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Herpetic gingivostomatitis in young children

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INTRODUCTION

Gingivostomatitis is the most common manifestation of primary herpes simplex virus (HSV) infection during childhood. Primary herpetic gingivostomatitis is characterized by ulcerative lesions of the gingiva and mucous membranes of the mouth (picture 1), often with perioral vesicular lesions (picture 2A-B).

The clinical features, diagnosis, management, and prevention of herpetic gingivostomatitis will be discussed here. Neonatal HSV infection is discussed separately. (See "Neonatal herpes simplex virus infection: Clinical features and diagnosis" and "Neonatal herpes simplex virus infection: Management and prevention".)

PATHOGENESIS

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 (eg, the trigeminal ganglion), where it remains latent. Reactivation results in recurrent HSV disease (eg, herpes labialis).

VIROLOGY

Herpetic gingivostomatitis is caused by herpes simplex virus type 1 [1].

EPIDEMIOLOGY

Primary herpetic gingivostomatitis typically occurs in children between six months and five years of age, but it can occur in older children and adolescents [1]. (See "Epidemiology, clinical manifestations, and diagnosis of herpes simplex virus type 1 infection".)

Herpetic gingivostomatitis occurs throughout the year, with no particular seasonal distribution [2]. In a retrospective review at a single institution, herpes simplex virus gingivostomatitis was diagnosed in 1.6 per 10,000 emergency department visits and 5.6 per 10,000 hospital admissions [3].

TRANSMISSION

Herpes simplex virus type 1 (HSV-1) infections usually result from direct contact with infected oral secretions or lesions. HSV infections can be transmitted from symptomatic or asymptomatic individuals with primary or recurrent HSV infection [4].

Children with primary gingivostomatitis typically shed HSV for at least one week and occasionally for several weeks (median three weeks) [4,5]. Intermittent asymptomatic reactivation and shedding occurs throughout life [4-6].

The incubation period for HSV infection beyond the neonatal period ranges from two days to two weeks, with a mean of four days [2,5,7]. (See "Epidemiology, clinical manifestations, and diagnosis of herpes simplex virus type 1 infection".)

CLINICAL FEATURES

Gingivostomatitis is the most common manifestation of primary herpes simplex virus (HSV) infection [1]. It occurs in 13 to 30 percent of affected children [8-11].

Primary herpetic gingivostomatitis is characterized by ulcerative lesions of the gingiva and mucous membranes of the mouth (picture 1), often with perioral vesicular lesions (picture 2A-B). Herpetic gingivostomatitis occurs approximately one week after contact with an infected child or adult (the contact case often is asymptomatic). It generally begins with a prodrome that lasts approximately four days and may include fever (>38°C [100.4°F]), anorexia, irritability, malaise, sleeplessness, and headache [1,12,13]. Caregivers may attribute these symptoms to teething in children whose primary teeth are erupting, but children who are teething do not have oropharyngeal lesions [14].

The eruption on the oral mucosa begins with red, edematous marginal gingivae that bleed easily and clusters of small vesicles (picture 1) [1,12,13]. The vesicles become yellow after rupture and are surrounded by a red halo. They coalesce to form large, painful ulcers of the oral and perioral tissues (picture 2A and picture 3). They bleed easily and may become covered with

a black crust [15]. The lesions involve the buccal mucosa, tongue, gingiva, hard palate, and pharynx; the lips and perioral skin are affected in approximately two-thirds of cases [1,8]. Mild lesions typically heal without scarring in approximately one week, but healing may require 14 to 21 days in severe cases [1,12]. (See 'Clinical course' below.)

Associated symptoms and signs may include bad breath, refusal to drink, anorexia, fever, arthralgia, headache, and submandibular or cervical lymphadenitis [1,8]. Refusal to drink may result in dehydration, which is the most frequent complication. (See 'Complications' below.)

After the primary infection, HSV migrates to the trigeminal ganglion, where it remains in a latent state unless it is reactivated. Reactivation can be induced by exposure to sunlight, cold, trauma, stress, or immunosuppression, and may occur in the oral cavity (recurrent stomatitis) or on the lips (herpes labialis) (picture 4). Herpes labialis is discussed separately. (See "Epidemiology, clinical manifestations, and diagnosis of herpes simplex virus type 1 infection" and "Treatment and prevention of herpes simplex virus type 1 in immunocompetent adolescents and adults", section on 'Recurrent infections'.)

CLINICAL COURSE

The natural history of herpes simplex virus type 1 gingivostomatitis was evaluated in a prospective study of 36 children who presented with clinical manifestations lasting <72 hours and were followed with examination and viral culture every two to three days until symptoms resolved [12]. The mean duration of signs and symptoms was as follows:

- Fever – 4.4 days (range 0 to 8 days)
- Oral lesions – 12 days (range 7 to 18 days)
- Extraoral lesions – 12 days (range 0 to 19 days)
- Eating difficulty – 9.1 days (range 4 to 17 days)
- Drinking difficulty – 7.1 days (no range provided)
- Drooling – 6.6 days (range 0 to 13 days)

Viral shedding persisted for a mean of 7.1 days (range 2 to 12 days) [12].

COMPLICATIONS

Complications of herpetic gingivostomatitis include [1,8]:

- Dehydration (the most common complication), which may require hospitalization for parenteral fluid therapy (see "Clinical assessment of hypovolemia (dehydration) in children")

- Herpetic whitlow (picture 5A-B) or herpetic keratitis (picture 6) from autoinoculation; herpetic lesions on the nose should prompt ophthalmologic evaluation for herpetic keratitis (given the proximity of the nose and eyes) (see "Overview of hand infections", section on 'Herpetic whitlow' and "Herpes simplex keratitis")

- Eczema herpeticum in children with atopic dermatitis and other dermatitides (picture 7A-B)

- Lip adhesions, which may be prevented through the application of lip barrier cream [16]

- Secondary bacteremia with upper respiratory bacteria (eg, *Streptococcus pyogenes, Kingella kingae)* or *Staphylococcus aureus* [17-19]; secondary bacteremia is uncommon but should be considered if the child's symptoms worsen (eg, new-onset fever) after a period of gradual recovery

- Herpes simplex virus (HSV) encephalitis (see "Herpes simplex virus type 1 encephalitis")

- Esophagitis (see "Herpes simplex virus infection of the esophagus")

- HSV epiglottitis and pneumonitis are rare complications in immunocompetent children [20] (see "Epidemiology, clinical manifestations, and diagnosis of herpes simplex virus type 1 infection", section on 'Severe manifestations')

Complications in immunocompromised patients include severe local lesions, disseminated HSV infection with visceral involvement (eg, hepatitis), HSV pneumonitis, and HSV encephalitis [1,4].

DIAGNOSIS

The diagnosis of gingivostomatitis generally is made clinically, based upon the typical appearance and location of oral and extraoral lesions (picture 1 and picture 2A) [8].

In cases where it is necessary to confirm an etiologic diagnosis, herpes simplex virus type 1 (HSV-1) can be diagnosed with viral culture, immunofluorescence, or polymerase chain reaction. (See "Epidemiology, clinical manifestations, and diagnosis of herpes simplex virus type 1 infection", section on 'Diagnosis'.)

The Tzanck smear, which demonstrates the cytopathic effect of herpes viruses, can be performed in patients with active lesions. However, it has limited utility because it is only helpful if it is positive and does not distinguish between HSV-1, HSV type 2, and varicella zoster virus. (See "Office-based dermatologic diagnostic procedures", section on 'Tzanck smear'.)

DIFFERENTIAL DIAGNOSIS

Herpes simplex virus (HSV) gingivostomatitis must be differentiated from a number of other conditions with oral lesions because the treatment, clinical course, and/or public health implications differ [8]. HSV gingivostomatitis can usually be differentiated from these conditions by the presence, appearance, and location of oral and extraoral lesions [12]. These conditions include:

- Herpangina – Herpangina, which is usually caused by group A coxsackieviruses, typically causes painful posterior pharyngeal lesions that do not bleed (picture 8), has a more acute onset and shorter duration than HSV gingivostomatitis, and occurs primarily in the summer and early fall [15]. (See "Hand, foot, and mouth disease and herpangina", section on 'Herpangina' and "Enterovirus and parechovirus infections: Clinical features, laboratory diagnosis, treatment, and prevention".)

- Hand, foot, and mouth disease (HFMD) – HFMD (picture 9A-C) is caused by a number of coxsackie A and B viruses. It occurs in the spring and early summer. The extremity lesions usually are bilateral (in contrast to herpetic whitlow, which typically is unilateral) [15]. The associated extremity lesions and seasonality are most helpful in distinguishing HFMD from herpetic gingivostomatitis, even if the oral lesions appear in the anterior oropharynx. Although the exanthem of HFMD typically involves the extremities, other sites may be involved (eg, the buttocks, torso, face); it is imperative to look for lesions at other sites. (See "Hand, foot, and mouth disease and herpangina", section on 'Clinical features' and "Enterovirus and parechovirus infections: Epidemiology and pathogenesis".)

- Oral candidiasis – Oral candidiasis is characterized by white plaques on the buccal mucosa, palate, tongue, or oropharynx (picture 10). It occurs in infants after exposure to the microorganisms of the vaginal tract, in children who are treated with antibiotics or inhaled glucocorticoids, and in immunocompromised children. (See "Oropharyngeal candidiasis in adults" and "Candida infections in children", section on 'Oropharyngeal candidiasis'.)

- Aphthous ulcers – Aphthae, also called canker sores, are painful oral lesions that appear as localized, shallow, round to oval ulcers with a grayish base (picture 11A-B). They are not preceded by vesicles and occur exclusively on nonkeratinized mucosal surfaces; lesions on the lips and perioral lesions exclude a diagnosis of aphthous ulcer. (See "Oral lesions", section on 'Erosive, ulcerative, and bullous lesions'.)

- Stevens-Johnson syndrome – Stevens-Johnson syndrome is characterized by a prodrome of malaise and fever, followed by the rapid onset of erythematous or purpuric macules and plaques. The skin lesions progress to epidermal necrosis and sloughing. Mucosal membranes are affected in at least 90 percent of patients (picture 12). (See "Stevens-Johnson syndrome and toxic epidermal necrolysis: Pathogenesis, clinical manifestations, and diagnosis".)

- Behçet syndrome – Behçet syndrome is characterized by recurrent oral aphthae and any of several systemic manifestations, including genital aphthae, ocular disease, skin lesions, gastrointestinal involvement, neurologic disease, vascular disease, or arthritis. (See "Clinical manifestations and diagnosis of Behçet syndrome".)

MANAGEMENT OF GINGIVOSTOMATITIS

Indications for hospitalization — Indications for hospitalization in children with herpetic gingivostomatitis include:

- Inability to maintain adequate hydration. (See "Clinical assessment of hypovolemia (dehydration) in children".)
- Immunocompromised host – Immunocompromised children with herpetic gingivostomatitis should be treated with intravenous (IV) or oral acyclovir and monitored closely for spread of infection. (See 'Immunocompromised children' below.)
- Eczema herpeticum.
- Encephalitis, epiglottitis, or pneumonitis – Children with herpes simplex virus (HSV) encephalitis, epiglottitis, or pneumonitis should be treated with IV acyclovir. (See "Acute viral encephalitis in children: Clinical manifestations and diagnosis", section on 'Clinical features' and "Epidemiology, clinical manifestations, and diagnosis of herpes simplex virus type 1 infection", section on 'Respiratory tract infections'.)
- Herpetic keratitis – Although herpetic keratitis usually can be treated with topical and/or oral medications, admission may be necessary if there are concerns about adherence to the treatment regimen. (See "Herpes simplex keratitis", section on 'Management'.)

Supportive care for all children

Fluid intake — Maintenance of hydration is a major component of the management of herpetic gingivostomatitis. Fluid intake should be encouraged to avoid dehydration. Children who are unable to drink sufficiently to maintain hydration should be hospitalized for parenteral fluid therapy [1].

The assessment of hydration status and treatment of dehydration are discussed separately. (See "Clinical assessment of hypovolemia (dehydration) in children" and "Maintenance intravenous fluid therapy in children" and "Treatment of hypovolemia (dehydration) in children".)

Pain control — Adequate pain control may facilitate fluid intake. Oral acetaminophen or ibuprofen may be administered if the child can take them. In severe cases, such as inability to sleep, oral opiates may be required. Opiates should be used with caution; potential adverse

effects include respiratory depression, central nervous system (CNS) depression, hypotension, and constipation.

Prevention of lip adhesions — We suggest application of a barrier cream (eg, petroleum jelly) to the lips to prevent adhesions in young children with HSV gingivostomatitis [16].

Indications for antiviral therapy

Immunocompetent children with severely limited intake

- **Children who present within 96 hours of disease onset** – For immunocompetent children with herpetic gingivostomatitis who have severely limited fluid intake or who have severe pain and who present within 96 hours of disease onset, we suggest oral acyclovir rather than supportive care alone. Oral acyclovir therapy also may be beneficial for children with less severe disease, particularly if they attend child care [21]. Small randomized trials suggest that initiation of oral acyclovir within three to four days of illness onset decreases the duration of symptoms by three to six days and possibly decreases the duration of viral shedding [22-24]. Whether it reduces the risk of complications or recurrence is unknown.

  Consensus regarding the optimal dose and duration of treatment with acyclovir is lacking [21]. We use acyclovir 15 mg/kg by mouth (maximum single dose 200 mg) five times per day for five to seven days, which is the regimen used in the largest published trial [22]. Although we advise administration five times per day, as the child improves (eg, healing of lesions, resolution of fever), acyclovir may be administered three times per day.

  Adverse effects of acyclovir include nausea, vomiting, diarrhea, headaches, and renal failure caused by crystallization in the renal tubules, which is more likely if the patient is dehydrated [21]. Theoretic concerns about the possible selection of acyclovir-resistant strains of HSV type 1 and earlier and more severe recurrences in treated patients have not been demonstrated in patients treated with short courses of acyclovir [21]. (See "Acyclovir: An overview", section on 'Toxicity'.)

  The use of oral acyclovir in the treatment of herpetic gingivostomatitis is supported by three small placebo-controlled randomized trials including a total of 149 children [22-24]. In the largest published trial, 61 children age one to six years with documented HSV gingivostomatitis and symptoms for <3 days were randomly assigned to treatment with oral acyclovir 15 mg/kg five times per day (maximum single dose 200 mg) or placebo for five to seven days [22]. Children in the acyclovir group had shorter median duration of lesions (-6 days, 95% CI -4 to -8 days), fever (-2 days, 95% CI -0.8 to -3.2 days), difficulty drinking (-3 days, 95% CI -1 to -5 days), and viral shedding (-4 days, 95% CI -3 to -5.1). Most participants received ≥80 percent of prescribed therapy (29 of 31 in the acyclovir group and 24 of 30 in the placebo group). Two children in each group had transient mild gastrointestinal

symptoms, but no serious adverse events were reported. The finding of reduced duration of symptoms is consistent with the other two randomized trials [23,24] and supported by observational studies [25,26].

- **Children who present ≥96 hours after illness onset** – For children who present ≥96 hours after illness onset, we provide supportive care. IV fluid therapy may be necessary to treat dehydration. (See 'Supportive care for all children' above.)

Immunocompromised children — For immunocompromised children with herpetic gingivostomatitis, we recommend treatment with IV or oral acyclovir rather than supportive care alone, **regardless of symptom duration before presentation**. The recommendation for systemic acyclovir is based upon randomized trials demonstrating that systemic acyclovir shortens the duration of symptoms and viral shedding in immunocompromised patients with mucocutaneous HSV (not limited to gingivostomatitis) [27-30]. Other treatment options include valacyclovir or famciclovir, if available. These medications require less frequent dosing and may be more bioavailable orally [15]. Whether any of these medications reduce the risk of complications or recurrence is unknown.

The efficacy of oral and IV acyclovir in the treatment of gingivostomatitis in immunocompromised patients has not been directly compared. Decisions about the route of therapy are individualized according to degree of immunosuppression, suspicion for dissemination, severity, and ability to absorb oral acyclovir from the gastrointestinal tract (eg, IV therapy is preferred for patients with gastrointestinal pathology in whom poor oral absorption is a concern) [15,31,32]. Consultation with a specialist in pediatric infectious disease is suggested. We use IV acyclovir if the infection is severe or life-threatening (eg, disseminated infection, CNS complications [eg, meningoencephalitis], hepatitis, pneumonitis). Patients who are treated orally warrant frequent reassessment for signs of dissemination.

We use the following regimens for initial treatment [32,33]:

- **IV** – Acyclovir 30 mg/kg per day IV divided in three doses (for children of all ages) for 10 to 14 days; dose adjustments for obese children are discussed separately (see "Acyclovir: An overview", section on 'Obesity')

  In the event that IV acyclovir is not available (eg, during a shortage; when existing supplies are reserved for neonates with HSV, individuals with HSV encephalitis, and pregnant women), alternatives to IV acyclovir are discussed separately. (See "Acyclovir: An overview", section on 'If there is an acyclovir shortage'.)

  The patient may be switched from IV acyclovir to oral acyclovir once the patient is clinically improved. Oral acyclovir is continued until healing is complete [32].

- **Oral** – Acyclovir 1000 mg/day orally divided in three to five doses (for children ≥2 years) for 10 to 14 days

  We discontinue oral acyclovir after 10 days if HSV signs and symptoms are clinically resolved.

Adverse effects of parenteral acyclovir therapy in immune-compromised children treated for mucocutaneous HSV include phlebitis in 14 percent of patients, obstructive nephropathy with transient increase in serum creatinine levels (5 to 10 percent of patients), hives (5 percent), nausea and vomiting (1 to 5 percent), and reversible neurologic symptoms such as agitation, lethargy, and disorientation (1 percent) [15]. Maintenance of adequate hydration (eg, keeping urine specific gravity below 1.010) may prevent development of obstructive nephropathy. (See "Acyclovir: An overview", section on 'Toxicity'.)

Use of systemic acyclovir for the treatment of herpetic gingivostomatitis in immunocompromised children is supported by several small placebo-controlled randomized trials in immunocompromised patients (including some children and adolescents) [27-30]. In three of these trials [27-29], IV acyclovir shortened the duration of development of new lesions (1 versus 3 days), the time to crusting of lesions (3 to 7 days versus 9 to 14 days), the time to healing of lesions (12 to 14 versus 18 to 28 days), the duration of pain (4 to 10 versus 7 to 16 days) and duration of viral shedding (3 versus 14 to 17 days); the rates of adverse reactions were similar between groups [27-29]. In the fourth trial, 21 hematopoietic cell transplant recipients (age 14 to 61 years) with mucocutaneous HSV infection were randomly assigned to oral acyclovir or placebo [30]. Oral acyclovir shortened the median duration of development of new lesions (1 versus 10 days), time to healing of lesions (8 versus 21 days), duration of pain (6 versus 16 days), and duration of viral shedding (2 versus >9 days) [30].

Failure to respond to antiviral therapy — Treatment failure should be considered if HSV lesions do not begin to resolve after five to seven days of initiation of antiviral therapy or if new lesions develop after three to four days of antiviral therapy [32].

- **Initial therapy with oral** acyclovir – We hospitalize children with gingivostomatitis who fail to respond to oral acyclovir therapy if they remain severely uncomfortable, are at risk for dehydration, and/or are immunocompromised. We initiate acyclovir 15 to 30 mg/kg per day IV divided in three doses while evaluating for other conditions in the differential diagnosis. (See 'Differential diagnosis' above.)

- **Initial therapy with IV** acyclovir – Acyclovir-resistant HSV should be suspected in children with a prolonged course of HSV stomatitis despite parenteral acyclovir [34,35]. Acyclovir-resistant HSV occurs in approximately 5 to 10 percent of immunocompromised patients [36]. Confirmation of acyclovir resistance generally requires viral culture; results may not be available for days to weeks. When acyclovir resistance is strongly suspected, a different

antiviral agent should be initiated pending culture and susceptibility results [31,32]. Foscarnet 80 to 120 mg/kg per day in two to three divided doses has been recommended as the drug of choice for acyclovir-resistant HSV [4,31,32,37]. Given that decreased thymidine kinase activity is the most common mechanism of acyclovir resistance, famciclovir, valacyclovir, and ganciclovir should also be avoided. (See "Acyclovir: An overview", section on 'Mechanism of resistance'.)

Unproven therapies

Topical antiviral agents — Topical antiviral agents (eg, acyclovir, penciclovir, docosanol) are not helpful in the treatment of primary herpes gingivostomatitis in immunocompetent patients and are not recommended. Although topical acyclovir appears to speed the resolution of lesions in immunocompromised patients [38], parenteral therapy is preferred. (See 'Immunocompromised children' above.)

"Magic mouthwash" and other topical therapies — We do not routinely suggest "magic mouthwash" to coat lesions and/or soothe pain given the lack of evidence of benefit from clinical trials, the potential for harm (eg, toxicity from systemic absorption, allergic reaction), and difficulty of application in young children [3].

"Magic mouthwash" consists of various combinations of diphenhydramine, magnesia-alumina (eg, Maalox), Kaolin pectin (eg, Kaopectate), sucralfate, and/or viscous lidocaine. There is no standardized "recipe," volume, frequency of administration, or mode of application (eg, swish and spit, swish and swallow, apply with swab) [3]. The inclusion of viscous lidocaine is controversial. In two separate randomized trials, oral fluid intake was similar among children presenting to the emergency department with acute infectious oral ulcers and decreased oral intake one hour after receiving viscous lidocaine or placebo (8.5 and 9.3 mL/kg, respectively) [39], or sucralfate or placebo (9.7 and 10.7 mL/kg, respectively) [40].

Zilactin, a nonprescription topical medication containing lidocaine and hydroxypropyl cellulose, which adheres to mucosa, may be used to protect lesions from trauma and irritants [41]. ORA5, another nonprescription topical therapy (0.11% iodine/potassium-iodide/copper sulfate solution) works by the same mechanism. Published studies regarding the efficacy and safety of Zilactin and ORA5 in young children with herpetic gingivostomatitis are lacking.

Topical therapies are potentially problematic for a number of reasons:

- Systemic absorption of diphenhydramine, lidocaine, or benzocaine may result in toxicity or adverse effects, such as sedation or seizures [3,42].
- Topical benzocaine may cause methemoglobinemia and should not be used in children younger than two years [43,44]. (See "Clinical use of topical anesthetics in children", section on 'Benzocaine' and "Methemoglobinemia", section on 'Acquired causes'.)

- Viscous lidocaine may predispose to self-injury if the child chews on anesthetized oral mucosa or chokes on secretions secondary to pharyngeal anesthesia [15,42].
- Most children in the gingivostomatitis age group are unable to swish and spit [3,45].
- Young children with painful oral lesions are unlikely to allow manipulation of inflamed mucosa for application with a swab [3].

MANAGEMENT OF COMPLICATIONS

- **Dehydration** – Dehydration is the most common complication of herpetic gingivostomatitis. The management of dehydration on children is discussed separately. (See "Maintenance intravenous fluid therapy in children" and "Treatment of hypovolemia (dehydration) in children".)
- **Secondary bacterial infection** – Antibiotics are not routinely administered to children with herpes simplex virus (HSV) gingivostomatitis unless a secondary bacterial infection is suspected. Secondary infections are uncommon but should be considered if there is worsening of the child's symptoms (eg, new onset of fever) after a period of gradual recovery. If a secondary bacterial infection is suspected, then empiric antibiotics with activity against *S. pyogenes*, *K. kingae,* and *S. aureus* (eg, amoxicillin or clindamycin in patients with penicillin allergy) may be administered awaiting the results of a blood culture to ensure appropriate antibiotic selection. The course of antibiotics is typically 7 to 10 days.

  Secondary bacteremia is treated with antimicrobial therapy targeted to the isolated pathogen:

  - *K. kingae* – *K. kingae* is usually susceptible to penicillin and cephalosporins (eg, cefazolin, cephalexin, cefotaxime, ceftriaxone, cefixime) [46,47]
  - *S. pyogenes* (see "Invasive group A streptococcal infections in children", section on 'Treatment')
  - *S. aureus* (see "Staphylococcus aureus bacteremia in children: Management and outcome", section on 'Management')
- **Lip adhesions** – Lip adhesions can resolve spontaneously with normal opening of the mouth but may require surgical release [16].
- **Complications related to spread of HSV –** The management the more common complications related to spread of HSV infection is discussed in separate topic reviews:

- Herpetic whitlow (picture 5A-B) (see "Overview of hand infections", section on 'Herpetic whitlow')
- Herpetic keratitis (picture 6) (see "Herpes simplex keratitis", section on 'Management')
- Eczema herpeticum (picture 7A-B) (see "Treatment of atopic dermatitis (eczema)", section on 'Viral infections')
- HSV esophagitis (see "Herpes simplex virus infection of the esophagus", section on 'Treatment')
- HSV encephalitis (see "Herpes simplex virus type 1 encephalitis", section on 'Treatment')

PREVENTION

Oral herpes simplex virus (HSV) infections are common in young children. Most of these infections are asymptomatic, with shedding of virus in the absence of clinical disease.

Child care — Children with gingivostomatitis who do not have control of oral secretions should be excluded from child care/school [4].

Isolation — Contact precautions are recommended for hospitalized children with severe mucocutaneous HSV disease (in addition to standard precautions) [4]. (See "Infection prevention: Precautions for preventing transmission of infection", section on 'Contact precautions'.)

SUMMARY AND RECOMMENDATIONS

- **Epidemiology and transmission** – Herpetic gingivostomatitis is caused by herpes simplex virus type 1 (HSV-1). HSV-1 gingivostomatitis typically occurs in children between six months and five years of age. It occurs throughout the year. HSV-1 infections usually result from direct contact with infected oral secretions or lesions. Children with primary gingivostomatitis typically shed HSV for at least one week (median three weeks).
- **Clinical features and complications** – Herpetic gingivostomatitis is characterized by ulcerative lesions of the gingiva and mucous membranes of the mouth (picture 1), often with perioral vesicular lesions (picture 2A). The oral and extraoral lesions follow a prodrome of fever and constitutional symptoms. The lesions begin as vesicles, which coalesce to form painful ulcers with generalized edematous and bleeding gingiva (picture 1). Associated findings include fever, bad breath, refusal to drink, anorexia, and submandibular or cervical lymphadenitis. (See 'Clinical features' above.)

Dehydration is the most common complication. Less common complications include spread of HSV to other sites (eg, herpetic whitlow (picture 5A-B), herpetic keratitis (picture 6), eczema herpeticum (picture 7A-B), encephalitis, esophagitis, pneumonitis, eczema herpeticum (picture 7A-B)), lip adhesions, and secondary bacteremia. (See 'Complications' above.)

- **Diagnosis** – The diagnosis of gingivostomatitis usually is made clinically based upon the typical appearance and location of oral and extraoral lesions (picture 1 and picture 2A). If necessary, HSV-1 can be confirmed with viral culture, immunofluorescence, or polymerase chain reaction. (See 'Diagnosis' above.)

- **Differential diagnosis** – The presence, appearance, and location of oral and extraoral lesions help to distinguish HSV-1 gingivostomatitis from other conditions in the differential diagnosis, including (see 'Differential diagnosis' above):

  - Herpangina (picture 8)
  - Hand, foot, and mouth disease (picture 9A-C)
  - Oral candidiasis (picture 10)
  - Aphthous ulcers (picture 11A-B)
  - Stevens-Johnson syndrome
  - Behçet syndrome

- **Supportive care** – Supportive care, with an emphasis on maintenance of hydration, is the mainstay of therapy. Pain control and application of a barrier cream (eg, petroleum jelly) to the lips to prevent adhesions are additional supportive measures. (See 'Supportive care for all children' above.)

- **Antiviral therapy**

  - Immunocompetent children – For immunocompetent children with herpetic gingivostomatitis with severely limited fluid intake or who have severe pain, and who present within 96 hours of disease onset, we suggest oral antiviral therapy with acyclovir rather than supportive care alone (**Grade 2B**). In randomized trials, initiation of oral acyclovir within three to four days of illness onset decreased the duration of symptoms by three to six days. (See 'Immunocompetent children with severely limited intake' above.)

    We use acyclovir 15 mg/kg by mouth (maximum single dose 200 mg) five times per day for five to seven days.

  - Immunocompromised children – For immunocompromised children with herpetic gingivostomatitis, we recommend treatment with intravenous (IV) or oral acyclovir rather than supportive care alone (**Grade 1B**). In small randomized trials, systemic acyclovir

shortened the duration of symptoms and viral shedding. (See 'Immunocompromised children' above.)

Decisions about the route of therapy are individualized according to degree of immunosuppression and suspicion for dissemination. We use IV acyclovir if the infection is severe or life-threatening (disseminated infection, central nervous system complications [eg, meningoencephalitis], hepatitis, pneumonitis). We use the following regimens for initial treatment:

- IV – Acyclovir 30 mg/kg per day IV divided in three doses (for children of all ages) for 10 to 14 days
- Oral – Acyclovir 1000 mg/day orally divided in three to five doses (for children ≥2 years) for 10 to 14 days

- **Treatment failure** – Treatment failure should be considered if HSV lesions do not begin to resolve after five to seven days of initiation of antiviral therapy or if new lesions develop after three to four days of antiviral therapy. (See 'Failure to respond to antiviral therapy' above.)

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GRAPHICS

Primary herpes simplex virus gingivostomatitis



Courtesy of Martha Ann Keels, DDS, PhD.

Graphic 58944 Version 1.0

Herpetic stomatitis



These three children demonstrate the spectrum of oral infection with herpes simplex virus, which ranges from asymptomatic to severe.

(A) The first patient has a single vesicle on his tongue.

(B) The second manifests widespread labial lesions.

(C) The third patient shows dissemination to the face. In the young child with facial involvement, fluorescein dye is dripping from the left eye after its instillation in an attempt to identify the typical dendritic ulcer seen with herpetic keratitis.

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Graphic 58542 Version 4.0

Herpetic gingivostomatitis



Scattered ulcerations with overlying slough on the tongue and lip of a child.

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Graphic 122954 Version 2.0

Herpes simplex virus lesion on the lip



Courtesy of Martha Ann Keels, DDS, PhD.

Graphic 73566 Version 1.0

Cold sores (fever blisters)



Cold sores are caused by reactivation of the herpes simplex virus. They are characterized by a vesicular eruption on the skin adjacent to the lips; the vesicles rupture to form ulcers and crusts that heal without scarring.

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Graphic 115299 Version 1.0

Herpetic whitlow



In addition to erythema, swelling, and pain, herpetic whitlow is characterized by the presence of vesicular or pustular lesions. Patients may also experience fever, lymphadenitis, and epitrochlear or axillary lymphadenopathy.

Reproduced with permission from: Nikkels AF, Peirard GE. Treatment of mucocutaneous presentations of herpes simplex virus infections. Am J Clin Dermatol 2002; 3:479. Copyright © 2002 Adis International.

Graphic 75510 Version 6.0

Herpetic whitlow



Grouped vesicles on an intensely erythematous base are characteristic of herpes simplex infection. The lesion is usually monolateral and is more often painful than pruritic.

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Graphic 52029 Version 8.0

Herpes simplex keratitis

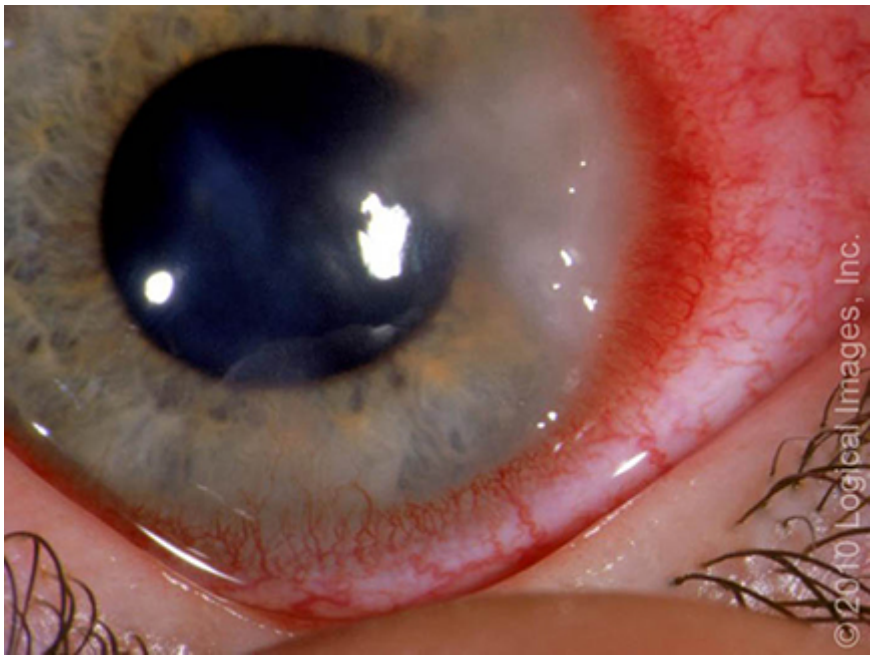


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Graphic 69359 Version 5.0

Eczema herpeticum



Hemorrhagic crusts and vesicles due to herpes simplex virus infection are present on the hand of this infant with underlying atopic dermatitis.

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Eczema herpeticum

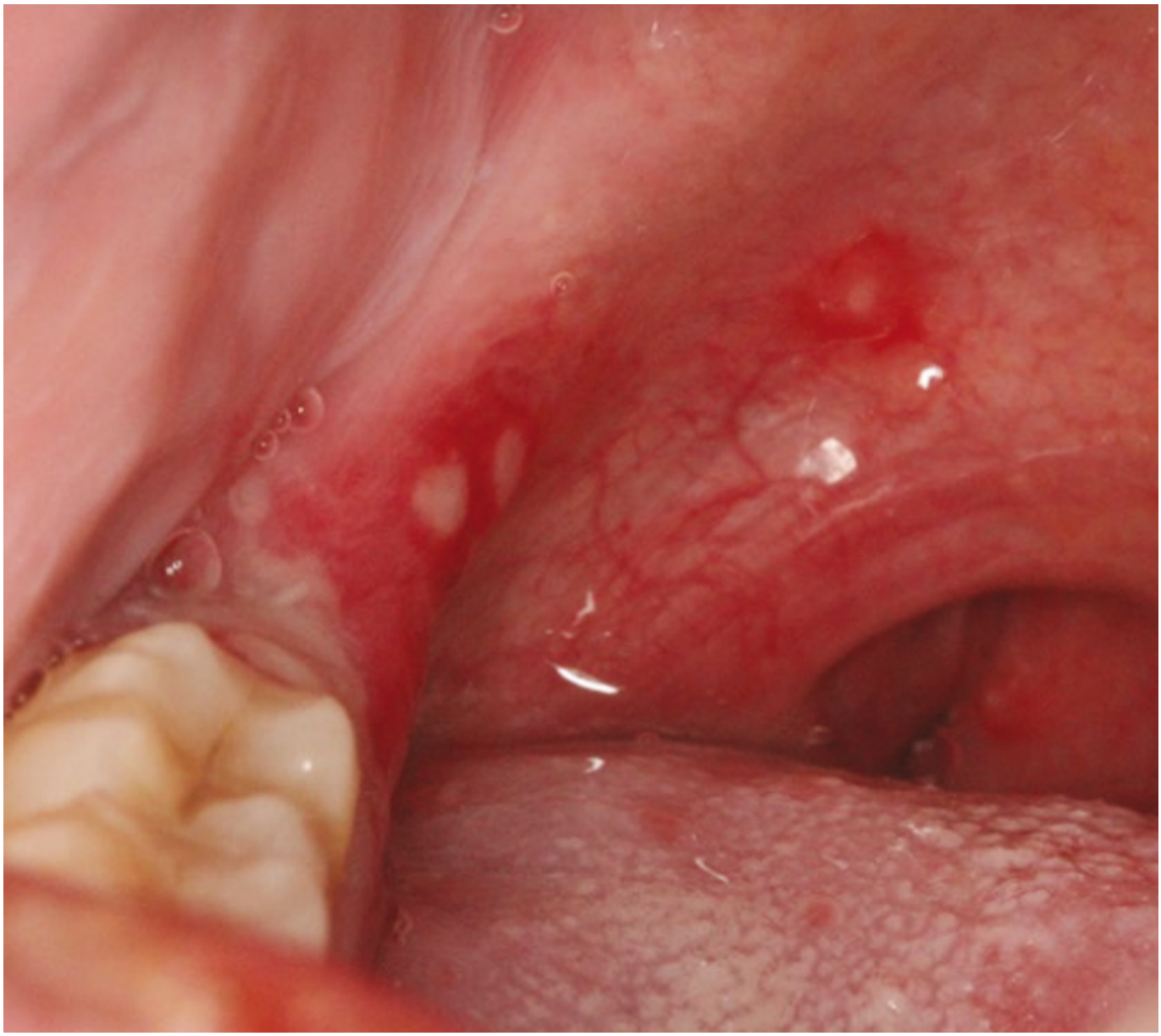


Hemorrhagic crusts and vesicles due to herpes simplex virus infection are present on the face of this infant with underlying atopic dermatitis.

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Graphic 64142 Version 5.0

Herpangina

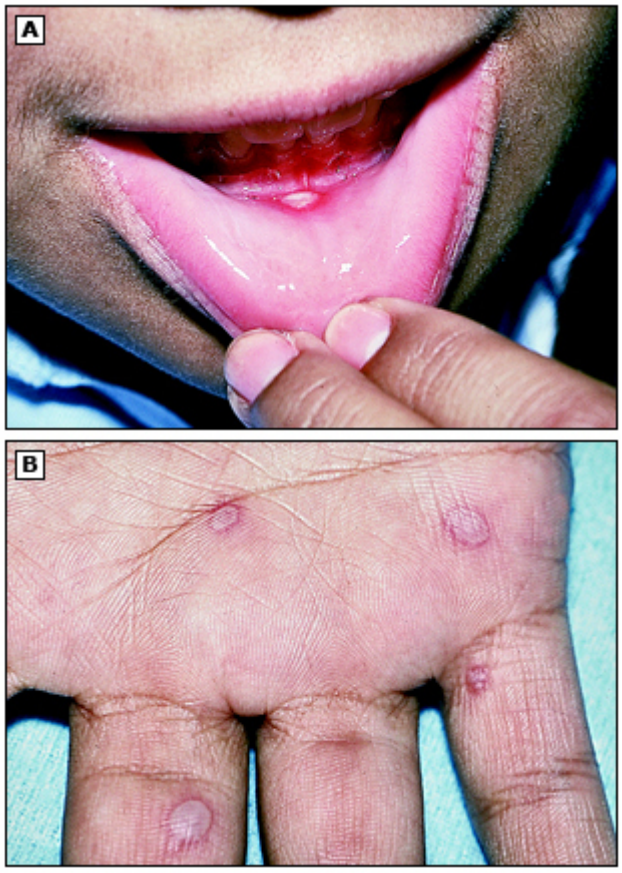


Small and symmetrical ulcers of herpangina on the soft palate and retromolar pad.

From: Mortazavi H, Safi Y, Baharvand M, Rahmani S. Diagnostic features of common oral ulcerative lesions: An updated decision tree. Int J Dent 2016. Available at: https://www.hindawi.com/journals/ijd/2016/7278925/. Copyright © 2016 The Authors (Accesse on March 6, 2020). Reproduced under the terms of the Creative Commons Attribution License 4.0.

Graphic 127342 Version 1.0

Hand-foot-and-mouth disease - lip and hand



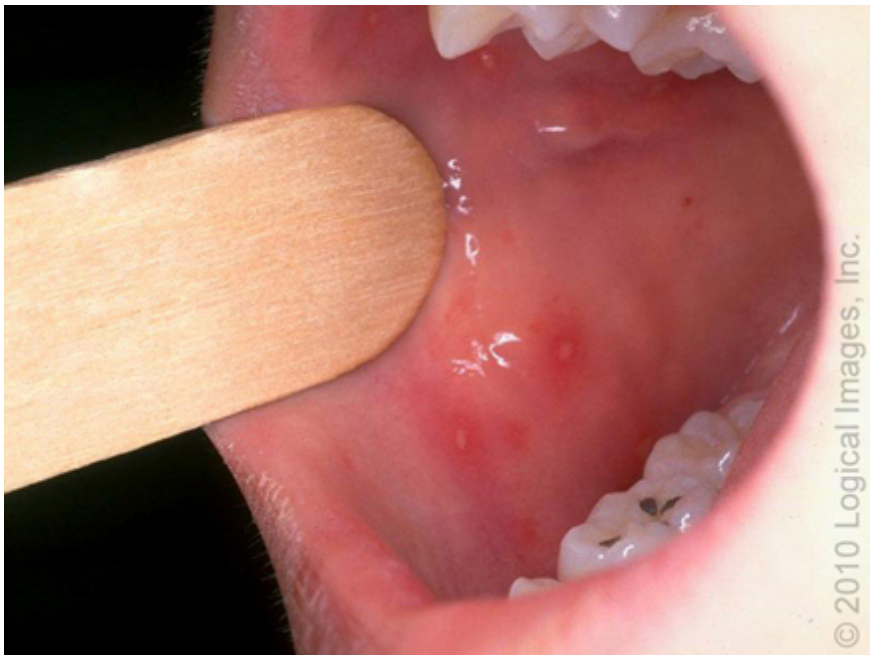
(A) Oral lesion: Note the oval shape and rim of erythema.

(B) Oval intact vesicles are noted on the palm.

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Hand-foot-and-mouth disease



Small ulcers are present on the oral mucosa.

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Graphic 58566 Version 8.0

Hand-foot-and-mouth disease

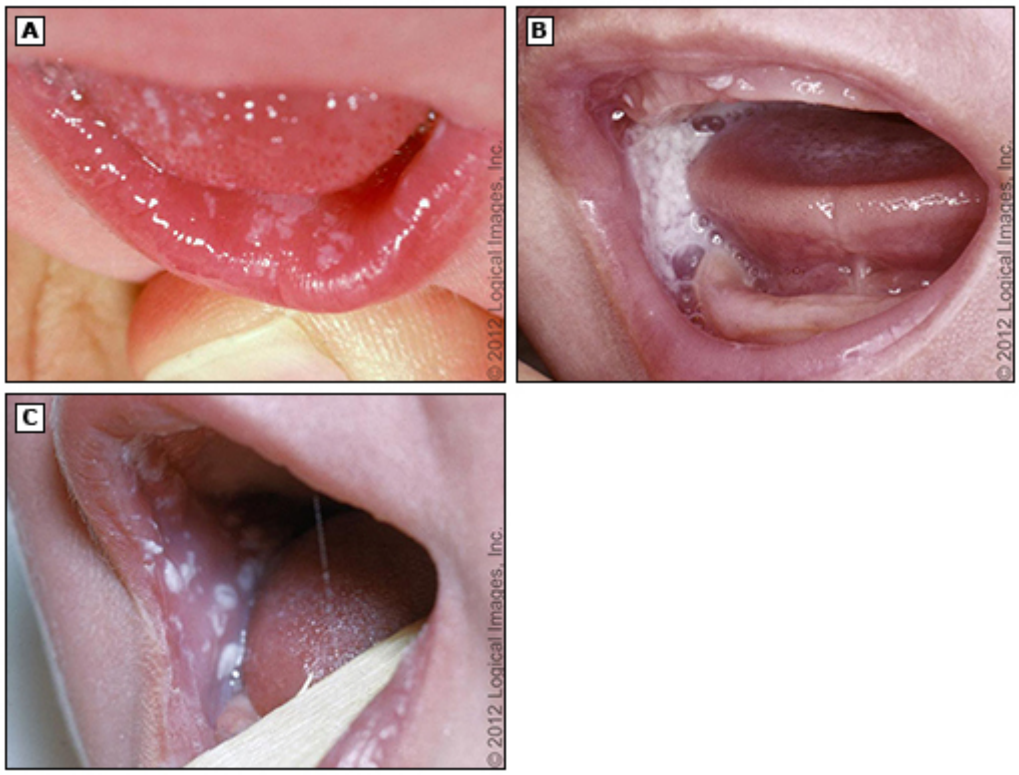


Multiple vesicular lesions on an erythematous base are present on the foot.

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Three examples of thrush (oral candidiasis) in an infant



Note the white plaques on the inner lip and tongue (A) and on the buccal mucosa (B and C).

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Aphthous ulcer



Courtesy of Martha Ann Keels, DDS, PhD.

Graphic 56488 Version 2.0

Aphthous ulcers



Round, yellow-gray ulcers are present on the oral mucosa.

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Mucosal changes in Stevens-Johnson syndrome/toxic epidermal necrolysis



Changes similar to those observed in SJS/TEN can also be observed in erythema multiforme majus.

SJS: Stevens-Johnson syndrome; TEN: toxic epidermal necrolysis.

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