Update on Oral Herpes Virus Infections

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KEYWORDS

• Herpes virus • Viral infection • Oral cavity • Mouth • Antivirals

KEY POINTS

- Oral herpes virus infections (OHVIs) are commonly encountered in clinical practice.
- OHVIs can resemble other types of oral mucosal diseases.
- Diagnosis of OHVIs is usually based on patient history and clinical examination findings, but adjunctive laboratory tests may be necessary to establish the diagnosis.
- Treatment of OHVIs usually consists of palliative care, but may include use of topical or systemic antiviral medications.
- Immunosuppressed patients with OHVIs are potentially at risk of developing life-threatening complications and may require aggressive treatment.

INTRODUCTION

There are 80 known herpes viruses, and at least 8 of them are known to cause infections in humans. These viruses include herpes simplex virus (HSV) -1 and -2, varicella – zoster virus (VZV) [human herpes virus {HHV} 3], Epstein – Barr virus (EBV) [HHV-4], Cytomegalovirus (CMV) [HHV-5], HHV-6, -7, and -8 [Kaposi's sarcoma herpes virus {KSHV}].[1,2] There are structural and behavioral characteristics that are common to the members of the herpes virus family (ie, they contain 4 layers: an inner core of double-stranded DNA, a protein capsid, the tegument, and a lipid envelope containing glycoproteins derived from the nuclear membrane of host cells).[1,2] Herpes viruses

A version of this article appeared as Stoopler, ET. Oral herpetic infections (HSV 1–8). Dent Clin N Am 2005;49:15–29.
Disclosures for authors: no disclosures.
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Dent Clin N Am 58 (2014) 265–280
http://dx.doi.org/10.1016/j.cden.2013.12.001 **dental.theclinics.com**
0011-8532/14/$ – see front matter

cause a primary infection when the person initially contacts the virus, and it remains latent within the nuclei of specific cells for the life of the individual. The site of latency differs among the herpes viruses, with HSV-1, HSV-2, and VZV remaining latent in the sensory nerve ganglia; EBV in B lymphocytes, oropharyngeal epithelial cells, and salivary gland tissue[3]; CMV in monocytes, bone marrow hematopoietic progenitor cells, epithelial cells, endothelial cells,[4] and possibly, salivary gland tissue[5]; and HHV-6 and HHV-7 in CD4 lymphocytes.[1,2] HHV-8 also remains latent in B lymphocytes circulating in the hematopoietic system.[6] After reactivation, herpes viruses can cause localized or disseminated recurrent infections. They are transmitted between hosts by direct contact with saliva or genital secretions. HHV-8 may be transmitted via organ transplantation.[7,8] Viruses are often shed in the saliva of asymptomatic hosts, who act as vectors for new primary infections in previously non-infected individuals.[9] EBV has been associated with malignancies in humans, such as nasopharyngeal carcinoma and B-cell lymphomas. Other malignancies are associated with EBV, including nasal T-cell/natural killer cell lymphoma seen most commonly in Southeast Asia.[10] HHV-8 has been definitively linked to malignant processes, such as KS, as well as several lymphoproliferative disorders and Castleman disease.[7]

HSV

HSV-1 and HSV-2 are the two major types of herpes viruses known to cause most common oral and perioral infections.[11,12] They can be distinguished by the distinct antibodies that are formed against each type of virus or by analysis of the nuclear DNA by restriction endonuclease analysis.[1,2] Classically, HSV-1 causes most cases of oral and pharyngeal infection, meningoencephalitis, and dermatitis above the waist; HSV-2 is implicated in most genital and anal infections.[1,2] Depending on sexual practices, both types can cause primary or recurrent infections in the oral, perioral, or genital area.[1,2] HSV infections of the finger (herpetic whitlow) develop after contact with infected saliva or bronchial secretions. The incidence of herpetic whitlow is 4 cases per 100,000 per year.[13]

PRIMARY HERPES SIMPLEX INFECTIONS

The incidence of primary infections with HSV-1 increases after 6 months of age as a result of loss of anti-HSV antibodies acquired from the mother during gestation. The incidence of primary HSV-1 infection reaches a peak between 2 and 3 years of age.[1,2] Primary HSV-1 infections may still occur in adolescents and adults, with occasional cases being reported in patients older than 60 years.[14] Incidence of primary HSV-2 infection does not increase until sexual activity begins. In a prevalence study between 1999 and 2004, 57.7% of the US population tested had HSV-1 antibodies. Data from the Centers for Disease Control showed that 16.2% of Americans aged between 14 and 49 years had HSV-2 antibodies.[15] This prevalence was higher among women (20.9%) compared with men (11.5%) and higher among Blacks (39.2%) compared with Whites (12.3%).[16]

Many primary herpes infections are subclinical or cause pharyngitis, which is difficult to distinguish from other upper respiratory viral infections. Symptomatic primary HSV disease is preceded or accompanied by systemic symptoms, which may include fever, headache, malaise, nausea, vomiting, and accompanying lymphadenopathy.[17,18] These prodromal symptoms are important to consider when clinically differentiating HSV infections from other vesiculoulcerative diseases of the oral cavity. In the oral cavity, vesicles and ulcers appear on the oral mucosa and generalized acute marginal gingivitis occurs 1 to 2 days after the prodromal symptoms appear (**Fig. 1**).