



## Cancer-Causing Viruses

Five viruses are being added to the Report on Carcinogens. All five are being listed as *known to be human carcinogens*, based on sufficient evidence from human studies. They all have been linked to cancer in humans. The viruses being added are:

- **Human immunodeficiency virus type 1 (HIV-1)**
- **Human T-cell lymphotropic virus type 1 (HTLV-1)**
- **Epstein-Barr virus (EBV)**
- **Kaposi sarcoma-associated herpesvirus (KSHV)**
- **Merkel cell polyomavirus (MCV)**

Given that about 12 percent of cancers worldwide are linked to viruses, and there are no vaccines available for any of these five viruses, prevention is critical for reducing potential cancer risks.

These five viruses are more likely to lead to cancer in people that have weakened immune systems, or immunosuppression.

These five viruses will be grouped with other viruses listed in previous reports, including hepatitis B, hepatitis C, and some human papillomaviruses.

### Key Points



- *All five viruses are known to be human carcinogens*
- *These five viruses are linked to more than 20 types of cancers*
- *People with weakened immune systems are more likely to develop these cancers*

**14<sup>th</sup>**  
**Report on  
Carcinogens**

### Viral exposures and cancers

#### **Human immunodeficiency virus type 1 (HIV-1)**

A virus spread through infected semen, vaginal fluids, or blood

##### **Sufficient evidence of cancer:**

- Cervical cancer
- Conjunctival eye cancer
- Hodgkin lymphoma
- Invasive anal cancer
- Kaposi sarcoma, a blood vessel cancer
- Non-Hodgkin lymphoma
- Non-melanoma skin cancer
- Penile cancer
- Vaginal/vulvar cancer

##### **Limited evidence of cancer:**

- Liver cancer
- Lung cancer
- Oral-related cancers

#### **Human T-cell lymphotropic virus type 1 (HTLV-1)**

A virus spread through contact with infected cells found in biological fluids or tissues

##### **Sufficient evidence of cancer:**

- Adult T-cell leukemia-lymphoma, a rare cancer

#### **Epstein-Barr virus (EBV)**

A herpes virus spread primarily by contact with infected saliva

##### **Sufficient evidence of cancer:**

- Burkitt lymphoma (endemic form)
- Extranodal natural killer/T-cell lymphoma (rare nasal type)
- Hodgkin lymphoma
- Immune-suppression-related non-Hodgkin lymphoma
- Nasopharyngeal carcinoma
- Some forms of stomach cancer

##### **Limited evidence of cancer:**

- Burkitt lymphoma (sporadic form)

#### **Kaposi sarcoma-associated herpesvirus (KSHV or HHV-8)**

A herpes virus spread through contact with infected saliva, blood, and bodily fluids

##### **Sufficient evidence of cancer:**

- Kaposi sarcoma, a blood vessel cancer
- Multicentric Castleman disease (plasmablastic variant)
- Primary effusion lymphoma

#### **Merkel cell polyomavirus (MCV or MCPyV)**

A virus where the spread is not fully understood, but close personal contact with infected saliva and skin, or from the environment, may contribute

##### **Sufficient evidence of cancer:**

- Merkel cell carcinoma, a rare skin cancer





## Human immunodeficiency virus type 1 (HIV-1)

### What is HIV and how are people exposed to it?

HIV is a virus that is spread through unprotected sexual activity, infected drug needles, during pregnancy from mother to child, and through infected breast milk. A significant number of people in the United States, approximately 1.2 million people, are infected with HIV. If left untreated, HIV can lead to the disease AIDS, acquired immunodeficiency syndrome.



### What evidence is there that HIV causes cancer?

There is sufficient human evidence to show that HIV increases the risk of seven types of cancer that are caused by infections from other viruses — Kaposi sarcoma; non-Hodgkin lymphoma; Hodgkin lymphoma; cervical, anal, vaginal/ vulvar, and penile cancers; and two other types of cancer — conjunctival eye cancer and non-melanoma skin cancer. Numerous studies in different populations provide evidence that people with HIV infection have a higher risk for these cancers compared to uninfected people of the same age.

Studies evaluating markers of a body's weakened immune system, or immunosuppression, such as decreased CD4 T cells, also support the link between these human viruses and cancer. Three of these cancers — Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer — are considered AIDS-defining cancers. A diagnosis of any of these three cancers means the HIV infection has progressed to AIDS.

There is only limited evidence from studies in humans for an association between HIV and lung cancer, liver cancer, or oral-related cancers, such as those occurring in the mouth or throat.

HIV-1 infection is associated with over 3,900 excess cancers in the United States. Fortunately, treatments referred to as HAART, highly active antiretroviral therapy, or cART, combination antiretroviral therapy, have been shown to reduce the level of HIV-1 in the blood and substantially decreased the risk of Kaposi sarcoma and non-Hodgkin lymphoma.

### How does HIV lead to cancer?

The HIV virus attacks the body's immune system, specifically white blood cells known as CD4 T cells that help fight off infection. An HIV infection can weaken the body's immune system and increase a person's risk of getting several infection-related cancers, such as those caused by other viruses. HIV also increases the risk of a few cancers not associated with infection from other viruses, however, it is not clear how HIV leads to these types of cancer.

### What are some things I can do to prevent transmission of the virus and, if infected, prevent my risk for cancer?

- Practice safe sex (use condoms and reduce sexual partners)
- Don't share needles or drug injection equipment
- If you are participating in high risk behaviors:
  - Get tested
  - Ask your doctor about PrEP, or pre-exposure prophylaxis
  - If you have been exposed to HIV, see a physician about post-exposure prophylaxis as soon as possible
- If infected, make choices that keep you healthy and protect others
  - Take prescribed treatments
  - Quit smoking

### For more prevention tips, visit:

#### Centers for Disease Control and Prevention

<http://www.cdc.gov/hiv/basics/prevention.html>

#### National Institute of Allergy and Infectious Diseases

<http://www.niaid.nih.gov/topics/hivaids/understanding/prevention>

#### National Cancer Institute

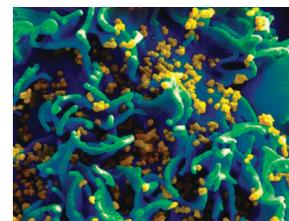
<http://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hiv-fact-sheet>

To view the NTP substance profile, go to [http://ntp.niehs.nih.gov/ntp/roc/content/profiles/viruses\\_hiv.pdf](http://ntp.niehs.nih.gov/ntp/roc/content/profiles/viruses_hiv.pdf)

## Human T-cell lymphotropic virus type 1 (HTLV-1)

### What is HTLV-1 and how are people exposed to it?

HTLV-1 is a virus that people are exposed to through contact with contaminated cells or biological tissues, such as breastfeeding, sharing of needles or syringes with infected individuals, organ transplants, or unprotected sexual activity. It is not transmitted by casual contact. Approximately 90,000 people in the United States are infected with HTLV-1, but only a very small number of infected people develop cancer or other diseases related to this virus.



This virus is most prevalent in Japan, the Caribbean, and the Middle East, with an estimated 5 million to 10 million people infected worldwide. Most HTLV-1-infected individuals have the virus in their bodies throughout their lifetime, but do not have any symptoms.



### What evidence is there that HTLV-1 causes cancer?

Human epidemiological studies and molecular studies show that HTLV-1 causes adult T-cell leukemia-lymphoma (ATLL). ATLL is a rare cancer that infects the body's T cells, specifically white blood cells known as CD4 T cells that help fight off infection.

### How does HTLV-1 lead to cancer?

A key HTLV-1 protein, called Tax, can initiate and promote cancer, especially in people who have a weakened immune system.

### What are some things I can do to prevent transmission of the virus and, if infected, prevent my risk for cancer?

- Practice safe sex (use condoms and reduce sexual partners)
- If infected, women should refrain from breastfeeding
- Periodic medical evaluations by a physician knowledgeable about this virus is recommended

### For more prevention tips, visit:

#### Centers for Disease Control and Prevention

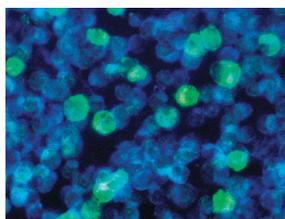
<http://www.cdc.gov/mmwr/preview/mmwrhtml/00021234.htm>

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## Epstein-Barr virus (EBV)

### What is EBV and how are people exposed to it?

EBV is a herpes virus, transmitted primarily through saliva. It may also be spread through contact with other types of bodily fluids, such as infected blood, genital fluids, and breast milk.



It is a common virus, infecting more than 90 percent of adults worldwide. Most people infected with EBV remain healthy and without symptoms. In some cases, EBV can cause infectious mononucleosis, also called mono. EBV was the first human virus ever linked to cancer, about 52 years ago.

### What evidence is there that EBV causes cancer?

Human epidemiological studies, clinical studies, and molecular studies show that Epstein-Barr virus can lead to four types of lymphoma — Burkitt, Hodgkin, Immune-suppression-related non-Hodgkin, and nasal type extranodal NK/T-cell lymphoma — and two types of epithelial cancer — nasopharyngeal cancer and some types of stomach cancer.

### How does EBV lead to cancer?

The way in which EBV leads to various EBV-related cancers is complex and continues to be researched. EBV is held in check by the immune system. For most EBV-related cancers, a weakened immune system can lead to the production of cancer-causing viral proteins. In addition, infectious agents, regional differences in diet, and an individual's genetic susceptibility and make-up can all potentially play a role in the development of some EBV-related cancers.

### What are some things I can do to prevent transmission of the virus and, if infected, prevent my risk for cancer?

- Don't share drinks, food, or personal items, such as toothbrushes, with people who have EBV infection

### For more prevention tips, visit:

#### Centers for Disease Control and Prevention

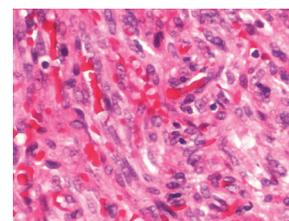
<http://www.cdc.gov/epstein-barr/about-ebv.html>

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## Kaposi sarcoma-associated herpesvirus (KSHV)

### What is KSHV and how are people exposed to it?

KSHV is a herpes virus transmitted from person to person, primarily through saliva. It can be transmitted from an infected mother to a child, and by contact with other infected family members. In adults, it can be



transmitted through sexual contact, primarily among men who have sex with men, and non-sexual routes, such as blood and organ transplants. Healthy individuals can be infected with the virus and show no signs or symptoms.

### What evidence is there that KSHV causes cancer?

There is sufficient human evidence linking KSHV to several cancers, including Kaposi sarcoma, a blood vessel cancer, and two rare lymphomas — primary effusion lymphoma, and a plasmablastic variant of multicentric Castleman disease. KSHV is part of the criteria for diagnosing all three of these cancers.

Kaposi sarcoma is a blood vessel cancer that mainly affects the skin, mouth, and lymph nodes. There are four types of Kaposi sarcoma. Approximately 90 percent of Kaposi sarcoma patients are infected with KSHV. More than 100 human studies have demonstrated a link between KSHV infection and all four types of Kaposi sarcoma.



Consistent human findings, coupled with information from tumor tissues, show that KSHV is also associated with primary effusion lymphoma. Additionally, studies of tumor tissue from KSHV-infected patients provide evidence for an association between KSHV infection and a plasmablastic variant of multicentric Castleman disease.

#### How does KSHV lead to cancer?

KSHV can cause cancer, especially in people with weakened immune systems, or immunosuppression, by transforming normal cells into cancer cells. Kaposi sarcoma is more likely to occur when an infected person becomes immunosuppressed, which can occur in transplant patients and patients receiving chemotherapy, and can be a major problem for persons with AIDS. Nevertheless, KSHV can also cause cancer in people not known to have impaired immune systems, suggesting that immunosuppression may not be required for cancer development.

#### What are some things I can do to prevent transmission of the virus and, if infected, prevent my risk for cancer?

- Practice safe sex (use condoms and reduce sexual partners)
- Patients diagnosed with Kaposi sarcoma should discuss treatment options with their physician

For more prevention tips, visit:

National Cancer Institute

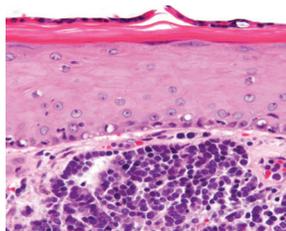
<http://www.cancer.gov/research/progress/snapshots/kaposi-sarcoma>

To view the NTP substance profile, go to [http://ntp.niehs.nih.gov/ntp/roc/content/profiles/viruses\\_kshv.pdf](http://ntp.niehs.nih.gov/ntp/roc/content/profiles/viruses_kshv.pdf)

### Merkel cell polyomavirus (MCV)

#### What is MCV and how are people exposed to it?

MCV is a common virus that was discovered in 2008. The virus infects the skin, but doesn't usually cause noticeable symptoms or lead to cancer. Healthy people continuously shed MCV from the skin surface throughout their lives, making its way into the environment. Therefore, practicing good hygiene may be beneficial. Close personal contact with saliva or skin may be how people are initially exposed to the virus during childhood.



#### What evidence is there that MCV causes cancer?

Human epidemiological studies of populations in different geographic locations, as well as clinical and molecular studies, show that MCV causes Merkel cell carcinoma, a rare but aggressive skin cancer. When cancer does occur, it is most common in elderly white men and people with weak immune systems. Tumors from almost all Merkel cell carcinoma patients contain integrated, mutated viral DNA, whereas cells from infected people without symptoms do not have the integrated form.

#### How does MCV lead to cancer?

MCV is thought to cause cancer through a complex process involving cancer-causing proteins and other environmental factors. People with weakened immune systems are more susceptible to getting cancer from this virus, because they are not able to suppress the infection. In some cases, the MCV DNA can integrate into a cell's healthy DNA in a mutated form, which can cause changes that lead to unregulated growth of the infected cell and potentially lead to Merkel cell carcinoma. Studies in cell culture and animal models show that certain mutated viral genes are needed for this type of cancer to develop. Ultraviolet light may be a key environmental factor that helps drive the development of Merkel cell carcinoma.

#### What are some things I can do to prevent transmission of the virus and, if infected, prevent my risk for cancer?

- Protect your skin from the sun by limiting your exposure to natural and artificial sunlight
- Monitor your skin, and consult a dermatologist if you notice changes. Merkel cell carcinoma typically appears as a relatively fast-growing, purple-colored bump on the skin.

For more prevention tips, visit:

National Cancer Institute

<http://www.cancer.gov/types/skin/patient/merkel-cell-treatment-pdq>

To view the NTP substance profile, go to [http://ntp.niehs.nih.gov/ntp/roc/content/profiles/viruses\\_mcv.pdf](http://ntp.niehs.nih.gov/ntp/roc/content/profiles/viruses_mcv.pdf)



National Toxicology Program  
U.S. Department of Health and Human Services

The Report on Carcinogens is prepared by the National Toxicology Program, an interagency group coordinated by the U.S. Department of Health and Human Services.

**The full report is available at**  
<http://ntp.niehs.nih.gov/go/roc14>.