***Review Article***

**An Overview of Herpes Virus: Clinical Features and Risk Factors**

**ABSTRACT**

Herpesviruses represent a pervasive and clinically significant group of DNA viruses capable of establishing lifelong infections in humans. Among more than 100 known herpes viruses, only 8 of them infect humans. Among them, herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), and varicella-zoster virus (VZV) are the most prevalent, contributing to a broad spectrum of diseases ranging from orolabial and genital lesions to severe neurological complications. Lethargy, malaise, and cervical or submandibular lymphadenopathy are associated symptoms. Worldwide, there are an estimated 4.85 billion people of all ages with prevalent HSV-1 infection. Moreover, there are an estimated 836 million people aged 15 years and above with prevalent HSV-2 infection, with prevalence again highest in the WHO Africa region. Despite decades of research, herpesviruses continue to pose major public health challenges due to their capacity for latency, reactivation, and evasion of host immune responses. This review provides a comprehensive overview of the epidemiology, virology, pathogenesis, clinical manifestations, diagnostic approaches, and current therapeutic strategies for managing herpesvirus infections. Emerging antiviral agents, vaccine development efforts, and novel therapeutic approaches, including gene editing and immunotherapies, are also discussed. Understanding these complex viral pathogens is essential for developing more effective prevention and treatment strategies. Future advancements in HSV's life cycle, protein interactions, and immune evasion mechanisms will pave the way for effective HSV vaccines to prevent or mitigate infections.

**Keywords:** Herpes simplex virus (HSV), Varicella-zoster virus (VZV), Herpesviridae, Reactivation, Genital herpes, Orolabial herpes

**INTRODUCTION**

Herpes simplex virus (HSV), known as herpes, is a common infection that can cause painful blisters or ulcers. It primarily spreads by skin-to-skin contact. It is treatable but not curable. Most people have no symptoms or only mild symptoms. The infection can cause painful blisters or ulcers that can recur over time (Musa et al., 2024). In regions such as sub-Saharan Africa, where as much as 80% of people living with HIV are seropositive for HSV-2, the dual burden compounds clinical disease and psychosocial sequelae and complicates treatment (Silva et al., 2022).

Medicines can reduce symptoms but can’t cure the infection. Recurrent symptoms of both oral and genital herpes may be distressing. Genital herpes may also be stigmatising and have an impact on sexual relationships. The virus replicates initially in epithelial cells, producing a characteristic vesicle on an erythematous base. It then ascends sensory nerves to the dorsal root ganglia, where, after an initial period of replication, it establishes latency. During reactivated infection, the virus spreads distally from the ganglion to initiate new cutaneous and/or mucosal lesions (Koca & Çetinkaya, 2025). Herpes simplex belongs to a group of eight related viruses, including HSV-1 and HSV-2, *varicella zoster* virus, *Epstein-Barr virus*, and *cytomegalovirus* (Bashir & Elhag, 2018). Worldwide, there are an estimated 4.85 billion people of all ages with prevalent HSV-1 infection. Moreover, there are an estimated 836 million people aged 15 years and above with prevalent HSV-2 infection, with prevalence again highest in the WHO Africa region. Infection with HSV is lifelong and is characterised by periodic recurrences of disease in a proportion of those infected (McCormick et al., 2022).

Among more than 100 known herpes viruses, only 8 of them infect humans. The structure of the herpes virus consists of

* Double-stranded DNA in the middle.
* Icosapentahedral capsid encircling the DNA
* A collection of tegument proteins envelops the capsid
* Outermost lipid bilayer envelope of membrane proteins and glycoproteins

**Subtypes**

* Alpha herpesviruses
* Beta herpesviruses
* Gamma herpesviruses

**CLASSIFICATION**

**Table 1: Classification of viruses**

|  |  |
| --- | --- |
| **Αlpha herpesviruses**  *Short replicative cycle, cause cytopathology in monolayer cell cultures, and have a wide host range* | Herpes simplex virus type 1(HSV 1)  Herpes simplex virus type 2(HSV 2)  Varicella-zoster virus(HHV 3) |
| **Βeta herpesviruses**  *Long replicative cycle and a limited host range* | Cytomegalovirus (HHV 5)  Human herpesviruses 6 (HHV 6) (variants A and B)  Human herpesviruses and 7 (HHV 7) |
| **Gamma herpesviruses**  *Very limited host range* | Epstein-barr virus (HHV 4)  Human herpesvirus 8 (HHV 8) [1] |

**HERPES SIMPLEX VIRUS 1**

The pathophysiology of HSV-1 infection generally consists of three stages: initial epithelial cell infection, latency (which mostly affects neurons) and reactivation. Primary and recurring vesicular eruptions, mostly in the vaginal and orolabial mucosa, are caused by HSV-1(2). HSV-1 is transmitted primarily through direct skin-to-mucosal contact (such as touching, kissing, and airborne droplets) and infects the skin and mucous membranes, including the central nervous system, eye, mouth, lips, metabolic system, respiratory system, and genitals (3).

**Risk factors**

* Activity that exposes one to the saliva of an infected patient, such as sharing cosmetics, drinkware or making contact with an infected person's mouth.
* Close shaving with a razor blade while suffering from an acute orolabial infection is the main risk factor for herpetic sycosis.
* High-contact sports, including boxing, rugby, and wrestling, are risk factors for herpes gladiatorum.
* Thumb sucking and nail biting in children with orolabial HSV-1 infection and working in the medical or dentistry field in adults are risk factors for herpetic whitlow.
* Mutations in the UNC-93B or toll-like receptor (TLR-3) genes are a significant risk factor for herpes encephalitis (2).

After starting to multiply at the infection site, HSV-1 moves in a retrograde manner down an axon and into the dorsal root ganglia (DRG). The DRG is where latency is determined. The virus can stay in a non-infectious condition for a variable length of time before reactivation. HSV-1 uses a number of strategies to avoid detection by the immune system. Inducing an intercellular buildup of CD1d molecules in antigen-presenting cells is one such approach. These CD1d molecules often travel to the cell surface, where the antigen is presented. There, they stimulate natural killer T-cells, which in turn boost the immune response. The immunological response is suppressed when CD1d molecules are intercellularly sequestered (2).

The clinical manifestations of mucocutaneous herpes simplex virus type 1 (HSV-1) disease are due to tissue destruction, a direct consequence of viral replication and cell lysis [1]. Inoculation of HSV-1 at mucosal surfaces or skin sites permits entry of the virus into sensory and autonomic nerve endings, through which it is transported to the cell nuclei (e.g., the trigeminal ganglion), where it remains latent. Reactivation results in recurrent HSV disease (e.g., herpes labialis) (4).

**Clinical features**

Children who have never been exposed to the virus before are typically the ones who get primary herpes gingivostomatitis. The majority of cases develop a prodrome of fever, anorexia, irritability and painful oral lesions, however, others may be asymptomatic. Lethargy, malaise, and cervical or submandibular lymphadenopathy are associated symptoms. Hyperaemia of the oral and perioral mucosa is the first symptom of herpetic gingivostomatitis. Vesicular lesions on the gingiva, palate, buccal and labial mucosa then progress quickly and finally burst. Ulcers bleed quickly and typically heal fully in two to three weeks without leaving any scars.

One-third of individuals with primary herpetic gingivostomatitis frequently develop recurrent herpes lesions. After experiencing burning and itching, the patient develops vesicular lesions in a specific location. Lesions typically appear on keratinised skin, such as the hard palate, perioral skin and vermillion border of the lips. Systemic illness, physical or emotional stress, trauma and exposure to sunshine may act as triggering factors. Every recurrence episode has the same lesions in the same location, and systemic symptoms like lymphadenopathy and malaise are minor (5).

**Treatment**

Supportive treatment is usually effective for herpes gingivostomatitis. It has been proposed that patients with active herpetic gingivostomatitis can avoid adhesions by using barrier lip lotions like petroleum jelly. Hydration is the most crucial element in the treatment of herpetic gingivostomatitis. Since pain management frequently results in adequate hydration, analgesics such as oral acetaminophen and mouth rinses are recommended to ease patient discomfort and improve fluid intake. It is crucial to remember that hospitalisation is necessary for patients who are unable to consume enough water to stay well hydrated (5).

**Differential diagnosis**

* Herpes zoster
* Primary chickenpox
* Behcet disease
* Herpetiform aphthae
* Erythema multiforme
* Acute necrotizing gingivostomatitis
* Reactive arthritis
* Cytomegalovirus ulceration
* Traumatic ulcers
* Burns, chemical and thermal
* Factitial injuries
* Vesiculobullous disease(5)

**HERPES SIMPLEX VIRUS 2**

The herpes simplex virus type 1 or type 2 can cause herpes genitalis, which can appear as a primary or recurring illness. Viral replication most frequently takes place in epithelial tissue, where it causes sensory neurons to go dormant before reactivating sporadically as localised recurrent lesions.HSV-2 is more commonly considered when patients present with genital lesions. It presents with nonspecific symptoms such as genital itching, irritation, and excoriations (6).

**Etiopathogenesis**

Direct contact with fluids (saliva) from a seropositive person carrying viral products, usually during sexual activity, is one of the risk factors for contracting an HSV-2 infection. The primary way that HSV-2 is spread is through sexual contact, which explains why it is more common after puberty. HSV is only contagious for a few days on moist surfaces because of its poor stability outside the body. As a result, transmission methods other than sexual contact are frequently negligible. Congenital HSV infection can develop from intrauterine transmission of primary or recurrent HSV infections in pregnant women (6)(7).

The virus primarily targets the skin and mucous membranes, where it first invades epithelial cells before intracellular replication takes place. The virus then lies dormant in the periaxonal sheath of the sensory nerves of the trigeminal, cervical, lumbosacral, or autonomic ganglia after the initial exposure and symptoms subside, which usually takes 10 to 14 days. In these areas, the patient's immune system frequently regulates viral replication, which stays dormant until reactivating later in life (6) (8).

**Treatment**

Nucleoside analogue-polymerase inhibitors and pyrophosphate analogue-polymerase inhibitors are examples of antiherpesviral drugs. Acyclovir, which has FDA approval for treating and inhibiting both HSV and VZV and has antiviral action against all herpesviruses, continues to be the cornerstone of treatment.

Acyclovir: Available in topical, oral, and IV formulations. The oral formulation has quite a poor bioavailability, which has been improved with valacyclovir. It has a low side effect profile, which allows it to be tolerated for long periods. Suppressive treatment with acyclovir can prevent or delay up to 80% of recurrences, thus reducing shedding by greater than 90%. Reported side effects include kidney toxicity and neutropenia when given at high doses. Given its chronicity of use, resistance has been reported in immunocompromised patients and those who are immunocompetent taking acyclovir as suppressive therapy for genital herpes. High dosages have been known to cause side effects such as neutropenia and renal damage.

* Primary herpes genitalis: 3 x 400 mg tablets PO daily for 7 to 10 days
* Severe primary herpes genitalis: 3 x 5 mg/kg IV daily for 5 to 7 days
* Recurrent herpes genitalis (less than 5 to 6 episodes/year): 400 mg PO twice a day for 3 days
* Prophylaxis: 2 x 400 mg PO daily for 6 months

*Valacyclovir is another formulation option*

* Primary herpes genitalis: 2 x 500 mg tablets PO daily for 7 to 10 days
* Recurrent herpes genitalis (less than 5 to 6 episodes/year): 2 x 500 mg PO twice daily for 3 days
* Prophylaxis: 1 x 500 mg PO daily for 6 months (6)

**Differential diagnosis**

Infectious genital ulcerative conditions

* Syphilis
* Chancroid
* Lymphogranuloma venereum
* Granuloma inguinale

Non-infectious genital ulcerative conditions

* Crohn disease
* Behcet syndrome
* Fixed drug eruptions
* Psoriasis
* Sexual trauma (6)

**VARICELLA ZOSTER VIRUS (HHV 3)**

The varicella-zoster virus (VZV) is the infectious agent that causes chickenpox, often known as varicella. Inhaled aerosolised droplets of an infected person can cause chickenpox. The average incubation time is roughly two weeks, however, symptoms start to appear ten to twenty-one days following exposure. Up to decades later, latent VZV may reactivate, either spontaneously or following one or more of a variety of triggering factors, to cause herpes zoster (shingles), which usually appears as a painful or pruritic cutaneous vesicular eruption that occurs in a characteristic dermatomal distribution.

**Clinical features**

The upper airway mucosa is the site of the first infection. After two to six days, the virus reaches the bloodstream, and ten to twelve days later, viremia strikes again. This is when the distinctive vesicle emerges. A skin rash that scabs over and forms tiny, irritating blisters is the outcome of chickenpox. Usually, it begins on the chest, back and face before spreading. It often lasts five to seven days and is accompanied by fever, exhaustion, pharyngitis, and headaches. Reactivation can cause herpes zoster (shingles), post-herpetic neuralgia and occasionally Ramsay Hunt syndrome type II.

*Complications* – stroke, encephalitis, segmental motor weakness and myelopathy, cranial neuropathies, Guillain–Barré syndrome, enteric features and zoster sine herpete (9)(10).

**Treatment**

Treatment is usually symptomatic. Topical calamine lotion may relieve pruritus. Daily cleansing with warm water helps avoid secondary bacterial infection. Acetaminophen may be used to reduce fever. Avoid aspirin as it may cause Reye syndrome.

*In children*, if acyclovir is administered within 24 hours of the rash beginning, symptoms are reduced by one day. However, it has little effect on the rate of complications and is not advised for people with good immune systems.

*In adults*, infection tends to be more severe, and treatment with antiviral drugs (acyclovir or valacyclovir) is advised if they can be started within 24 to 48 hours of rash onset. Although oral therapy is typically the preferred method of treatment, immunocompromised patients may benefit from injectable antivirals.

**Differential diagnosis**

* Insect bites
* Impetigo
* Smallpox
* drug eruptions
* dermatitis herpetiformis(9)

**Prophylaxis**

A live attenuated vaccine (OKA varicella vaccine) against VZV received FDA approval in March 1995 (11).

**HHV 4**

Epstein-Barr virus is a herpesvirus with double-stranded DNA surrounded by proteins. There are two kinds of EBV subtypes: type 1 and type 2. The virus causes B cells to differentiate into memory B cells, which subsequently travel into the circulatory system or become latent until a stimulus prompts reactivation (12). In 1964, Epstein-Barr virus (EBV) was identified by electron microscopic examination of suspension cultures of African Burkitt lymphoma cells (13).

**Clinical features**

EBV is the first human tumour-causing virus to be found (14). In the 1980s, EBV was discovered to be related to non-Hodgkin lymphoma and oral hairy leukoplakia in patients with acquired immunodeficiency syndrome (AIDS) (15,16). It has the ability to avoid immune surveillance and generate persistent latent infections, while also contributing to a wide range of diseases (17).

In younger children, EBV infection is typically moderate or asymptomatic. When a primary infection happens in adolescence, clinical illness typically results. At least 90% of infectious mononucleosis cases are caused by EBV. The symptoms of EBV-induced mononucleosis include fever, pharyngitis, lymphadenopathy, hepatosplenomegaly, and malaise. The infection usually resolves on its own. Mononucleosis, sometimes known as the kissing disease, is contracted by teenagers and young adults in their early twenties by close contact with an EBV-infected individual. It can also cause tumours in the lymphoid tissue as well as naso- and oropharyngeal epithelial tissue (18).

**Differential diagnosis**

* Bacterial pharyngitis
* Viral pharyngitis
* Cytomegalovirus infection (19)

**Treatment**

Epstein-Barr virus is managed symptomatically with drugs that lower fever and discomfort. Nucleosides are the only group of antiviral medicines that have been investigated for treating EBV infections in controlled clinical studies. Some of the antivirals are acyclovir, valacylovir, ganciclovir and valganciclovir. Corticosteroids can be helpful in patients who develop airway impairment or autoimmune problems induced by EBV infection (13).

**HHV 5**

HHV 5 is often commonly known as cytomegalovirus, and it belongs to the family of herpesviruses. Cytomegalovirus (CMV) is a prevalent virus that causes mild to severe end-organ damage in immunocompromised patients with congenital CMV illness (20). The cytomegalovirus is distributed in bodily fluids including saliva, urine, breast milk, sperm, and blood (21). Human CMV infections are frequently connected with the salivary glands. After infection, CMV frequently remains dormant, although it might reactivate at any time. (20)

**Differential diagnosis**

* HIV
* HHV 6 infection
* Viral hepatitis
* Epstein-Barr virus
* Infectious mononucleosis (20)

**Treatment**

IV ganciclovir, IV foscarnet, IV cidofovir and oral valganciclovir are antiviral options for CMV retinitis. IV ganciclovir 6 mg/kg body weight/dose is administered 12 hourly as the initial treatment for HIV-infected infants with CMV disease (22).

**HHV 6**

HHV-6 is the collective name for the double-stranded DNA viruses HHV-6A and HHV-6B. In the immunocompromised host, HHV-6A is more common. HHV-6B, on the other hand, has been found to be the causative agent of roseola infantum in the paediatric population (23).

**Etiopathogenesis**

HHV-6A and HHV-6B both proliferate in T-cells, but their receptors for cellular entry differ. HHV-6A uses the human cluster differentiation 46 (CD46), whereas HHV-6B uses the primary receptor cluster differentiation 134 (CD134) (24). Studies show that the virus is carcinogenic and damaging to autoimmune cells. HHV-6 attaches to the CD46 cellular receptor on CD4 cells, where it mostly infects and undergoes replication. Viral replication occurs after HHV-6 enters cells through receptor-mediated endocytosis. The virus's DNA resides in peripheral blood mononuclear cells (PBMC) following the initial infection.

**Clinical features**

Roseola infantum is characterised by high fever, mild skin rash, periorbital oedema, conjunctivitis, inflammation of the tympanic membranes, lymphadenopathy, gastrointestinal (GI) symptoms including liver dysfunction and hepatitis, bulging fontanelles and respiratory tract infections. when the fever subsides, there is development of a blanching maculopapular rash that is rose-pink, 2 to 5 mm in size, and has a halo around it. The rash usually spreads centrifugally and lasts for one to two days. Fever, graft versus host disease (GVHD), graft rejection symptoms, interstitial pneumonitis, myelitis, and rash are common symptoms in transplant recipients.

**Differential diagnosis**

* Infectious mononucleosis
* Cytomegalovirus infection
* Viral hepatitis, Herpes simplex virus infection
* Meningitis Rubella Viral pneumonia
* DRESS syndrome (Drug rash with eosinophilia and systemic symptoms (23).

**Treatment**

Treatment for children with roseola infantum is supportive (25). Management with ganciclovir has established benefits in patients undergoing stem-cell transplantation and is the recommended antiviral of choice (23).

**HHV 7**

HHV-7 belongs to the Roseola virus genus within the Betaherpesvirinae subfamily. Like HHV-6, it causes initial infection in most people during childhood (26). Human herpesvirus 7 (HHV-7) is a common virus linked to a variety of human diseases, including fever syndromes, dermatological lesions, neurological disorders and transplantation.

Recurrent or (re)infection of HHV-7 has been linked with multiple complications in transplant recipients, in spite of the presence of other concomitant infections. These complications include CNS disease, hepatitis, bronchiolitis, pneumonia, transplant rejection and CMV disease. It is also associated with a variety of clinical syndromes outside the context of transplantation and in immunocompetent individuals, including mononucleosis-like illnesses, acute respiratory distress syndrome, interstitial pneumonia, hepatitis, myocarditis, fibromyalgia, connective tissue disease and periodontitis (27). From a practical standpoint, immunocompetent individuals with uncomplicated skin manifestations linked to HHV-7, especially roseola infantum and pityriasis rosea, require only symptomatic and supportive care (28).

**HHV 8**

As the AIDS epidemic unfolded in the 1980s, human herpesvirus/Kaposi sarcoma herpesvirus (HHV-8) was identified as a causative factor of Kaposi sarcoma. Kaposi sarcoma, in its most recognised manifestation, appears in patients with immunodeficiency (29).

**Etiopathogenesis**

All variants of Kaposi sarcoma contain human herpesvirus-8 (HHV-8). HHV-8 disrupts various normal cellular processes and necessitates cofactors such as cytokines or particular proteins for the development of Kaposi sarcoma. Transmission occurs mainly through saliva during childhood and through sexual contact, with some instances of infection via blood transfusion or intravenous drug use. Family members who are seropositive will frequently transmit the infection to other relatives, especially in regions where HHV-8 is endemic. By infecting endothelial cells, HHV-8 activates the mTOR pathway, induces mesenchymal differentiation in the cells, and fosters abnormal angiogenesis (30)

**Differential diagnosis**

The differential diagnosis of HSV-8 on mucocutaneous surfaces comprises

* Nevi
* Pyogenic granuloma
* Bacillary angiomatosis
* Hemangioma
* Angiosarcoma
* Melanoma(31)

**Treatment**

Patients suffering from HIV-related Kaposi sarcoma show a good response to HAART. In individuals suffering from severe Kaposi sarcoma, combining HAART with chemotherapy is preferred (31).

**Conclusion**

In conclusion, understanding the complexities of viral pathogens is essential for developing more effective prevention and treatment strategies. Future advancements in HSV's life cycle, protein interactions, and immune evasion mechanisms will pave the way for effective HSV vaccines to prevent or mitigate infections.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

Option 2:

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc. have been used during the writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

1.

2.

3.

**REFERENCES:**

1. Whitley RJ. Herpesviruses. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 68. Available from: https://www.ncbi.nlm.nih.gov/books/NBK8157/
2. Saleh D, Yarrarapu SNS, Sharma S. Herpes Simplex Type 1. 2023 Aug 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29489260.
3. Su D, Han L, Shi C, Li Y, Qian S, Feng Z, Yu L. An updated review of HSV-1 infection-associated diseases and treatment, vaccine development, and vector therapy application. Virulence. 2024 Dec;15(1):2425744. doi: 10.1080/21505594.2024.2425744. Epub 2024 Nov 13. PMID: 39508503; PMCID: PMC11562918.
4. Blevins JY. Primary herpetic gingivostomatitis in young children. Pediatr Nurs. 2003 May-Jun;29(3):199-202. PMID: 12836996.
5. Aslanova M, Ali R, Zito PM. Herpetic Gingivostomatitis. [Updated 2023 Jun 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526068/
6. Mathew Jr J, Sapra A. Herpes Simplex Type 2. 2024 Mar 13. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 32119314.
7. Sauerbrei A. Herpes Genitalis: Diagnosis, Treatment and Prevention. Geburtshilfe Frauenheilkd. 2016 Dec;76(12):1310-1317. [[PMC free article](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5177552/)] [[PubMed](https://pubmed.ncbi.nlm.nih.gov/28017972)]
8. Mbopi-Keou FX, Robinson NJ, Mayaud P, Belec L, Brown DW. Herpes simplex virus type 2 and heterosexual spread of human immunodeficiency virus infection in developing countries: hypotheses and research priorities. Clin Microbiol Infect. 2003 Mar;9(3):161-71. doi: 10.1046/j.1469-0691.2003.00550.x. PMID: 12667248.
9. Ayoade F, Kumar S. Varicella-Zoster Virus (Chickenpox). 2022 Oct 15. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 28846365.
10. Kennedy PGE, Gershon AA. Clinical Features of Varicella-Zoster Virus Infection. Viruses. 2018 Nov 2;10(11):609. doi: 10.3390/v10110609. PMID: 30400213; PMCID: PMC6266119.
11. McCrary ML, Severson J, Tyring SK. Varicella zoster virus. J Am Acad Dermatol. 1999 Jul;41(1):1-14; quiz 15-6. doi: 10.1016/s0190-9622(99)70398-1. PMID: 10411403.
12. Hoover K, Higginbotham K. Epstein-Barr Virus. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 32644711.
13. Odumade OA, Hogquist KA, Balfour HH Jr. Progress and problems in understanding and managing primary Epstein-Barr virus infections. Clin Microbiol Rev. 2011 Jan;24(1):193-209. doi: 10.1128/CMR.00044-10. PMID: 21233512; PMCID: PMC3021204.
14. Yu H, Robertson ES. Epstein-Barr Virus History and Pathogenesis. Viruses. 2023 Mar 9;15(3):714. doi: 10.3390/v15030714. PMID: 36992423; PMCID: PMC10056551.
15. Ziegler JL, Drew WL, Miner RC, Mintz L, Rosenbaum E, Gershow J, Lennette ET, Greenspan J, Shillitoe E, Beckstead J, Casavant C, Yamamoto K. Outbreak of Burkitt's-like lymphoma in homosexual men. Lancet. 1982 Sep 18;2(8299):631-3. doi: 10.1016/s0140-6736(82)92740-4. PMID: 6125777.
16. Greenspan JS, Greenspan D, Lennette ET, Abrams DI, Conant MA, Petersen V, Freese UK. Replication of Epstein-Barr virus within the epithelial cells of oral "hairy" leukoplakia, an AIDS-associated lesion. N Engl J Med. 1985 Dec 19;313(25):1564-71. doi: 10.1056/NEJM198512193132502. PMID: 2999595.
17. Silva JM, Alves CEC, Pontes GS. Epstein-Barr virus: the mastermind of immune chaos. Front Immunol. 2024 Feb 7;15:1297994. doi: 10.3389/fimmu.2024.1297994. PMID: 38384471; PMCID: PMC10879370.
18. Slots, J., Saygun, I., Sabeti, M. and Kubar, A. (2006), Epstein–Barr virus in oral diseases. Journal of Periodontal Research, 41: 235-244. <https://doi.org/10.1111/j.1600-0765.2006.00865.x>
19. Taylor GH. Cytomegalovirus. Am Fam Physician. 2003 Feb 1;67(3):519-24. PMID: 12588074.
20. Gupta M, Shorman M. Cytomegalovirus. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29083720.
21. Akpan US, Pillarisetty LS. Congenital Cytomegalovirus Infection. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 31082047.
22. Ngai JJ, Chong KL, Oli Mohamed S. Cytomegalovirus Retinitis in Primary Immune Deficiency Disease. Case Rep Ophthalmol Med. 2018 Sep 19;2018:8125806. doi: 10.1155/2018/8125806. PMID: 30327738; PMCID: PMC6169215.
23. King O, Al Khalili Y. Herpes Virus Type 6. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 31082042.
24. Pantry SN, Medveczky PG. Latency, Integration, and Reactivation of Human Herpesvirus-6. Viruses. 2017 Jul 24;9(7):194. doi: 10.3390/v9070194. PMID: 28737715; PMCID: PMC5537686.
25. John L Kiley ,Human Herpesvirus 6 (HHV-6) Infection Treatment & Management https://emedicine.medscape.com › 219019-treatment
26. Human Herpesvirus 7 - an overview ScienceDirect.com https://www.sciencedirect.com › topics › neuroscience
27. Verbeek R, Vandekerckhove L, Van Cleemput J.2024.Update on human herpesvirus 7 pathogenesis and clinical aspects as a roadmap for future research. J Virol98:e00437-24.https://doi.org/10.1128/jvi.00437-24
28. Wolz MM, Sciallis GF, Pittelkow MR. Human herpesviruses 6, 7, and 8 from a dermatologic perspective. Mayo Clin Proc. 2012 Oct;87(10):1004-14. doi: 10.1016/j.mayocp.2012.04.010. Epub 2012 Jul 21. PMID: 22819486; PMCID: PMC3538396.
29. Stănescu L, Foarfă C, Georgescu AC, Georgescu I. Kaposi's sarcoma associated with AIDS. Rom J Morphol Embryol. 2007;48(2):181-7. PMID: 17641807.
30. Mariggiò G, Koch S, Schulz TF. Kaposi sarcoma herpesvirus pathogenesis. Philos Trans R Soc Lond B Biol Sci. 2017 Oct 19;372(1732):20160275. doi: 10.1098/rstb.2016.0275. PMID: 28893942; PMCID: PMC5597742.
31. Bishop BN, Lynch DT. Kaposi Sarcoma. [Updated 2023 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK534839/>
32. Musa, M., Enaholo, E., Aluyi-Osa, G., Atuanya, G. N., Spadea, L., Salati, C., & Zeppieri, M. (2024). Herpes simplex keratitis: A brief clinical overview. World Journal of Virology, 13(1), 89934.
33. Koca, R., & Çetinkaya, E. A. (2025). Herpes Simplex Viruses in Children. In Pediatric Airway Diseases (pp. 859-879). Cham: Springer Nature Switzerland.
34. Bashir, R. A., & Elhag, W. I. (2018). Molecular Detection of Herpes Simplex Virus Types [1 and 2] in Oropharyngeal Squamous Cell Carcinoma (OSCC) in Khartoum Dental Education Hospital. *Journal of Advances in Medicine and Medical Research*, *26*(9), 1–6.
35. McCormick, I., James, C., Welton, N. J., Mayaud, P., Turner, K. M. E., Gottlieb, S. L., ... & Looker, K. J. (2022). Incidence of herpes simplex virus keratitis and other ocular disease: global review and estimates. *Ophthalmic epidemiology*, *29*(4), 353-362.
36. Silva, S., Ayoub, H. H., Johnston, C., Atun, R., & Abu-Raddad, L. J. (2022). Estimated economic burden of genital herpes and HIV attributable to herpes simplex virus type 2 infections in 90 low-and middle-income countries: A modeling study. *PLoS medicine*, *19*(12), e1003938.