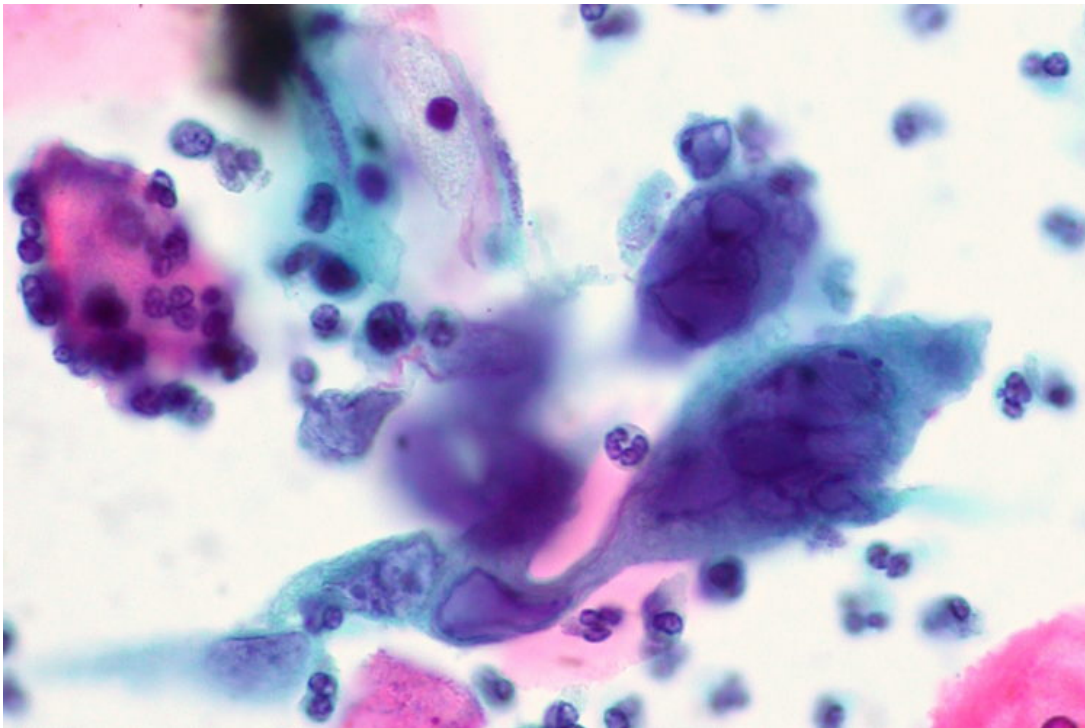


Herpes Simplex (HSV, Herpes Simplex Virus Infection) — Symptoms and Treatment

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Herpes simplex virus (HSV) infections are caused by either HSV type 1 or 2. The former is more commonly associated with non-genital herpes, while the type 2 variant is more likely to be responsible for genital herpes. The most common presenting sign is ulcers. While the healing process is excellent and subsequent scarring rare, topical and systemic antiviral therapies may be indicated to accelerate healing and prevent complications in immunosuppressed individuals.



Classification of Herpes Simplex Virus (HSV) Infections

- Herpes simplex virus type 1 (HSV-1), associated with oral-labial herpes
- Herpes simplex virus type 2 (HSV-2), associated with genital herpes

The most common presenting sign of HSV infections is ulcers. While the healing process is usually excellent and subsequent scarring is rare, topical and systemic antiviral therapies may be indicated to accelerate the healing of lesions and prevent complications in immunosuppressed individuals.

Epidemiology of HSV Infections

HSV-1 infections are common in young adults. Approximately **60% of the people in the United States are seropositive** and have been previously infected. HSV-1 is usually responsible for non-genital herpetic lesions, but of late, it is being commonly identified in genital lesions.

Additionally, it appears that the incidence of HSV **infections is closely related to race**. It is estimated that 35% of African American children are seropositive by the age of 5 years as compared to 18% of Caucasian children in a similar age category.

Patients presenting with **genital ulcers** are most likely infected with HSV-2, which is the most common cause in sexually active individuals. The incidence of HSV-2 genital infections is approximately **half a million per year**. Approximately 25% of American adults are HSV seropositive.

HSV infections are more common in **women than men** and the **risk of infection increases with age**. As indicated, the infection rate among African Americans is higher compared to that in Caucasians. Patients who are seropositive for HSV-1 are less likely to acquire HSV-2 due to cross-immunity.

Pathophysiology of HSV Infections

Transmission is common among asymptomatic individuals who may shed the virus and spread infection via skin-to-skin, skin-to-mucosa, and mucosa-to-skin contact.

HSV affects the **skin and mucous membranes**. **Primary herpetic gingivostomatitis** is caused by an initial infection with HSV-1.

The virus is transmitted through **the mucous membranes via direct exposure** to an infected individual. It can also be transmitted via **respiratory droplets**.

Upon entering via the mucous membranes or compromised skin, the virus replicates and induces cell lysis.

The next step in pathogenesis involves **the migration of viral particles** upwards towards the trigeminal, facial, or autonomic nerve ganglia, where the **virus replicates** and **enters a dormant state**. These sites are thought to be protected from the immune system and allow the virus to remain dormant without being detected until reactivation. This retrograde migration is independent of virus multiplication and local inflammation.

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

Clinical Presentation of HSV Infections

The clinical presentation of HSV infections depends on **two main factors**, namely, whether the patient was seronegative before acquiring the virus, i.e. presence of **primary infection**, and the **type of infection**. HSV-1 is more commonly found in oral,

facial, and pharyngeal infections and those involving the CNS. On the other hand, HSV-2 more commonly affects the genital areas.

Primary herpetic gingivostomatitis is the primary infection of the oral and mucous membranes caused by HSV-1. Patients present with **multiple small mouth ulcers**; however, the disease can go unnoticed in many patients.

Patients may describe a **burning sensation** before the onset of the ulcer. **Fever, malaise, dysphagia,** and **headaches** are common in primary infections but are less likely during recurrent infections. Most patients with primary herpetic gingivostomatitis recover within two weeks without 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. Symptoms may include **discomfort** in the face or around the lips during HSV-1 infections. **Recurrences** are typically **characterized by fever. Subsequent episodes** can be painful for the patient and might cause embarrassment due to the unsightly appearance of lesions. **Cold sores** and **fever blisters** are the most common presentations of recurrent HSV-1 infections.

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

Patients with **primary genital herpes infections** are usually **asymptomatic**. HSV-2 is commonly implicated; however, HSV-1 infections are steadily rising.

Diagnostic Workup for HSV Infections

HSV infections are clinically diagnosed. Several **laboratory tests** are available to confirm the diagnosis.

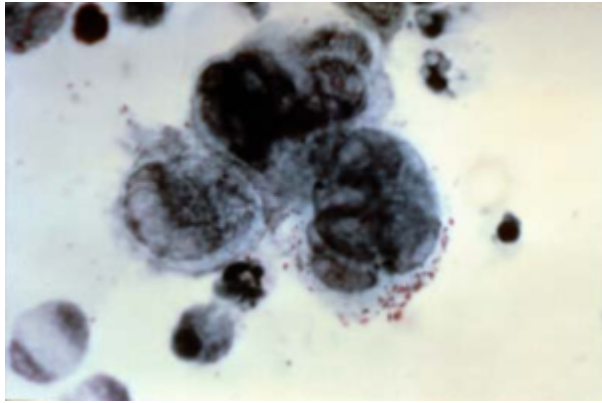


Image: "Herpes Tzanck smear. Positive Tzanck test showing three multinucleated giant cells in the center." by National Institute of Allergy and Infectious Diseases (NIAID) - NIH Image Bank > Herpes Tzanck Smear
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Viral cultures, cytological examination of Tzanck smears of the vesicular fluid, and the detection of viral DNA using **polymerase chain reaction** are a few routinely used methods to confirm HSV infections.

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

Viral cultures are the gold standard to confirm the diagnosis of HSV infections. Vesicles are swabbed and contents are later cultured. The presence of **multinucleated giant cells** that show ballooning degeneration is the hallmark cytopathological feature of an HSV infection. This finding can be easily identified after a day or two after isolation of the virus and inoculation of the culture.

Polymerase chain reactions can detect viral DNA and are useful when the culture is negative. Unfortunately, these tests are relatively expensive compared to other techniques.

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

Treatment of HSV Infections

Management of HSV infections starts with **prevention**. Children who develop oral ulcers that are found to be herpetic should be encouraged to **avoid contact** with others owing to the contagious nature of HSV infections. Additionally, adults who develop genital ulcers should **abstain from sex** until the ulcers heal completely.

The currently available treatment options for HSV infections aim to ameliorate symptoms, accelerate recovery, and lower the risk of recurrence. **None of these treatments are known to cure the disease.**

Antivirals should be used **within the first 48 hours** of infection since viral replication is maximum within this time window.

Docosanol 10% cream is an alcohol-based preparation known to be effective in the management of recurrent oral and labial HSV infections. **Penciclovir** is another effective option in the management of recurrent herpetic infections. These topical antivirals are usually inferior in efficacy compared to systemic antiviral therapy.

Acyclovir and **valacyclovir** are two possible options for the systemic treatment of HSV infections. **Orally administered antivirals** are more effective, show better efficacy in controlling symptoms, and lead to faster healing and recovery.

Patients **resistant to acyclovir** should be prescribed **foscarnet** or **cidofovir**.

Management of **recurrent genital herpes** consists of therapy with **acyclovir**, **valacyclovir**, or **famciclovir**. These antivirals should be systemically administered for the treatment of primary and recurrent genital herpes. **Immunocompromised patients** with recurrent genital herpes should be started on **valacyclovir** or **famciclovir**; however, the **dosage should be doubled**.

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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