symptoms are due to the patient's immune response
  - Because immune symptoms kills infected liver cells
  - Incubation period: About one month
  - Include fever, fatigue, nausea, anorexia, and jaundice
  - Children are less likely to develop symptoms because of cell-mediated immune responses are not fully developed

## Hepatitis A

- Infection does not cause chronic liver disease
- Complete recovery occurs most of the time
  - In almost 99% of the patients
  - About 15 percent of people infected with hepatitis A virus will have prolonged or relapsing symptoms during the first six to nine months after being infected – but less than 2 months in most patients
  - Recovery will protect you from virus for life
- Asymptomatic patients can release virion in feces and can infective even without developing symptoms
  - A person can transmit the disease 2 weeks before the symptoms appear
- Vaccine is available for children and adults

## Hepatitis A

#### **Protect Yourself**

- Get vaccinated
- Be aware when you travel
- Ensure proper hygiene and take precautions with food and drink
- Avoid peeled fruit and raw vegetables, salads, dairy products with unpasteurized milk, and raw or undercooked meat, fish and shellfish and any food sold by street vendors.
- Swim only in chlorinated pools
- Do not share food, drinks or cigarettes

## Hepatitis A

#### How soon before travel should I get the hepatitis A vaccine?

You should get the first dose of hepatitis A vaccine as soon as you plan international travel to a country where hepatitis A is common. Two weeks or more before departure is ideal, but getting the vaccine any time before travel will provide some protection.

For optimal protection, older adults, people who are immunocompromised, and people with chronic liver disease or other chronic medical conditions who are planning to depart in less than 2 weeks should receive the first dose of vaccine and can get a shot of immune globulin at the same time, at a separate injection site.

#### I'm leaving for my trip in a few days, can I still get the hepatitis A vaccine?

Experts say that the first dose of hepatitis A vaccine can be given any time before departure. This will provide some protection for most healthy people.

#### What should I do if I am traveling internationally but cannot receive hepatitis A vaccine?

Travelers who are allergic to a vaccine component or who are younger than 12 months should receive a single dose of immune globulin (IG). Immune globulin provides effective protection against hepatitis A virus infection for up to 2 months, depending on the dosage given. If you are staying longer than two months, you can get another dose of IG for continued protection.

#### TABLE **25.3** Comparison of Hepatitis Viruses

Feature	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
Common Names of Disease	Infectious hepatitis	Serum hepatitis	Non-A, non-B hepatitis; chronic hepatitis	Delta agent hepatitis	Hepatitis E, enteric hepatitis
Virus Family (genus)	Picornaviridae (Hepatovirus)	Hepadnaviridae (Orthohepadnavirus)	Flaviviridae (Hepacivirus)	Arenaviridae (Deltavirus)	Hepeviridae (Orthohepevirus)
Genome	+ssRNA	dsDNA	+ssRNA	-ssRNA	+ssRNA
Envelope?	Naked	Enveloped	Enveloped	Enveloped	Naked
Transmission	Fecal-oral	Needles; sex	Needles; sex	Needles; sex	Fecal-oral
Severity (mortality rate)	Mild (<0.5%)	Occasionally severe (1–2%)	Usually subclinical (0.5–4%)	Requires coinfection with hepatitis B virus; may be severe (high)	Mild (1–2%) except in pregnant women (20%)
Chronic Carrier State?	No	Yes	Yes	No	No
Other Disease Associations	<u> </u>	Hepatic cancer	Hepatic cancer	Cirrhosis	_

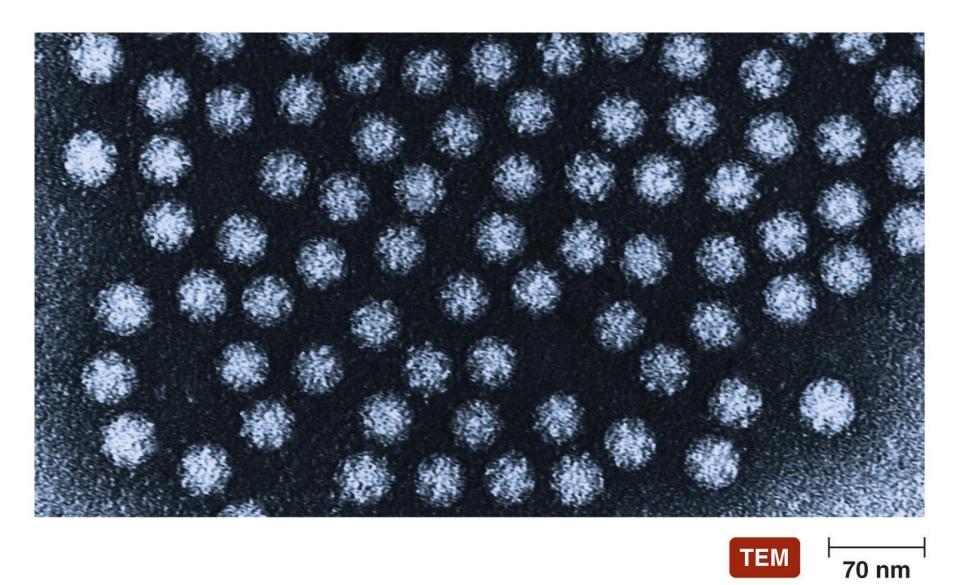
#### Acute Gastroenteritis

- Caliciviruses and astroviruses can cause acute gastroenteritis
- Can cause outbreaks where people live in close quarters
  - Day care centers, schools, hospitals, prisons, cruise ships, university dormitories
- Caliciviruses cause diarrhea, nausea, and vomiting
  - Noroviruses cause most (90%) cases of viral gastroenteritis
- Astroviruses cause diarrhea but no vomiting
- Incubation period: About 24 hours
- Symptoms may relive in 12 60 hours

#### Acute Gastroenteritis

- No specific treatment except replacement of fluid and electrolytes
- Prevention involves adequate sewage and water treatment, frequent handwashing, and disinfection of contaminated surfaces

Figure 25.6 Viruses of the families *Caliciviridae* and *Astroviridae* have naked, star-shaped capsids.



## Hepatitis E

- Also known as enteric hepatitis
- Caused by hepatitis E virus
  - Formerly classified as a calicivirus
- Fatal in 20% of pregnant women but 4% in rest of the population
- The disease is self-limiting
- Treatment: Rehydration and rest
- Prevent by interrupting the fecal-oral route of transmission
  - Good hygiene, water purification, and adequate sewage treatment

#### Diseases of +RNA Arboviruses

- Yellow Fever
  - Disease involving degeneration of the liver, kidneys, and heart as well as massive hemorrhaging
  - Caused by yellow fever virus
  - Spreads through the bite of infected mosquitoes the Aedes species in Africa and the Haemagogus species in South America
    - Bites during the daytime, mostly around sunrise and sunset
  - Mortality can approach 20%
  - Still remains a significant cause of death worldwide
  - Vaccine available for travelers



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Home → Public Health Agency of Canada → Travel Health → Yellow Fever Vaccination Centres in Canada

### **Travellers Going to Yellow Fever Areas**

Update on Recent Yellow Fever Vaccine Shortage:

There is currently a shortage of the yellow fever vaccine in Canada. It is important for travellers to contact a designated Yellow Fever Vaccination Centre well in advance of their trip to ensure that the vaccine is available.

Click on a question to read the answer.

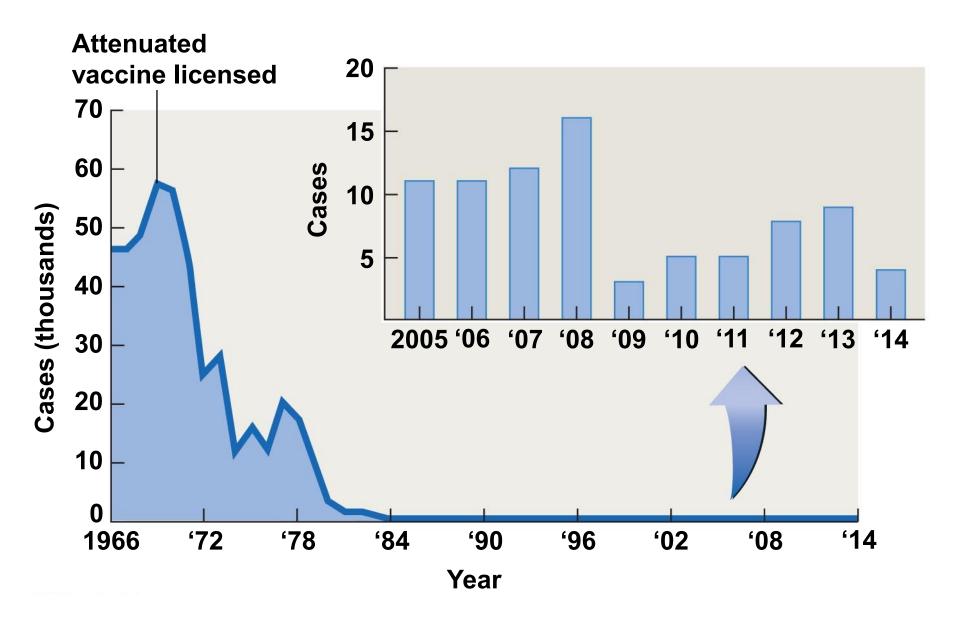
- Rubella
  - Also called "German measles" or "three-day measles"
  - Rubella virus is the causative agent
  - One of the five childhood diseases that produces skin lesions
    - Others: Measles, chickenpox, roseola, fifth disease
  - Infection begins in respiratory system but spreads throughout the body
  - Characterized by a rash of flat, pink to red spots
  - Infections in children are usually not serious
  - Adults can develop arthritis or encephalitis

- Rubella
  - Infection of pregnant women can cause congenital defects
    - Was not considered a serious disease until 1941
    - Norman Gregg, an Australian Ophthalmologist, recognized infection in pregnant women resulted in sever congenital defects in their babies
      - Cardiac abnormalities, deafness, blindness, mental retardation, microcephaly, and growth retardation
  - Vaccination effective at reducing the incidence of rubella
    - Live vaccine contraindicated in pregnant and immunocompromised individuals

Figure 25.13 The rash of rubella.



Figure 25.14 The efficacy of vaccination against rubella.



- Hepatitis C
  - Caused by hepatitis C virus (HCV)
  - Accounts for about 20% of hepatitis cases in the United States
  - Spread through needles, organ transplants, and sexual activity
  - Chronic infection with few if any symptoms
  - Severe liver damage (20% of cases) and liver failure (5% of cases) can occur over time
  - Sofosbuvir cures most people with HCV within 12 weeks
  - No vaccine is available

- Diseases of Coronaviruses
  - Named for the corona-like halo formed by their envelopes
  - Transmitted via large droplets from the upper respiratory tract
  - Second most common cause of colds
  - Coronavirus respiratory syndromes
    - Include severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)
    - Fatality rate: 10% in SARS, and 50% in MERS
    - Symptoms include high fever and respiratory distress
    - No treatment or vaccine is available
  - Quarantine of infected individuals and use of face masks help prevent SARS and MERS

Figure 25.15 Coronaviruses.

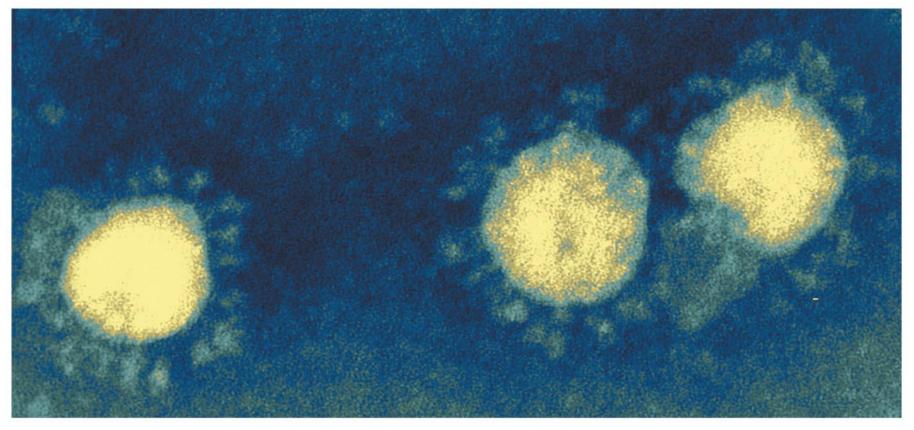


Figure 25.16 Prevention of coronavirus respiratory syndromes.



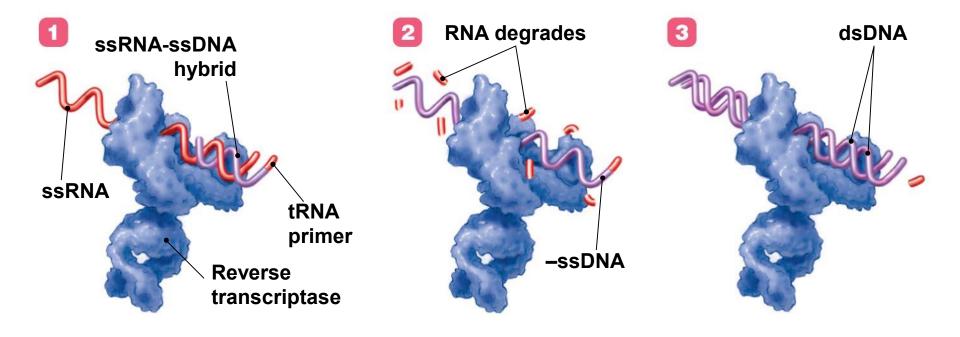


(a) (b)

#### Retroviruses

- Studied more than any other group of viruses
- Have polyhedral capsids with spiked envelopes
- Genomes contain two identical molecules of positive ssRNA
- Retroviruses don't conform to the "central dogma"
- Retroviruses transcribe dsDNA from ssRNA using reverse transcriptase
- Two types of retroviruses:
  - Viruses that are primarily oncogenic
  - Viruses that are primarily immunosuppressive

Figure 25.17 Action of reverse transcriptase, depicted here as three distinct steps.



- Oncogenic Retroviruses (Deltaretrovirus)
  - Human T-lymphotrophic virus 1 (HTLV-1)
    - Identified in patient with adult acute T-cell lymphocytic leukemia
    - Tax protein activates cell growth genes in helper T cells
  - HTLV-2 causes a rare cancer called hairy-cell leukemia
  - HTLV-5 has not been linked to cancer
  - HTLV-1 and HTLV-2 infect lymphocytes and are transmitted via sexual intercourse, blood transfusion, and contaminated needles
  - No specific antiviral treatment
  - Infections are chronic, and long-term prognosis of patients is poor
  - Infections prevented with same behavior changes needed to prevent HIV

- Immunosuppressive Retroviruses (Lentivirus) and Acquired Immunodeficiency Syndrome
  - Acquired immunodeficiency syndrome (AIDS)
    - Not a disease but a syndrome
    - Defined as certain opportunistic or rare infections along with infection by HIV or a severe decrease in the number of helper T cells and a positive test for HIV
    - Several infections and diseases define AIDS
  - Two major types of HIV:
    - HIV-1 is prevalent in the United States, Canada and Europe
    - HIV-2 is prevalent in West Africa

**Table 25.5 Opportunistic Infections and Tumors of AIDS Patients** 

#### TABLE **25.5** O

### Opportunistic Infections and Tumors of AIDS Patients

Туре	Manifestations
Bacterial Infections (19–21) <sup>a</sup>	Tuberculosis, especially extrapulmonary (Mycobacterium)
	Rectal gonorrhea (Neisseria)
	Recurrent fever and septicemia due to Salmonella, Haemophilus, or Streptococcus
Fungal Infections (22)	Pneumocystis pneumonia
	Thrush, disseminated in trachea, lungs, esophagus (Candida)
	Histoplasmosis (Histoplasma)
Protozoal Infections (23)	Toxoplasmosis (Toxoplasma)
	Chronic diarrhea (Cryptosporidium, Isospora)
Viral-Induced Tumors (24)	Kaposi's sarcoma (especially when associated with HHV-8)
	Lymphoma (induced by Epstein-Barr virus)
Viral Infections (24)	Cytomegalovirus disseminated in brain, lungs, retina, etc.
	Human herpesvirus 1 and 2 disseminated in lungs, GI tract, etc.
	Progressive multifocal leukoencephalopathy (JC virus)
	Oral hairy leukoplakia (Epstein-Barr virus)
Others	Wasting disease; called <i>slim</i> in Africa (cause unknown)
	Dementia

<sup>&</sup>lt;sup>a</sup>Numbers in parentheses refer to chapters where relevant material is discussed.

- Immunosuppressive Retroviruses (Lentivirus) and Acquired Immunodeficiency Syndrome
  - Structure of HIV
    - Several infections and diseases define AIDS
    - Two antigenic glycoproteins found in the viral envelope:
      - gp120 (glycoprotein with molecular weight of 120 kilodaltons)
        - Primary attachment molecule of HIV
        - Antigenically variable during prolonged infection
      - gp41
        - Promotes fusion of the viral envelope to target cell
      - Viral characteristics impede immune clearance of HIV

#### TABLE **25.6**

### Characteristics of HIV That Challenge the Immune System

Characteristic	Effect(s)
Retrovirus with a genome that consists of two copies of +ssRNA	Reassortment of viral genes possible; reverse transcription produces much mutation and thus genetic variation; genome integrates into host's chromosome
Targets helper T cells especially but also macrophages, dendritic cells, and muscle cells and possibly liver, nerve, and epithelial cells	Permanently infects key cells of host's immune system
Antigenic variability	Numerous antigenic variations due to mutations helps virus evade host's immune response
Induces formation of syncytia (fusion of infected cells with neighboring cells)	Increases routes of infection; intracellular site helps virus evade immune detection

- Immunosuppressive Retroviruses (Lentivirus) and Acquired Immunodeficiency Syndrome
  - Origin of HIV
    - Likely arose from mutation of simian immunodeficiency virus (SIV)
    - May have emerged in the human population in the 1920s but the first human case was not documented until 1981
    - Whether the two HIV types are derived from the same or different SIV strains is unknown

Figure 25.19 The replication cycle of HIV.

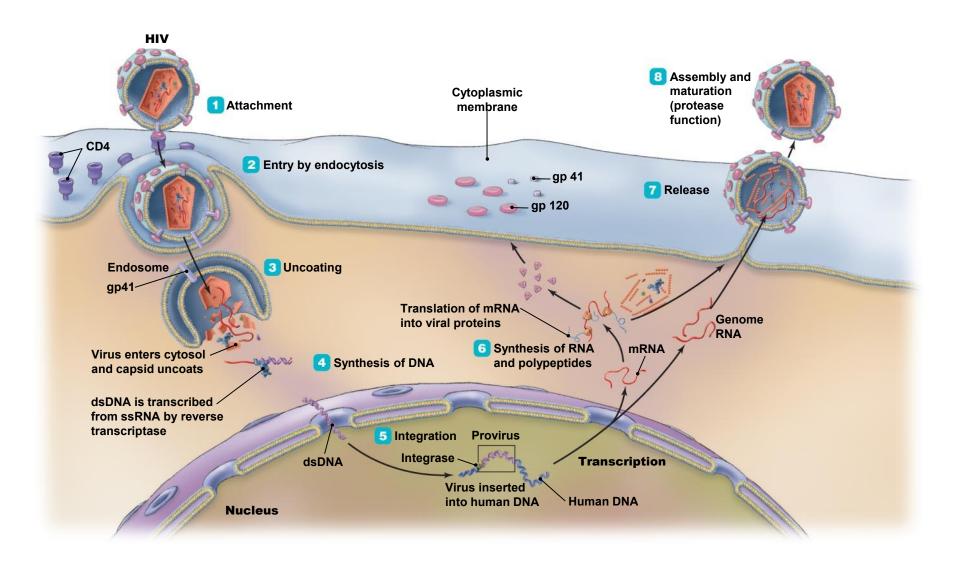
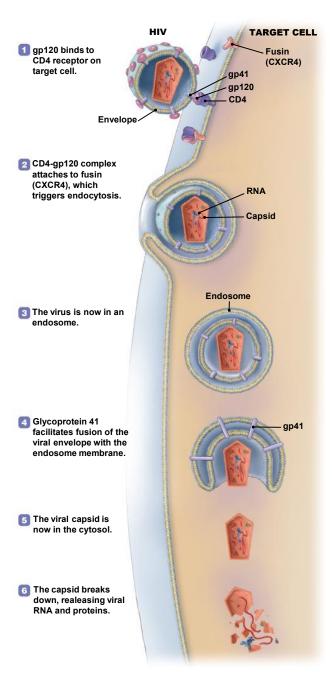


Figure 25.20 The process by which HIV attaches to and enters a host cell.



- Immunosuppressive Retroviruses (Lentivirus) and Acquired Immunodeficiency Syndrome
  - Details of Synthesis and Latency
    - Reverse transcriptase transcribes dsDNA from ssRNA
      - Antigenic variants of HIV result from errors introduced in the genome during transcription
    - dsDNA provirus enters the nucleus
      - Viral integrase inserts provirus into a human chromosome
      - Integrated DNA passed to progeny cells during replication
      - Provirus can remain dormant for years
    - Macrophages and monocytes are major reservoirs of HIV

- Immunosuppressive Retroviruses (Lentivirus) and Acquired Immunodeficiency Syndrome
  - Details of Release, Assembly, and Maturation
    - HIV exits cell at lipid rafts in the cytoplasmic membrane
      - Lipid raft components become the viral envelope
    - Capsomeres form immature capsid outside the cell
    - Viral protease releases proteins that produce a mature virus
      - Protease inhibitors used to treat HIV
  - Pathogenesis of AIDS
    - Only humans replicate HIV
    - HIV destroys the immune system

Figure 25.21 The course of AIDS follows the course of helper T cell destruction.

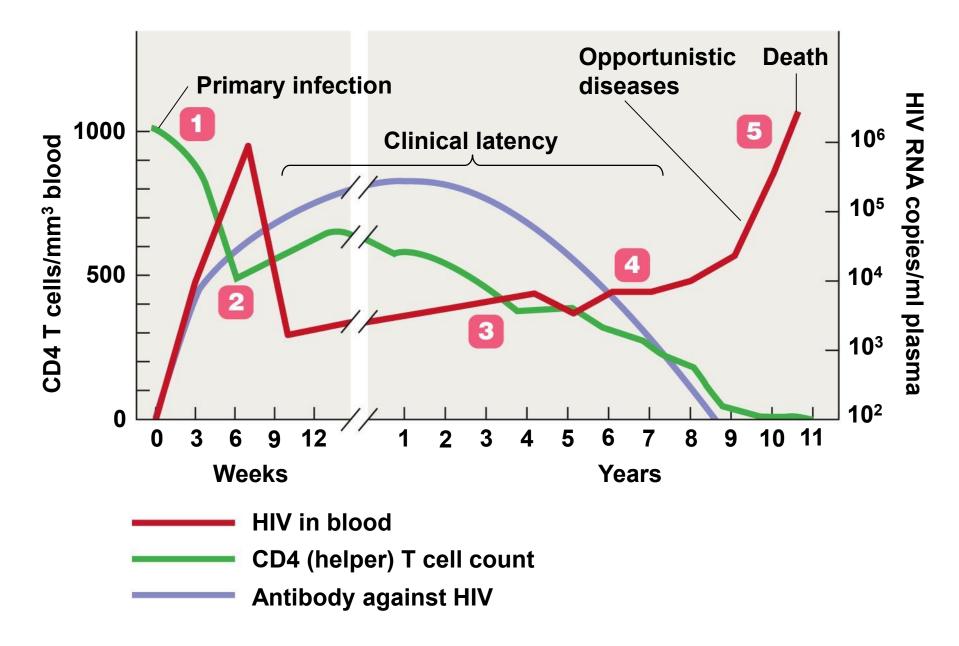


Figure 25.22 Some diseases associated with AIDS. A) Disseminated herpes B) Kaposi sarcoma

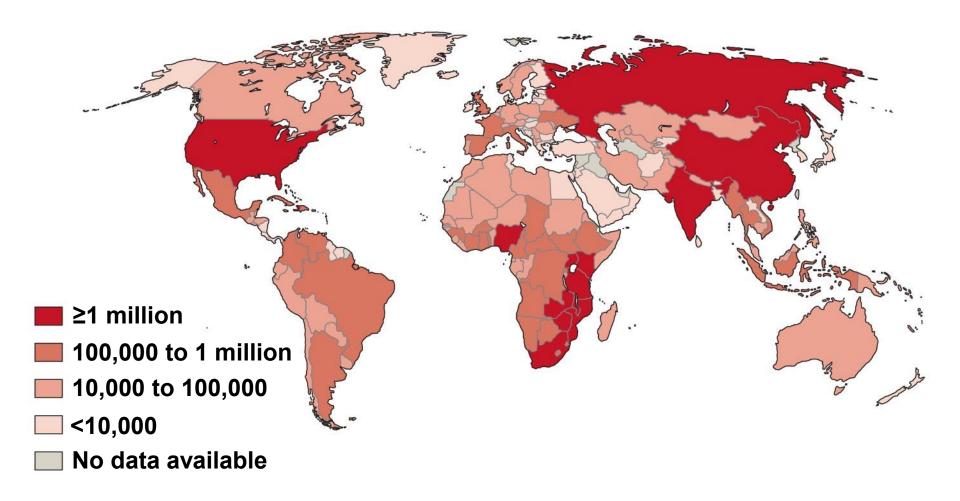


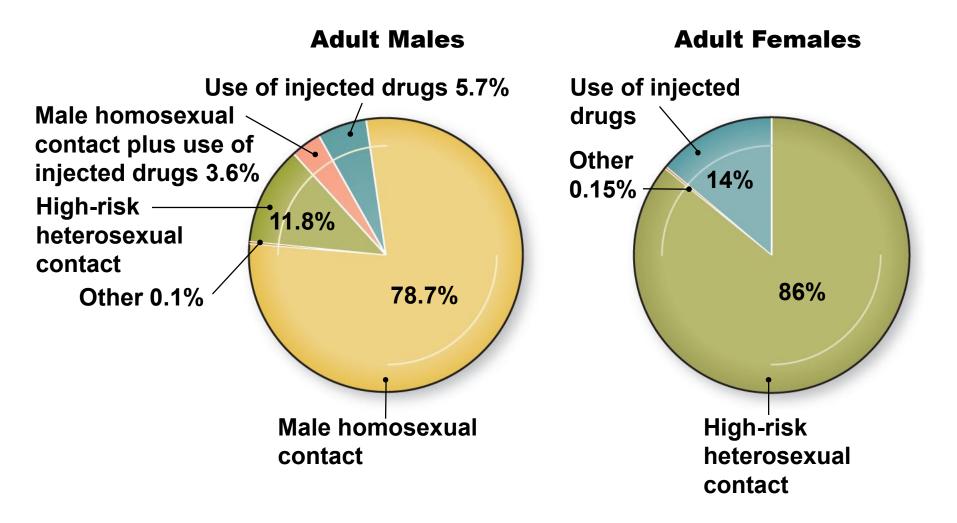
(a)



- Immunosuppressive Retroviruses (Lentivirus) and Acquired Immunodeficiency Syndrome
  - Epidemiology of AIDS
    - AIDS first recognized in young male homosexuals in the U.S.
    - AIDS is now found worldwide
    - HIV found in blood, semen, saliva, vaginal secretions, and breast milk can cause infections
      - Blood and semen more infective than other secretions
      - Infected fluid must be injected or contact a tear or lesion in the skin or mucous membranes

Figure 25.23 The global distribution of HIV/AIDS.





- Immunosuppressive Retroviruses (Lentivirus) and Acquired Immunodeficiency Syndrome
  - Epidemiology of AIDS
    - Some behaviors increase the risk of HIV infection
      - Anal intercourse
      - Sexual promiscuity sex with multiple partners
      - Intravenous drug use
      - Intercourse with someone in these categories
    - A few cases of casual HIV spread have been documented
      - Sharing razors, toothbrush, and from mouth to mouth kissing