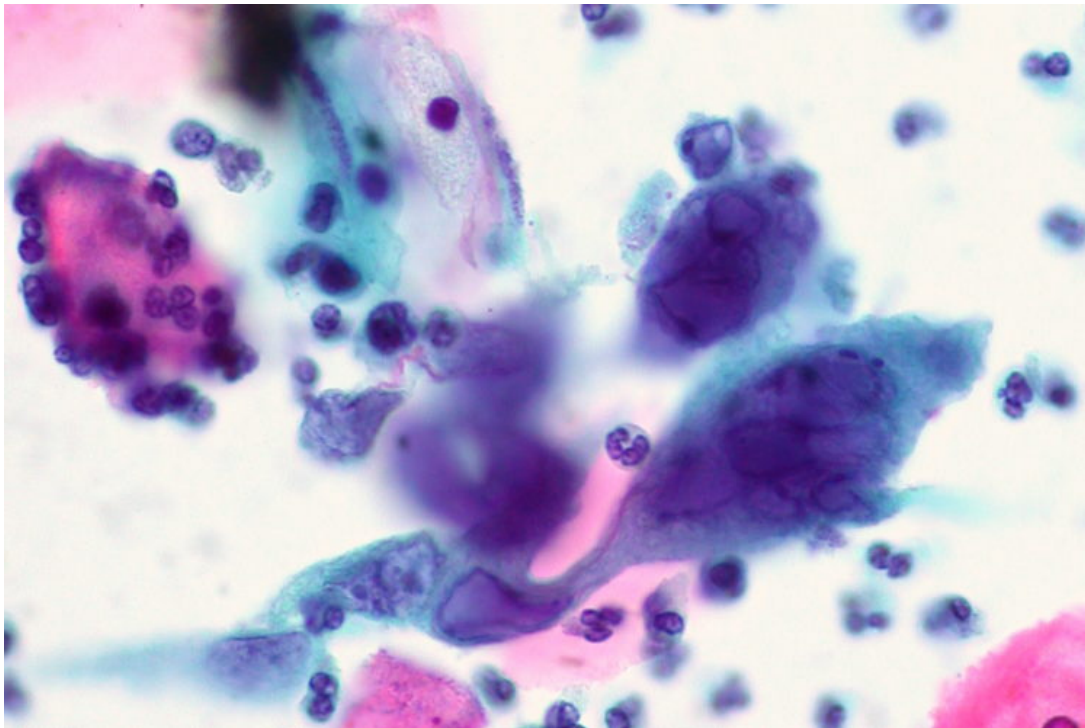


Herpes Simplex (HSV, Herpes Simplex Virus Infection) — Symptoms and Treatment

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Herpes simplex virus infections are caused by either herpes simplex virus type 1 or 2. Type 1 viruses are more commonly associated with non-genital herpes, while type 2 viruses are more likely to be responsible for genital herpes diseases. The most common presenting sign is ulcers. While the healing process is usually excellent and subsequent scarring is very rare, topical and systemic antiviral therapy might be indicated to fasten the healing process or prevent complications in the immunosuppressed.



Definition of Herpes Simplex Virus Infections

Herpes simplex virus infections are caused by:

- Herpes simplex virus type 1 which is associated with oral-labial herpes.
- Herpes simplex virus type 2 which is associated with genital herpes.

The most common presenting sign is ulcers. While the healing process is usually excellent and subsequent scarring is very rare, topical, and systemic antiviral therapy might be indicated to fasten the healing process or prevent complications in the immunosuppressed.

Epidemiology of Herpes Simplex Virus Infections

Herpes simplex virus type 1 infection among humans is very common more so among young adults. Approximately **60% of the people in the United States carry the viral DNA** and have been infected before. This virus is usually responsible for non-genital herpetic lesions but, due to the recent changes in sexual practices, the virus is becoming more commonly identified in genital lesions.

Additionally, it seems that the **infection rate** with herpes simplex virus is **closely related to race**. It is estimated that 35% of African American children who are aged 5 years carry the virus, while only 18% of white children are seropositive.

Patients presenting with **genital ulcers** are most likely infected with herpes simplex virus type 2 which is the most common etiology of genital ulcers in humans who are sexually active. The incidence of herpes simplex type 2 genital infection is approximately **half a million per year**. Approximately 25% of American adults already carry herpes simplex type 2 virus and are seropositive.

Possible risk factors for herpes simplex virus infections include **female gender and older age**. As we have explained, the viral infection rate among blacks is higher compared to whites. Patients who are seropositive for herpes simplex virus type 1 are less likely to acquire herpes simplex virus type 2 due to cross-immunity.

Pathophysiology of Herpes Simplex Virus Infections

Transmission is common among asymptomatic individuals who shed the virus to others via skin-skin, skin-mucosa, and mucosa-skin contacts.

Herpes simplex viruses affect the **skin** and **mucous membranes**. When the patient acquires the herpes simplex virus type 1 for the first time, he or she usually develops **primary herpetic gingivostomatitis**.

The viruses are transmitted through **direct exposure of the mucous membranes** to an infected individual. Additionally, the viruses can be transmitted by **respiratory droplets**.

Once the viruses enter the mucous membranes or the damaged skin, they start replicating and inducing lysis of the infected cells.

The next pathogenic step would be the **migration of the viral particles** upwards towards the trigeminal, facial, or autonomic nerve ganglions. There the **virus replicates** and then **enters a dormant state**. This site is thought to be protected from the immune system and allows the virus to stay dormant until reactivation without being detected by our immune system. This retrograde migration is independent of virus multiplication and local inflammation.

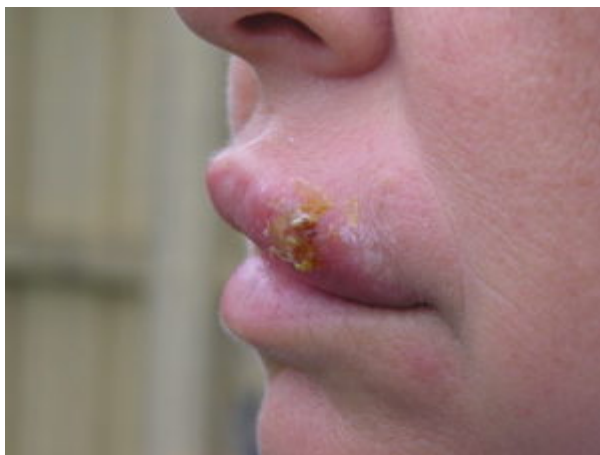
Reactivation of the virus replication is not a new infection. It is, in fact, a process of reactivation of viral DNA replication, down-migration of the new viral particles to the dermatomes supplied by the affected nerve, and the presentation of recurrent symptoms of **skin vesicles, ulcers, and crusting**. The process of reactivation can happen due to **stress, physical illness, a flu illness** or without any apparent reason.

Clinical Presentation of Herpes Simplex Virus Infections

The clinical presentation of the different herpes simplex viruses' infections depends on **two main factors**: whether the patient was seronegative before acquiring the virus, i.e. **primary infection**, and the **type of the acquired virus**. Herpes simplex virus type 1 is more commonly found in oral, facial, pharyngeal and central nervous system herpetic disease. On the other hand, herpes simplex virus type 2 more commonly affects the genital areas.

Primary herpetic gingivostomatitis is the primary infection caused by herpes simplex virus type 1 of the oral and mucous membranes. Patients can present with **multiple small mouth ulcers**, but the disease can go unnoticed in many patients.

Patients can describe a **burning sensation** before the onset of the ulcer. **Fever, malaise, dysphagia, and headaches** are common in primary infections, but less likely with recurrent infections. Most patients with primary herpetic gingivostomatitis recover within two weeks without any subsequent sequelae.



[Image](#): "Cold Sore in Herpes Labialis." by Ben Tillman - Own Work. License: Public Domain

Recurrent oral or genital herpetic disease is usually milder than primary infections. The symptoms can include **discomfort** in the face or around the lips for herpes simplex virus type 1. **Recurrences** can be painful for the patient and might cause embarrassment due to the disfiguring appearance of the lesions. Most patients usually develop a **fever illness** before the reactivation of the virus. **Cold sores** and **fever blisters** are the most common form of recurrent herpes simplex type 1 disease.

Before the onset of the ulcer in the outer vermilion border and cutaneous region of the lip, patients can describe a **prodrome of pain and a burning sensation**. Six hours later, small vesicles start appearing which eventually rupture and form a crust. These lesions heal within two weeks, but **virus shedding** can happen for approximately three weeks since the onset of the symptoms.

Patients with **primary genital herpes infections** are usually **asymptomatic**. The most commonly implicated virus is the herpes simplex type 2 but, recently, type 1 cases are becoming more recognized.

Diagnostic Workup for Herpes Simplex Virus Infections

The diagnosis of herpes simplex virus infections is usually a clinical one. If the treating physician wishes to confirm the diagnosis, several **laboratory tests** are available.

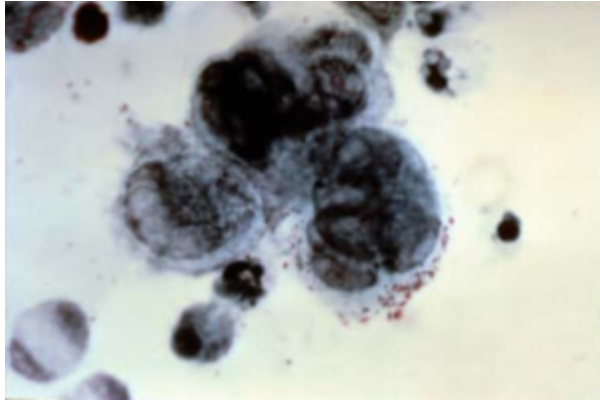


Image: "Herpes Tzanck smear. Positive Tzanck test, showing three multinucleated giant cells in center." by National Institute of Allergy and Infectious Diseases (NIAID) - NIH Image Bank > Herpes Tzanck Smear
<http://media.nih.gov/imagebank/display.aspx?ID=239>. License: Public Domain

Viral cultures, cytological smears with Tzanck preparation of the vesicular fluid content and the detection of the virus DNA by **polymerase chain reaction** are possible methods to confirm the diagnosis of herpes simplex.

Tzanck preparation is the most commonly used method to confirm the diagnosis. The fluid content of a newly formed vesicle is examined under light microscopy after staining with Giemsa or Papanicolaou stain to identify the presence of certain cytological abnormalities that are known to be related to herpes viruses infections. **Unfortunately, this method cannot differentiate between varicella-zoster and herpes simplex infections.**

Viral cultures are the gold standard to confirm the diagnosis of herpes simplex virus infection. The vesicles are swabbed and the contents are later cultured. The presence of **multinucleated giant cells** that show ballooning degeneration is the hallmark cytopathological feature of herpes simplex virus infection. This finding can be easily identified one to two days after the virus isolation and inoculation in the culture.

Polymerase chain reaction tests can identify the virus DNA and are useful when the culture is negative. Unfortunately, these tests are still relatively expensive compared to other techniques.

Patients with primary herpes simplex virus infections do not have any preformed antibodies against the virus antigens; therefore, **serologic testing** might be useful in differentiating recurrent from primary disease. Patients with anti-herpes simplex virus IgG antibodies and the appearance of IgM antibodies are indicative of recurrence disease.

Treatment of Herpes Simplex Virus Infections

Management of herpes simplex virus infections starts with **prevention**. Children who

develop oral ulcers that are found to be herpetic should be encouraged to **avoid contact** with other children because the virus is highly contagious. Additionally, people who develop genital ulcers should **abstain from sex** until the ulcers completely heal, if possible.

The currently available treatment options for herpes simplex virus infections aim to ameliorate the symptoms, fasten the recovery and lower the risk of recurrence. **None of the currently available treatments are known to cure the disease.**

Most of the currently available **antiviral therapies** should be used **within the first 48 hours** of the disease because maximum viral replication happens within this time window.

Docosanol 10% cream is an alcohol-based treatment that is known to be effective in the management of recurrences of oral and labial herpes simplex disease. **Penciclovir** is another option that was found to be effective in the management of recurrent herpes infections. These topical antivirals are usually inferior in efficacy when compared to systemic antiviral therapy.

Acyclovir and **valacyclovir** are two possible options for the systemic treatment of herpes simplex infections. **Oral therapy** is known to have better accessibility to the infected sites, better efficacy in symptoms control and faster recovery time and healing effect.

Patients with **extensive disease** that is **resistant to acyclovir** should be prescribed **foscarnet** or **cidofovir**.

Management of **recurrent genital herpes** consists of **acyclovir**, **valacyclovir** or **famciclovir**. These antivirals should be given systemically for primary and recurrent genital herpes. **Immunocompromised patients** with recurrent genital herpes disease should take **valacyclovir** or **famciclovir**, but the **dosage should be double**.

References

Fatahzadeh, Mahnaz and Robert A. Schwartz. 2007. "Human Herpes Simplex Virus Infections: Epidemiology, Pathogenesis, Symptomatology, Diagnosis, and Management." *Journal of the American Academy of Dermatology* 57(5):737-63.

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