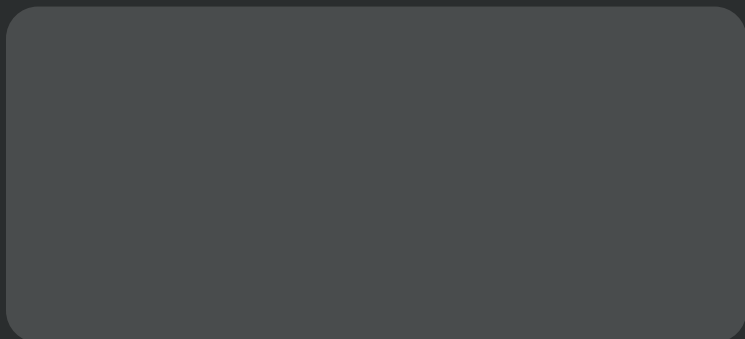




80152611 © CherriesJd | Dreamstime.com

Big fat happy herpes family: Oral manifestations of human herpesvirus infections

A peer-reviewed article written by Sherri Lukes, MS, RDH, FAADH; & Stacey McKinney, MEd, PHDH, RDH



PUBLICATION DATE: MARCH 2023

EXPIRATION DATE: APRIL 2026

EARN
3 CE
CREDITS

Big fat happy herpes family: Oral manifestations of human herpesvirus infections

Abstract

Many viruses affecting the US population have intra- and extraoral manifestations; this is especially true of the herpes family of viruses. This course is an evidence-based presentation of the human herpesvirus (HHV) infections that produce symptoms in and around the oral cavity. Treatment options and therapies for alleviating discomfort from oral lesions will be discussed as well as potential conditions/lesions to be included in the differential diagnosis. Dental professionals play a major role in assisting with diagnosis of HHV infections.

Educational objectives

Upon completion of the course, participants will be able to:

1. Describe the pathogenesis of human herpesvirus (HHV) infections affecting the oral cavity and head/neck region
2. Identify oral lesions associated with HHV infections
3. Discuss treatment options and palliative procedures for alleviating symptoms of HHV infections
4. Explain the hygienist's role in assisting the dentist with diagnosis of HHV infections



Go online to take this course.
DentalAcademyofCE.com

QUICK ACCESS code 22125

This continuing education (CE) activity was developed by Endeavor Business Media with no commercial support.

This course was written for dentists, dental hygienists, and dental assistants, from novice to skilled.

Educational methods: This course is a self-instructional journal and web activity.

Provider disclosure: Endeavor Business Media neither has a leadership position nor a commercial interest in any products or services discussed or shared in this educational activity. No manufacturer or third party had any input in the development of the course content.

Presenter disclosure: Author discloses that they do have a leadership or financial relationship to disclose related to this continuing education activity.

Requirements for successful completion: To obtain three (3) CE credits for this educational activity, you must pay the required fee, review the material, complete the course evaluation, and obtain an exam score of 70% or higher.

CE planner disclosure: Laura Winfield, Endeavor Business Media dental group CE coordinator, neither has a leadership nor commercial interest with the products or services discussed in this educational activity. Ms. Winfield can be reached at lwinfield@endeavorb2b.com or 800-633-1681.

Educational disclaimer: Completing a single continuing education course does not provide enough information to result in the participant being an expert in the field related to the course topic. It is a combination of many educational courses and clinical experience that allows the participant to develop skills and expertise.

Image authenticity statement: The images in this educational activity have not been altered.

Scientific integrity statement: Information shared in this CE course is developed from clinical research and represents the most current information available from evidence-based dentistry.

Known benefits and limitations of the data: The information presented in this educational activity is derived from the data and information contained in the reference section.

Registration: Rates for print CE have increased due to the manual nature of producing and grading courses in this format. For a lower-cost option, scan the QR code or go to dentalacademyofce.com to take this course online. **MAIL/FAX:** \$69 for three (3) CE credits. **DIGITAL:** \$39 for three (3) CE credits.

Cancellation and refund policy: Any participant who is not 100% satisfied with this course can request a full refund by contacting Endeavor Business Media in writing.

Provider information:

Dental Board of California: Provider RP5933. Course registration number CA code: 03-5933-22125. Expires 7/31/2024.

"This course meets the Dental Board of California's requirements for three (3) units of continuing education."



Endeavor Business Media is a nationally approved PACE program provider for FAGD/MAGD credit. Approval does not imply acceptance by any regulatory authority or AGD endorsement. 11/1/2019 to 10/31/2024. Provider ID# 320452. AGD code: 730



American Academy of Dental Hygiene
Approved provider through December 31, 2024

Endeavor Business Media is designated as an approved Provider by the American Academy of Dental Hygiene, Inc. #AADHPNW (January 1, 2023–December 31, 2024). Approval does not imply acceptance by a state or provincial Board of Dentistry. Licensee should maintain this document in the event of an audit. AADH code: ADHEBM-010-4-2023-3

ADA CERP® | Continuing Education
Recognition Program

Endeavor Business Media is an ADA CERP-recognized provider. ADA CERP is a service of the American Dental Association to assist dental professionals in identifying quality providers of dental continuing education. ADA CERP does not approve or endorse individual courses or instructors, nor does it imply acceptance of credit hours by boards of dentistry. Concerns or complaints about a CE provider may be directed to the provider or to ADA CERP at ada.org/cerp.



Introduction

Viruses are obligate parasites, completely dependent upon their hosts for survival and reproduction. They are the simplest and smallest microorganisms that infect humans and must infect a living cell to reproduce. Although viruses share several features with living organisms, such as the presence of genetic material, deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), they are not considered to be alive. Virus structure includes either DNA or RNA, which is surrounded by a protein coat also known as the capsid or envelope.¹ These two structures are called the nucleocapsid or core (virion) of the virus, which is responsible for causing infection. Unlike cells, which contain all of the structures needed for growth and reproduction (organelles), viruses are composed of only an outer coat (capsid), the genome, and in some cases, a few enzymes. Together these make up the virion, or virus particle.²

To be able to enter a cell, the virus must find a cell with a surface receptor specific for that particular virus. The matching of a virus with a specific cell type is termed “tropism.” When a match occurs, the virion penetrates the cell wall and enters the cytoplasm. It sheds its envelope, disintegrates, and DNA viruses enter the nucleus, fusing to the host’s DNA, while RNA viruses typically stay in the cytoplasm.¹ Retroviruses are an exception in that they use the host’s DNA to replicate their RNA genome.³

Viruses are primarily classified by their phenotypic characteristics such as morphology, type of nucleic acid, mode of replication, host organisms, and the type of disease they cause. Ultimately, all viruses alter the metabolic and protein synthesis pathways of the host to serve their own needs, causing death to the host cell and allowing replicated viruses to infect cells of adjacent tissue. Some viruses have the ability to enter a stage of latency.³ Latency occurs when the virus has entered a host cell, yet there are no detectable clinical lesions or antigens. This is an important aspect of some viruses, as latency appears to play a role in carcinogenesis as the persistence among select viruses. As highlighted in this course, the human herpesviruses all share a characteristic

ability to remain latent within the body over long periods of time, remaining with the individual for life.^{2,4,5}

Human herpesviruses

The term “herpes” comes from the ancient Greek word meaning “to creep or crawl,” which suggests the tendency for spreading, latency, or recurrent infection. There are more than 100 known herpesviruses with eight affecting humans, known collectively as the family *Herpetoviridae*.⁶ They are double-stranded DNA viruses numbering 1-8 and consist of herpes simplex virus types 1 and 2 (HSV1 or HHV-1, HSV2 or HHV-2), varicella-zoster virus (VZV or HHV-3), Epstein-Barr virus (EBV or HHV-4), cytomegalovirus (CMV or HHV-5), and human herpesviruses 6, 7, and 8 (HHV-6, HHV-7, HHV-8).⁷

Herpes simplex viruses and varicella zoster viruses are all neurotropic whereas the remaining “family members,” EBV, CMV, and HHV 6, 7, and 8, are considered lymphotropic.^{3,8} All human herpesviruses can enter and replicate in epithelial cells. In addition, some herpesviruses have oncogenic potential. Dental practitioners will primarily encounter oral manifestations of HSV-1, VZV, and EBV infection; therefore, this article concentrates on those three members of the herpes family.^{4,5}

Herpes simplex virus type 1

Approximately 75%–90% of the population is or will be infected with the ubiquitous herpes simplex virus type 1 (HSV-1).⁷ It enters the body through breaks in the skin and mucous membranes, with an incubation period of one to 26 days.⁶ Primary infection is usually in childhood or adolescence and most commonly subclinical, or producing only mild symptoms. A small percentage of the population infected with HSV-1 will experience a clinical infection with significant symptoms known as acute primary herpetic gingivostomatitis.¹ In the acute form, the infected person will present with multiple shallow intraoral ulcers on both keratinized and moveable mucosa with variable pain. Lesions begin as vesicles but immediately rupture, forming shallow ulcers.^{1,4,5} As the name implies, most

cases will present with significant gingivitis. Vesicles may also be present on the lips and/or periorally. In both mild and severe cases, persons experience fever and lymphadenopathy lasting two to 20 days. They may even experience myalgia and malaise with discomfort during eating and swallowing food. Treatment for acute HSV-1 is mostly palliative in nature, including analgesics, antipyretics, and other supportive therapies.^{4,5,9,10} After diagnosis by the dentist, hygienists can recommend over-the-counter (OTC) products, whereas any prescription remedy must be prescribed by the dentist.

Upon entering the body, HSV-1 infects the peripheral nerves and migrates to a regional ganglion where it remains latent and undetected by the immune system and protected from therapeutic agents.^{11,12} It remains in the latent phase for the life of the individual unless reactivated.^{3,12} Reactivation results in migration along the nerve axon to surface epithelial cells and can be triggered by a number of factors including stress, illness, trauma, cold, sunlight, menstrual cycle, and/or any other factors that may suppress the immune system.^{11,12} The lay term “cold sore” was the result of herpetic lesions following an upper respiratory infection. Most reactivation of HSV-1, or recurrent HSV-1, includes migration to the lip or perioral region, resulting in formation of multiple vesicles that typically begin at the vermilion border and spread either onto the lip or perioral skin.^{9,10} Recurrent outbreaks affecting the lips is known as herpes labialis, easily identified by dental professionals. Vesicle formation is preceded by a prodromal stage of tingling, itching, or feeling of fullness in the area where lesions will appear.^{4,5,11} Lesions remain three to 10 days, eventually rupturing and/or crusting before resolving.^{4,5,12}

Not nearly as common as recurrent herpes labialis are recurrent intraoral HSV-1 lesions.^{9,10,12} Unlike herpes labialis, the vesicular stage is rarely visualized intraorally. Patients present with multiple punctate red and shallow ulcerations as the epithelium covering the vesicle immediately ruptures, forming a cluster of small ulcerations that over the course of a few days will often coalesce, forming

one large ulcerative lesion.⁵ In most cases, the lesions will appear only on keratinized or bound-to-bone tissue, which includes the hard palate and attached gingiva^{6,9,10} (**figure 1**). Pain and duration of lesions vary, but typically are similar to those of herpes labialis. The most common area is on the palatal slope of the attached gingiva near the junction of the attached gingiva and hard palate, the region of the greater palatine foramen.^{4,5,13}

Those affected by recurrent herpes lesions may report myriad “treatment” modalities. There are multiple OTC products for providing relief from HSV-1 lesions with varying efficacy claims by the manufacturers. Patients may try multiple products before seeking prescription therapies. The only FDA-approved OTC medicament is docosanol, a long-chain alcohol, applied topically.¹² Patients may swear by additional OTC products and homeopathic regimens as being efficacious for their extra- and intraoral herpetic lesions. Though evidence is limited, many patients report effectiveness of OTC rinses, green tea extract products, medical grade kanuka honey, L-lysine, vitamin C supplements, and home remedy type topical medicaments.¹⁴⁻¹⁷

Prescription options include the antiviral topical medicaments acyclovir and penciclovir.^{6,9,10} Topical penciclovir has been shown to be most effective, followed by acyclovir and docosanol.^{4,12} Systemic acyclovir, valacyclovir, and famciclovir may be prescribed as well.^{6,10} Both topical and systemic prescription medications are most effective if begun during the prodromal phase of the outbreak.^{4,11}

Before gloves were worn routinely by dental professionals, many experienced primary or secondary HSV infection of the fingers known as herpetic whitlow.^{9,18,19} Infection from oral lesions of patients were the result of the virus penetrating minor breaks in the skin. Self-inoculation is a possibility with both herpetic whitlow as well as ocular herpes infections.^{6,18} Care must be taken by patients with herpetic lesions against autoinoculation. Dental professionals can discourage patients from digitally manipulating oral lesions as well as from rubbing their eyes during a herpetic episode.

Herpes simplex type two (HSV-2) is similar structurally to HSV-1 and is considered a sexually transmitted disease, affecting the genital region.^{1,6,9,12} It behaves like HSV-1 in that it remains latent after primary infection and produces similar lesions with recurrent episodes.^{3,7} Most oral herpetic lesions are due to HSV-1; however, a very small percentage may be caused by HSV-2 as a result of oral-genital contact. The lesions caused by the two viruses appear the same clinically. The primary difference in the two viruses is the oncogenic potential of HSV-2.⁴ Prescription antiviral medication is the treatment of choice.

Diagnosis of most herpetic infections, both primary and recurrent, is made from clinical findings alone; however, if laboratory confirmation is required, the most common sampling methods for diagnosis are the cytological smear and tissue biopsy.^{4,9}

Differential diagnosis

When diagnosing herpes simplex lesions, the dental professional must be cognizant of similar-appearing lesions. For the uncommon acute primary herpetic gingivostomatitis, other conditions can have comparable clinical appearances. The intraoral lesions of Coxsackievirus infections (hand, foot, and mouth) and herpangina can appear very similar to those of primary HSV-1. Coxsackie infections are more common in children than primary herpes infections.²⁰ The intraoral lesions of Coxsackie infections can be very similar to herpesviruses, but there are typically lesions on the hands and feet as

well.^{1,4} The characteristic gingivitis seen in acute primary herpetic gingivostomatitis can help differentiate from Coxsackie infections as well.^{4,5} Herpangina lesions are similar to primary HSV-1, but they tend to be in the posterior palatal and tonsillar pillar areas rather than throughout the oral cavity, and there are no lesions on hands and feet.

When differentiating between recurrent intraoral herpes simplex lesions and aphthous ulcers, location of the lesions is key. Though coalescing herpetic lesions (**figure 1**) may appear clinically similar to aphthae, they will be on keratinized tissue, and aphthous ulcers are almost always on nonkeratinized (non-bound-to-bone) or mucosal tissue. This includes a much greater surface area than keratinized or bound-to-bone tissue; the soft palate, tonsillar pillars, labial and buccal mucosa, ventral tongue, and floor of the mouth are all considered mucosal tissue. Etiology and treatment options are different for aphthous ulcers as illustrated in **Table 1**.^{4,5}

Varicella-zoster virus

The varicella-zoster virus (VZV) is a member of the herpes family and shares many features with HSV.^{6,12} The primary infection manifests as the childhood disease known as varicella or chicken pox, followed by a latency period and the potential recurrent manifestation as herpes zoster or shingles.^{1,9,21,22} Ninety percent of adults have been exposed and harbor the latent form. VZV infection differs from that of HSV in that the mode of contact is inhalation of droplets that enter through the respiratory system, replicating there before spreading via the bloodstream.^{3,21,23} The virus is believed to infect the dorsal root ganglia and remains latent until reactivated.^{6,21,22} Primary infection is highly contagious, producing epithelial vesiculo-pustular lesions in varying degrees on the skin and mucous membranes.^{3,4,6} Systemic symptoms may include malaise, fever, pharyngitis, and rhinitis.²² Oral lesions as well as lesions along the remaining gastrointestinal tract may be present, the latter resulting in gastrointestinal symptoms. Oral vesicles rupture spontaneously, appearing similar



FIGURE 1. Intraoral herpetic lesion demonstrating ulcer coalescence

Table 1	
Recurrent intraoral herpes simplex	Recurrent aphthous stomatitis
Herpes	Aphthous
Etiology: viral	Etiology: immune mediated
Intraoral lesion on keratinized tissue	Intraoral lesion on nonkeratinized tissue
Intraoral lesion begins as a vesicle	Intraoral lesion begins as an ulcer
Lay term: fever blister/cold sore	Lay term: canker sore
Prescription TX: antiviral medications <i>acyclovir, penciclovir, valacyclovir</i>	Prescription TX: corticosteroids <i>triamcinolone acetonide, fluocinonide, betamethasone dipropionate</i>

to aphthous ulcers, and are not particularly painful.^{6,9} Skin lesions may continue to appear for approximately one week, be highly pruritic, and heal with scarring if they become secondarily infected.⁹ Treatment before vaccines became available was primarily symptomatic.²² In the prevaccine era, chicken pox was a very common exanthematous disease of childhood, but since vaccine development, incidence has been reduced by greater than 90%.^{3,23} Breakthrough infections have been reported. Diagnosis is achieved primarily from clinical presentation but can be confirmed with additional laboratory tests prescribed by the dentist or upon referral by the primary care provider.^{9,24}

Reactivation occurs in 10%–20% of the population, primarily among the elderly or immunocompromised, with the resultant lesions of zoster, or shingles.^{3,9,10,22} A painful, unilateral vesicular rash appears on the skin and follows the distribution of the affected peripheral nerves in varying severity (**figure 2**).^{6,9,10} Intraoral lesions may also be present, appearing clinically as unilateral fragile vesicles spontaneously producing oral ulcerations. Lesions produce pain on both skin and mucous membranes. Before eruption of vesicles, patients may experience pain and/or paresthesia in the affected area and may continue to experience pain after the lesions have healed (postherpetic neuralgia).^{9,10,22}



FIGURE 2. Unilateral skin lesions of herpes zoster (shingles)

Treatment consists of systemic antiviral medications such as acyclovir, valacyclovir, and famciclovir, beginning as early in the course of the disease as possible for best results.^{6,9,10,22} Other supportive therapies include antipruritics, antipyretics, and analgesics.⁶ Care must be taken to avoid secondary infection of skin and mucosal lesions. For relief of oral lesions, a rinse can be compounded by a pharmacy and may include an antibiotic, antihistamine, antifungal, steroid, local anesthetic, and/or an antacid to enhance coating of the ingredients in the mouth.⁴

A herpes zoster vaccine is available, administered in two doses, and recommended primarily for healthy adults age 50 and older, even if a person does not recall having had chicken pox.^{3,23} The only vaccine currently available in the US has been shown to be 90% effective at preventing shingles as well as the painful complication of postherpetic neuralgia.

Epstein-Barr virus

Another ubiquitous virus, Epstein-Barr virus (HHV-4), is harbored by most (70%–95%) of the adult population.^{4,25,26} It is primarily transmitted via the saliva but may be transmitted sexually as well.^{26,27} Epstein-Barr virus (EBV) has tropism for B-lymphocytes and epithelial cells with a structure similar to HSV and VZV.^{25,27} Infection during childhood typically results in mild illness; however, among adolescents and young adults it results commonly in infectious mononucleosis.¹ Symptoms of mononucleosis include lymphadenopathy, malaise, pharyngitis, fatigue, fever, thrombocytopenia, and splenomegaly. Intraoral symptoms include hyperplastic tonsils and palatal petechiae.^{1,4,5,25} Laboratory tests confirm diagnosis. Treatment consists of palliative measures and rest. Symptoms may persist for weeks, and care should be taken to not overexert, risking splenic damage and/or rupture.^{4,28}

Epstein-Barr virus has also been implicated in hairy leukoplakia, an intraoral lesion presenting as an opportunistic infection primarily in HIV-positive individuals.^{4,5,25,27} The presence of EBV in hairy leukoplakia as well as the normal epithelium of patients with AIDS has been

confirmed.^{4,5} Linear, corrugated, white hyperkeratotic lesions appear bilaterally on the tongue and cannot be scraped off.²⁷ They may eventually spread onto the dorsal or lingual surfaces. In HIV-positive individuals, it may be among the first signs of infection and immunosuppression, thus an important condition to identify for patients.²⁵ Dental professionals may be the first to discover potential HIV infection. Hairy leukoplakia may also present in severely immunocompromised individuals such as transplant recipients who are on large doses of immunosuppressant drugs.²⁷ No specific treatment is indicated for hairy leukoplakia.

Other conditions to consider in the differential diagnosis of hairy leukoplakia can include frictional hyperkeratosis (tongue chewing), contact stomatitis from cinnamon or other agents, lichen planus, benign migratory glossitis, and hyperplastic candidiasis.²⁷ It is incumbent on the dental professional to do a thorough health history to determine the actual cause of the lesions for appropriate referral and follow-up.

Other significant manifestations of EBV infection include Burkitt's lymphoma and nasopharyngeal carcinoma.^{4,5,25} Named after the British surgeon Denis Burkitt, Burkitt's lymphoma is a form of non-Hodgkin's lymphoma starting in immune cells, the B lymphocytes. It affects the jaws of children, primarily boys, and is endemic in Africa. The maxilla is affected more than the mandible. Rapid tumor growth causes visible enlargement of the affected area and is rapidly fatal if left untreated. Intensive chemotherapy can achieve long-term survival in more than half of those with Burkitt's lymphoma. It is rare in the United States.^{4,5}

Nasopharyngeal carcinoma is a cancer that occurs in the nasopharynx. It can be difficult to detect early on as the nasopharynx is not easily examined and the symptoms are similar to other common conditions such as nasal congestion. Affecting only one in 100,000 Americans, it is more common in adult males. Along with Epstein-Barr virus infection, additional risk factors include tobacco and alcohol use, vitamin C-deficient diets, and other environmental carcinogens.

Treatment includes radiotherapy, chemotherapy, or both. Nasopharyngeal carcinoma and Burkitt's lymphoma are both rare in the United States.⁴

Herpesviruses and periodontal disease

Of particular interest to the dental professional is the recent research examining the relationship between HSV-1 and periodontal disease. It has been suggested that the presence of herpesviruses in gingival crevicular fluid (GCF) and subgingival plaque in periodontally diseased sites gives credence to a viral role in the disease. Markers of herpesvirus activation have also been exhibited in the GCF from periodontal lesions.²⁹

Progressive severe periodontitis has been shown to be closely linked to a synergistic effect between herpesviruses and periodontal bacteria. Active herpesvirus infections can impede the humoral immune response and stimulate upgrowth of periodontopathic bacteria. In turn, major pathogenic bacteria may induce latent herpesviruses to reactivate. This synergism may exacerbate periodontal breakdown. A proposed anti-infective therapy of antivirals, antibiotics, antiseptics, and conventional scaling and root planing procedures has been proposed. Additional research is warranted in this area.^{30,31}

Conclusion

A working knowledge of the human herpesviruses, specifically those affecting the oral cavity, is essential for dental professionals. As dentists and hygienists become more involved in interdisciplinary care of patients, we must rise to the top as those in health care most knowledgeable about the conditions, thus the most appropriate providers to diagnose and treat oral lesions resulting from the various herpesviruses.

References

1. Ramesh N. Oral manifestations of viral diseases. *Drug Intervention Today*. 2019;12(2):9.
2. Sapp PJ, Eversole LR, Wysocki GP. *Contemporary Oral and Maxillofacial Pathology*. Mosby; 2004:208.
3. Lopez-Munoz AD, Rastrojo A, Martin R, Alcami A. Herpes simplex virus 2 (HSV-2) evolves faster in cell culture than HSV-1 by generating greater genetic

diversity. *PLoS Pathog*. 2021;17(8):e1009541. doi:10.1371/journal.ppat.1009541

4. Neville B, Damm D, Allen C, Chi A. *Oral and Maxillofacial Pathology*. Saunders/Elsevier; 2016:218-230, 242-243, 395-396, 560-562.
5. Regezi JA, Sciubba JJ, Jordan RCK. *Oral Pathology Clinical Pathologic Correlations*. Elsevier; 2017:1-10, 87-88, 338-339.
6. Santosh ABR, Muddana K. Viral infections of oral cavity. *J Family Med Prim Care*. Jan 2020;9(1):36-42. doi:10.4103/jfmpc.jfmpc_807-19
7. Zhu S, Viejo-Borbolla A. Pathogenesis and virulence of herpes simplex virus. *Virulence*. 2021;12(1):2670-2702. doi:10.1080/21505594.2021.1982373
8. Steiner I. The neurotropic herpes virus: herpes simplex and varicella-zoster. *Lancet*. 2007;6(11):1015-1028.
9. Stoopler ET, Greenberg MS. Update on herpesvirus infections. *Dent Clin North Am*. 2003;47(3):517-532. doi:10.1016/s0011-8532(03)00018-1
10. Stoopler ET, Sollecito TP. Oral mucosal diseases: evaluation and management. *Med Clin North Am*. 2014;98(6):1323-1352. doi:10.1016/j.mcna.2014.08.006
11. Boes H, Goulioumis V, Wechsler A, et al. Clinical study on the effectiveness of three products in the treatment of herpes simplex labialis. *Sci Rep*. 2020;10(1):6465. doi:10.1038/s41598-020-63530-6
12. Fatahzadeh M, Schwartz RA. Human herpes simplex labialis. *Clin Exp Dermatol*. 2007;32(6):625-630. doi:10.1111/j.1365-2230.2007.02473.x
13. Gurenlian J. Differentiating herpes simplex virus and recurrent aphthous ulcerations. *Access*. 2003;17(2).
14. Semprini A, Singer J, Braithwaite I, et al. Kanuka honey versus acyclovir for the topical treatment of herpes simplex labialis: a randomized controlled trial. *BMJ Open*. 2019;9:e026201. doi:10.1136/bmjopen-2018-026201
15. Polanski H, Javaherian A, Itzkovitz, E. Clinical trial of herbal treatment Gene-Eden-VIR/Novirin in oral herpes. *J Evid Based Integr Med*. 2018;23:1-9.
16. Mailoo VJ, Ramples S. Lysine for herpes simplex prophylaxis: a review of the evidence. *Integr Med*. 2017;16(3):42-46.
17. McCarthy JP, Browning WD, Veit G. Treatment of herpes labialis: comparison of two OTC drugs and untreated controls. *J Esthet Restor Dent*. 2012;24(2):103-109.
18. Feder H, Long S. Herpetic whitlow. *Am J Dis Child*. 1983;137:3.
19. Rubright JH, Shafritz AB. The herpetic whitlow. *J Hand Surg Am*. 2011;36(2):340-342. doi:10.1016/j.jhsa.2010.10.014
20. Centers for Disease Control and Prevention. Hand, foot, and mouth disease (HFMD). Accessed February 13, 2022. <https://www.cdc.gov/hand-foot-mouth/about/transmission.html>
21. Sahara S, Jahangir A, Glaser A, et al. Case report: aseptic meningitis secondary to varicella-zoster virus (VZV) without an exanthem post MMR vaccination. *BMC Infect Dis*. 2021;21(1):1-5. doi:10.1186/s12879-021-06453-5
22. Gilden D, Mahalingam R, Nagel MA, et al. Review: the neurobiology of varicella zoster virus infection. *Neuropathol Appl Neurobiol*. 2011;37(5):441-463. doi:10.1111/j.1365-2990.2011.01167.x

23. Centers for Disease Control and Prevention. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2007;56(No. RR-04).
24. Centers for Disease Control and Prevention. About chickenpox. Accessed February 14, 2022. <https://www.cdc.gov/chickenpox/about/index.html>
25. De Melo Silva J, Pinheiro-Silva R, Dhyani A, Pontes GS. Cytomegalovirus and Epstein-Barr infections: prevalence and impact on patients with hematological diseases. *BioMed Res Int.* 2020;1-14. doi:10.1155/2020/1627824
26. Centers for Disease Control and Prevention. About Epstein-Barr virus (EBV). Accessed March 7, 2022. <https://www.cdc.gov/epstein-barr/about-ebv.html>
27. Braz-Silva PH, Santos RTM, Schussel JL, Gallottini M. Oral hairy leukoplakia diagnosis by Epstein-Barr virus in situ hybridization in liquid-based cytology. *Cytopathology.* 2014;25(1):21-26. doi:10.1111/cyt.12053
28. Lennon P, Crotty M, Fenton JE. Infectious mononucleosis. *BMJ.* 2015;350:h1825. doi:10.1136/bmj.h1825
29. Cappuyns I, Gugerli P, Mombelli A. Viruses in periodontal disease—a review. *Oral Dis.* 2005;11:219-229.
30. Slots J. Primer on etiology and treatment of progressive/severe periodontitis: a systemic health perspective. *Periodontol 2000.* 2020;00:1-5.
31. Khinda PK, Rao D, Sodhi SPS, Salaria S. Herpes viruses: role in periodontitis. *J Crit Rev.* 2020;7(10):2798-2803.



Sherri Lukes, MS, RDH, FAADH, has been a dental hygienist for 41 years. As associate professor emerita, Southern Illinois University, Sherri taught oral pathology, public health, and multicultural dental hygiene courses. She now presents CE courses nationally and internationally. She holds a

pathology fellowship in the American Academy of Dental Hygiene, is past president of the Illinois Dental Hygienists' Association, and a member of the American Academy of Oral Medicine. She can be reached at smlukes@siu.edu.



Stacey McKinney, MSED, PHDH, RDH, is an assistant professor and program director in the dental hygiene program at Southern Illinois University Carbondale. Her teaching responsibilities focus on preventive oral care, teaching methodologies, and advanced periodontics. She

has more than 10 years of clinical dental hygiene experience in community-based and general practice. Stacey is a member of the American Dental Hygienists' Association, Illinois Public Health Association, and American Dental Education Association. She can be reached at smckinney8@siu.edu.

ONLINE COMPLETION

Use this page to review questions and answers. Visit dentalacademyofce.com and sign in. If you have not previously purchased the course, select it from the Course Library and complete your online purchase. Once purchased, click the "Start Course" button on the course page. You will have an opportunity to review an online version of the article. When finished, click the "Next" button to advance to the quiz. Click "Start Quiz," complete all the program questions, and submit your answers. An immediate grade report will be provided. Upon receiving a grade of 70% or higher, your verification form will be provided immediately for viewing and printing. Verification forms can be viewed and printed at any time in the future by visiting the site and returning to your Dashboard page.

QUICK ACCESS code **22125**

QUESTIONS

- The smallest and simplest microorganisms to affect humans are:
 - Bacteria
 - Viruses
 - Protozoa
 - Spirochetes
- The matching of a virus with a specific cell type is termed:
 - Tropism
 - Integration
 - Endocytosis
 - Replication
- All of the following are used to classify viruses except:
 - Host organisms
 - Type of disease they cause
 - Morphology
 - Protein pathways
- Which of the herpesviruses are considered neurotropic?
 - EBV and CMV
 - HSV and EBV
 - HSV and VZV
 - HHV 6, 7, 8
- When the initial infection of HSV-1 produces symptoms of fever, malaise, and generalized oral ulcerations and gingivitis, the condition is termed:
 - Herpes labialis
 - Acute primary herpetic gingivostomatitis
 - Herpetic aphthous stomatitis
 - Herpangina
- Which of the following is true regarding recurrent intraoral herpes?
 - Occurs on movable, mucosal linings
 - Frequently seen on the ventral tongue
 - Also termed herpetiform aphthous
 - Commonly occurs on slope of hard palate
- A 16-year-old patient presents with palatal petechiae, hyperplastic tonsils, sore throat, enlarged lymph nodes, and severe malaise. These are typical symptoms of:
 - Infectious mononucleosis, cytomegalovirus infection
 - Acute primary herpetic gingivostomatitis, herpes simplex type 1 infection
 - Infectious mononucleosis, Epstein-Barr virus infection
 - Herpangina, Coxsackie virus infection
- The following viral infection should be considered in the differential diagnosis of acute primary herpetic gingivostomatitis based on intraoral findings:
 - Coxsackie virus infection
 - Human papillomavirus infection
 - Paramyxovirus infection
 - Epstein-Barr virus infection
- Which of the following viral infections is most commonly characterized by intraoral lesions in those who are HIV positive?
 - CMV
 - HSV
 - EBV
 - VZV
- Burkitt's lymphoma, a form of non-Hodgkin's lymphoma, commonly affects what area of the facial region?
 - Maxilla
 - TMJ
 - Mandible
 - Trigeminal nerve

Use this page to review questions and answers. Visit dentalacademyofce.com and sign in. If you have not previously purchased the course, select it from the Course Library and complete your online purchase. Once purchased, click the "Start Course" button on the course page. You will have an opportunity to review an online version of the article. When finished, click the "Next" button to advance to the quiz. Click "Start Quiz," complete all the program questions, and submit your answers. An immediate grade report will be provided. Upon receiving a grade of 70% or higher, your verification form will be provided immediately for viewing and printing. Verification forms can be viewed and printed at any time in the future by visiting the site and returning to your Dashboard page.

QUESTIONS

11. Cells contain all necessary structures for growth and reproduction. Viruses contain all of the following except:
 - A. Capsid
 - B. Genome
 - C. Cell membrane
 - D. Enzymes
12. When a virus enters a host cell without a detectable clinical lesion, it is called:
 - A. Interphase
 - B. Mitosis
 - C. Cytokinesis
 - D. Latency
13. All of the following are characteristics of the herpesvirus family except:
 - A. Can establish virus latency in the host
 - B. Has the tendency for spreading
 - C. Are non-cancer causing
 - D. Can cause recurrent infections
14. There are _____ herpesviruses that affect humans, collectively known as *Herpetoviridae*.
 - A. 6
 - B. 8
 - C. 12
 - D. 15
15. Identify the correct medicinal treatment for acute HSV-1.
 - A. Antipyretic
 - B. Antihistamine
 - C. Antiemetic
 - D. Anti-inflammatory
16. When infected with HSV-1, the virus remains latent unless reactivated. Activation can be triggered by factors that may suppress the immune system such as stress or trauma.
 - A. Both statements are true.
 - B. Both statements are false.
 - C. The first statement is true; the second is false.
 - D. The first statement is false; the second is true.
17. Hairy leukoplakia occurs when infected with which virus?
 - A. Epstein-Barr virus
 - B. Herpes simplex virus
 - C. Mononucleosis
 - D. Coxsackie virus
18. Which of the following is the most likely condition included in the differential diagnosis for a patient diagnosed with hairy leukoplakia?
 - A. Squamous cell carcinoma
 - B. Lichen planus
 - C. Linea alba
 - D. Leukoedema
19. The lay term for the reactivation of HSV-1 is:
 - A. Aphthous ulcer
 - B. Chicken pox
 - C. Cold sore
 - D. Shingles
20. Recurrent intraoral herpes lesions are commonly found on:
 - A. Keratinized tissue
 - B. Soft palate
 - C. Labial and buccal mucosa
 - D. Non-bound-to-bone tissues
21. The mode of contact for varicella-zoster virus is:
 - A. Oral/vaginal sex
 - B. Unwashed hands
 - C. Human blood
 - D. Inhalation of droplets
22. An 8-year-old presents with epithelial vesiculo-pustular lesions on the skin and mucous membranes along with malaise, fever, and rhinitis. These symptoms are typical of:
 - A. Infectious mononucleosis
 - B. Acute primary herpetic gingivostomatitis
 - C. Varicella-zoster virus infection
 - D. Coxsackie virus infection
23. HSV-1 and caries have been shown to have a significant relationship. Severe periodontal conditions have also been linked to a symbiotic effect between herpes and periodontal bacteria.
 - A. Both statements are true.
 - B. Both statements are false.
 - C. The first statement is true; the second is false.
 - D. The first statement is false; the second is true.
24. The prodromal stage of itching, tingling, or feeling full around the vermilion border could warrant diagnosis of:
 - A. Recurrent herpes labialis
 - B. Angular cheilitis
 - C. Candidiasis
 - D. Pemphigus vulgaris
25. Prescription treatment for recurrent aphthous stomatitis includes:
 - A. Acyclovir
 - B. Penciclovir
 - C. Fluocinonide
 - D. Valacyclovir
26. The vaccine for which of the following is administered in two doses and recommended for adults 50 years and older to prevent shingles?
 - A. Herpes zoster
 - B. Hep A
 - C. Tdap
 - D. Pneumococcal polysaccharide
27. The protein coat surrounding the DNA or RNA is also called:
 - A. Nucleus
 - B. Capsid
 - C. Helix
 - D. Thymine
28. Identify which of the following is correct regarding intraoral recurrent HSV-1 lesions:
 - A. Vesicular stage is always visualized intraorally
 - B. Lesion will appear on nonkeratinized tissue
 - C. Presents as multiple punctate red ulcerations
 - D. Appears on the buccal mucosa
29. The only FDA-approved medication for HSV-1 lesions is:
 - A. Kanuka honey
 - B. Vitamin C supplements
 - C. Green tea extract products
 - D. Docosonal
30. Diagnosis for most herpetic infections can be made from clinical findings, although the most common method for sampling includes:
 - A. Cytological smear
 - B. Fine-needle aspiration
 - C. Swab
 - D. Skin sample

PUBLICATION DATE:	MARCH 2023
EXPIRATION DATE:	APRIL 2026

ANSWER SHEET

Big fat happy herpes family: Oral manifestations of human herpesvirus infections

NAME: _____ TITLE: _____ SPECIALTY: _____

ADDRESS: _____ EMAIL: _____ AGD MEMBER ID (IF APPLIES): _____

CITY: _____ STATE: _____ ZIP: _____ COUNTRY: _____

TELEPHONE (PRIMARY): _____ TELEPHONE (OFFICE): _____

REQUIREMENTS FOR OBTAINING CE CREDITS BY MAIL/FAX: 1) Read entire course. 2) Complete info above. 3) Complete test by marking one answer per question. 4) Complete course evaluation. 5) Complete credit card info or write check payable to Endeavor Business Media. 6) Mail/fax this page to DACE. If you have any questions, please contact dace@endeavor2b.com or call (800) 633-1681. A score of 70% or higher is required for CE credit.

COURSE CAN ALSO BE COMPLETED ONLINE AT A LOWER COST. Scan the QR code or go to dentalacademyofce.com to take advantage of the lower rate.



Educational Objectives

- Describe the pathogenesis of human herpesvirus (HHV) infections affecting the oral cavity and head/neck region
- Identify oral lesions associated with HHV infections
- Discuss treatment options and palliative procedures for alleviating symptoms of HHV infections
- Explain the hygienist's role in assisting the dentist with diagnosis of HHV infections

Course Evaluation

- Were the individual course objectives met?

Objective #1: Yes	No	Objective #3: Yes	No
Objective #2: Yes	No	Objective #4: Yes	No

Please evaluate this course by responding to the following statements, using a scale of Excellent = 5 to Poor = 0.

- | | | | | | | |
|---|-------|----|---|---|---|---|
| 2. To what extent were the course objectives accomplished overall? | 5 | 4 | 3 | 2 | 1 | 0 |
| 3. Please rate your personal mastery of the course objectives. | 5 | 4 | 3 | 2 | 1 | 0 |
| 4. How would you rate the objectives and educational methods? | 5 | 4 | 3 | 2 | 1 | 0 |
| 5. How do you rate the author's grasp of the topic? | 5 | 4 | 3 | 2 | 1 | 0 |
| 6. Please rate the author's effectiveness. | 5 | 4 | 3 | 2 | 1 | 0 |
| 7. Was the overall administration of the course effective? | 5 | 4 | 3 | 2 | 1 | 0 |
| 8. Please rate the usefulness and clinical applicability of this course. | 5 | 4 | 3 | 2 | 1 | 0 |
| 9. Please rate the usefulness of the references. | 5 | 4 | 3 | 2 | 1 | 0 |
| 10. Do you feel that the references were adequate? | Yes | No | | | | |
| 11. Would you take a similar course on a different topic? | Yes | No | | | | |
| 12. If any of the continuing education questions were unclear or ambiguous, please list them. | _____ | | | | | |

13. Was there any subject matter you found confusing? Please describe.

14. How long did it take you to complete this course?

15. What additional dental continuing education topics would you like to see?

Mail/fax completed answer sheet to:

Endeavor Business Media

Attn: Dental Division
7666 E. 61st St. Suite 230, Tulsa, OK 74133
Fax: (918) 831-9804

Payment of \$69 is enclosed (this course can be completed online for \$39. Scan the QR code or go to dentalacademyofce.com to take advantage of the lower rate).

Make check payable to Endeavor Business Media

If paying by credit card, please complete the following:

MC Visa AmEx Discover

Acct. number: _____

Exp. date: _____ CVC #: _____

Billing address: _____

Charges on your statement will show up as Endeavor.

- | | |
|---------------------|---------------------|
| 1. (A) (B) (C) (D) | 16. (A) (B) (C) (D) |
| 2. (A) (B) (C) (D) | 17. (A) (B) (C) (D) |
| 3. (A) (B) (C) (D) | 18. (A) (B) (C) (D) |
| 4. (A) (B) (C) (D) | 19. (A) (B) (C) (D) |
| 5. (A) (B) (C) (D) | 20. (A) (B) (C) (D) |
| 6. (A) (B) (C) (D) | 21. (A) (B) (C) (D) |
| 7. (A) (B) (C) (D) | 22. (A) (B) (C) (D) |
| 8. (A) (B) (C) (D) | 23. (A) (B) (C) (D) |
| 9. (A) (B) (C) (D) | 24. (A) (B) (C) (D) |
| 10. (A) (B) (C) (D) | 25. (A) (B) (C) (D) |
| 11. (A) (B) (C) (D) | 26. (A) (B) (C) (D) |
| 12. (A) (B) (C) (D) | 27. (A) (B) (C) (D) |
| 13. (A) (B) (C) (D) | 28. (A) (B) (C) (D) |
| 14. (A) (B) (C) (D) | 29. (A) (B) (C) (D) |
| 15. (A) (B) (C) (D) | 30. (A) (B) (C) (D) |

EXAM INSTRUCTIONS
All questions have only one answer. If mailed or faxed, grading of this examination is done manually. Participants will receive confirmation of passing by receipt of a Verification of Participation form. The form will be mailed within two weeks after receipt of an examination.

COURSE EVALUATION AND FEEDBACK
We encourage participant feedback. Complete the evaluation above and e-mail additional feedback to Rachel McIntyre (rmcintyre@endeavor2b.com) and Laura Winfield (lwinfield@endeavor2b.com).

COURSE CREDITS AND COST
All participants scoring 70% or higher on the examination will receive a verification form for three (3) continuing education (CE) credits. Participants are urged to contact their state dental boards for CE requirements. The cost for courses ranges from \$20 to \$110.

PROVIDER INFORMATION
Endeavor Business Media is an ADA CERP-recognized provider. ADA CERP is a service of the American Dental Association to assist dental professionals in identifying quality providers of continuing dental education. ADA CERP neither approves nor endorses individual courses or instructors, nor does it imply acceptance of credit hours by boards of dentistry. Concerns about a CE provider may be directed to the provider or to ADA CERP at ada.org/cerp.

Endeavor Business Media is designated as an approved PACE program provider by the Academy of General Dentistry. The formal continuing dental education programs of this program provider are accepted by the AGD for fellowship, mastership, and membership maintenance credit. Approval does not imply acceptance by a state or provincial board of dentistry or AGD endorsement. The current term of approval extends from 11/1/2019 to 10/31/2024. Provider ID# 320452. AGD code: 730.

Dental Board of California: Provider RP5933. Course registration number CA code: 03-5933-22125. Expires 7/31/2024. *This course meets the Dental Board of California's requirements for three (3) units of continuing education.*

Endeavor Business Media is designated as an approved provider by the American Academy of Dental Hygiene Inc. #AADHPNW (January 1 2022 - December 31, 2024). Approval does not imply acceptance by a state or provincial board of dentistry. Licensee should maintain this document in the event of an audit.

RECORD KEEPING
Endeavor Business Media maintains records of your successful completion of any exam for a minimum of six years. Please contact our offices for a copy of your CE credits report. This report, which will list all credits earned to date, will be generated and mailed to you within five business days of receipt.

CANCELLATION AND REFUND POLICY
Participants who are not 100% satisfied can request a refund by contacting Endeavor Business Media in writing.

IMAGE AUTHENTICITY
The images in this educational activity have not been altered.
© 2021 Academy of Dental Therapeutics and Stomatology, a division of Endeavor Business Media