Genital Herpes : A Review

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ABSTRACT

Genital herpes simplex virus (HSV) infection is a recurrent, lifelong disease with no cure. Being one of the commonest cause of genital ulcer disease HSV infection is to be diagnosed and treated by recommended antivirals.

Key words: HSV, Genital herpes, Acyclovir

INTRODUCTION

Genital herpes simplex virus (HSV) infection is a recurrent, lifelong disease with no cure. HSV is an enveloped, linear, double-stranded DNA virus whose only known hosts are humans. The two types of HSV (i.e., HSV-1 and HSV-2) are distinguished by antigenic differences in their envelope proteins. HSV-1 normally is associated with oral infections and HSV-2 with genital infections, but either type can infect a person anywhere on the skin. At least 50 million persons in the United States have genital HSV infection, and an estimated 500,000 to 700,000 cases of symptomatic first-episode genital HSV infections occur annually. Coinfection of HSV-2 and HIV-1 may result in more efficient transmission of HIV-1 and an increased rate of HIV replication during HSV reactivation. The strongest predictor for genital HSV infection is a person's number of lifetime sex partners).[1,2]

TABLE

Risk Factors for Genital Herpes Infection

History of sexually transmitted diseases

History of undiagnosed genital lesions or discharge

Human immunodeficiency virus infection

Multiple sex partners

Partner diagnosed with genital HSV infection

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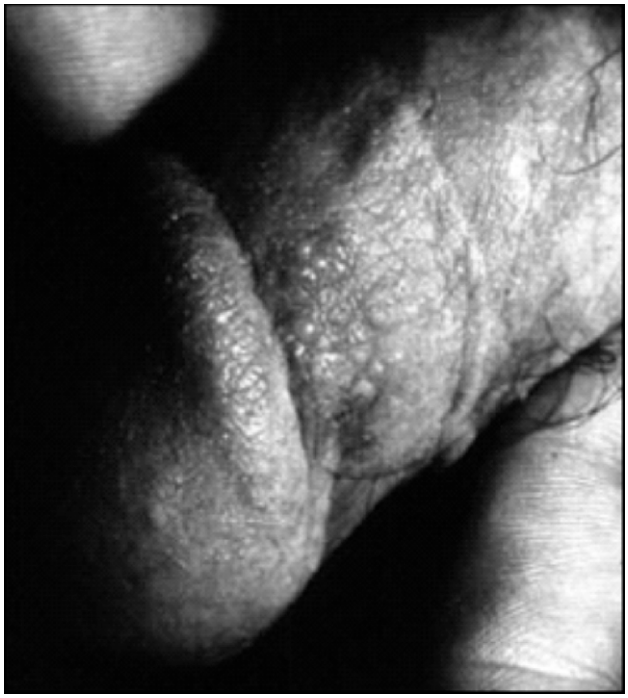
The natural history of HSV infection includes acute or subclinical first-episode mucocutaneous infection, establishment of viral latency, and subsequent reactivation. The herpes virus enters the body through the skin or mucous membranes by direct sexual contact with the secretions or mucosal surfaces of an infected person. The virus multiplies at the epithelial layer and then ascends along the sensory nerve roots to the dorsal root ganglion, where it becomes latent. With reactivation, the virus travels from the dorsal root ganglion back down the nerve root to create a mucocutaneous outbreak, or it may produce no detectable symptoms. Most infected persons(nearly 80 %) have unrecognized symptomatic or completely asymptomatic infections.

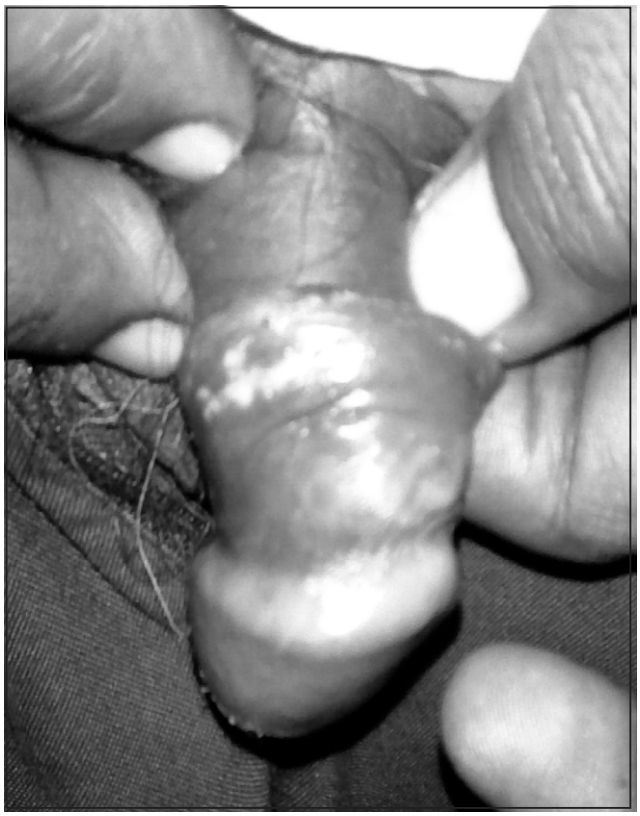
CLINICAL FEATURES---

"Classic" outbreaks of primary genital HSV infection begin with a prodrome lasting two to 24 hours that is characterized by localized or regional pain, tingling, and burning. Patients also may have constitutional symptoms such as headache, fever, inguinal lymphadenopathy, anorexia, and malaise.7 As the disease progresses, papules, vesicles on an erythematous base, and erosions appear over hours to days. Patterns of HSV-1 and HSV-2 infection appear identical: vesicles usually are uniform in size, and the tense center umbilicates to form a depressed center.

These lesions usually crust and then re-epithelialize and heal without scarring. In women, ulcers can occur on the introitus, urethral meatus, labia, and perineum. In men, ulcers often appear on the shaft or glans of the penis. In both men and women, lesions may appear on the perianal area, thighs, or buttocks(2,6)

Genital herpes





There are two types of first-episode, clinically apparent eruptions.

The first is a nonprimary clinical eruption in a patient who has been infected previously with any type of HSV. The second type is a true primary infection, which is the first HSV infection in a seronegative patient. First-episode infections have more numerous and scattered vesicles and more systemic symptoms. Approximately 80 percent of primarily infected persons develop constitutional symptoms.

Primary lesions last two to six weeks and can be extremely painful, containing large quantities of infectious HSV particles. Vesicles appear approximately six days after sexual contact. Viral shedding lasts longer in first-episode infections, usually 15 to 16 days, and new lesions will continue to form for about 10 days after the initial infection.

For unknown reasons, women have more severe disease, constitutional symptoms, and complications than do men. This may be a result of the larger affected surface area in women and the ability of the virus to spread more easily over moist surfaces.

Systemic complications : Complications associated with genital HSV infection include:[3,4]

- disseminated HSV
- aseptic meningitis
- autonomic dysfunction with urinary retention
- vertical transmission from an infected mother to her newborn
- increased risk of HIV transmission.

Recurrent HSV outbreaks usually are milder than the initial episode .Antibodies for one type of HSV seem to provide partial protection against infection with the other serotype: women infected with HSV-1 have a 5 to 20 percent lower annual rate of seroconversion to HSV-2 compared with uninfected women.[1]

Recurrence rates for HSV-2 vary greatly, but the median is four recurrences per year, and the median time to first recurrence is 50 days. Approximately 90 percent of patients have at least one recurrence during the first year Mens have more recurrences than women. Although HSV-1 can cause up to 33 percent of initial outbreaks, HSV-2 infections recur six times more frequently.

Recurrences are spontaneous, but various factors such as fever; nerve or tissue damage; physical or emotional

stress; exposure to heat, cold, and ultraviolet light; immunosuppression; menses; concurrent infection; fatigue; and sexual intercourse have been associated with recurrences[1,7]

Diagnosis

- Diagnosis is usually made clinically, but laboratory tests should be used to confirm the diagnosis
- This can be done with **Virological tests like viral culture, PCR, or Serological tests**[3]
- To obtain a sample from an active clinical lesion for laboratory analysis:
- choose the most recent of the vesicles and gently lift the roof of the vesicle with a needle tip or scalpel blade to expose the underlying material
- instill collected swab in viral culture media and send to the lab as per usual practice (takes 5 days to culture)
- alternatively, transfer swab to a glass slide and send for immediate direct immunofluorescence testing (rapid detection).[3]
- **Cell culture and PCR** are the preferred HSV tests for persons who seek medical treatment for genital ulcers or other mucocutaneous lesions. The sensitivity of viral culture is low, especially for recurrent lesions, and declines rapidly as lesions begin to heal. PCR assays for HSV DNA are more sensitive and are increasingly used in many settings (8,9). **PCR is the test of choice for detecting HSV in spinal fluid for diagnosis of HSV infection of the central nervous system (CNS).**
- Type specific serology can be done, however, this can only be used to determine past infection or asymptomatic HSV infection; this test is helpful for determining between HSV-1 and HSV-2.4. Accurate type-specific HSV serologic assays are based on the HSV-specific glycoprotein G2 (HSV-2) and glycoprotein G1 (HSV-1). . The sensitivities of these glycoprotein G type-specific tests for the detection of HSV-2 antibody vary from 80%–98%. IgM testing for HSV is not useful, because the IgM tests are not type-specific and might be positive during recurrent episodes of herpes **(10)**
- A Tzanck smear showing multinucleated giant cells has been used historically, but may not always be practical in a clinic setting.
- Consider testing for other bacterial causes of ulcerative lesions, such as Treponema pallidum and Haemophilus*ducreyi*, depending on the demographics of the population.

Treatment Rationale(1 ,2)

Treatment is aimed at reducing patient discomfort, transmission of the virus, duration of the outbreak,and risk of complications.

- Treatment should be initiated as soon as possible without waiting for laboratory results (ideally within 72 hours of symptom onset in order to minimize duration and severity of illness).
- Conservative measures include analgesics and sitz baths to alleviate the pain.
- Intermittent urinary catheterization may be necessary if urinary retention results from autonomic dysfunction.
- Counseling is must part of the treatment.

1.Table 2: Treatment of Genital Herpes(1,2)

Drug name	Dosage for Primary or First Episode	Dosage for Treatment of Recurrent Disease Outbreak	Dosage for the Suppression of 50%-78% of Recurrent Disease
Acyclovir (Zovirax ®)	400 mg three times a day for 7-10 days	(i). 800 mg twice a day or (ii). 400 mg three times a day, each for 5 days	400 mg twice daily; shown to be safe and effective for at least 3 years; has also been used for much longer periods
Famciclovir (Famvir ®)	250 mg three times a day for 7 – 10 days	125 mg twice a day for 5 days	250 mg twice daily
Famciclovir (Famvir ®)	250 mg three times a day for 7 – 10 days	125 mg twice a day for 5 days	250 mg twice daily
Valacyclovir (Valtrex ®)	1g twice a day for 7 10 days	500 mg twice a day for 5 days	i). 500 mg once daily for people with less than 10 episodes/yr; (ii). 1 g once daily for those with more than 10 episodes/yr

FIRST CLINICAL EPISODE

Study of acyclovir showed that treatment decreased constitutional symptoms by three days, local pain by two days, viral shedding by seven days, time until all lesions were crusted by three days, and time until all lesions were healed by six days.Antvirals decrease by several days the time until all lesions are crusted and healed, as well as localized pain, constitutional symptoms, and viral shedding.

EPISODIC THERAPY

Episodic therapy is advised for HSV-infected patients who have mild and infrequent recurrences. Treatment

started during the prodromal phase or within one day of lesion onset diminish symptoms and infectivity during recurrences, rather than reduce the frequency of recurrences.

SUPPRESSIVE THERAPY

It is recommended for patients with more than six episodes per year. It reduces recurrences by 70 to 80 percent(7)

Severe Disease

Intravenous (IV) acyclovir therapy is recommended for severe HSV disease or complications that necessitate hospitalization (e.g., disseminated infection, pneumonitis, or hepatitis) or CNS complications (e.g., meningoencephalitis). The recommended regimen is acyclovir 5–10 mg/kg IV every 8 hours for 2–7 days or until clinical improvement is observed, followed by oral antiviral therapy to complete at least 10 days of total therapy. Acyclovir dose adjustment is recommended for impaired renal function.(2)

Genital herpes in HIV infected individuals

HIV infected patients have more frequent, prolonged episodes of herpes genitalis with slower response to acyclovir even in the absence of overt acyclovir resistance. Patient unresponsive to acyclovir can be treated with topical trifluridine 8 hourly or IV foscarnet 50mg/kg twice daily until complete healing.[11]

Vaccines against HSV

The most promising candidate vaccine are those based on recombinant HSV glycoprotein B and D. Though it does not provide sterilizing immunity and is not cost effective, it prevents the development of symptomatic genital herpes and reduce latent infection.[12]

Conclusion:

Herpes genitalis, the most common cause of genital ulceration in the developed world is an incurable life long illness with high recurrence rate.Diagnosis is mainly clinical. Acyclovir is the drug of choice. Valacyclovir and famcyclovir have their own advantage of convenient dose schedule. Trifluridine and foscarnet are the safer and effective drugs in case of drug resistance. Most anti HSV drugs reduce symptoms, recurrences and viral shedding of HSV.Vaccine is the only practical measure to control disease and the spread of infection.

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