

Chapter 3

Characterization of Viral Exposures in United States Occupational Environments

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Abstract Viruses are considered to be the most abundant biological particles and have the capability to infect all forms of life leading to a variety of diseases. American workers in specific occupational environments are threatened by viral exposures, highlighting the importance to recognize the type and risk of exposure, as well as the preventive measures that can be taken to reduce the risk of exposure. For example, healthcare workers can potentially be exposed to air and blood-borne pathogens, such as hepatitis and the human immunodeficiency virus. These types of exposures have led to the development of preventive equipment and regulations intended to reduce viral exposures in occupational settings. This chapter will discuss the characteristics of viruses and the occupationally relevant viruses of which people in varying occupations can potentially encounter. Regulatory guidelines and protective strategies will also be reviewed.

Keywords Virus · viral exposure · occupational exposure

3.1 Introduction

Viruses are abundant microbiological agents (Lawrence et al. 2009) that are capable of infecting all forms of life including but not limited to humans, plants, animals, fungi, bacteria, protozoa, and archaea. The United States workforce, especially health care workers, first responders, industrial workers, and biowaste workers are at risk of occupational exposure to a broad diversity of viruses including hepatitis, human immunodeficiency virus (HIV), Ebola virus, influenza and adenoviruses. Preventative guidelines including administrative and engineering controls, as well as use of personal protective equipment (PPE) have been published by various government agencies, and these avoidance strategies and exposure control plans have

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been modernized and recently revised (CDC 1988, 2016b, c, v; Kuhar et al. 2013; Garner 1996; Siegel et al. 2007; West and Cohen 1997).

Viruses are acellular and conflict within the scientific community exists as to whether or not viruses are living. Only able to replicate inside living cells, viruses rely on the host cell's reproductive machinery (Sze and Tan 2015). They are generally smaller than bacteria and therefore must be visualized using scanning or transmission electron microscopy. Viral particles range in diameter from 20 nm to approximately 300 nm; approximately one hundredth the size of a bacterium (Sekar and Kathiresan 2013). Stains are used to enhance the visualization of the viral particles, such as fluorescent antibodies that specifically tag antigens specific to the viral particles or uranyl acetate and phosphotungstic acid to enhance the contrast for electron microscopy (Smith and Melnick 1962). Negative staining can also enhance the contrast by staining the background instead of the viral proteins (Kiselev et al. 1990). Complete independent viral particles that have not yet infected, or are in the process of infecting, living cells are called "virions" and consist of two components. The genetic material of the virus, whether it is DNA or RNA, is contained within the protective proteinaceous coat termed the "capsid." Identical protein subunits termed "capsomeres" collectively construct the capsid, which can be enveloped with a layer of lipids formed from the host cell. This envelope, which aids in the infection of a host cell, consists of components from both the viral and the host cell's membranes.

3.1.1 Structure of Viral Capsids

Depending on the virus, virions differ in morphology, size and symmetry. There are four primary morphologies: helical, icosahedral, prolate and enveloped. The majority of viruses contain either a helical or icosahedral capsid (Lidmar et al. 2003; Vernizzi and Olvera de la Cruz 2007) and more commonly will be encountered in an occupational environment. Helical viruses are rigid or flexible rod-shaped (Prasad and Schmid 2012) formed by capsomeres specifically arranged in a helix around a central axis. The genetic material is located either inside the central cavity protected by the capsid or may be attached directly to the capsid. Fig. 3.1 illustrates the longitudinal view of an influenza virion, which is an example of a helical virus (Brown et al. 2010) that can be encountered in healthcare settings. Another example of a helical virus is the tobacco mosaic virus (TMV) discovered in 1898 (Harrison and Wilson 1999). Although humans cannot be infected by TMV, antibodies against TMV can be produced as shown in a study that measured anti-TMV antibodies in cigarette and smokeless tobacco users (Liu et al. 2013).

More commonly, viruses have an icosahedral shape where capsids are composed of 60 repeating identical subunits that give rise to 20 equilateral triangles arranged in a symmetrical manner (Prasad and Schmid 2012). This formation allows for the least amount of genetic material needed to code for the structural proteins that make up the capsid and for a closed capsid to protect the genetic material. An example of a virus with an icosahedral structure is an adenovirus, shown in Fig. 3.2. Other examples of icosahedral viruses include the rhinoviruses,

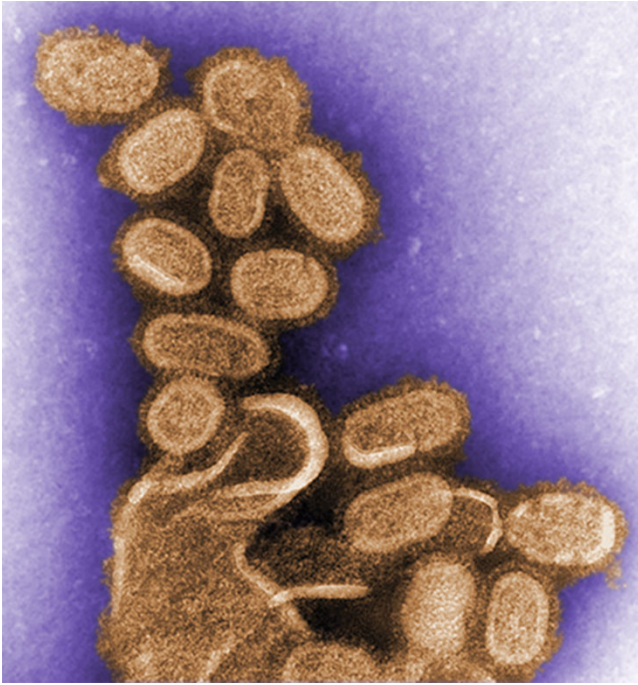


Fig. 3.1 Longitudinal transmission electron microscopic image of influenza virions. A negative-stained transmission electron microscopic (TEM) image illustrating 1918 influenza virions

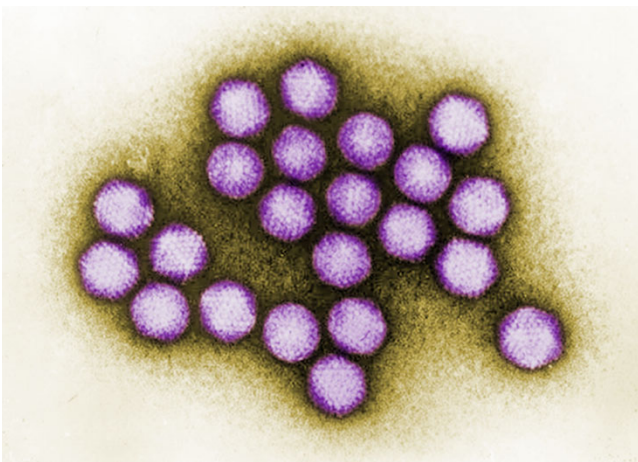


Fig. 3.2 Transmission electron microscopic image of a single adenovirus virion. A colorized transmission electron microscopic (TEM) image of adenovirus

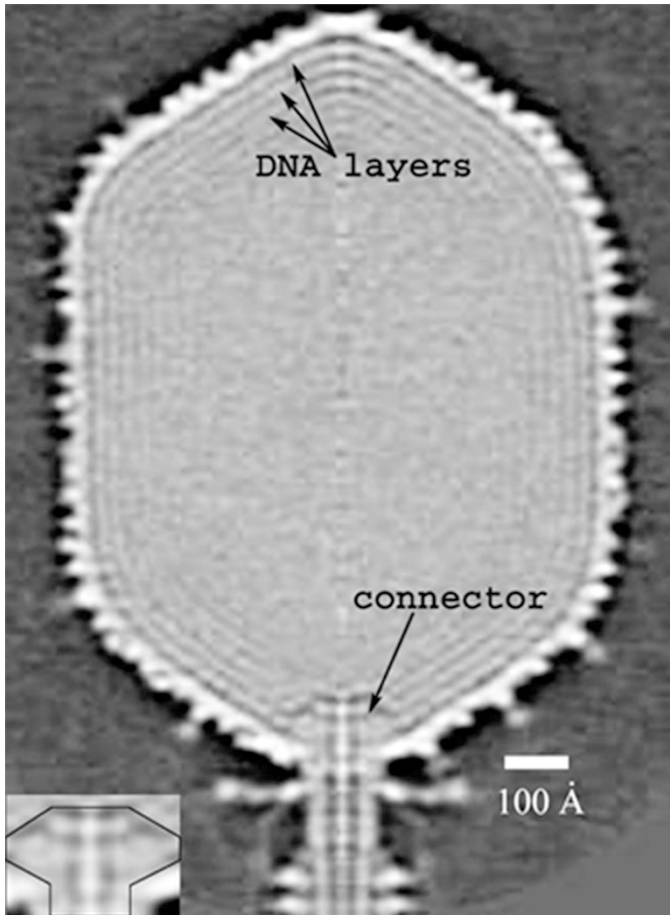


Fig. 3.3 Cryo-electron microscopic image of a T4 bacteriophage. A Cryo-electron microscopic image of the prolate head of bacteriophage T4 (Fokine et al. 2004)

which belong to the family of viruses that cause the common cold, as well as the virus responsible for poliomyelitis, poliovirus (Lodish et al. 2000). Unlike the frequency of acquiring the common cold in the healthcare or service sector, for example (Turner 2007), poliovirus has decreased 99% over the past 20 years, with only 74 cases reported worldwide in 2015 (WHO 2016d) and could be encountered by American emergency responders that visit third-world countries or by infected travelers visiting the United States. Variants to the icosahedral structure are known as “prolate” structures, such as those seen in bacteriophages (Fokine et al. 2004) as depicted in Fig. 3.3. Phage capsids have a variety of sizes and morphologies that are similar to human pathogenic viruses (Ackermann and Prangishvili 2012) and infect different bacterial species. These viruses are used as

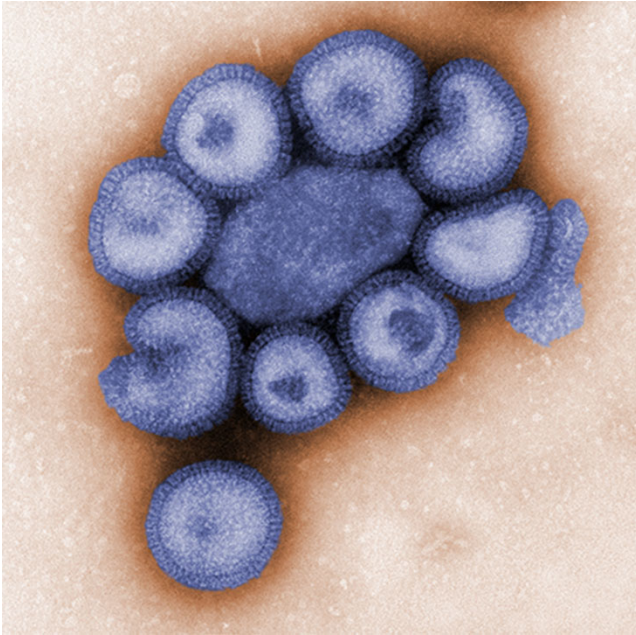


Fig. 3.4 Cross-sectional transmission electron microscopic image of influenza virions. A colored negative-stained transmission electron microscopic (TEM) image of influenza virus particles

bactericidal agents in “phage therapy” to treat bacterial infections in humans (Abedon et al. 2011).

Viruses such as influenza, herpes virus, and HIV are enveloped viruses that acquire a lipid envelope from the outer or inner membrane of a host cell (Prasad and Schmid 2012). This envelope contains proteins that are coded by both the viral and the host’s genome and are required for the infectivity of the virus. Viruses that contain an envelope are more stable under low relative humidity and low temperatures (Duchaine 2016). A cross-sectional image of influenza virions shown in Fig. 3.4 demonstrates the envelope of the virion.

3.2 Classification of Viruses

Viruses are classified according to the Baltimore classification system developed in 1971 (Baltimore 1971). This system classifies viruses based on the type of genome, such as single- or double-stranded and deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) (Prasad and Schmid 2012), as well as the method of replication (Baltimore 1971). The type of genetic material found in a

virus depends on the nature and function of the virus. The diversity between the different genomes illustrate the complexity of viruses. Viruses with the largest genomes, including the Mimivirus, Megavirus and Pandoravirus, infect amoebas, with the latter having the largest known genome of all the viruses (Philippe et al. 2013). Having one of the simplest genomes, the circoviruses are the smallest viruses and infect eukaryotic cells (Mankertz et al. 2004).

Viruses contain either RNA or DNA as their genetic material; however, some viruses contain both RNA and DNA at different times during the life cycle. An example of a virus that contains both RNA and DNA is HIV. The replication of the viral genome will also vary, depending on whether the genome is composed of RNA or DNA. For instance, viral RNA replicates primarily in the cell's cytoplasm, whereas DNA viruses replicate in the cell's nucleus.

The viral genome can be linear, circular or segmented in shape. Along with the different shapes of the viral genome, the structure of the nucleic acid will also differ. Viruses can contain single stranded DNA (ssDNA) in which the virus relies on the host's replication machinery, such as the host's DNA polymerase, in order for the ssDNA to be made into double stranded DNA (dsDNA). The dsDNA is then transcribed to messenger RNA (mRNA) after which translation can take place. Single stranded DNA viruses, such as parvovirus, have the ability to infect archaea, bacteria, plants and animals (Koonin et al. 2006). The difference between dsDNA viruses compared to ssDNA viruses is that the virus does not require DNA polymerase to create a complimentary DNA strand to be then transcribed into mRNA because the DNA is already double stranded. Double stranded DNA viruses, such as adenoviruses and herpes viruses, have the ability to infect archaea, bacteria, unicellular eukaryotes and animals (Koonin et al. 2006). Hepatitis A and C, as well as enteroviruses, contain positive-sense ssRNA genomes. A positive-sense RNA genome allows for the genome to be immediately translated in the host cell's cytoplasm. Negative-sense ssRNA viruses, such as Ebola, influenza, measles and mumps, requires an RNA polymerase to produce a positive-sense RNA strand in order for translation to occur. Viruses with dsRNA, such as rotavirus, have the ability to infect bacteria, unicellular eukaryotes, fungi, plants and animals (Koonin et al. 2006).

Lastly, reverse transcribing viruses possess either an ssRNA or a dsDNA genome. HIV contains an ssRNA genome where a reverse transcriptase copies the ssRNA into a complementary DNA strand, and then a DNA polymerase creates a sense DNA strand, making dsDNA. This dsDNA moves into the nucleus of the host cell and integrates into the host's genome. During replication of the host's genome, the dsDNA is transcribed to mRNA from which the viral proteins are then translated. Reverse transcribing viruses that contain dsDNA genome, such as Hepatitis B, use proteins in the host cell to move to the nucleus where the dsDNA serves as a template for mRNA following transcription. The mRNA can then move back into the cytoplasm where it will be reverse transcribed to DNA, allowing for the process to repeat multiple times.

The viral genome can be mutated through different mechanisms to result in new viral strains. First, DNA or RNA bases can mutate to other bases; however,

the resultant proteins may be unchanged. Although the proteins may not be initially altered, the accumulation of point mutations may eventually change the viral proteomic profile over time. RNA viruses are more prone to mutations compared to DNA viruses (Domingo et al. 1996). Recombination of the viral genome can also alter the resultant proteins. This type of mutation can render the virus resistant to vaccinations and antiviral drugs, which is detrimental to the prevention against disease development that follow exposures encountered in occupational environments.

3.3 Infection and Effects on Host Cell

Infection generally involves contact between a virus and the host's epithelial surface (Janeway et al. 2001). Viral capsid proteins attach to receptors on the host's outer surface. Glycoproteins or glycolipids serve as the attachment receptors, such as heparin sulfate proteoglycans (de Haan et al. 2005; Vlasak et al. 2005). The attachment process of HIV requires CD4 along with CCR5 or CXCR4 (Grove and Marsh 2011), while rhinoviruses attach to the intercellular adhesion molecule 1 (Norkin 1995). Endocytosis or membrane fusion enables the virus to penetrate the host cell; however, this process may differ depending on the host cell. Penetration into plant or bacterial cell walls is typically more challenging compared to animal cells due to the thickness and complexity of the outer surface composition. Once the virus has entered into the host cell, the capsid is uncoated to release the viral genome. Replication of the viral genome takes place inside the host cell using the host's replication machinery. After the viral components are produced, developed and assembled, they are released from the host cell. This process either occurs by lysis of the host cell when releasing non-enveloped virus or by budding and scission to release enveloped viral particles (Sze and Tan 2015).

Once the virus has migrated out of the host cell, the cytopathic effects caused by the viral infection can result in host cell death through lysis or apoptosis (Roulston et al. 1999). In contrast, there is no visible change to the host cell for some viruses, such as herpes virus (Sissons et al. 2002). These viruses lie dormant inside of the host cell with viral genetic material floating in the nucleus or cytoplasm and can cause chronic infection over long periods of time.

3.3.1 *Host Diversity*

Viruses can infect a wide diversity of hosts. The infections caused by most viruses are species-specific. On one hand, some viruses can only infect a limited number of hosts and are considered to have a narrow range of hosts. An example of a virus with a narrow range of hosts is the smallpox virus, which only infects humans. On the other hand, other viruses can infect multiple species and are considered to

have a broad range of hosts. An example of a virus with a broad range is the rabies virus, which can infect animals and be transmitted to humans. Emerging viral diseases affecting humans, wildlife and agricultural have resulted from viruses infecting new novel hosts, a process known as a “host shift” (Longdon et al. 2014) or a “host switch” (Parrish et al. 2008). These shifts have caused pandemics in the human population, such as HIV from chimpanzees (Sharp and Hahn 2010), severe acute respiratory syndrome from bats (Li et al. 2005), and influenza virus from aquatic birds (Webby and Webster 2001). Although the reservoirs of the influenza virus are in aquatic birds, swine also serve as another zoonotic source as evidenced by the 2009 H1N1 outbreak (Novel Swine-Origin Influenza et al. 2009; Fraser et al. 2009; Gatherer 2009). Rodents are also carriers of viruses, like the hantavirus (CDC 2016e), whereas bats and wild carnivores are zoonotic sources of rabies (CDC 2011; England 2013). Recently, Influenza A (H7N2) virus was detected in an animal shelter worker who was exposed to infected cats (CDC 2016f).

3.4 Viral Transmission Routes

Depending on the origin of the virus, transmission occurs through a variety of mechanisms. Direct transmission occurs through direct physical contact with an infected person’s bodily fluids or through indirect transmission by contact with contaminated surfaces or objects (fomites). Viruses, such as HIV and hepatitis, are transmitted by direct contact with bodily fluids, including blood, mucous secretions, urine or feces, from an infected person or through contact with contaminated drug delivery equipment, like needles. Potential exposure to blood-borne diseases can be encountered in occupations involving the use of needles as tools, such as tattooists and piercers, emergency first responders, maintenance and waste workers, or in healthcare environments. Also in a healthcare environment, patients or staff can be exposed to viruses through the use of surgical or medical instruments like catheters or sharp instruments. A sharps injury occurs when a sharp object penetrates the skin, such as a needle, scalpel, or bone fragment. Of all reported sharps injuries, nurses and healthcare assistants accounted for 42%, whereas doctors accounted for 41% (Riddell et al. 2015). Industrial workers are potentially exposed to blood-borne diseases through sharps or a traumatic injury.

To reduce the risk of viral exposures, the Centers for Disease Control and Prevention (CDC) has set guidelines to prevent transmission of infectious agents in healthcare settings (Garner 1996; Siegel et al. 2007). The Universal Precautions guidelines were developed in 1987 as an addition to the 1983 “Guideline for Isolation Precautions in Hospitals” to include the recommendation that blood and body fluid precautions be used for all patients regardless of their blood-borne infection status (CDC 1988). These precautions were set in place to reduce the risk of exposure to blood-borne diseases, specifically for healthcare workers. The Standard Precautions guidelines were proposed in 1996, consisting of precautions

that are standard for all patients and includes blood-borne, airborne, and other important pathogens (West and Cohen 1997). The guidelines discuss hand and respiratory hygiene, the use of PPE, such as gloves, gowns, eyewear and face-masks, prevention of sharps injuries, and sanitation practices. By following the recommendations of the guidelines, the risk of viral exposures can be reduced.

Other viruses infect the host via a vector, such as insects like the mosquito. This type of vector-borne transmission can spread through a bite or through contact with the host. This is the route used by the virus involved in the recent disease outbreak caused by the Zika virus. The swine influenza virus is an example of a zoonotic virus that is transmitted from animals to humans. Workers in a meat processing facility and a pig farm have been found to be at greater risk to swine influenza virus compared to people not working in those occupations (Myers et al. 2006; Gray et al. 2007). Hantavirus is another example of a zoonotic virus. As previously mentioned, hantaviruses are carried by rodents and can lead to a rare, but sometimes lethal disease in humans called hantavirus pulmonary syndrome. Contracted through exposure to rodent urine, droppings or saliva, workers in construction, utility, pest control and house cleaning services are at risk of hantavirus pulmonary syndrome exposure (CDC 2016e).

Airborne transmission occurs when a virus is spread by traveling on dust particles or on small respiratory droplets. Viruses can travel on different sizes of airborne particles formed when a person coughs, sneezes, talks or exhales. The larger respiratory droplets that form travel short distances (Mubareka et al. 2009), compared to droplet nuclei that are small and responsible for transmission over long range distances. An example of an airborne virus is the influenza virus, which can be transmitted by direct contact with infected people in a healthcare environment for example or by exposure to fomites that have been contaminated when the droplet nuclei settle out of the air and dry on a surface, a situation that may be encountered in healthcare or academic occupational environments. The viability of the viral particle on the fomites depends on the virus, the environmental conditions surrounding the fomite and whether or not the droplet nuclei is moist or dry. Viral exposure can occur through inhalation of aerosolized droplet nuclei into the respiratory tract of a person, also potentially encountered in healthcare or academic occupational environments. One study determined that professionals in healthcare settings could be exposed to infectious doses of influenza virus within 1.8 meters of an infected patient (Bischoff et al. 2013). Another study detected low concentrations of influenza viral RNA in aerosols located in patients' rooms of which healthcare workers frequently encountered (Leung et al. 2016). The National Institute for Occupational Safety and Health (NIOSH) has developed a bioaerosol sampler that allows for the collection of size-fractionated aerosols (Cao et al. 2011; Lindsley et al. 2010b), which enabled further research into influenza transmission. Subsequent studies utilizing the influenza virus as a model illustrated that infectious viral particles are collected in the smallest particle (airborne) fraction, as well as in the larger (droplet) fraction (Noti et al. 2012) and that more viable influenza particles are detected after coughing than exhaling (Lindsley et al. 2016).

3.5 Viral Exposures in Occupational Settings

Viral exposures are encountered in a wide variety of occupations. An earlier review described methods for sampling airborne viruses in various environments such as hospitals, office buildings, restaurants and schools (Verreault et al. 2008). Most of the studies reviewed occurred before 2008 and do not include recent viral outbreaks. Current examination of viral exposures lead to the identification of viruses that are frequently encountered in occupational environments or have been a recent focus in the United States. Although viral exposures can occur in many different occupational environments, the healthcare sector has one of the greatest risk of exposure to a large variety of infectious viruses.

Environments within the healthcare sector include, but are not limited to, hospitals, medical offices, assisted-living facilities, and dental offices. Viruses in these occupational environments can be transmitted from patient to patient, healthcare worker to patient or patient to healthcare worker as hypothesized in a review on Hepatitis C transmission in a healthcare environment (Pozzetto et al. 2014). One study reported the detection of human cytomegalovirus in the air of hospital rooms, a mode of transmission not previously considered, which demonstrates a potential route of exposure to healthcare workers and patients (McCluskey et al. 1996). Respiratory syncytial virus has also been detected in the air of hospital rooms housing infected patients in which the viral RNA was detected up to 7 m away from the patients for up to 7 days (Aintablian et al. 1998). Severe acute respiratory syndrome (SARS) coronavirus was identified on fomites in a hospital room belonging to a patient with SARS, as well as at a nurses' station. These data suggest generation of aerosol particles containing SARS coronavirus (Booth et al. 2005). Collectively, these studies further highlight the potential exposure for both patients and healthcare workers in a healthcare setting.

Laboratory-associated occupations also serve as potential sources of adverse viral exposures. Researchers that handled clinical samples of the Ebola virus became infected at a government hospital in Sierra Leone (Silver 2015). Individuals that work in biotechnological laboratories, as well as healthcare environments, that use lentiviral vectors for gene delivery systems are also at risk of viral exposure (Howard et al. 2017). Viral exposures may also occur in manufacturing or industrial occupational environments. Human adenovirus was detected in air samples collected from a landfill, a waste recycling plant, an incineration plant, and waste collection vehicles, all serving as environments with a potential risk for viral exposure (Carducci et al. 2013). Modeling systems for airborne viruses used in industry could possibility lead to viral exposures for workers in these facilities. For example, bacteriophages are not only used by the FDA to test the effectiveness of filtration devices (Duchaine 2016), but are also used as surrogates for enteric viruses in wastewater treatment studies (Grabow 2001). Rhinoviruses have been detected in office buildings with low outdoor air supply, suggesting that occupants are at an increased risk of viral exposure from infected colleagues

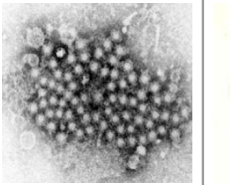


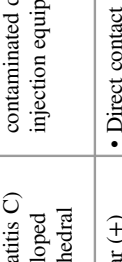
(Myatt et al. 2004). Other occupational environments where people are susceptible to viral exposures, such as influenza and norovirus, are in the service sector, including schools and daycare settings, as well as agricultural environments (Division of Viral Diseases et al. 2011; CDC 2016h). Areas of construction serve as environments where blood-borne pathogens can be encountered through traumatic or sharp injuries. The following section and Table 3.1 details the viruses that have more recently been characterized in occupational environments.

3.5.1 *Viral Hepatitis*

In 2014, Hepatitis B affected approximately 850,000 people in the United States (Roberts et al. 2016; Wasley et al. 2010). Hepatitis B and Hepatitis C are transmitted through bodily fluids or by contact with contaminated drug-injection equipment. Sewage workers at waste plants, as well as healthcare workers and patients in healthcare environments can be exposed to both viruses. Hepatitis B (CDC 2016s) is normally an acute infection, but for some, the disease can become chronic. The risk of the infection becoming chronic is related to the age of the infected person. For all viral hepatitis cases, routine blood tests, serological tests, reverse transcription polymerase chain reaction (RT-PCR) to detect viral RNA, and genotyping tests are used to diagnose viral hepatitis. This virus can be prevented by following the recommendations of the Standard Precautions guidelines, including the use of PPE, proper handling of sharps and patient care equipment, avoiding close physical contact and vaccination. Similar to Hepatitis B, Hepatitis C is transmitted by contact with contaminated drug-injection equipment and is also an acute infection, which can become chronic in some. In 2014, 30,500 cases of acute and an estimated 2.7–3.9 million cases of chronic Hepatitis C occurred in the United States (CDC 2016s). Hepatitis C exposure in healthcare environments is less common, but sharps injuries can still occur. Unlike Hepatitis B, a vaccine is not available for Hepatitis C (Riddell et al. 2015), so it is important to avoid sharps injuries or sharing drug-injection equipment with those people infected with Hepatitis C.


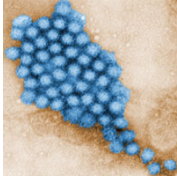
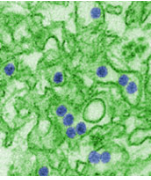
Even more uncommon than Hepatitis C exposure in the healthcare environment are exposures to Hepatitis A. Hepatitis A is transmitted by the fecal-oral route or consumption of contaminated food or water. It does not result in a chronic disease and there is no available vaccine (CDC 2016s). Another rare exposure risk in the United States is Hepatitis D. It is transmitted through contact with infectious blood; however, it only occurs in people who are infected with Hepatitis B. Hepatitis D virus is incomplete and therefore, needs Hepatitis B in order to replicate. There is no vaccination for Hepatitis D, so the best prevention strategy is to be vaccinated against Hepatitis B (CDC 2016s). Hepatitis E is also rare in the United States; however, one study reported a significant association between occupational exposure to Hepatitis E and swine (De Schryver et al. 2015). Hepatitis E is transmitted by ingestion of fecal matter through contaminated food or water.

Table 3.1 Prevalent viral exposures encountered in United States occupational environments

Disease	Genome	Transmission	Occupation	Treatment	Virus	Reference
Hepatitis	<ul style="list-style-type: none"> • Circular dsDNA (Hepatitis B) • (+)ssRNA (Hepatitis C) • Enveloped icosahedral 	<ul style="list-style-type: none"> • Direct contact with bodily fluids from infected person(s) • Contact with contaminated drug-injection equipment 	<ul style="list-style-type: none"> • Healthcare workers 	<ul style="list-style-type: none"> • Vaccine for Hepatitis B, but no vaccine for Hepatitis C 		Photo courtesy of CDC/E.H. Cook, Jr.; CDC Public Health Image Library (PHIL) ID#: 8153
HIV	<ul style="list-style-type: none"> • Linear (+) ssRNA-RT • Viral envelope 	<ul style="list-style-type: none"> • Direct contact with bodily fluids from infected person(s) • Contact with contaminated drug-injection equipment 	<ul style="list-style-type: none"> • Healthcare workers • Research laboratories 	<ul style="list-style-type: none"> • Antiretroviral treatments, but no cure is available 		Photo courtesy of National Institute of Allergy and Infectious Diseases (NIAID); PHIL ID#: 18142
Adenovirus	<ul style="list-style-type: none"> • Linear dsRNA • Non-enveloped icosahedral 	<ul style="list-style-type: none"> • Direct contact with bodily fluids from infected person(s) • Contact with contaminated surfaces 	<ul style="list-style-type: none"> • Healthcare workers • Military 	<ul style="list-style-type: none"> • Available vaccine only approved for military use 		Photo courtesy of CDC/Dr. G. William Gary, Jr.; PHIL ID#: 10010
Influenza	<ul style="list-style-type: none"> • Segmented • (-)ssRNA • (Influenza A) • Linear (-) ssRNA (Influenza B) • Viral envelope 	<ul style="list-style-type: none"> • Airborne and spreads by coughing and sneezing • Contact with contaminated areas and surfaces 	<ul style="list-style-type: none"> • Healthcare workers • General public • Poultry and meat processing facilities 	<ul style="list-style-type: none"> • Flu vaccine 		Photo courtesy of CDC/Cynthia Goldsmith; CDC PHIL ID#: 11745

(continued)

Table 3.1 (continued)

Disease	Genome	Transmission	Occupation	Treatment	Virus	Reference
Ebola	<ul style="list-style-type: none"> • Linear (-) ssRNA • Viral envelope 	<ul style="list-style-type: none"> • Direct contact with bodily fluids from infected person(s) 	<ul style="list-style-type: none"> • Healthcare workers • Response teams • Research laboratories 	<ul style="list-style-type: none"> • No vaccine, but two potential candidates 		Photo courtesy of CDC/Dr. F. A. Murphy; CDC PHIL ID#: 10815
Norovirus	<ul style="list-style-type: none"> • Linear (+) ssRNA • Non-enveloped icosahedral 	<ul style="list-style-type: none"> • Contaminated food and water • Direct and indirect contact with infected person(s) or contaminated surfaces • Airborne transmission 	<ul style="list-style-type: none"> • Healthcare workers • Food handling services • Cruise ships • Military 	<ul style="list-style-type: none"> • No vaccine 		Photo courtesy of CDC/Dr. Charles D. Humphrey; PHIL ID#: 10706
Zika	<ul style="list-style-type: none"> • Linear (+) ssRNA • Enveloped icosahedral 	<ul style="list-style-type: none"> • Transmitted by mosquitos 	<ul style="list-style-type: none"> • Occupations requiring travel to infected areas • Research laboratories 	<ul style="list-style-type: none"> • No vaccine 		Photo courtesy of CDC/Cynthia Goldsmith; CDC PHIL ID#: 20541

Despite Hepatitis E not resulting in a chronic infection, there is a vaccine available (CDC 2016s). Although these latter types of viral hepatitis are uncommon, each are important to review as lapses in standard precautions and a break in safety protocols can lead to an increased risk of exposure.

To reduce the risk of exposure to viral hepatitis and other blood-borne pathogens, the CDC has set guidelines to prevent transmission of infectious agents in healthcare settings that include standard precautions, which protect the healthcare worker and patient (Garner 1996) as previously mentioned. Guidelines reported in 2007 regarding the prevention of infectious agent transmission in healthcare settings, discuss transmission-based precautions dependent upon the specific disease, as well as type and duration of precautions recommended for selected infections (Siegel et al. 2007). If the virus can be transmitted through bodily fluids, healthcare workers have to be able to assess the risk of exposure by considering the injury type, the bodily fluid involved, the risk for transmission of blood-borne viruses and then test the source patient to determine if blood-borne viruses are present. Although these precautions were recommended to reduce the risk of exposure to blood-borne diseases for healthcare workers, these practices can be applied to prevent exposure in any occupational environment that poses a risk. Exposure Control Plans also need to be executed to ensure the workers have accurate information regarding potential exposures. CDC has also implemented engineering controls and personal protective equipment resources to help reduce exposure to blood-borne infectious diseases, such as viral hepatitis and HIV (CDC 2016b).

3.5.2 *Human Immunodeficiency Virus*

As of 2010, there were approximately 35,000–38,000 new cases of HIV and 16,000–18,000 deaths per year in the United States (CDC 2016g; Mohebbati et al. 2010). In 2015, the CDC reported that approximately 1.2 million people in the United States were living with HIV infection (CDC 2016f). Even though rates are falling (Wyżgowski et al. 2016; CDC 2001), new cases of HIV are reported every year. HIV is transmitted by exposure to infected bodily fluids and is diagnosed through serological testing, as well as detection of the virus through RT-PCR assays. The CDC recommends that all individuals in a healthcare setting aged 13–64 years be tested for HIV, regardless of the exposure risk (Panneer et al. 2014). One review reported 57 documented cases of HIV infections transmitted in an United States healthcare environment after having a negative serology at the time of assumed exposure (Mohebbati et al. 2010). HIV is a lentivirus, a subgroup of retroviruses, characterized by long incubation periods. Lentiviruses can integrate large amounts of viral RNA into the DNA of host cells and as a result, lentiviral vectors have become an important research tool as a delivery system for gene therapy strategies. As previously mentioned, workers in biotechnological laboratories or healthcare environments that use these lentiviral vectors are also at risk of viral exposure (Howard et al. 2017). Individuals who work in laboratories that conduct

research on HIV are also susceptible to exposure; however, with the protective measures taken to limit exposure to contaminated blood and other bodily fluids, exposure to HIV has decreased over time, specifically in the United States. From 2005 to 2014, HIV infections in the United States have decreased approximately 19% (CDC 2016f). To reduce the risk of exposure, the CDC recommends following the 2007 guidelines for isolation precautions preventing transmission of infectious agents, such as HIV (Siegel et al. 2007). Included in these recommendations are proper use of PPE, such as gloves, safety glasses, and gowns to reduce the risk of exposure. In 2013, an update of the United States Public Health Service guidelines for the management of occupational exposures to HIV was released and included recommendations for the management of healthcare workers who had been exposed to HIV (Kuhar et al. 2013). Administration of antiretroviral drugs to reduce the replication of the virus is also effective following exposure to HIV.

3.5.3 *Adenoviruses*

Adenoviruses are the most common illness of the respiratory system in healthcare environments and in the military, and can cause a wide range of symptoms (CDC 2015), including common cold-like symptoms, pharyngitis, bronchitis, pneumonia, diarrhea, conjunctivitis or gastroenteritis. Adenoviruses are transmitted by direct personal contact with an infected person or by contact with contaminated surfaces. One study suggested that the crowding of personnel at military stations lead to adenovirus outbreaks, highlighting the importance of vaccinations (Gray et al. 2000). Another study reported the exposure of healthcare workers to Adenovirus Serotype 14 from infected military trainees (Centers for Disease and Prevention 2007). In 2008, adenoviral transmission was documented between healthcare workers and two patients identified as having Adenovirus Serotype 14 (Louie et al. 2008). Good hygiene and sanitation practices, as well as avoiding close contact with infected people or contaminated areas, are prevention strategies to minimize the spread of the virus. Currently, the only available vaccine is for military use, which was approved in 2011 by the Food and Drug Administration (CDC 2015).

3.5.4 *Influenza*

Influenza virus is a respiratory illness that can affect anyone potentially leading to hospitalization or even death. There are three different types of influenza virus. Influenza type A and B are responsible for the annual influenza outbreaks. Type C also causes the flu, but the symptoms are not as profound as types A and B. Influenza A viruses are found among animals and humans, while influenza B viruses are mainly found in humans. The virus can be transmitted by contact with surfaces or areas where an infected person has touched or sneezed. The

virus has also recently been shown to become airborne via coughing (Lindsley et al. 2016). Throughout the world, there are approximately 3–5 million severe influenza cases reported annually with 250,000–500,000 resulting deaths (WHO 2016c). Since 2010, the CDC estimates that 140,000–710,000 influenza cases in the United States have resulted in hospitalizations, resulting in 12,000–56,000 deaths (CDC 2016k).

The influenza virus is diagnosed via several methods including lateral flow and membrane-based immunoassays, as well as RT-PCR assays from nasal swabs. Sensitive real time semi-quantitative PCR assays, such as the viral replication assay developed at NIOSH (Blachere et al. 2011), can detect viable viral RNA influenza quickly and accurately compared to traditional methods (Blachere et al. 2009; Lindsley et al. 2010a; Lindsley et al. 2010b) that cannot distinguish between infectious and non-infectious virus. Prevention of the influenza virus includes proper sanitation practices, such as hand washing and decontamination of infected areas. Guidelines developed by the CDC, such as wearing PPE, will reduce the risk of exposure to the influenza virus (Siegel et al. 2007). An annual flu vaccine is available and is recommended for people older than 6 months (CDC 2016h). The vaccination is composed of inactivated or recombinant strains of influenza virus that research conducted at the collaborating centers of the World Health Organization (WHO) has deemed most probable to be encountered in the upcoming season (CDC 2016h). Trivalent vaccines are most commonly used and the current configuration immunizes workers against two Influenza A (H1N1 and H3N1) viruses and one Influenza B virus. There is also a quadrivalent vaccine that protects against the same three viral strains as the trivalent vaccine, but also includes a second Influenza B virus (CDC 2016h). The National 2009 H1N1 Flu Survey conducted by the CDC from October 2009 through June 2010 found that of 28,710 employed adults, 10.5% of workers employed in real estate and the rental and leasing industry, 10.2% workers in accommodation and food services industry, 11.0% workers in food preparation services, and 8.3% of workers in community and social services reported having an influenza-like illness. It is important to note that the number of workers vaccinated for the seasonal influenza or H1N1 in the aforementioned groups was low (Luckhaupt et al. 2014). A study conducted at NIOSH measured viral particles of influenza in air samples collected from a hospital emergency department and found that over 50% of the virus was detected in the airborne droplets located in waiting rooms, triage rooms and in personal samplers worn by emergency department physicians (Blachere et al. 2009). Even though the CDC, the Advisory Committee on Immunization Practices, and the Healthcare Infection Control Practices Advisory Committee recommend that all United States healthcare workers get vaccinated annually, only 64.3% of healthcare workers were vaccinated during the early 2014–2015 season (CDC 2016j). Changes and updates to the previous recommendations of immunization practices have already been reported for the 2016–2017 influenza season (CDC 2016i).

Workers in the poultry and swine industries are susceptible to zoonotic infections, and exposures have been reported in recent studies (Fragaszy et al. 2016; Gray et al. 2007). Workers in pig farms and their wives have been found to be at

a greater risk of exposure to swine influenza virus compared to a control population not exposed to swine (Gray et al. 2007). Veterinarians, farmers and workers who process meat have also been reported to be exposed to swine flu (Myers et al. 2006; O'Brien and Nonnenmann 2016). In December 2016, a New York animal shelter worker was infected with a novel avian lineage influenza (H7N2) virus. The worker was thought to have acquired the virus through close, prolonged unprotected exposure to infected cats (CDC 2016l).

3.5.5 *Ebola*

The Ebola virus disease, also known as Ebola hemorrhagic fever made headlines from December 2013 to January 2016 due to an outbreak in West Africa, including the countries of Guinea, Liberia and Sierra Leone (CDC 2016d). Symptoms included fever, sore throat, muscular pain and headaches followed by vomiting diarrhea and rash. The virus is transmitted into the human population through direct contact with blood or other bodily secretions of infected animals, then transmitted from human to human by contact with bodily fluids of infected individuals (WHO 2016a). To diagnose the Ebola virus, blood samples are tested for viral RNA by RT-PCR and viral proteins by an enzyme-linked immunosorbent assay (ELISA). During the outbreak, approximately 25,000 cases of Ebola exposure were reported, with 41% of those cases ending in death (Suwantararat and Apisarntharak 2015). Healthcare-related infections with the Ebola virus accounted for 2.5–12% of total cases and the fatality rate was reported in up to 73% of the emergency responders and healthcare workers in direct contact with infected patients (Suwantararat and Apisarntharak 2015). There were five reported exposures that were confirmed in the United States, with four of the cases being healthcare workers (Lyon et al. 2014; Chevalier et al. 2014). The CDC has published guidelines for healthcare workers during the management of patients in United States hospitals during an Ebola virus outbreak (CDC 2016c). The guidelines instruct workers on the selection of the correct PPE, the proper use of PPE, and techniques for donning and doffing PPE. Fig. 3.5 shows a responder wearing PPE during the Ebola outbreak. Preventative measures discussed in the guidelines include strict adherence to PPE recommendations and incubation periods when responders returned to the United States (CDC 2016c). Currently, there are no approved vaccinations against Ebola (CDC 2016d); however, there are potential candidates (WHO 2016b).

3.5.6 *Norovirus*

Gastroenteritis-causing norovirus is a highly contagious virus found in healthcare occupations, food handling services, the military, schools and on cruise ships. The Vessel Sanitation Program at CDC assists with preventing and controlling

Fig. 3.5 Personal protective equipment. An emergency responder displaying the proper use of personal protective equipment



gastroenteritis illnesses such as the norovirus in the cruise ship industry (CDC 2016r). Norovirus is easily transmitted by contaminated food and water, hands and communal objects, and by direct contact with infected individuals (CDC 2016p). It is suggested that norovirus can be carried through the air to replicate in the host (Duchaine 2016). Recently, molecular analysis of air collected from areas in healthcare facilities revealed evidence of human norovirus (Bonifait et al. 2015). Norovirus is diagnosed through enzyme immunoassays or RT-PCR assays and has no current vaccine. Similar to norovirus, rotavirus causes gastroenteritis and is spread among infants and young children through the fecal-oral route. It is transmitted by contaminated food, water and objects as well as by direct bodily contact. Diagnosis is made through the detection of rotavirus antigen in stool samples. Unlike norovirus, rotavirus has an available vaccine (CDC 2016q). Both viral diseases are prevented through proper hygiene and sanitation practices, as well as avoiding infected and symptomatic people (MacCannell et al. 2011). Washing vegetables and fruits and disinfecting contaminated areas also limits the risk of exposure. Due to the age of the population at risk of rotavirus exposure, it is not common for occupational exposures.

3.5.7 *Zika Virus*

Beginning in 2015, the Zika virus has been a major focus for public health officials. Zika virus is a mosquito-borne illness that was first identified in Uganda (WHO 2016e) and can be transmitted through mosquito bites and possibly blood transfusions, although the latter is unconfirmed (CDC 2016v). In pregnant women, Zika can be transmitted to the fetus and cause birth defects, such as microcephaly. Symptoms that normally last 2–7 days include mild fever, skin rashes, muscle and joint pain, and conjunctivitis. A blood or urine test can confirm the presence of Zika virus. In March 2016, the Food and Drug Administration approved a new Triplex RT-PCR Assay to test for Zika (CDC 2016o). The CDC suggested that avoiding mosquito bites by wearing protective clothing or applying bug repellents are methods to reduce the risk of exposure. Currently, there is no vaccine against Zika viral infection. In 2016, the CDC responded to an outbreak of Zika in North and South America. Along with NIOSH, the Occupational Safety and Health Administration (OSHA) developed guidelines for protecting workers from occupational exposure to Zika virus, including workers in outdoor environments, business travelers, as well as healthcare and laboratory workers (CDC 2016v). There are reports of locally acquired cases of Zika in Florida that are not associated with travel exposure (CDC 2016w). More recently, five cases of locally acquired Zika were reported in Texas (CDC 2016w). Laboratorians are an additional occupational group at risk of contracting Zika as shown in a case study of a Pittsburgh worker who acquired Zika through laboratory transmission, specifically by a needle stick (CDC 2016w).

3.5.8 *Other Potential Occupational Viral Exposures*

Although not as prevalent in occupational environments, there are other viruses that pose a risk for potential exposure. Viral meningitis, defined as the inflammation of the spinal cord and brain, is the most common type of meningitis. This disease is caused by non-polio enterovirus, mumps, herpes virus, measles, influenza, and arboviruses. Viral meningitis is most common in immunocompromised people and young children (CDC 2016t). The disease can be diagnosed by X-ray of the head, blood collection for culturing, or drawing fluid from around the spinal cord to further test for cellular, sugar and protein levels. There is no specific treatment for viral meningitis. Although viral meningitis may not be commonly found in many occupational environments, the causal agents are found in occupational settings, such as schools (Crocker et al. 2015; Sosa et al. 2009). Non-polio enterovirus can be encountered in a healthcare environments (Midgley et al. 2015; Midgley et al. 2014). If symptoms are present, they are similar to the common cold. Non-polio enterovirus is transmitted through feces, or eye, nose and mouth secretions

and can be diagnosed through serotype identification and molecular testing. Exposure to the virus can be minimized by washing hands and avoiding direct contact with infected people or contaminated objects. Currently there is no treatment for non-polio enterovirus (CDC 2016a). According to the CDC, mumps can be encountered in healthcare and school environments (CDC 2016n). Transmitted through eye, nose and mouth secretions, mumps is spread through coughing, sneezing or talking and by direct contact with infected people or contaminated objects. The disease is diagnosed using antibody measurements, viral culturing, and RT-PCR assays. A vaccine is available that protects against measles, mumps and rubella (MMR). There is also an MMRV vaccine for children which includes protection against varicella (chickenpox). A third cause of viral meningitis is measles. It is highly contagious and is transmitted through coughing and sneezing. In 2015, there was an outbreak at an amusement park in California exposing both the general public and the park workers (Zipprich et al. 2015), as well as another outbreak in an Ohio Amish community in 2014 (CDC 2016m). Measles is diagnosed using RT-PCR and genetic sequencing and is prevented with the MMR vaccine. Arboviruses, such as the West Nile virus are another group of viruses that can potentially cause viral meningitis. This disease is transmitted to humans by mosquitoes; therefore, insect repellent and protective clothing are preventative measures taken to reduce the risk of exposure. West Nile virus is diagnosed by antibody testing, viral culturing or RT-PCR assays to detect viral RNA. Less than 1% of those infected develop life threatening illnesses (CDC 2016u). Currently, there is no treatment available to treat the West Nile virus, but the same precautions for the Zika virus should be taken to reduce exposure to workers in occupations that require travel (CDC 2016v).

3.6 Conclusion

In summary, viral exposures can occur in many occupational environments with the healthcare environment having some of the greatest risk for exposure to a broad diversity of viruses. Table 1 depicts the most prevalent viral exposures encountered in occupational environments, characteristics of those viruses, and current treatment strategies against the viral exposure. The CDC, along with many other governmental agencies, have developed guidelines that are often updated to provide the most current preventative methods to protect workers from potential viral exposures (Garner 1996). Regardless of the virus, the “2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings” cover an array of recommendations to protect workers at risk for different viral exposures (Siegel et al. 2007). The CDC offers available resources for workers, especially in the healthcare sector, to assist in limiting potential viral exposures through proper use of selection and the donning of PPE (CDC 2016b, c), as depicted in Fig. 3.5. It is important to follow appropriate prevention practices, such as good hygiene, proper sanitation and disinfection strategies, as well

as wearing the correct PPE to limit viral exposure in occupational environments. Knowledge of the available federal and state guideline documents for specific viruses, as well as Exposure Control Plans developed by employers will help reduce occupational exposures to viruses. Taking preventative measures to limit the risk of exposures and following vaccination recommendations can reduce the spread of viral exposure in occupational environments.

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References

- Abedon ST, Kuhl SJ, Blasdel BG et al. (2011) Phage treatment of human infections. *Bacteriophage* 1(2):66–85. doi:[10.4161/bact.1.2.15845](https://doi.org/10.4161/bact.1.2.15845)
- Ackermann HW, Prangishvili D (2012) Prokaryote viruses studied by electron microscopy. *Arch. Virol* 157(10):1843–1849. doi:[10.1007/s00705-012-1383-y](https://doi.org/10.1007/s00705-012-1383-y)
- Aintablian N, Walpita P, Sawyer MH (1998) Detection of *Bordetella pertussis* and respiratory syncytial virus in air samples from hospital rooms. *Infect Control Hosp Epidemiol* 19(12): 918–923. doi:[10.2307/30142018](https://doi.org/10.2307/30142018)
- Baltimore D (1971) Expression of animal virus genomes. *Bacteriol Rev* 35(3):235–241
- Bischoff WE, Swett K, Leng I et al. (2013) Exposure to Influenza virus aerosols during routine patient care. *J Infect Dis* 207(7):1037–1046. doi:[10.1093/infdis/jis773](https://doi.org/10.1093/infdis/jis773)
- Blachere FM, Cao G, Lindsley WG et al. (2011) Enhanced detection of infectious airborne influenza virus. *J Virol Methods* 176(1–2):120–124. doi:[10.1016/j.jviromet.2011.05.030](https://doi.org/10.1016/j.jviromet.2011.05.030)
- Blachere FM, Lindsley WG, Pearce TA et al. (2009) Measurement of airborne influenza virus in a hospital emergency department. *Clin Infect Dis* 48(4):438–440. doi:[10.1086/596478](https://doi.org/10.1086/596478)
- Bonifait L, Charlebois R, Vimont A et al. (2015) Detection and quantification of airborne norovirus during outbreaks in healthcare facilities. *Clin Infect Dis* 61(3):299–304. doi:[10.1093/cid/civ321](https://doi.org/10.1093/cid/civ321)
- Booth TF, Kournikakis B, Bastien N et al. (2005) Detection of airborne severe acute respiratory syndrome (SARS) coronavirus and environmental contamination in SARS outbreak units. *J Infect Dis* 191(9):1472–1477. doi:[10.1086/429634](https://doi.org/10.1086/429634)
- Brown JC, Newcomb WW, Wertz GW (2010) Helical virus structure: the case of the rhabdovirus bullet. *Viruses* 2(4):995–1001. doi:[10.3390/v2040995](https://doi.org/10.3390/v2040995)
- Cao G, Noti JD, Blachere FM et al. (2011) Development of an improved methodology to detect infectious airborne influenza virus using the NIOSH bioaerosol sampler. *J Environ Monit* 13(12):3321–3328. doi:[10.1039/c1em10607d](https://doi.org/10.1039/c1em10607d)
- Carducci A, Federigi I, Verani M (2013) Virus occupational exposure in solid waste processing facilities. *Ann Occup Hyg*. doi:[10.1093/annhyg/met043](https://doi.org/10.1093/annhyg/met043)
- CDC (1988) Update: universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. *MMWR Morb Mortal Wkly Rep* 37(24):377–382. 387-378
- CDC (2001) HIV and AIDS – United States, 1981–2000. *MMWR Morb Mortal Wkly Rep* 50(21):430–434
- CDC (2011) Rabies. Centers for Disease Control and Prevention. <https://www.cdc.gov/rabies/>. Accessed November 27, 2016
- CDC (2015) Adenoviruses. Centers for Disease Control and Prevention. <http://www.cdc.gov/adenovirus/index.html>. Accessed November 27, 2016

- CDC (2016a) About non-polio enterovirus. Centers for Disease Control and Prevention. <https://www.cdc.gov/non-polio-enterovirus/about/index.html>. Accessed November 27, 2016
- CDC (2016b) Bloodborne infectious diseases: HIV/AIDS, Hepatitis B, and Hepatitis C. Centers for Disease Control and Prevention. <https://www.cdc.gov/niosh/topics/bbp/controls.html>. Accessed November 27, 2016
- CDC (2016c) Ebola (Ebola virus disease). Centers for Disease Control and Prevention. <http://www.cdc.gov/vhf/ebola/healthcare-us/ppe/guidance.html>. Accessed November 27, 2016
- CDC (2016d) Ebola (Ebola virus disease). Centers for Disease Control and Prevention. <http://www.cdc.gov/vhf/ebola/index.html>. Accessed November 27, 2016
- CDC (2016e) Hantavirus. Centers for Disease Control and Prevention. <https://www.cdc.gov/hantavirus/>. Accessed November 27, 2016
- CDC (2016f) HIV in the United States: at a glance. Centers for Disease Control and Prevention. <http://www.cdc.gov/hiv/statistics/overview/ata glance.html>. Accessed November 27, 2016
- CDC (2016g) HIV surveillance reports. Centers for Disease Control and Prevention. <http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Accessed November 27, 2016
- CDC (2016h) Influenza (flu). Centers for Disease Control and Prevention. <http://www.cdc.gov/flu/index.htm>. Accessed November 27, 2016
- CDC (2016i) Influenza (flu). Centers for Disease Control and Prevention. <https://www.cdc.gov/flu/professionals/acip/index.htm>. Accessed November 27, 2016
- CDC (2016j) Influenza (flu). Centers for Disease Control and Prevention. <https://www.cdc.gov/flu/healthcareworkers.htm>. Accessed November 27, 2016
- CDC (2016k) Influenza (flu). Centers for Disease Control and Prevention. <https://www.cdc.gov/flu/protect/keyfacts.htm>. Accessed November 27, 2016
- CDC (2016l) Influenza (flu). Centers for Disease Control and Prevention. <https://www.cdc.gov/flu/spotlights/avian-influenza-cats.htm>. Accessed January 5, 2017
- CDC (2016m) Measles (Rubeola). Centers for Disease Control and Prevention. <https://www.cdc.gov/measles/index.html>. Accessed November 27, 2016
- CDC (2016n) Mumps. Centers for Disease Control and Prevention. <https://www.cdc.gov/mumps/>. Accessed November 27, 2016
- CDC (2016o) New CDC laboratory test for Zika virus authorized for emergency use by FDA. Centers for Disease Control and Prevention. <https://wwwdev.cdc.gov/media/releases/2016/s0318-zika-lab-test.html>. Accessed November 27, 2016
- CDC (2016p) Norovirus. Centers for Disease Control and Prevention. <https://www.cdc.gov/norovirus/>. Accessed November 27, 2016
- CDC (2016q) Rotavirus. Centers for Disease Control and Prevention. <https://www.cdc.gov/rotavirus/about/transmission.html>. Accessed November 27, 2016
- CDC (2016r) Vessel sanitation program. Centers for Disease Control and Prevention. <https://www.cdc.gov/nceh/vsp/>. Accessed November 27, 2016
- CDC (2016s) Viral hepatitis. Centers for Disease Control and Prevention. <http://www.cdc.gov/hepatitis/index.htm>. Accessed November 27, 2016
- CDC (2016t) Viral meningitis. Centers for Disease Control and Prevention. <https://www.cdc.gov/meningitis/viral.html>. Accessed November 27, 2016
- CDC (2016u) West Nile virus. Centers for Disease Control and Prevention. <https://www.cdc.gov/westnile/>. Accessed November 27, 2016
- CDC (2016v) Zika virus. Centers for Disease Control and Prevention. <http://www.cdc.gov/zika/index.html>. Accessed November 27, 2016
- CDC (2016w) Zika virus. Centers for Disease Control and Prevention. <http://www.cdc.gov/zika/index.html>. Accessed November 27, 2016
- Centers for Disease C, Prevention (2007) Acute respiratory disease associated with adenovirus serotype 14 – four states, 2006–2007. *MMWR Morb Mortal Wkly Rep* 56(45):1181–1184
- Chevalier MS, Chung W, Smith J et al. (2014) Ebola virus disease cluster in the United States – Dallas County, Texas, 2014. *MMWR Morb Mortal Wkly Rep* 63(46):1087–1088

- Crocker C, Civen R, Keough K et al. (2015) Aseptic meningitis outbreak associated with echovirus 30 among high school football players – Los Angeles County, California, 2014. *MMWR Morb Mortal Wkly Rep* 63(51):1228
- de Haan CAM, Li Z, te Lintelo E et al. (2005) Murine Coronavirus with an extended host range uses heparan sulfate as an entry receptor. *J Virol* 79(22):14451–14456. doi:[10.1128/jvi.79.22.14451-14456.2005](https://doi.org/10.1128/jvi.79.22.14451-14456.2005)
- De Schryver A, De Schrijver K, Francois G et al. (2015) Hepatitis E virus infection: an emerging occupational risk? *Occup Med (Lond)* 65(8):667–672. doi:[10.1093/occmed/kqv154](https://doi.org/10.1093/occmed/kqv154)
- Division of Viral Diseases NCFI, Respiratory Diseases CfDC, Prevention (2011) Updated norovirus outbreak management and disease prevention guidelines. *MMWR Recomm Rep* 60 (RR-3):1–18
- Domingo E, Escarmis C, Sevilla N et al. (1996) Basic concepts in RNA virus evolution. *FASEB J* 10(8):859–864
- Duchaine C (2016) Assessing microbial decontamination of indoor air with particular focus on human pathogenic viruses. *Am J Infect Control* 44(9, Supplement):S121–S126. doi:[10.1016/j.ajic.2016.06.009](https://doi.org/10.1016/j.ajic.2016.06.009)
- England PH (2013) Zoonotic diseases (zoonoses): guidance, data and analysis. <https://www.gov.uk/government/publications/list-of-zoonotic-diseases/list-of-zoonotic-diseases>. Accessed November 27, 2016
- Fokine A, Chipman PR, Leiman PG et al. (2004) Molecular architecture of the prolate head of bacteriophage T4. *Proc Natl Acad Sci U S A* 101(16):6003–6008. doi:[10.1073/pnas.0400444101](https://doi.org/10.1073/pnas.0400444101)
- Fragaszy E, Ishola DA, Brown IH et al. (2016) Increased risk of A(H1N1)pdm09 influenza infection in UK pig industry workers compared to a general population cohort. *Influenza Other Respir Viruses* 10(4):291–300. doi:[10.1111/irv.12364](https://doi.org/10.1111/irv.12364)
- Fraser C, Donnelly CA, Cauchemez S et al. (2009) Pandemic potential of a strain of influenza A (H1N1): early findings. *Science* 324(5934):1557–1561. doi:[10.1126/science.1176062](https://doi.org/10.1126/science.1176062)
- Garner JS (1996) Guideline for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 17(1):53–80
- Gatherer D (2009) The 2009 H1N1 influenza outbreak in its historical context. *J Clin Virol* 45 (3):174–178. doi:[10.1016/j.jcv.2009.06.004](https://doi.org/10.1016/j.jcv.2009.06.004)
- Grabow WOK (2001) Bacteriophages: update on application as models for viruses in water. *Water SA* 27(2):251–268
- Gray GC, Goswami PR, Malasig MD et al. (2000) Adult adenovirus infections: loss of orphaned vaccines precipitates military respiratory disease epidemics. For the Adenovirus Surveillance Group. *Clin Infect Dis* 31(3):663–670. doi:[10.1086/313999](https://doi.org/10.1086/313999)
- Gray GC, McCarthy T, Capuano AW et al. (2007) Swine workers and swine influenza virus infections. *Emerg Infect Dis* 13(12):1871–1878. doi:[10.3201/eid1312.061323](https://doi.org/10.3201/eid1312.061323)
- Grove J, Marsh M (2011) The cell biology of receptor-mediated virus entry. *J Cell Biol* 195(7):1071–1082. doi:[10.1083/jcb.201108131](https://doi.org/10.1083/jcb.201108131)
- Harrison BD, Wilson TM (1999) Milestones in the research on tobacco mosaic virus. *Philos Trans R Soc Lond B Biol Sci* 354(1383):521–529
- Howard J, Murashov V, Schulte P (2017) Synthetic biology and occupational risk. *J Occup Environ Hyg* 14(3):224–236. doi:[10.1080/15459624.2016.1237031](https://doi.org/10.1080/15459624.2016.1237031)
- Janeway CJ, Travers P, Walport M et al. (2001) Infectious agents and how they cause disease. Immunobiology: the immune system in health and disease, 5th edn. Garland Science, New York
- Kiselev NA, Sherman MB, Tsuprun VL (1990) Negative staining of proteins. *Electron Microsc Rev* 3(1):43–72. doi:[10.1016/0892-0354\(90\)90013-1](https://doi.org/10.1016/0892-0354(90)90013-1)
- Koonin EV, Senkevich TG, Dolja VV (2006) The ancient Virus World and evolution of cells. *Biol Direct* 1:29. doi:[10.1186/1745-6150-1-29](https://doi.org/10.1186/1745-6150-1-29)
- Kuhar DT, Henderson DK, Struble KA et al. (2013) Updated US Public Health Service guidelines for the management of occupational exposures to human immunodeficiency virus and

- recommendations for postexposure prophylaxis. *Infect Control Hosp Epidemiol* 34(9): 875–892. doi:[10.1086/672271](https://doi.org/10.1086/672271)
- Lawrence CM, Menon S, Eilers BJ et al. (2009) Structural and functional studies of archaeal viruses. *J Biol Chem* 284(19):12599–12603. doi:[10.1074/jbc.R800078200](https://doi.org/10.1074/jbc.R800078200)
- Leung NHL, Zhou J, Chu DKW et al. (2016) Quantification of influenza virus RNA in aerosols in patient rooms. *PLoS One* 11(2):e0148669. doi:[10.1371/journal.pone.0148669](https://doi.org/10.1371/journal.pone.0148669)
- Li W, Shi Z, Yu M et al. (2005) Bats are natural reservoirs of SARS-like coronaviruses. *Science* 310(5748):676–679. doi:[10.1126/science.1118391](https://doi.org/10.1126/science.1118391)
- Lidmar J, Mirny L, Nelson DR (2003) Virus shapes and buckling transitions in spherical shells. *Phys Rev E* 68(5):051910
- Lindsay WG, Blachere FM, Beezhold DH et al. (2016) Viable influenza A virus in airborne particles expelled during coughs versus exhalations. *Influenza Other Respir Viruses* 10(5):404–413. doi:[10.1111/irv.12390](https://doi.org/10.1111/irv.12390)
- Lindsay WG, Blachere FM, Davis KA et al. (2010a) Distribution of airborne influenza virus and respiratory syncytial virus in an urgent care medical clinic. *Clin Infect Dis* 50(5):693–698. doi:[10.1086/650457](https://doi.org/10.1086/650457)
- Lindsay WG, Blachere FM, Thewlis RE et al. (2010b) Measurements of airborne influenza virus in aerosol particles from human coughs. *PLoS One* 5(11):e15100. doi:[10.1371/journal.pone.0015100](https://doi.org/10.1371/journal.pone.0015100)
- Liu R, Vaishnav RA, Roberts AM et al. (2013) Humans have antibodies against a plant virus: evidence from tobacco mosaic virus. *PLoS One* 8(4):e60621. doi:[10.1371/journal.pone.0060621](https://doi.org/10.1371/journal.pone.0060621)
- Lodish H, Berk A, Zipursky S et al. (2000) *Molecular Cell Biology*. Section 6.3 Viruses: Structure, Function, and Uses, 4th edn. W. H. Freeman, New York
- Longdon B, Brockhurst MA, Russell CA et al. (2014) The evolution and genetics of virus host shifts. *PLoS Pathogens* 10(11):e1004395. doi:[10.1371/journal.ppat.1004395](https://doi.org/10.1371/journal.ppat.1004395)
- Louie JK, Karon AE, Holodniy M et al. (2008) Severe pneumonia due to adenovirus serotype 14: a new respiratory threat? *Clin Infect Dis* 46(3):421–425. doi:[10.1086/525261](https://doi.org/10.1086/525261)
- Luckhaupt SE, Calvert GM, Li J et al. (2014) Prevalence of influenza-like illness and seasonal and pandemic H1N1 influenza vaccination coverage among workers – United States, 2009–10 influenza season. *MMWR Morb Mortal Wkly Rep* 63(10):217–221
- Lyon GM, Mehta AK, Varkey JB et al. (2014) Clinical care of two patients with Ebola virus disease in the United States. *New Engl J Med* 371(25):2402–2409. doi:[10.1056/NEJMoal409838](https://doi.org/10.1056/NEJMoal409838)
- MacCannell T, Umscheid CA, Agarwal RK et al. (2011) Guideline for the prevention and control of norovirus gastroenteritis outbreaks in healthcare settings. *Infect Control Hosp Epidemiol* 32(10):939–969. doi:[10.1086/662025](https://doi.org/10.1086/662025)
- Mankertz A, Çaliskan R, Hattermann K et al. (2004) Molecular biology of Porcine circovirus: analyses of gene expression and viral replication. *Veterinary Microbiology* 98(2):81–88. doi:[10.1016/j.vetmic.2003.10.014](https://doi.org/10.1016/j.vetmic.2003.10.014)
- McCluskey R, Sandin R, Greene J (1996) Detection of airborne cytomegalovirus in hospital rooms of immunocompromised patients. *J Virol Methods* 56(1):115–118
- Midgley CM, Jackson MA, Selvarangan R et al. (2014) Severe respiratory illness associated with enterovirus D68 – Missouri and Illinois, 2014. *MMWR Morb Mortal Wkly Rep* 63(36):798–799
- Midgley CM, Watson JT, Nix WA et al. (2015) Severe respiratory illness associated with a nationwide outbreak of enterovirus D68 in the USA (2014): a descriptive epidemiological investigation. *Lancet Respir Med* 3(11):879–887. doi:[10.1016/S2213-2600\(15\)00335-5](https://doi.org/10.1016/S2213-2600(15)00335-5)
- Mohebbati A, Davis JM, Fry DE (2010) Current risks of occupational blood-borne viral infection. *Surg Infect (Larchmt)* 11(3):325–331. doi:[10.1089/sur.2010.025](https://doi.org/10.1089/sur.2010.025)
- Mubareka S, Lowen AC, Steel J et al. (2009) Transmission of influenza virus via aerosols and fomites in the guinea pig model. *J Infect Dis* 199(6):858–865. doi:[10.1086/597073](https://doi.org/10.1086/597073)
- Myatt TA, Johnston SL, Zuo Z et al. (2004) Detection of airborne rhinovirus and its relation to outdoor air supply in office environments. *Am J Respir Crit Care Med* 169(11):1187–1190. doi:[10.1164/rccm.200306-760OC](https://doi.org/10.1164/rccm.200306-760OC)

- Myers KP, Olsen CW, Setterquist SF et al. (2006) Are swine workers in the United States at Increased risk of infection with zoonotic influenza virus? *Clin Infect Dis*42(1):14–20. doi:[10.1086/498977](https://doi.org/10.1086/498977)
- Norkin LC (1995) Virus receptors: implications for pathogenesis and the design of antiviral agents. *Clin Microbiol Rev* 8(2):293–315
- Noti JD, Lindsley WG, Blachere FM et al. (2012) Detection of infectious influenza virus in cough aerosols generated in a simulated patient examination room. *Clin Infect Dis* 54(11): 1569–1577. doi:[10.1093/cid/cis237](https://doi.org/10.1093/cid/cis237)
- Novel Swine-Origin Influenza AVIT, Dawood FS, Jain S et al. (2009) Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med* 360(25):2605–2615. doi:[10.1056/NEJMoa0903810](https://doi.org/10.1056/NEJMoa0903810)
- O'Brien KM, Nonnenmann MW (2016) Airborne influenza a is detected in the personal breathing zone of swine veterinarians. *PLoS One* 11(2):e0149083. doi:[10.1371/journal.pone.0149083](https://doi.org/10.1371/journal.pone.0149083)
- Panneer N, Lontok E, Branson BM et al. (2014) HIV and hepatitis c virus infection in the United States: whom and how to test. *Clin Infect Dis* 59(6):875–882. doi:[10.1093/cid/ciu396](https://doi.org/10.1093/cid/ciu396)
- Parrish CR, Holmes EC, Morens DM et al. (2008) Cross-species virus transmission and the emergence of new epidemic diseases. *Microbiol Mol Biol Rev* 72(3):457–470. doi:[10.1128/MMBR.00004-08](https://doi.org/10.1128/MMBR.00004-08)
- Philippe N, Legendre M, Doutre G, et al. (2013) Pandoraviruses: amoeba viruses with genomes Up to 2.5 Mb reaching that of parasitic eukaryotes. *Science* 341(6143):281–286. doi:[10.1126/science.1239181](https://doi.org/10.1126/science.1239181)
- Pozzetto B, Memmi M, Garraud O et al. (2014) Health care-associated hepatitis C virus infection. *World J Gastroenterol* 20(46):17265–17278. doi:[10.3748/wjg.v20.i46.17265](https://doi.org/10.3748/wjg.v20.i46.17265)
- Prasad BVV, Schmid MF (2012) Principles of virus structural organization. In: Rossmann MG, Rao VB (eds) *Viral molecular machines*. Springer, US, Boston, MA, p 17–47. doi:[10.1007/978-1-4614-0980-9_3](https://doi.org/10.1007/978-1-4614-0980-9_3)
- Riddell A, Kennedy I, Tong CY (2015) Management of sharps injuries in the healthcare setting. *BMJ* 351:h3733. doi:[10.1136/bmj.h3733](https://doi.org/10.1136/bmj.h3733)
- Roberts H, Kruszon-Moran D, Ly KN et al. (2016) Prevalence of chronic hepatitis B virus (HBV) infection in U.S. households: National Health and Nutrition Examination Survey (NHANES), 1988–2012. *Hepatology* 63(2):388–397. doi:[10.1002/hep.28109](https://doi.org/10.1002/hep.28109)
- Roulston A, Marcellus RC, Branton PE (1999) Viruses and apoptosis. *Ann Rev Microbiol* 53:577–628. doi:[10.1146/annurev.micro.53.1.577](https://doi.org/10.1146/annurev.micro.53.1.577)
- Sekar A, Kathiresan K (2013) Bacterial viruses in marine environment and their ecology role and bioprospecting potential: a review. *Int J Curr Microbiol Appl Sci* 2(7):151–163
- Sharp PM, Hahn BH (2010) The evolution of HIV-1 and the origin of AIDS. *Philos Trans R Soc Lond B Biol Sci* 365(1552):2487–2494. doi:[10.1098/rstb.2010.0031](https://doi.org/10.1098/rstb.2010.0031)
- Siegel JD, Rhinehart E, Jackson M et al. (2007) 2007 Guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control* 35(10 Suppl 2):S65–164. doi:[10.1016/j.ajic.2007.10.007](https://doi.org/10.1016/j.ajic.2007.10.007)
- Silver S (2015) Laboratory-acquired lethal infections by potential bioweapons pathogens including Ebola in 2014. *FEMS Microbiol Lett* 362(1):1–6. doi:[10.1093/femsle/fmu008](https://doi.org/10.1093/femsle/fmu008)
- Sissons JG, Bain M, Wills MR (2002) Latency and reactivation of human cytomegalovirus. *J Infect* 44(2):73–77. doi:[10.1053/jinf.2001.0948](https://doi.org/10.1053/jinf.2001.0948)
- Smith KO, Melnick JL (1962) A method for staining virus particles and identifying their nucleic acid type in the electron microscope. *Virology* 17(3):480–490. doi:[10.1016/0042-6822\(62\)90143-5](https://doi.org/10.1016/0042-6822(62)90143-5)
- Sosa LE, Gupta S, Juthani-Mehta M et al. (2009) Meningitis in a college student in Connecticut, 2007. *J Am Coll Health* 58(1):12–14. doi:[10.3200/JACH.58.1.12-14](https://doi.org/10.3200/JACH.58.1.12-14)
- Suwantarat N, Apisarnthanarak A (2015) Risks to healthcare workers with emerging diseases: lessons from MERS-CoV, Ebola, SARS, and avian flu. *Curr Opin Infect Dis* 28(4):349–361. doi:[10.1097/QCO.0000000000000183](https://doi.org/10.1097/QCO.0000000000000183)

- Sze CW, Tan Y-J (2015) Viral membrane channels: role and function in the virus life cycle. *Viruses* 7(6):3261–3284. doi:[10.3390/v7062771](https://doi.org/10.3390/v7062771)
- Turner RB (2007) Rhinovirus: more than just a common cold virus. *J Infect Dis* 195(6):765–766. doi:[10.1086/511829](https://doi.org/10.1086/511829)
- Vernizzi G, Olvera de la Cruz M (2007) Faceting ionic shells into icosahedra via electrostatics. *Proc Natl Acad Sci* 104(47):18382–18386. doi:[10.1073/pnas.0703431104](https://doi.org/10.1073/pnas.0703431104)
- Verreault D, Moineau S, Duchaine C (2008) Methods for sampling of airborne viruses. *Microbiol Mol Biol Rev* 72(3):413–444. doi:[10.1128/MMBR.00002-08](https://doi.org/10.1128/MMBR.00002-08)
- Vlasak M, Goesler I, Blas D (2005) Human rhinovirus type 89 variants use heparan sulfate proteoglycan for cell attachment. *J Virol* 79(10):5963–5970. doi:[10.1128/jvi.79.10.5963-5970.2005](https://doi.org/10.1128/jvi.79.10.5963-5970.2005)
- Wasley A, Kruszon-Moran D, Kuhnert W et al. (2010) The prevalence of hepatitis B virus infection in the United States in the era of vaccination. *J Infect Dis* 202(2):192–201. doi:[10.1086/653622](https://doi.org/10.1086/653622)
- Webby RJ, Webster RG, (2001) Emergence of influenza A viruses. *Philos Trans R Soc Lond B Biol Sci* 356(1416):1817–1828. doi:[10.1098/rstb.2001.0997](https://doi.org/10.1098/rstb.2001.0997)
- West KH, Cohen ML (1997) Standard precautions – a new approach to reducing infection transmission in the hospital setting. *J Intraven Nurs* 20(6 Suppl):S7–10
- WHO (2016a) Ebola virus disease. World Health Organization. <http://www.who.int/mediacentre/factsheets/fs103/en/>
- WHO (2016b) Final trial results confirm Ebola vaccine provides high protection against disease. World Health Organization. <http://www.who.int/mediacentre/news/releases/2016/ebola-vaccine-results/en/>
- WHO (2016c) Influenza (Seasonal). World Health Organization. <http://www.who.int/mediacentre/factsheets/fs211/en/>. Accessed November 27, 2016
- WHO (2016d) Poliomyelitis. World Health Organization. <http://www.who.int/mediacentre/factsheets/fs114/en/>. Accessed November 27, 2016
- WHO (2016e) Zika virus. World Health Organization. <http://www.who.int/mediacentre/factsheets/zika/en/>
- Wyżgowski P, Rosiek A, Grzela T et al. (2016) Occupational HIV risk for health care workers: risk factor and the risk of infection in the course of professional activities. *Ther Clin Risk Manag* 12:989–994. doi:[10.2147/TCRM.S104942](https://doi.org/10.2147/TCRM.S104942)
- Zipprich J, Winter K, Hacker J et al. (2015) Measles outbreak – California, December 2014–February 2015. *MMWR Morb Mortal Wkly Rep* 64(6):153–154