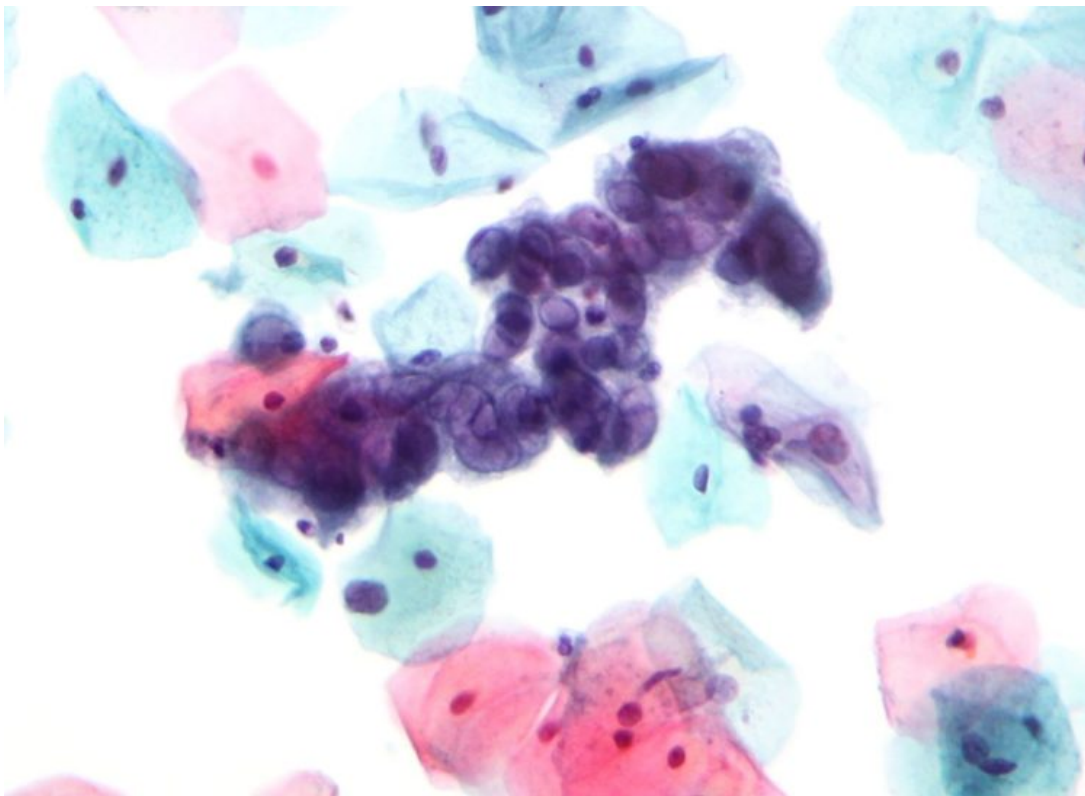


Genital Herpes — Symptoms and Treatment

[See online here](#)

Genital herpes is caused by either herpes simplex virus type 2 (70% of the cases) or herpes simplex virus type 1 (30% of the cases). The patient can present with primary disease characterized by severe genital vesicles that are fluid-filled, or recurrent milder disease of dermatomal vesicular and ulcerative disease. Affected individuals can also be asymptomatic. Treatment of primary and recurrent genital herpes consists of acyclovir or valacyclovir for one week. Suppressive antiviral therapy is indicated in patients with frequent recurrent genital herpes.



Definition and Epidemiology of Genital Herpes

Genital herpes is defined as the **development of ulcerative genital disease due to infection by either herpes simplex type 1 or type 2 viruses**. The genital lesions might be due to primary infection, which is defined as the occurrence of genital herpetic lesions for the first time in a patient who is immunologically naïve to the virus, or recurrent.

Genital herpes is a sexually transmitted viral infection characterized by acute and recurrent painful, clustered genital vesicles which ulcerate, low-grade fever, and regional lymphadenopathy.

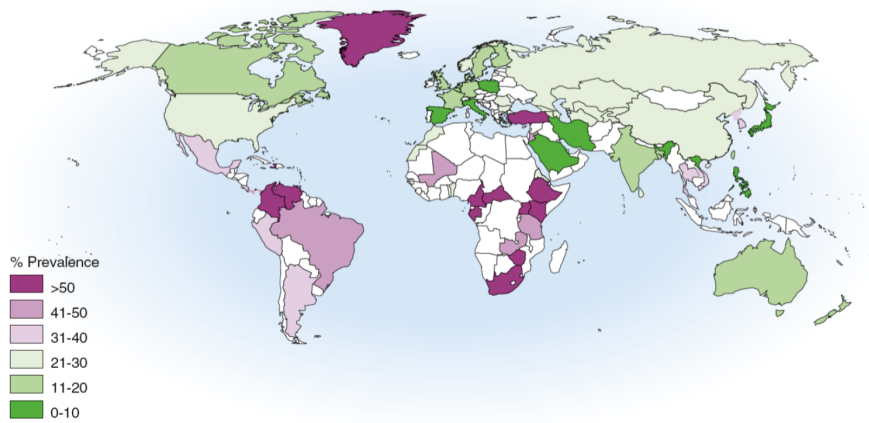


FIGURE 138-1 Global seroprevalence of herpes simplex virus type 2 infection.

High-yield

Genital herpes is a **common sexually transmitted disease with an estimated number of 40 to 60 million of affected individuals in the United States**. The annual incidence of infection by herpes simplex type 2 is estimated to be around 1 to 2 million cases. Most of these patients are in fact asymptomatic with only approximately 800,000 new clinical cases of genital herpes identified per year in the United States.

Genital herpes is **more common in Africa, especially in countries that have human immunodeficiency (HIV) virus epidemics**. The estimated prevalence of genital herpes in populations that have a significant prevalence of HIV in Africa is approximately 70 %.

Genital herpes primary infection is more **common among young adolescents who have started sexual activities recently**. Recurrent genital herpes disease is usually seen in patients who are sexually active. **Immunodeficient patients** are at risk of developing more severe recurrent genital herpes with possibly invasive systemic illness.

- Worldwide pandemic over the past two decades
- 23 million new cases/year worldwide
- Seroprevalence: ~17 % of adults
- Lifetime incidence:
 - White women: 25 %
 - White men: 20 %
 - Black women: 80 %
 - Black men: 60 %

Etiology of Genital Herpes

The **most common cause of genital herpes is herpes simplex virus type 2**. In the past, herpes simplex virus type 2 was considered as genital herpes, while herpes simplex virus type 1 was known as oral herpes. Modern studies have demonstrated that genital herpes is caused by herpes simplex type 2 in 70–90 % of the cases and by herpes simplex type 1 in 10–30 % of the cases. Conversely, orolabial herpes is caused by herpes simplex type 1 in 80–90 % of the cases and herpes simplex type 2 in 10–20 % of the cases.

The **most likely cause of the increase of incidence of herpes simplex virus type 1 genital herpes is the introduction of new sexual practices**, including oral sexual intercourse. Genital herpes can also be acquired from non-genital herpetic lesions that are found on the fingers, eyes or lips of an infected individual.

While genital herpes is more common in HIV epidemic areas, the current hypothesis is that herpes simplex infection increases the risk of HIV transmission and not the other way around. Genital herpes **causes skin breakdowns and ulcerations** which make it easier for the HIV virus to gain entry and infect the individual.

Transmission

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

- Person-to-person transmission: intimate contact (genital-genital)
- Virus inoculated onto susceptible mucosal surfaces or through small skin cracks
- Replication begins in cells of epidermis and dermis
- Sensory & autonomic nerve endings infected → potential for lifelong reactivation
- Transported via axons to nerve cell bodies in regional ganglia → high-level replication
- **Sacral root ganglia - s2 - s5 (most common)**
- Contiguous neural tissue

Pathophysiology

After exposure, replication begins in epithelial cells of epidermis and **dermis causing lysis of infected cells, vesicle formation and local inflammation.** This is known as primary infection.

After primary infection at the inoculation site, HSV ascends via the sensory & autonomic nerve endings infected where latency is established creating a potential for lifelong reactivation. This retrograde migration is independent of virus multiplication and local inflammation.

HSV reactivates from the latent stage to travel in an anterograde manner to the skin and mucous membranes where it causes recurrent disease and episodes. **The transport is via axons to nerve cell bodies in regional ganglia → high-level replication: Sacral root ganglia - s2 - s5 (most common) & Contiguous neural tissue.**

Recurrent infection

Asymptomatic viral shedding (2/3 subclinical)

- [Women: cervix, vulva, anus, urethra](#)
- [Men: penile skin, urethra, anus, semen](#)

Pregnancy

- Few infants at risk
- [C-section](#): only women who shed at delivery

Clinical Presentation of Genital Herpes

The clinical presentation of genital herpes should be classified into primary, first-time presentation and recurrent presentation.

Primary genital herpes

Patients presenting with their first episode of genital herpes **usually present with an erythematous lesion that later develops a group of vesicles and pustules** that become eroded to become genital ulcers that are severely painful.

The distribution of the primary lesions in men is usually on the prepuce and subpreputial areas of the penis. Women have herpetic lesions on the vagina, vulva, and cervix.

Patients with primary genital herpes are more likely to develop systemic features such as fever. Healing usually takes place within one month and leaves no scarring behind.

Lymphadenopathy is sometimes evident in these patients.

Recurrent genital herpes

It is usually of a milder severity and is more confined to a single dermatome. The lesions heal in one week to ten days instead of one month. **Recurrent genital herpes can happen up to 5 times per year**, but the frequency of the recurrences decreases with time.

Most cases, however, are in fact asymptomatic. Patients usually develop a very mild disease that goes unrecognized. **Asymptomatic genital herpes is more common in patients who have recurrent genital herpes.** During the reactivation phase of the virus, they can shed and infect other individuals without knowing so because they are asymptomatic.

The reactivation phase presents as features specific to certain dermatomes such as ocular HSV, trigeminal nerve involvement and herpetic facial paralysis.

Diagnostic Workup for Genital Herpes

While clinical examination and history taking are helpful in the evaluation of the patient presenting with genital ulcers, laboratory investigations are usually needed to confirm the diagnosis and direct the treatment plan. **These tests include:**

- **Direct microscopy/ Tzank test** where fluid from the vesicles is smeared into a slide and then stained with Giemsa to identify acantholytic keratinocytes. It is diagnostic in 75 % of the cases.
- **Antigen detection tests** where monoclonal antibodies specific for HSV-1 and 2 are detected and differentiated on smears.
- **Viral cultures from the herpetic lesions** can provide definite proof about the presence of herpes simplex virus. Unfortunately, herpes virus cultures are usually difficult to maintain, therefore, polymerase chain reaction testing is becoming more acceptable as a gold-standard diagnostic modality.

Patients who develop new antibodies against herpes simplex type 1 or 2 might be considered as having a primary infection if they were seronegative before. Therefore, **serologic testing is usually more useful in the sexual partner of the affected individual who did not develop the disease yet**, because the availability of a serologic baseline in the current patient is unlikely.

The differentiation between herpes simplex virus type 1 and type 2 is important for counseling purposes. While the initial genital herpes disease is usually

severe in both conditions, recurrent genital herpes by patients affected with herpes simplex virus type 1 is far less common compared to herpes simplex virus type 2. Serologic testing is not useful in the differentiation between the two types, but polymerase chain reaction testing is usually sufficient.

Treatment of Genital Herpes

	1st clinical episode: treatment for 7 to 10 days	Recurrent episodes: duration of the treatment variable
Acyclovir	<ul style="list-style-type: none"> • 400 mg PO tid or 200 mg PO 5 times daily 	<ul style="list-style-type: none"> • 400 mg PO tid x 5 d • 800 mg PO bid x 5 d • 800 mg PO tid x 2 d
Valacyclovir	<ul style="list-style-type: none"> • 1 g PO bid 	<ul style="list-style-type: none"> • 500 mg PO bid x 3 d • 1,000 mg PO daily x 5 d
Famciclovir	<ul style="list-style-type: none"> • 250 mg PO tid 	<ul style="list-style-type: none"> • 125 mg PO bid x 5 d • 1,000 mg PO bid x 1 d • 500 mg PO once; then 250 mg bid x 2 d

The treatment of genital herpes depends on whether this is a primary presentation or a recurrent one. Patients with primary genital herpes can receive acyclovir 200 mg orally five times a day for 5 days. This dosing might be inconvenient, which is why valacyclovir is becoming a more attractive option for the treatment of primary genital herpes. Valacyclovir 500 mg to 1000 mg twice a day is usually sufficient. This treatment plan should be continued for 5 days.

The choice to prolong antiviral treatment should be based on the formation of any new lesions during active treatment. If the patient does not develop any new lesions, most recommendations are to stop the antiviral therapy after 5 days. Patients who develop new lesions should receive antiviral therapy for 5 more days, i.e., a total of 10 days.

In a recent review published by the British Medical Journal, the authors recommended acyclovir 400 mg three times a day for one week as the initial therapy for primary genital herpes.

Patients with recurrent genital herpes should receive acyclovir or valacyclovir in similar dosage to primary infection. Patients with 6 or more recurrences of genital herpes per year might benefit from suppressive antiviral therapy. Suppressive antiviral therapy is effective in decreasing the recurrence rate by as much as 80 %. Acyclovir 400 mg twice a day, or valacyclovir 500 mg once a day are excellent options as suppressive therapies against recurrent genital herpes. Suppressive therapy should be discontinued after 12 months.

Patients with the confirmed asymptomatic shedding of herpes simplex virus type 2 should receive valacyclovir.

- Acyclovir 400 mg twice a day (safety and efficacy established for 6 years) OR
- Valacyclovir 500 mg orally once a day OR
- Valacyclovir 1 g orally once a day OR
- Famciclovir 250 mg orally twice a day (safety and efficacy established for 1 year)

Treating genital herpes in pregnant women should receive more attention because of the risk of transmission to the fetus. Patients who acquire the virus for the first time during the first or second trimester of pregnancy should receive routine antiviral therapy, in addition to four weeks of suppressive antiviral therapy before the planned vaginal delivery. Patients who develop genital herpes after the 34th week of

gestation should always be delivered by [cesarean section](#).

Pregnant women with a known history of recurrent genital herpes should receive suppressive antiviral therapy with acyclovir in the last four weeks of pregnancy. Vaginal delivery is possible in these women, as long as they do not have an active genital herpetic disease.

Counseling

- Sex partners should be informed
- Sexual transmission can occur during asymptomatic periods
- Persons with genital herpes should remain abstinent when lesions or prodromal symptoms present

References

Sen P, Barton SE. Genital herpes and its management. BMJ: British Medical Journal. 2007;334(7602):1048-1052. doi:10.1136/bmj.39189.504306.55

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