

Oral herpes simplex (HSV-1)

Synonyms: oral herpes labialis, cold sore

What is oral herpes simplex?

Of the herpes viruses, herpes simplex virus type 1 (HSV-1) is usually the cause of oral infection. After primary infection, HSV-1 becomes latent, usually in the dorsal root ganglia of the trigeminal nerve. Rarely, herpes simplex virus type 2 (HSV-2) may cause primary infection of the oral cavity, typically in association with orogenital sex; however, recurrent oral HSV-2 disease is rare.

Oral herpes simplex epidemiology^[1]

- Around 40% of young adults who are seropositive for HSV-1 have recurrent cold sores.
- Recurrences occur typically between two and six times a year.
- A study of the global burden of HSV-1 reported an estimated worldwide prevalence of HSV-1 infection among those aged 0-49 years in 2012 of 67%. Prevalence increased with age and was high across all regions but highest in Africa (87% overall prevalence) and lowest in the Americas (40-50%).^[2]

Risk factors

- Transmission is due to viral shedding into saliva and can occur by direct contact with saliva (eg, kissing). Viral shedding into saliva may occur during asymptomatic infection but it is thought that the risk of infection is much smaller than during symptomatic infection.
- Viral shedding can occur up to 60 hours after the onset of symptoms.^[1]

- Factors that may trigger a recurrence of oral herpes simplex include immunosuppression (eg, corticosteroids), upper respiratory tract infections, fatigue, emotional stress, physical trauma, exposure to sun (ultraviolet light), trauma and menstruation.
- Obesity may increase susceptibility to HSV-1 infection.^[3]

Oral herpes simplex symptoms

Infection with HSV can cause pain and blistering within the mouth (gingivostomatitis or recurrent oral ulceration) or on or around the lips (cold sores or herpes labialis).



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Primary infection

- This occurs most often in infancy or childhood. It may or may not be symptomatic.
- Gingivostomatitis is the most common presentation in young children. It presents with vesicles and ulcers on the tongue, lips, gums, buccal mucosa and hard and soft palates. Pain, inability to swallow, drooling and dehydration are common. There may be associated fever, cervical lymphadenopathy, halitosis, lethargy, irritability and loss of appetite.
- Pharyngitis is a more common presentation in adolescents, with lesions in the throat associated with viral symptoms similar to those of infectious mononucleosis.
- Herpetic whitlow may occasionally occur via spread to the fingers.

Recurrent infection

- Cold sore lesions are the most common form of recurrent disease. They tend to occur in the same location, be unilateral and recur two or three times a year on average.
- Prodromal symptoms may occur 6–24 hours before the appearance of a lesion and include tingling, pain and/or itching in the perioral area.
- Cold sores are usually seen on the lips and extend to the skin around the mouth. Other areas on the face, chin, or nose are sometimes involved. Lesions begin as erythematous areas that swell into papules. These become vesicles, which then collapse into ulcers. This takes 1–3 days. The ulcers crust over and the skin returns to normal within about two weeks.
- Oral mucosal lesions are rare and not generally associated with fever. They are usually restricted to small clusters of microvesicles that rupture to leave punctate ulcers, typically on the palatal gingiva. Immunocompromised people may develop chronic ulcers, often on the tongue.

Differential diagnosis

- Differential diagnosis of herpes simplex gingivostomatitis:
 - [Aphthous ulcers](#) – do not cause fever; lesions are more likely to be on non-keratinised mucosa.
 - [Hand, foot and mouth disease](#) – lesions may also be seen on the hands or feet.
 - [Herpes zoster](#) of the second or third division of the trigeminal nerve.
 - [Infectious mononucleosis](#).
 - [Erythema multiforme](#).
 - [Stevens–Johnson syndrome](#).
 - [Behçet's disease](#).
 - [Leukaemia](#).

- Differential diagnosis of cold sores:
 - Aphthous ulcers - are not unilateral and are more likely to be on non-keratinised mucosa.
 - [Chickenpox](#).
 - [Impetigo](#).
 - Lip cancer.
 - Primary oral chancre of [syphilis](#).
- Signs of possible oral cancer include:
 - Ulceration of the oral mucosa persisting for more than three weeks.
 - Oral swellings persisting for more than three weeks.
 - All red or red and white patches of the oral mucosa.
 - The level of suspicion is further increased if the person is a heavy smoker, heavy alcohol drinker, aged over 45 years or male.
- The National Institute for Health and Care Excellence (NICE) guidance on referral for suspected cancer recommends urgent referral:^[4]
 - By a doctor for unexplained ulceration in the oral cavity lasting for more than three weeks.
 - By a dentist for:
 - A lump on the lip or in the oral cavity consistent with oral cancer; or
 - A red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia.

Investigations

- Tests are not usually necessary in immunocompetent people, as history and examination will usually confirm the diagnosis.^[1]

- Viral culture from swabs of lesions has been considered the gold standard but is limited by the short time period of viral shedding and the relatively low number of viral particles present in samples. Also, the risk of a false negative increases from 48 hours after the lesions have appeared.^[5]
- Rapid detection based on polymerase chain reaction (PCR) is available when required (eg, immunocompromised patients, severe infection).^[6]

Oral herpes simplex treatment and management^[1]

- Cold sores or gingivostomatitis are usually mild and self-limiting and so can be managed symptomatically. Reassure the patient that lesions will heal without scarring.
- A soft diet may be needed: drinking should also be encouraged to prevent dehydration.
- Give advice to reduce the risk of transmission:
 - Avoid touching the lesions.
 - Wash hands with soap and water immediately after touching the lesions, such as after applying medication.
 - Topical medications should be dabbed on rather than rubbed in, to minimise trauma.
 - Topical medications or other items that come into contact with a lesion area – eg, lipstick or lip gloss – should not be shared with others.
 - Avoid kissing until the lesions have completely healed.
 - Avoid oral sex until all lesions have completely healed.
 - There is a risk of transmission to the eye if contact lenses become contaminated.
 - Children with cold sores do not need to be excluded from nurseries and schools.

- Advise to seek medical advice if the person's condition deteriorates (eg, the lesion spreads, a new lesions develops after the initial outbreak, persistent fever, inability to eat) or no improvement is seen after 7-10 days.

Drug treatment ^[1]

- Paracetamol and ibuprofen are effective in relieving pain and pyrexia.
- NICE advises against prescribing topical anaesthetic or analgesic preparations, mouthwash or lip barrier preparations. If patients find these helpful they can be bought over the counter, although they are not all licensed for use in children.
- Choline salicylate gel for pain control of cold sores can be bought over the counter (this is contra-indicated under the age of 16 due to Reye's syndrome).
- Topical antiviral agents:
 - Aciclovir 5% (age range is not specified by the manufacturer).
 - The benefits of topical antivirals are small and cold sores usually resolve within 7-10 days even without treatment.
 - Treatment needs to be initiated at the onset of symptoms before vesicles appear and should be bought over the counter rather than being prescribed.
 - Topical antivirals need to be applied frequently for a minimum of 4-5 days.

- Oral antiviral agents:
 - For immunocompetent individuals, oral antivirals are not routinely indicated for the treatment of cold sores but may be indicated in severe episodes. If possible this should be done from the time of the prodrome - ie before vesicles appear.
 - Seek specialist advice for people who are immunocompromised (including people with HIV).
 - Aciclovir is active against herpes viruses but does not eradicate them. It can be used as systemic and topical treatment of herpes simplex infections of the mucous membranes and is used orally for severe herpetic stomatitis.
 - Valaciclovir is an ester of aciclovir. It is licensed for herpes simplex infections of the skin and mucous membranes.
 - Inosine pranobex can be used for mucocutaneous herpes simplex but its efficacy remains unproven and the BNF has marked it as 'less suitable for prescribing'.^[7]
 - The development of aciclovir resistance has led to the study of new antiviral targets, new antiviral mechanisms and new antiviral molecules from which it is hoped novel therapies will emerge.^[8]
- Intravenous antiviral agents:
 - Foscarnet sodium is licensed for use in immunocompromised patients with mucocutaneous herpes simplex infection who do not respond to aciclovir.

Laser treatment

Laser therapy decreases pain and reduces the number of recurrences. It is particularly useful for elderly patients, due to the low frequency of side-effects. However, large-scale double-blind trials have not yet been conducted.^[9] Laser devices can be bought over the counter by patients.^[10]

Referral

- Seek advice for managing immunocompromised individuals who have cold sores, including people with HIV – an immunocompromised person with a severe infection may need admission.
- Seek specialist advice if neonatal herpes is suspected (this is rare; it may present with skin, eye and/or mouth symptoms) and consider doing this if the patient is pregnant, particularly in her third trimester. The risk of transmission to the baby from kissing is greatest when infection develops in the third trimester, as maternal antibodies have not had time to develop.
- Consider admission if the person is unable to swallow due to pain and is at risk of dehydration, or has a complication such as a secondary bacterial infection.

Complications

- [Dehydration](#), especially in children.
- Recurrent lesions at the same site may occasionally cause atrophy and scarring.
- Secondary bacterial infection, including impetigo, can occur.
- Eczema herpeticum can complicate [atopic eczema](#).
- [Bell's palsy](#) is possibly a complication of herpes simplex infection.
- Rare complications include dissemination, herpes encephalitis, meningitis, corneal dendritic ulcers (ocular herpes simplex) and erythema multiforme.

Prognosis

- Oral herpes simplex is usually a self-limiting disease.
- Lesions (whether due to primary infection or recurrent disease) usually heal within 7-10 days, without scarring.^[1]

Oral herpes simplex prevention

- Sunscreen may be useful for people who have recurrences triggered by sunlight but the evidence is equivocal.^{[1] [11]}

- A Cochrane review found evidence that long-term use of oral antivirals can prevent herpes simplex labialis, although the benefit is small and NICE advises that this is not usually recommended in people who are otherwise healthy.^[1] The review found no evidence to confirm the preventative efficacy of any other measures, including topical therapy and laser treatment.^[12]

Further reading

- [Vogel JL, Kristie TM](#); The dynamics of HCF-1 modulation of herpes simplex virus chromatin during initiation of infection. *Viruses*. 2013 May 22;5(5):1272–91. doi: 10.3390/v5051272.
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- [Kriesel JD, Bhatia A, Thomas A](#); Cold sore susceptibility gene-1 genotypes affect the expression of herpes labialis in unrelated human subjects. *Hum Genome Var*. 2014 Nov 20;1:14024. doi: 10.1038/hgv.2014.24. eCollection 2014.

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Authored by:	Peer Reviewed by: Dr Colin Tidy, MRCP	
Originally Published: 21/11/2023	Next review date: 19/05/2022	Document ID: doc_2258

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