Oral Manifestations

This is a PDF version of the following document:
Section 1: Basic HIV Primary Care
Topic 2: Oral Manifestations

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Topic Overview

Background

The oral manifestations of HIV disease are manifold, prevalent, and clinically significant. The recognition and management of HIV-related oral manifestations remains an important area of study for clinicians who provide medical care to persons with HIV infection. Oral lesions may be the first clinical sign of HIV infection and can cause significant morbidity. This topic will focus on common HIV-related oral conditions, including oral candidiasis, oral hairy leukoplakia, ulcerative disease, and oral malignancies.

Oral Health

With the advent of effective antiretroviral therapy, the overall prevalence of HIV-related oral manifestations has decreased. In addition, with the improved long-term health of persons living with HIV there has been a renewed focus on the importance of preventative oral health through regular dental care. Good oral health allows for appropriate eating and speaking, as well as increased quality of life as measured by self-confidence, social acceptance, and employability. Dental decay, gingivitis, and periodontal disease are common problems for individuals with HIV. Causes of dental decay include inadequate dental hygiene, poor diet, xerostomia, changes in immune cells in the salivary glands, and changes that result from chronic methamphetamine use (“meth mouth”). The challenge of salivary gland damage from HIV infection in addition to the xerostomic effects of many HIV medications creates a difficult environment to treat both caries and periodontal disease. Unfortunately, barriers to good oral health include lack of insurance coverage, lack of dentists who are trained or willing to see individuals with HIV infection (even for routine periodontal care), patient fear of dentists, and a lack of awareness of the importance of oral health.

Oral Examination

A comprehensive oral examination should include both visual and tactile components, beginning with careful inspection the face, neck, lips and mouth (including the roof, floor and sides of the mouth, the tongue, the tonsillar pillars and the back of the throat) and followed by manual palpation. A detailed patient history is often helpful in directing the examiner to explore a particular area in greater detail. The American College of Prosthodontist has produced an excellent oral examination video titled Oral Cancer Screening Exam.
Oral Candidiasis

Background

Oropharyngeal candidiasis is seen frequently among individuals with HIV infection and is an indicator of immune suppression.[4, 5] It occurs most often in patients with CD4 cell counts less than 200 cells/mm³. *Candida albicans* is the most common species involved, but non-*albicans* species (*C. dubliniensis, C. glabrata, C. tropicalis*) can also cause disease.[6] In addition, *Candida glabrata* is associated with azole resistance among patients with advanced immunosuppression, particularly those who have received repeated or prolonged courses of oral fluconazole.[7] The introduction and widespread use of effective antiretroviral therapy has led to a marked decrease in the prevalence of oral candidiasis. Although HIV-related immune suppression is typically the most important risk factor for developing oral candidiasis, other causes for oral candidiasis include antibiotic use, corticosteroids, chemotherapeutic drugs, and diabetes. By maximizing immune status with effective antiretroviral therapy, most cases of candidiasis can be avoided.

Clinical Manifestations

Among individuals with HIV infection, there are four different manifestations of oral candidiasis: pseudomembranous candidiasis (thrush), atrophic (erythematous) candidiasis, angular cheilitis (perleche) and rarely, hyperplastic candidiasis. Pseudomembranous candidiasis manifests as painless, creamy white plaques or patches that may involve any oral mucosal surface, including the palate (Figure 1), buccal mucosa (Figure 2), gingiva (Figure 3), and tongue (Figure 4); the pseudomembranous plaques can be easily scraped off with a tongue blade. Erythematous candidiasis typically presents as flat red patches most commonly on the hard palate (Figure 5) and surface of the tongue (Figure 6). Patients with either pseudomembranous or erythematous disease often complain of burning sensation and of altered taste. Angular cheilitis manifests as erythema and splitting of the corners of the mouth (Figure 7); if not treated, this can progress to a chronic, non-healing lesion.

Diagnosis

A presumptive diagnosis of oropharyngeal candidiasis is based on typical clinical appearance or on a favorable response to an empiric trial of antifungal medication.[7] A definitive diagnosis of oropharyngeal candidiasis requires obtaining a direct smear and performing a potassium hydroxide (KOH) wet mount or Gram’s stain and seeing characteristic yeasts. Fungal cultures are reserved for patients who do not respond to first-line therapy or for cases of suspected antifungal resistance.

Treatment

In the Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents, oral fluconazole is the drug of choice for treating oropharyngeal candidiasis based on its efficacy, convenience, and tolerance (Table 1).[7] Topical therapy reduces the risk of systemic drug exposure and adverse events, and is also considered acceptable first-line therapy for mild-moderate oral disease. Topical therapies include miconazole buccal tablets, clotrimazole lozenges (troche), or nystatin suspension or nystatin lozenges (pastille).[7] Alternative therapy consists of either itraconazole or posaconazole oral solutions, and a delayed-release solid formulation of posaconazole was also recently made available; systemic therapy with itraconazole or ketoconazole is not recommended due to reduced efficacy, increased risk for drug-drug interactions, and poorer tolerability.[7] Treatment is generally given for 10 to 14 days. Episodic treatment of clinical episodes is strongly preferred over chronic suppressive therapy, mainly because of the risk of developing antifungal drug resistance with chronic therapy. In addition, routine primary prophylaxis is not recommended because oral candidiasis has relatively low attributable morbidity and acute treatment is highly effective.[7]
Fluconazole-Resistant Candidiasis

Refractory oropharyngeal candidiasis in AIDS patients emerged in response to the widespread and frequent use of fluconazole; in earlier years of the epidemic, it occurred in approximately 5% of patients with HIV infection.[7,8] Studies have identified multiple risk factors for the development of fluconazole-resistant candidiasis, including low CD4 cell count, advanced immunosuppression, greater number of fluconazole-treated episodes, and longer median duration of fluconazole therapy.[9] The Guidelines for the Prevention and Treatment of Opportunistic Infections provide recommended and alternative treatment options for refractory oropharyngeal candidiasis.[7]
Oral Hairy Leukoplakia

Background

Oral hairy leukoplakia (OHL) occurs in up to 20% of individuals with HIV infection, typically among those with moderate to advanced immune suppression. As with other opportunistic infections, the prevalence of OHL has decreased with the advent of effective antiretroviral therapy. In most reports, Epstein-Barr virus (EBV) has been strongly associated with OHL although the mechanism by which EBV infects the oral epithelium has not been fully elucidated.

Clinical Manifestations

Patients with OHL present with raised, white, corrugated lesions most often on the lateral aspect of the tongue. Less often, OHL can manifest with extensive oral mucosal involvement, including the buccal mucosa and pharynx. The OHL lesions are adherent and not removed when scraping the lesion with a tongue blade. This feature serves to distinguish OHL from oral candidiasis, since pseudomembranous candidiasis lesions typically are easily removed by scraping with a tongue blade. In most patients, OHL does not cause symptoms, but some individuals may complain of glossodynia.

Diagnosis

The diagnosis of OHL is usually made based on clinical findings. To confirm the diagnosis, though this is rarely required, a biopsy can be performed, which will show characteristic histopathologic findings, namely cellular nuclear changes (acanthosis, Cowdry type A inclusions, ground glass and nuclear beading), absence of an inflammatory infiltrate, regions of ballooning cells, and epithelial hyperplasia. Further confirmation can be made by identify replicating EBV in the histologic sample, but this is rarely done.

Treatment

In most patients, OHL resolves after treatment of the underlying HIV infection with effective antiretroviral therapy and thus no specific OHL therapy is generally required. If patients desire treatment due to symptoms or cosmetic reasons, reports have described benefit from valacyclovir and from topical agents, such as podophyllin resin combined with acyclovir cream. Patients should also be instructed to brush their tongues with a toothbrush or use a tongue scraper.
Aphthous Stomatitis

Background

Aphthous stomatitis affects up to 15% of persons with HIV infection and the incidence has not significantly changed since the advent of effective antiretroviral therapy.[20, 21] The cause of these ulcers remains unclear, but may represent an overstimulation of tumor necrosis factor, perhaps stimulated by an unidentified pathogen. Other possible etiologies include trauma and stress, systemic disease, nutritional deficiencies, and food allergies.[22] When compared with aphthous lesions in immunocompetent individuals, patients with HIV typically have oral ulcers that are more extensive, more frequent in occurrence, and slower to heal.[21]

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Aphthous stomatitis manifests as round to oval lesions with a raised red halo on non-keratinized mucosal surfaces in the mouth, including the lip (Figure 10), or tongue (Figure 11), often with a yellow-gray pseudomembranous covering.[23] Aphthous stomatitis lesions are characterized as minor, major, or herpetiform based on the size and number of lesions. Minor lesions are 0.2 to 0.5 cm in diameter and typically persist for 7 to 10 days; major lesions are greater than 0.5 cm in diameter (sometimes are up to 2 cm in diameter) and often persist for weeks.[24] Herpetiform lesions manifest as a crop of lesions with each lesion smaller than 1 to 2 mm in diameter, but these small lesions can coalesce into large lesions. Aphthous stomatitis lesions often can cause intense pain, particularly when patients ingest spicy, salty or acidic foods or beverages.[22, 25] This disorder is referred to as recurrent aphthous stomatitis in patients who have repeated episodes.

Diagnosis

No causative agent has been identified for aphthous stomatitis. The diagnosis of aphthous stomatitis is based on clinical presentation and exclusion of other possible causes, including HSV, syphilis, neoplasm, or drug reaction.

Treatment

Topical anesthetics are helpful for pain control of all lesions. Minor lesions can be treated with a mucosal binding agent and topical corticosteroid, ideally combined in a dental paste preparation. In contrast, more severe lesions may require systemic or intralesional corticosteroids, or the immunomodulator, thalidomide.[21, 26] Antiretroviral therapy is an important component in treating aphthous stomatitis.[25] Objective evidence shows most efficacy from corticosteroids and antimicrobials used topically, although a meta-analysis concluded there was insufficient evidence to support any single treatment.[27, 28] In general, treatment of aphthous ulcers should focus on both acute ulcer control and also on preventing recurrences, and treatment algorithms should follow a stepwise progression, starting with topical preparations and proceeding if necessary to first- and second-line systemic therapies.[21] The following summarizes several key aspects of treatment options:

- **Chlorhexidine**: Chlorhexidine gluconate and bioadherent oral rinse gel mouth rinses reduce the severity and pain of ulceration but not the frequency.
- **Anti-Inflammatory Agents**: In patients with mild-moderate aphthous lesions, anti-inflammatory agents can help; a spectrum of topical agents such as benzydamine mouthwash and amlexanox paste may help. Benzydamine hydrochloride mouthwash, though no more beneficial than a placebo, can produce transient pain relief.
- **Topical Corticosteroids**: The use of topical corticosteroids remains the mainstays of treatment, with a recent randomized placebo-controlled trial showing a statistically significant improvement in healing ratio in patients treated with dexamethasone ointment.
compared with placebo.[29] A spectrum of different topical corticosteroids can be used. At best, topical corticosteroids reduce painful symptoms but not the rate of ulcer recurrence. The commonly used preparations are as follows: (1) hydrocortisone muco-adhesive buccal tablets 2.5 mg used 4 times daily, (2) triamcinolone acetonide 0.1 dental paste applied to ulcer 4 times daily, or (3) betamethasone sodium phosphate as a 0.5 mg tablet dissolved in 15 mL of water to make a mouth rinse, used 4 times daily for 4 minutes each time.

- **Safety of Topical Corticosteroids**: Hydrocortisone and triamcinolone topical preparations are popular because neither causes significant adrenal suppression, but ulcers typically recur unless effective antiretroviral therapy is also used. Betamethasone, fluocinonide, fluocinolone, fluticasone, and clobetasol are more potent and more effective than hydrocortisone and triamcinolone, but they carry an increased risk for adrenocortical suppression and a predisposition to candidiasis. All corticosteroids, even when given in non-oral formulation, have the potential to induce serious complications, such as Cushing’s syndrome in patients with HIV infection taking ritonavir or cobicistat, as well as with some protease inhibitors.[30] Corticosteroids should be used with caution in these patients.

- **Tetracyclines**: Topical tetracyclines may reduce the severity of ulceration, but they do not alter the recurrence rate. A doxycycline capsule of 100 mg in 10 mL of water administered as a mouth rinse for 3 minutes or tetracycline 500 mg plus nicotinamide 500 mg administered 4 times daily may provide relief and reduce ulcer duration. Avoid tetracyclines in children younger than 12 years who might ingest them and develop tooth staining.

- **Thalidomide**: In patients with severe aphthous lesions, the medication thalidomide (200 mg per day for 4 weeks) has been shown to significantly improve healing and resolution. The use of thalidomide is hampered by its pregnancy category X classification and the requirement that clinicians need to enroll in a special thalidomide distribution program.
Herpes Simplex Virus

Background

Infections with herpes simplex virus (HSV) occur frequently in persons with HIV infection and more than 95% of individuals with HIV infection test seropositive for either HSV-1 or HSV-2.[31] Infection with HSV is characterized by periodic reactivation, during which shedding from mucosal surfaces is increased. Shedding of HSV persists despite highly active antiretroviral therapy among patients coinfected with both HSV and HIV.[32]

Clinical Manifestations

Oral herpes manifests most often as lesions on the outer mouth region (Figure 12), inner lips (Figure 13), tongue (Figure 14), or palate (Figure 15); oral herpes is usually caused by infection with HSV-1, but HSV-2 can cause oral lesions. Individuals with their first episode of oral HSV may have more severe and extensive lesions (Figure 16). Oral infection with HSV-1 and HSV-2 are indistinguishable from a clinical perspective. Patients classically experience a sensory prodrome followed by evolution of the lesion(s) from papule to vesicle to crusting stage.[31] If untreated, symptoms persist 5 to 10 days; antiviral therapy initiated at onset of the prodrome can shorten the symptomatic period or even abort the outbreak. Patients with HIV infection and a CD4 count less than 100 cells/mm³ may have deep, extensive and non-healing ulcers[33] and are more likely to develop acyclovir-resistant HSV.[31]

Diagnosis

The clinical diagnosis of HSV lesions can be difficult since HSV lesions can mimic many other infections, particularly when present in the ulcerated form. Therefore, establishing the diagnosis via laboratory testing is recommended.[34] Performing HSV DNA PCR testing is the most sensitive method for diagnosis, but viral culture and antigen detection are also frequently used for diagnostic purposes.

Treatment

The recommended therapy for oral HSV lesions consists of a 5 to 10 day course of oral valacyclovir 1 g twice daily, famciclovir 500 mg twice daily, or acyclovir 400 mg three times daily; intravenous acyclovir 5 mg/kg every 8 hours may be required for severe mucocutaneous disease (Table 2).[31] Long-term suppressive therapy reduces the number of recurrences of mucocutaneous HSV disease in patients with HIV infection. Thus, for patients who have severe outbreaks or who want to minimize the frequency of recurrences suppressive therapy can be used with valacyclovir 500 mg twice daily, famciclovir 500 mg twice daily, or acyclovir 400 mg twice daily.[31] The efficacy and safety of antiviral suppression of HSV for longer than 1 year in immunocompetent patients and beyond 6 months in patients with HIV infection have not been established.
Kaposi's Sarcoma

Background

Kaposi’s sarcoma is a vascular tumor caused by human herpes virus-8 (HHV-8), also known as KS-associated herpes virus (KSHV). Kaposi’s sarcoma remains the most frequent HIV-associated oral malignancy, with a peak incidence occurring among men who have sex with men aged 25 to 59 years. In the current era of the HIV epidemic, as patients are living longer, the overall frequency of malignancies has increased but rates of Kaposi’s sarcoma have dramatically decreased.[35] Research suggests a relationship between immunodeficiency and malignancy, possibly through a mechanism of decreased immune surveillance.

Clinical Manifestations

When Kaposi’s sarcoma involves the mouth, lesions are usually located on the gums (Figure 17) or hard palate (Figure 18) and can appear macular, nodular, raised, or ulcerated, with color ranging from red to purple.[1] Patients frequently present with both intraoral and cutaneous lesions. In addition, patients with intraoral lesions may have lesions lower in the gastrointestinal tract.

Diagnosis

The diagnosis of Kaposi’s sarcoma is usually strongly suspected based on characteristic clinical findings. A definitive diagnosis requires biopsy of the oral lesion(s). Classic findings on pathology include neovascularization with aberrant proliferation of small vessels, atypical spindle-shaped cells with leukocytic infiltration, and hemosiderin-laden macrophages.

Treatment

Combination antiretroviral therapy is recommended for all patients with HIV-related Kaposi’s sarcoma and these lesions often regress with antiretroviral therapy alone.[36] When lesions do not resolve or the initial manifestations are severe, additional treatment may involve a combination of radiation, intralesional chemotherapy, topical therapy or surgical excision.[37] Systemic cytotoxic chemotherapy is generally reserved for treatment of disseminated disease beyond the oral cavity.
Human Papillomavirus

Background

Despite current widespread use of effective antiretroviral therapy for persons with HIV infection, oral lesions associated with human papillomavirus (HPV) have increased in recent years. [38] Oral HPV infection is common among individuals with HIV infection, particularly men who have sex with men, and these infections more frequently involve the oncogenic subtype 16. [38] Previous studies have shown an oral HPV prevalence of 20 to 40% among men with HIV infection compared to an overall prevalence of 6.9% among men and women without HIV infection. [38, 39] A recent analysis of pooled data from 17 prospective studies in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) between 1996 and 2009 found that HPV-related and HPV-unrelated head and neck squamous cell cancers are both elevated in individuals with HIV infection, possibly due to immunosuppression. [40] In addition, other studies have shown an increase (up to 6-fold in one study) in oral warts among patients taking antiretroviral therapy, possibly related to immune reconstitution. [20]

Clinical Manifestations

Oral warts can be cauliflower-like, spiked, or raised with a flat surface. [] Lesions may be white, red, or the color of normal mucosa. Oral warts typically arise at the base of the tongue or tonsillar region (Figure 20), where they can easily be missed on routine oral examination. In addition, oral warts may appear on the lips or gingiva. (Figure 21) It is difficult to differentiate benign and malignant lesions based on visual examination alone.

Diagnosis

The diagnosis of HPV-related oral disease is often made on the basis of a typical clinical appearance; if needed, biopsy can confirm the diagnosis. Due to the increased frequency of oral lesions and oral cancers in immunocompromised patients, clinicians should maintain a low threshold for performing a biopsy on any suspicious lesion. It is important to note that lesions, including malignant ones, may not be readily visible on routine oral examination and may remain asymptomatic until they are at later stage.

Treatment

No clear standard for the treatment of HPV-related oral lesions has been established, but approaches to therapy may involve surgery, laser therapy, or cryotherapy. The specific treatment chosen is usually based on the location of the lesions, extent of disease, and whether or not the lesions are malignant.
**Summary Points**

- Periodontal disease can complicate management of other chronic health conditions, including HIV, and routine dental care and hygiene are essential components of good oral health.
- Oral candidiasis remains a common opportunistic infection among individuals with HIV infection and fluconazole-resistant candidiasis can complicate management, especially in patients with advanced immunosuppression who receive repeated or prolonged courses of fluconazole.
- Oral candidiasis is generally a clinical diagnosis and first-line therapy includes either oral fluconazole or topical azole therapy. Primary prophylaxis and chronic suppressive therapy are discouraged due to cost, low attributable morbidity, efficacy of acute therapy, and risk of promoting further drug resistance.
- Oral hairy leukoplakia is strongly linked with Epstein-Barr virus and generally causes asymptomatic hyperkeratotic lesions on oral mucosal surfaces. Treatment of underlying HIV with effective antiretroviral therapy usually leads to resolution of OHL lesions.
- Antiretroviral therapy is an important component in treatment of recurrent aphthous stomatitis.
- Oral herpes is usually caused by HSV-1, but HSV-2 can also cause oral lesions. Treatment consists of acyclovir, valacyclovir, or famciclovir.
- The incidence of Kaposi’s sarcoma has decreased significantly following the widespread use of antiretroviral therapy, though KS remains the most frequent HIV-associated oral malignancy and may regress with antiretroviral treatment alone.
- Oral HPV infection is very common among individuals with HIV infection, HPV can cause both benign and malignant oral lesions, and HPV-associated head and neck cancers are on the rise.
Citations


Figures

Figure 1 Pseudomembranous Candidiasis on Palate

Photograph from David H. Spach, MD
Figure 2 Pseudomembranous Candidiasis on Buccal Mucosa

Photograph from David H. Spach, MD
Figure 3 Pseudomembranous Candidiasis on Gingiva (Gums) and Lips
Figure 4 Pseudomembranous Candidiasis on Tongue

Photograph from David H. Spach, MD
Figure 5 Erythematous Candidiasis on Palate

Photograph from David H. Spach, MD
Figure 6 Erythematous Candidiasis on Tongue

Photograph from David H. Spach, MD
Figure 7 Angular Cheilitis

Photograph from David H. Spach, MD
Figure 8 (Image Series) - Oral Hairy Leukoplakia on Lateral Tongue (Image Series) - Oral Hairy Leukoplakia on Lateral Tongue
Image 8A: Anterior View

Photograph from David H. Spach, MD
Figure 8 (Image Series) - Oral Hairy Leukoplakia on Lateral Tongue
Image 8B: Lateral View

Photograph from David H. Spach, MD
Figure 9 Oral Hairy Leukoplakia on Buccal Mucosa

Photograph from David H. Spach, MD
Figure 10 Aphthous Stomatitis on Lip

Photograph from David H. Spach, MD
**Figure 11 Aphthous Lesion on Tongue**

The black arrow points to large aphthous lesion on lateral tongue.

Photograph from David H. Spach, MD
Figure 12 Focal HSV Lesions on Lower Lip and Face

Characteristic focal cluster of vesicular lesions with a surrounding erythematous base.

Photograph from David H. Spach, MD
Figure 13 Oral HSV Lesion on Inner Lip

Photograph from David H. Spach, MD
Figure 14 HSV Lesion on Tongue and Outer Lip

Photograph from David H. Spach, MD
Figure 15 HSV Oral Lesion Involving Palate and Uvula

The black arrows are pointing to aphthous lesions—the right lesion is on the soft palate and the left is at the base of the uvula.

Photograph from David H. Spach, MD
**Figure 16 First Episode of Oral HSV**

Note the extensive number of lesions and the involvement of the entire lip region.

Photograph from David H. Spach, MD
Figure 17 Oral Kaposi's Sarcoma on Lower Gum

The white arrow pointing to isolated Kaposi's sarcoma lesion on lower gum region

Photograph from David H. Spach, MD
Figure 18 Multiple Oral Kaposi's Sarcoma Lesions on Palate

Photograph from Deborah A. Stimpson, PA
Figure 19 Extensive Nodular Oral Kaposi's Sarcoma on Palate

Photograph from Brian R. Wood, MD
Figure 20 Intraoral Wart on Tonsillar Region

Photograph from Michael A. Siegel, DDS, MS
Figure 21 Oral Warts on Upper Gingiva

Photograph from Michael A. Siegel, DDS, MS
Table 1. **Guidelines for the Prevention and Treatment of Opportunistic Infections**

**Treatment of Oropharyngeal Candidiasis: Initial Episodes**

<table>
<thead>
<tr>
<th>Preferred Therapy (Duration: 7-14 Days)</th>
</tr>
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<tbody>
<tr>
<td>• Fluconazole 100 mg PO once daily (AI)</td>
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</tbody>
</table>

**Alternative Therapy**

- Clotrimazole troches 10 mg PO 5 times daily (BI), or
- Miconazole mucoadhesive buccal tablet 50 mg: Apply to mucosal surface over the canine fossa once daily (do not swallow, chew, or crush tablet). Refer to product label for more detailed application instructions, (BI) or
- Itraconazole oral solution 200 mg PO daily (BI), or
- Posaconazole oral suspension 400 mg PO BID for one day, then 400 mg daily (BI), or
- Nystatin suspension 4–6 mL QID or 1–2 flavored pastilles 4–5 times daily (BII)

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

**Source:**

Table 2. **Guidelines for the Prevention and Treatment of Opportunistic Infections**

**Recommendations for Treating Oropharyngeal Herpes Simplex Virus (HSV) Infections**

<table>
<thead>
<tr>
<th>Treating Oropharyngeal Lesions (Duration: 5-10 Days)</th>
</tr>
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<tbody>
<tr>
<td>• Valacyclovir 1 g PO BID (AIII), or</td>
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<tr>
<td>• Famciclovir 500 mg PO BID (AIII), or</td>
</tr>
<tr>
<td>• Acyclovir 400 mg PO TID (AIII)</td>
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<table>
<thead>
<tr>
<th>Treating Severe Mucocutaneous HSV Infections (AIII)</th>
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<tbody>
<tr>
<td>• Initial therapy acyclovir 5 mg/kg IV q8hr</td>
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<tr>
<td>• After lesions begin to regress, change to oral therapy as above.</td>
</tr>
<tr>
<td>• Continue treatment until lesions have completely healed.</td>
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</table>

**Chronic Suppressive Therapy**

*Indications:*

- For patients with severe recurrences (AI), or
- Patients who want to minimize the frequency of recurrences (AI), or
- To reduce the risk of genital ulcer disease in patients with CD4 cell counts <250 cells/mm$^3$ who are starting antiretroviral therapy (BI)

*Treatment:*

- Valacyclovir 500 mg PO BID (AI), or
- Famciclovir 500 mg PO BID (AI), or
- Acyclovir 400 mg PO BID (AI)
- Evaluate ongoing need for suppressive therapy annually.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Source:
