

An Overview of 8 Viruses That Can Cause Cancer

BY DIBASH KUMAR DAS, PHD

Approximately 10 percent of cancer cases worldwide are thought to be caused by viruses (*Nat Genet* 2020; <https://doi.org/10.1038/s41588-019-0558-9>). Viruses can be roughly divided into two types—those that have DNA as their genetic material and those that have RNA. The effects of both types of viruses on cancer development are highly complicated. Both have been found to be associated with cancers of different types, and one type can cause various types of cancer.

Compared to other viruses, oncogenic viruses are unusual because they infect, rather than kill their host cells. This allows oncogenic viruses to cause lasting, persistent infections. Many virus-associated cancers can take years to become symptomatic as the viruses depend on weakened host immunity, environmental factors, and host cellular mutations. Here we briefly review eight known oncologic viruses.

Epstein-Barr Virus

Epstein-Barr virus (EBV), one of the nine known human herpesvirus types in the herpes family, is estimated to infect more than 90 percent of the global population (*Front Oncol* 2018; doi: 10.3389/fonc.2018.00211). The mechanism of transmission is generally unclear, although it is most often spread through saliva. EBV can also be contracted through coughing, sneezing, blood, semen, and close contact.

The virus is best known for causing mononucleosis. EBV infection also increases the likelihood for the development of several different types of lymphoma, including Burkitt's lymphoma, Hodgkin's lymphoma, HIV-associated lymphoma, and post-transplant lymphoma. Additionally, EBV infection may contribute to nasopharyngeal cancer and stomach cancer. There is currently no vaccine for EBV.

Hepatitis B Virus

Hepatitis B virus (HBV), an enveloped DNA hepadnavirus, is prevalent on every continent with over 250 million people worldwide infected (*Nat Rev Gastroenterol Hepatol* 2020; <https://doi.org/10.1038/s41575-020-0296-6>). HBV is a leading cause of hepatocellular carcinoma (HCC), which is the third-leading cause of cancer deaths worldwide (*Liver Cancer* 2020; <https://doi.org/10.1159/000508568>).

HBV can incorporate itself into the human genome and replicate within liver cells, directly boosting carcinogenic activity through multiple signaling pathways in the liver. HBV infections are highly contagious and transmitted via contact with contaminated blood, sweat, or tears. It can also be spread through sharing IVs, sexual contact, and from mother to child.

The World Health Organization and CDC both recommend the HBV vaccine for all infants and children up to age 18 years. The CDC further recommends that adults in high-risk groups be vaccinated, including individuals at risk by sexual exposure and by exposure to blood.

Hepatitis C Virus

Hepatitis C virus (HCV), an RNA virus, is prevalent on every continent with over 70 million people globally infected. It is the most com-

mon cause of HCC. Similar to HBV, HCV also causes viral hepatitis; though it is less likely than HBV to cause symptoms.

HCV cannot incorporate into the human genome. The development of HCV is multifactorial, and its progression can take 20-40 years (*Gastroenterol Clin North Am* 2015; doi: 10.1016/j.gtc.2015.07.003). Consequently, people with an HCV infection may not be aware they have the disease. HCV is more likely to cause a chronic infection, as the immune system attacks the virus over time, liver fibrosis develops, and can result in cirrhosis and HCC.

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HCV is transmitted primarily through blood-blood contact and most people become infected by sharing needles or other equipment used to prepare and inject drugs. There is no vaccine for HCV. However, treatments can cure most people with hepatitis C in 8-12 weeks.

Human Immunodeficiency Virus

Human immunodeficiency virus (HIV) is a retrovirus that can cause the chronic, potentially life-threatening condition of acquired immunodeficiency syndrome (AIDS). More than 35 million people live with HIV worldwide.

HIV infects and destroys helper T cells in the immune system. As the number of T cells decreases, the immune system has a more difficult time fighting infections. HIV infection also causes certain B cells to grow, increasing the risk of overproduction and mutation. This weakening of the immune system caused by HIV infection can increase the risk of developing certain types of lymphomas, such as non-Hodgkin lymphoma, Hodgkin lymphoma, primary CNS lymphoma, leukemia, and myeloma. In addition to lymphomas, HIV increases the risk of Kaposi's sarcoma, cervical cancer, and cancers of the anus, liver, mouth and throat, and lungs.

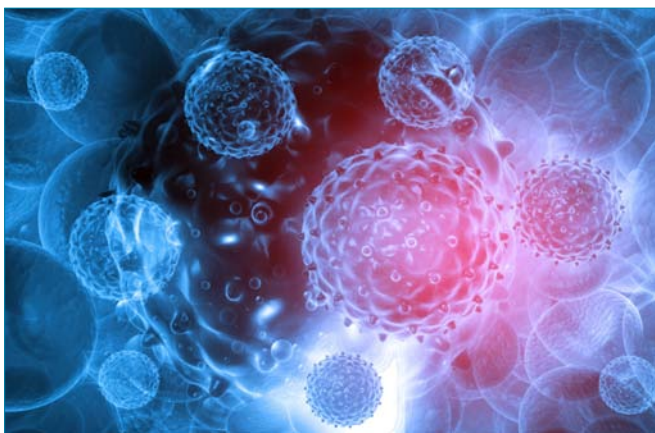
HIV spreads through bodily fluids, including blood, semen, and vaginal fluids. It can also be spread from a mother with HIV to the baby. While there is no cure, HIV can be controlled with treatment.

Human Herpesvirus 8

The human herpesvirus-8 (HHV-8), also called Kaposi sarcoma-associated herpesvirus, belongs to the family of DNA viruses known as Herpesviridae. It primarily causes Kaposi sarcoma, a type of cancer that affects the skin and soft organs. HHV8 is also associated with B-cell lymphoproliferative disorders such as primary effusion lymphoma and multicentric Castleman disease. An important consideration is that infection by multiple viruses is likely to be synergistic; the likelihood of HHV-8-associated cancers is significantly higher amongst individuals living with HIV.

Infection with HHV-8 is rare. It is estimated that only 1-5 percent of people in North America and Northern Europe are infected. Mediterranean populations have a higher infection rate (10-20%) and Sub-Saharan Africa has the highest rate (30-80%). In the U.S., gay men also have a higher infection rate (~40%).

HHV-8 is mostly spread through sexual contact and via saliva. Transmission also may occur through organ transplants and blood



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transfusions. There are several medications in various stages of clinical trials that target the various stages of the pathogenesis of HHV-8 associated diseases. The most favorable patient outcome for HHV-8-associated cancers involves a multidisciplinary approach.

Human Papillomavirus

Human papillomavirus (HPV) is the most common sexually transmitted virus in the world and is present in about 43 million Americans. It is transmitted via skin-skin contact with sexual intercourse being the most common route. When the HPV genome becomes integrated into human chromosomes, it interrupts an open reading frame and causes the overexpression of two viral oncogenes, which can eventually lead to cancer.

There are over 200 known genetically different strains of HPV. It is important to note that most HPV infections are cleared within 2 years. However, long-term HPV infection can lead to cellular changes and the development of several cancers.

There are 14 high-risk strains of HPV that can cause cancer in men and women, including anal, cervical, penile, throat, vaginal and vulvar, and head and neck cancers. Two high-risk strains, 16 and 18, are thought to be responsible for over 70 percent of cervical cancer cases. The HPV vaccine, available for individuals up to 45 years of age, prevents approximately 70-80 percent of cancer cases.

Human T-Cell Leukemia Virus Type

Human T-cell leukemia virus type, also called human T-lymphotrophic virus (HTLV-1) is a retrovirus which can infect T cells, B lymphocytes, monocytes, and fibroblasts. Globally, roughly 5-10 million people are infected. HTLV-1 is more common outside of the U.S. in areas such as Japan, the Caribbean, the Middle East, and in regions of Central Africa

and South America. Although HTLV-1 infection rarely causes serious disease, approximately 1-5 percent of people who have the virus get an aggressive type of cancer called acute T-cell leukemia/lymphoma (ATL).

Despite the association of HTLV-1 with cancer, its cancer-causing mechanisms remain unclear due to difficulties propagating this virus in tissue culture. Symptoms and its development are different for each person. Potential means of HTLV transmission include sexual or blood-blood contact, organ transplant, sharing needles with infected people, and from mother to child during birth or through breastfeeding. HTLV-1 is considered a lifelong condition and currently there are no cures or treatment.

Merkel Cell Polyomavirus

Merkel cell polyomavirus (MCV or MCPyV) is a recently discovered virus that infects the skin. MCV typically has no symptoms nor leads to cancer. But in some people, MCV causes a rare skin cancer that affects Merkel cells, leading to Merkel cell carcinoma (MCC). This neuroendocrine cancer has a disease-associated mortality of 46 percent, and it commonly occurs in sun-exposed individuals with weakened immune systems. Researchers are also looking to see if MCV is associated with other types of skin cancer, such as squamous cell carcinoma and basal cell carcinoma.

It remains unclear how MCV is transmitted; researchers believe skin-to-skin contact is most likely, along with encountering contaminated objects or surfaces. There are currently no vaccines for MCV infections; however, MCC is treatable, especially when found at an early stage.

Steps that can be taken to reduce the risk of getting oncoviruses include getting proper vaccinations, as well as getting screened as early detection is typically the most opportune time to treat cancers. Additionally, avoiding high-risk behaviors such as unprotected sex, illegal drugs, and sharing syringes/needles can significantly decrease a person's risk of infection. **OT**

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Learning Objectives for This Month's Activity:

After participating in this activity, readers should be better able to: 1. Distinguish the prevalence and distinct pathophysiology associated with eight oncologic viruses. 2. Summarize the mechanism of transmission, associated cancers, and recommendations for prevention of infection with specific oncologic viruses.

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