

# Chapter 18

## Viral Infections of Humans

### Learning Objectives

Chapter 18 introduces a wide variety of important human viral diseases and serves as an introduction to Medical Virology. It is considered to be a key chapter in the education of students of the health care professions.

### Terms Introduced in This Chapter

After reading Chapter 18, you should be familiar with the following terms. These terms are defined in Chapter 18.

<b>Acute coryza</b>
<b>Arthropod-borne virus</b>
<b>Chikungunya virus</b>
<b>Dengue virus</b>
<b>Ebola virus</b>
<b>Epstein–Barr virus</b>
<b>Hantavirus pulmonary syndrome (HPS)</b>
<b>Herpes labialis</b>
<b>Herpes simplex viruses</b>
<b>Human polyoma viruses</b>
<b>Koplik spots</b>
<b>Middle East respiratory syndrome (MERS)</b>
<b>Papillomaviruses</b>
<b>Parotitis</b>
<b>Reye's syndrome</b>
<b>Rubella virus</b>
<b>Rubeola virus</b>
<b>Severe acute respiratory syndrome (SARS)</b>
<b>Shingles</b>
<b>Vaccinia virus</b>
<b>Varicella virus</b>
<b>Variola virus</b>
<b>Viral load</b>
<b>Viral rhinitis</b>
<b>Zika virus</b>



## Review of Key Points

- Viruses can only infect cells bearing appropriate surface receptors; thus, viruses are specific as to the type of cell(s) that they can infect.
- Viruses multiply within host cells, and it is during their escape from those cells—by either cell lysis or budding—that the host cells are destroyed. This cell destruction leads to most of the symptoms of the viral infection, which vary depending upon the location of the infection.
- Chickenpox and shingles are caused by varicella-zoster virus.
- German measles is caused by rubella virus, whereas measles is caused by rubeola virus.
- Smallpox is caused by variola viruses, whereas monkeypox is caused by monkeypox virus.
- All human warts are caused by papillomaviruses. Genital warts can become malignant.
- The common cold is also known as acute viral rhinitis and acute coryza.
- The hantaviruses that cause hantavirus pulmonary syndrome are transmitted by inhalation of aerosolized rodent feces, urine, and saliva.
- Severe acute respiratory syndrome (SARS) and Middle East Respiratory virus syndrome (MERS-CoV) are caused by two types of coronavirus.
- Many different viruses can cause diarrhea, including adenoviruses, noroviruses, and rotaviruses.
- Hepatitis, or inflammation of the liver, can have many causes, including alcohol, drugs, and viruses. When it is caused by a virus, it is called viral hepatitis.
- The hepatitis caused by hepatitis A virus is referred to as infectious hepatitis.
- Hepatitis B virus is the only DNA virus that causes hepatitis.
- Cold sores (fever blisters) and genital herpes are caused by herpes simplex viruses.
- Viremia refers to the presence of viruses in the bloodstream.
- Acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV).
- Infectious mononucleosis is caused by Epstein–Barr virus, which also causes several types of cancer.
- Viruses that cause cancer are called oncogenic viruses or oncoviruses.
- Mumps (infectious parotitis) is caused by mumps virus.
- Ebola virus and Marburg virus are two of the viruses that cause viral hemorrhagic diseases.
- Dengue fever and yellow fever are mosquito-borne diseases, transmitted primarily by mosquitoes belonging to the genus *Aedes*.
- Poliomyelitis (polio) is caused by polioviruses, and rabies is caused by rabies virus.
- Viral meningitis, which can be caused by many different viruses, is also known as aseptic meningitis, nonbacterial meningitis, and abacterial meningitis.

- Several different arthropod-borne viruses (arboviruses) cause viral encephalitis.
- Chikungunya virus and Zika virus are newly introduced viruses in South and North America and the Caribbean.

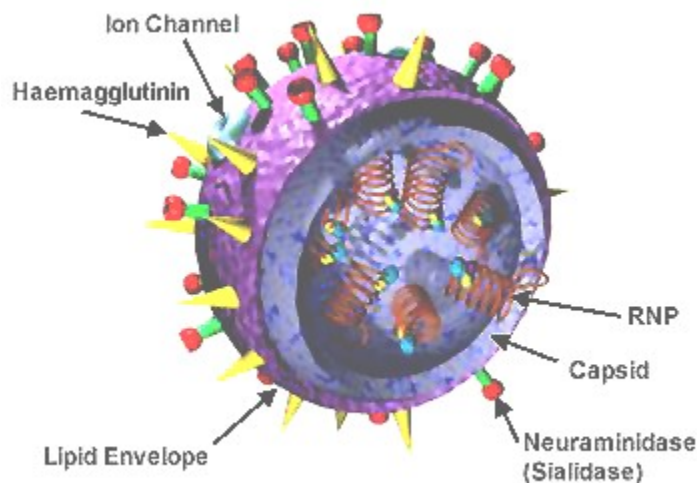


## A Closer Look

### • Influenza Viruses

Influenza viruses belong to a family of RNA viruses called Orthomyxovirus. There are three genera of influenza viruses called Influenza virus A, Influenza virus B, and Influenza virus C. Each genus contains only one species called Influenza A, Influenza B, and Influenza C. Influenza A infects humans, other mammals (including pigs and horses), and birds, and causes all flu epidemics. Influenza B primarily infects humans, but also infects seals. Influenza C infects humans and pigs. Although all three species infect humans, type A viruses are the most virulent human pathogens among the three and cause the most severe disease.

Influenza A viruses are classified based upon viral surface proteins called hemagglutinin (H or HA) and neuraminidase (N or NA). See the following diagram. Hemagglutinin is a lectin (a carbohydrate-binding protein) that mediates binding of the virion to target cells and entry of the viral genome into the target cell. Neuraminidase is an enzyme that is involved in the release of progeny virions from infected cells. As of April 2013, there were 16 known H subtypes and 9 known N subtypes. Examples of subtypes are H1N1 (“swine flu”) and H5N1 (“bird flu”).



Model of an Influenza Virus. (Courtesy of The National Institutes of Health and en.Wikipedia.)

The antigenic properties of [influenza viruses](#) are determined by both [hemagglutinin](#) and [neuraminidase](#). Influenza viruses frequently alter their surface proteins in order to evade a host immune response—a process known as antigenic variation. There are two types of antigenic variation: (1) [antigenic drift](#), which results from a change in few amino acids, and (2) [antigenic shift](#), which is the outcome of acquiring new structural proteins. Antigenic shift occurs when the genes for structural proteins are acquired from other animal hosts resulting in a sudden dramatic

change in viral genome. Antigenic shift is the primary reason why a new influenza vaccine is required every year.

### • Bird Flu

Avian influenza A/H5N1, or “bird flu,” is primarily a viral disease of birds. Wild birds carry the virus in their intestines, but they do not become ill. Domesticated birds, such as chickens, ducks, and turkeys, become infected by contact with contaminated saliva, or nasal, respiratory, or fecal material from infected birds. Fecal–oral transmission is the most common mode of spread between birds. Domesticated birds can become very sick and die, and contact with these birds can cause human illness. As of April 2013, highly pathogenic avian influenza (HPAI) A (H5N1) has caused more than 600 sporadic cases of human infection since November 2003, with high mortality. These cases have occurred in 15 countries in Asia, Africa, the Pacific, Europe, and the Near East. Most human cases of HPAI H5N1 infection are thought to have occurred as a result of direct or indirect contact with sick or dead infected poultry. The CDC has advised travelers to endemic areas to avoid poultry farms, contact with animals in live food markets, and any surfaces that appear to be contaminated with feces from poultry or other animals. Seasonal influenza vaccination will not prevent infection with avian influenza. New strains of bird flu virus continue to emerge.

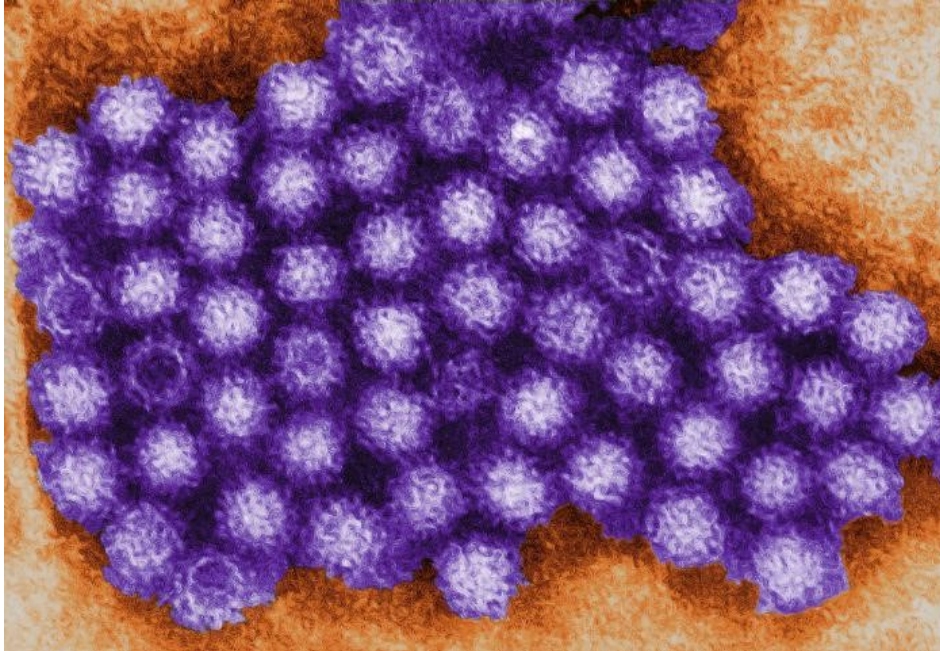
### • Swine Flu

Some influenza viruses primarily infect humans (human flu viruses), whereas others primarily infect pigs (swine flu viruses) or birds (avian flu viruses). Pigs are susceptible to all three of these types—human, swine, and avian flu viruses. When pigs are simultaneously infected with more than one type of flu viruses, the genetic information from these viruses can combine to produce a new (or novel) strain. Because of the genetic recombination that occurs in pigs, pigs are sometimes referred to as “mixing bowls.”

In June of 2009, the World Health Organization (WHO) declared a pandemic caused by a new strain of swine origin, called Novel H1N1 (swine flu). See the following transmission electron micrograph. This strain was the most common cause of human influenza in 2009. By the start of 2010, H1N1 had caused about 17,000 deaths, worldwide. It had been reported in all 50 states in the United States and in more than 70 other countries. H1N1 is spread primarily through coughing and sneezing, but may also be spread by touching contaminated objects and then touching one’s nose or mouth. Novel H1N1 (or 2009 H1N1, as it is also called) causes a wide range of flu-like symptoms, including fever, cough, sore throat, body aches, headache, chills, and fatigue. As of August 23, 2009, the WHO had recorded more than 209,438 laboratory-confirmed cases worldwide, with approximately 2,185 deaths. The laboratory-confirmed cases represent an underestimation of total cases, as many countries perform laboratory testing only for persons with severe illness. During August, 2009, Novel H1N1 was the predominant influenza virus in circulation worldwide. An H1N1 vaccine became available, and was being administered, in the fall of 2009. In August, 2010, the WHO declared the H1N1 influenza pandemic was over, but new strains of swine flu virus continue to emerge.

## • Norovirus

Norovirus is often in the news. It is the most common cause of acute gastroenteritis (inflamed stomach and intestines) in the United States, causing about 21 million illnesses per year. Norovirus is also the most common cause of foodborne disease outbreaks in the United States. Cases of norovirus infection often occur among people in confined spaces (e.g., cruise ships). Norovirus is very contagious. One acquires the virus from an infected person, contaminated food or water, or by touching contaminated surfaces (e.g., door handles and hand rails). Infection leads to stomach pain, nausea, diarrhea, and vomiting, and sometimes fever, headache, and body aches. The vomiting and diarrhea can lead to dehydration. Although most people get better within 1 to 3 days, norovirus illness can be serious, especially for young children and older adults. The best way to avoid becoming infected with norovirus is to practice proper hand washing and general cleanliness. There is no specific medicine to treat norovirus illness. Infected individuals should drink plenty of liquids (e.g., sports drinks and over-the-counter oral rehydration fluids).



Digitally Colorized Transmission Electron Micrograph of Norovirus Virions. (Courtesy of Charles D. Humphrey and the CDC.)

## • West Nile Virus

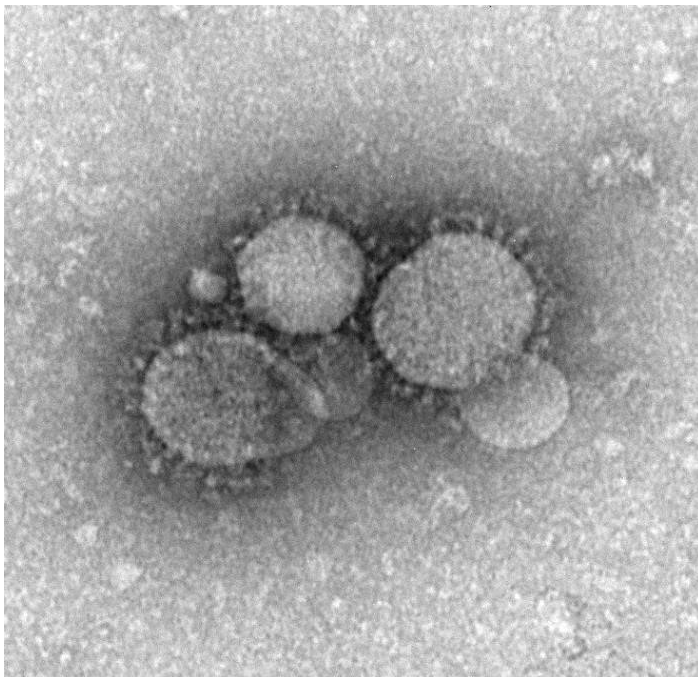
West Nile Virus (WNV) is a flavivirus that has been described in Africa, Europe, west and central Asia, the Middle East, and, most recently, North America. It is closely related to St. Louis encephalitis virus. WNV can infect humans, birds, mosquitoes, horses, and some other mammals. Humans become infected primarily by mosquitoes, but WNV transmission has also been reported via blood transfusion, organ transplantation, transplacental transfer, and breastfeeding. WNV can cause very severe central nervous system (CNS) infections, referred to as West Nile encephalitis, West Nile meningitis, and West Nile meningoencephalitis. West Nile fever is another manifestation of WNV disease, characterized by fever, headache, tiredness, aches, and sometimes rash. WNV was first identified in the West Nile region of Uganda in 1937. The first human and equine cases of West Nile disease in North America occurred in the United

States in 1999; a total of 62 cases were reported to the CDC that year. Since then, numerous cases have been reported every year. As of December 2016, only Alaska has been free from human cases of West Nile Virus although Hawaii and Puerto Rico have reported only one case each. Over 46,000 human cases of West Nile Virus infection have been reported to the CDC since the beginning of the outbreak. Of these cases, 51% were classified as neuroinvasive diseases and 49% were classified as non-neuroinvasive disease. As a precaution, people should use a mosquito repellent to avoid bites and should never handle dead birds with their bare hands.

- **Middle East Respiratory Syndrome Coronavirus**

Middle East Respiratory Syndrome (MERS) is a viral respiratory disease that was first identified in Saudi Arabia in 2012. It is caused by a coronavirus, originally called novel coronavirus 2012, but renamed MERS-coronavirus (MERS-CoV). Coronaviruses, named for the club-like projections that emanate from the viral membrane (see the following figure), have long been known to cause a variety of respiratory diseases, ranging from the common cold to severe SARS. MERS-CoV appears to be circulating widely throughout the Arabian Peninsula, where most MERS cases originated. Individuals who have been diagnosed elsewhere (including Europe and the United States) initially developed their infection in the Middle East. As of May 2018, more than 2200 laboratory-confirmed MERS cases have occurred, including 787 deaths. The disease has about a 35% mortality rate. Most of the people who died had an underlying medical condition.

Although most people infected with MERS-CoV developed severe respiratory illness with symptoms of fever, cough, shortness of breath, and pneumonia, some infected people had mild symptoms or no symptoms at all. The virus does not seem to pass easily from person to person unless there is close contact. Clusters of cases have occurred in health care facilities. Although the source of the virus is uncertain, very similar coronaviruses have been found in camels. MERS is yet another example of an emerging infectious disease. The WHO has labeled MERS a “threat to the entire world.”



Transmission Electron Micrograph of MERS-CoV. (Courtesy of Maureen Metcalfe, Azaibi Tamin, and the CDC.)

- **Zika Virus**

Zika virus was first recognized in 1947 and is named after the Zika Forest region in Uganda (Africa). The first human cases were detected in 1952 and since then outbreaks have occurred sporadically in tropical Africa, Southeast Asia, and the Pacific Islands. Because Zika virus infection is similar to other viral infections, and for the most part, the infections are self-limited, many infections likely occurred but did not reach the levels needed to alert public health authorities. It was not until 2015, when Zika virus arrived somewhere in South America that the virus attained notoriety. In July of 2015, Brazilian Health authorities noted an increase in cases of Guillain–Barré Syndrome (GBS), a neurologic autoimmune syndrome that is often self-limited. GBS has been noted to occur following infections with certain organisms although the exact trigger is not known. This was followed in October 2015 by a report from Brazil on an increase in babies born with rare congenital abnormalities such as microcephaly (small head). The virus quickly spread throughout South and Central America and the islands of the Caribbean prompting the World Health Organization to declare a public health emergency. In 2017, a few cases of locally acquired Zika virus infection have been noted in Florida and South Texas. However, most cases of Zika virus infection diagnosed in the United States have been in patients with a travel history to an endemic area. Much is now known about the virus, how it spreads, the symptoms associated with the infection, and the birth abnormalities that are caused by the virus. Vaccine development is a high priority to stem the spread of the virus, but as of 2017, no vaccine has been licensed for use.

**How is Zika virus transmitted?**

- Mosquito bites (*Aedes aegypti* and *Aedes albopictus*)
- From an infected pregnant woman to her fetus
- Through sex
- Through blood transfusion (rarely)

**What are the symptoms of Zika virus infection?**

- Many infected people will be asymptomatic, others may have:
- Fever
- Rash
- Headache
- Joint pain
- Red eyes
- Muscle pain

**What are the complications associated with Zika virus infection?**

- Guillain–Barré Syndrome
- Microcephaly in babies (see pictures below)
- Blindness in babies

**How is Zika virus infection diagnosed?**

- Molecular-based (PCR) tests of urine, blood

- Antibody studies

### How is Zika infection treated?

- Presently there are no antiviral agents that are used to treat Zika virus infection

### How do you avoid Zika virus infection?

- Protect yourself from mosquito bites
  - Wear long-sleeved shirts and long pants
  - Treat your clothing and gear with permethrin or buy pre-treated items
  - Use insect repellent (Environmental Protection Agency (EPA)-approved insect repellents)

More information on the status of Zika virus can be obtained from the Centers for Disease Control website ([www.cdc.gov](http://www.cdc.gov))



Baby with Typical Head Size



Baby with Microcephaly



Baby with Severe Microcephaly







## Increase Your Knowledge

Students seeking additional information about the major viral diseases of humans should consult one of the following books or visit one of the following Web sites:

1. Beers MH, et al., eds. *The Merck Manual of Medical Information*. 2nd ed. Whitehouse Station, NJ: Merck & Company; 2008. The Merck Manual is also available online at <http://www.merck.com>
2. The Centers for Disease Control and Prevention (CDC), <http://www.cdc.gov>. You can use the “A–Z Index” to find information about many different infectious diseases.
3. Learn about emerging viral diseases at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2496997/>
4. Read the latest information on the H1N1 swine flu virus at the CDC Web site <http://www.cdc.gov/H1N1flu/qa.htm>
5. Learn more about viral and other infectious diseases at “The Big Picture Book of Viruses,” [http://www.virology.net/Big\\_Virology/BVDiseaseList.html](http://www.virology.net/Big_Virology/BVDiseaseList.html)
6. Additional information about many of the viral diseases discussed in this chapter can be found at <https://www.cdc.gov>
7. The American Society for Microbiology offers various podcasts on their website. “This Week in Virology” covers interesting topics pertaining to viruses. It can be accessed at <https://www.asm.org/podcasts>



## Critical Thinking

1. A friend of yours has read that there is a connection between HIV infection and immunosuppression. However, she doesn't have a clue as to how the two events are connected. Explain to her the mechanism by which HIV-infected individuals become immunosuppressed, and why AIDS patients die of overwhelming infections caused by a variety of different types of pathogens.
2. Why do dogs get certain viral diseases (e.g., canine parvovirus infection) that humans do not get, and vice versa?



## Additional Chapter 18 Self-Assessment Exercises

(Note: Do not peek at the answers before you attempt to solve these self-assessment exercises.)

### Matching Questions

- |    |                        |       |    |                         |
|----|------------------------|-------|----|-------------------------|
| A. | Ebola virus            | _____ | 1. | Measles                 |
| B. | Herpes simplex virus   | _____ | 2. | Viral hemorrhagic fever |
| C. | Variola virus          | _____ | 3. | Chickenpox              |
| D. | Varicella-zoster virus | _____ | 4. | Smallpox                |
| E. | Rubeola virus          | _____ | 5. | Cold sores              |

- 
- |    |                       |       |    |                          |
|----|-----------------------|-------|----|--------------------------|
| A. | Rotavirus             | _____ | 1. | German measles           |
| B. | West Nile virus       | _____ | 2. | Infectious mononucleosis |
| C. | Rubella virus         | _____ | 3. | Diarrhea                 |
| D. | A type of coronavirus | _____ | 4. | Encephalitis             |
| E. | Epstein–Barr virus    | _____ | 5. | SARS                     |

### True/False Questions

- \_\_\_\_\_ 1. All human warts are caused by viruses belonging to the genus *Papillomavirus*.
- \_\_\_\_\_ 2. Chickenpox and shingles are caused by the same virus.
- \_\_\_\_\_ 3. Koplik spots are a sign of smallpox.
- \_\_\_\_\_ 4. Mumps is a rather mild disease, without any serious complications.
- \_\_\_\_\_ 5. West Nile virus is most commonly transmitted by tick bite.
- \_\_\_\_\_ 6. Epstein–Barr virus is associated with several types of cancer.
- \_\_\_\_\_ 7. Some cases of genital herpes are caused by the same virus that causes cold sores.
- \_\_\_\_\_ 8. Smallpox virus, monkeypox virus, and chickenpox virus are all considered to be pox viruses.
- \_\_\_\_\_ 9. Epstein–Barr virus is a type of herpes virus.
- \_\_\_\_\_ 10. Genital warts can become malignant.

## Answers to the Additional Chapter 18 Self-Assessment Exercises

### Matching Questions

1. E
2. A
3. D
4. C
5. B

1. C
2. E
3. A
4. B
5. D

### True/False Questions

1. True
2. True
3. False (Koplik spots are a sign of measles.)
4. False (Mumps can lead to very serious complications.)
5. False (West Nile virus is most commonly transmitted by mosquito bite.)
6. True
7. True
8. False (Smallpox virus and monkeypox virus are pox viruses; chickenpox virus is a type of herpes virus.)
9. True
10. True