

Newer trends in the management of genital herpes

Amiya Kumar Nath, Devinder Mohan Thappa

Department of Dermatology
and STD, Jawaharlal Institute
of Postgraduate Medical
Education and Research
(JIPMER), Pondicherry - 605
006, India

Address for correspondence:
Dr. Devinder Mohan Thappa,
Department of Dermatology
and STD, JIPMER,
Pondicherry - 605 006, India.
E-mail: dmthappa@gmail.com

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ABSTRACT

Management of genital herpes is complex. Apart from using the standard antivirals, an ideal management protocol also needs to address various aspects of the disease, including the psychological morbidity. Oral acyclovir, valacyclovir or famciclovir are recommended for routine use. Long-term suppressive therapy is effective in reducing the number of recurrences and the risk of transmission to others. Severe or disseminated disease may require intravenous therapy. Resistant cases are managed with foscarnet or cidofovir. Genital herpes in human immunodeficiency virus-infected individuals usually needs a longer duration of antiviral therapy along with continuation of highly active anti retroviral therapy (HAART). Genital herpes in late pregnancy increases the risk of neonatal herpes. Antiviral therapy and/or cesarean delivery are indicated depending on the clinical circumstance. Acyclovir appears to be safe in pregnancy. But, there is limited data regarding the use of valacyclovir and famciclovir in pregnancy. Neonatal herpes requires a higher dose of acyclovir given intravenously for a longer duration. Management of the sex partner, counseling and prevention advice are equally important in appropriate management of genital herpes. Vaccines till date have been marginally effective. Helicase–primase inhibitors, needle-free mucosal vaccine and a new microbicide product named VivaGel may become promising treatment options in the future.

Key words: Acyclovir, Famciclovir, Genital herpes, HIV, Pregnancy, Valacyclovir

INTRODUCTION

Genital herpes is the most common cause of ulcerative sexually transmitted infection in the world.^[1] Appropriate management of genital herpes is complex. The most important aspect of the management revolves around the judicious use of antiviral agents.^[1] As the results of various randomized studies come to light, treatment protocols for the management of genital herpes under different clinical circumstances undergo constant update.

Many patients with genital herpes may have atypical manifestations.^[2] Therefore, the sensitivity and the specificity of a clinical diagnosis is unacceptably low (39% sensitivity at best with a 20% false-positive diagnosis).^[3] It should also be borne in mind that undiagnosed cases are the most common source of new transmission.^[3] Hence, clinical diagnosis of genital herpes should be confirmed by laboratory testing.

INVESTIGATIONS

Investigations should be routinely utilized to improve the diagnostic accuracy of genital herpes. They are especially useful when the manifestations of genital herpes are atypical or when met with special circumstances like neonatal herpes.^[3-5]

Tzanck smear can be helpful in the rapid diagnosis of genital herpes lesions (by identifying multinucleate giant cells), but it is less sensitive than viral culture. Immunofluorescence staining increases the sensitivity and specificity of a Tzanck smear preparation.

Histopathology is occasionally required in chronic herpes infection in human immunodeficiency virus (HIV)-infected individuals wherein morphology and clinical course are atypical.

Viral culture is the 'gold standard' for herpes simplex

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virus (HSV) diagnosis. Cytopathic effects appear in 2–3 days after inoculation in human diploid fibroblast cultures or green monkey kidney cell cultures. Sensitivity of the tissue culture depends on the stage of clinical lesions – isolation is successful in about 80% of primary infections and in 25–50% of recurrent infections. Viral isolation is least successful in lesions that have begun to heal.

HSV direct detection tests include electron microscopy, HSV antigen detection (immunoperoxidase tests, immunofluorescence, enzyme immunoassay), HSV–DNA detection (DNA hybridization) and HSV–PCR.

Immunofluorescence

Direct fluorescent antibody test (DFA) is used for the detection of HSV antigen in smear, tissues or culture. The sensitivity of the DFA test for the detection of HSV in genital specimens varies between 70 and 90% of culture-positive specimens.

Rapid assay

HSV antigen is extracted from the clinical specimen with a buffered solution. The extract is added to a test device and any antigen present is immobilized on a membrane. When treated peroxidase-labeled anti-HSV monoclonal antibody with substrate is added, a colored spot is obtained on the membrane. The sensitivity of this test is slightly lower than that of enzyme-linked immunosorbent assay (ELISA).

HSV–PCR

PCR is more sensitive (four times) and faster than viral culture. Because the type of HSV infection affects prognosis and subsequent counseling, type-specific testing to distinguish HSV-1 from HSV-2 is recommended. Although PCR has been the diagnostic standard for HSV infections of the central nervous system (CNS), until now viral culture has been the test of choice for HSV genital infection. However, HSV–PCR, with its consistently and substantially higher rate of HSV detection, will likely replace viral culture as the gold standard for the diagnosis of genital herpes in people with active mucocutaneous lesions, regardless of anatomic location or viral type.^[6]

Serology

These tests detect antibodies to HSV in blood and it includes ELISA, complement fixation test and Western blot. Accurate type-specific HSV serologic assays are based on the HSV-specific glycoprotein G2 (HSV-2) and glycoprotein G1 (HSV-1).

Serology can rule out a prior HSV infection. HSV antibodies are absent in the acute stage but gradually appear, increase over subsequent weeks and persist for life.^[1] Seroconversion and a four-fold rise in antibody titers in acute and convalescent sera are seen after a true primary (first episode) infection.^[4] Seroconversion in pregnancy is associated with a high risk of neonatal herpes.^[4] Recurrent episodes are rarely associated with an increase in antibody titers.^[1,4] Newer type-specific ELISAs can discriminate between HSV-1 and HSV-2 antibodies.^[1] Serology is useful in recurrent lesions, atypical lesions, healing lesions, culture-negative cases, unrecognized infection and in evaluation of the sex partner.^[1] These tests may also be used to establish whether a herpetic outbreak is due to newly acquired infection for medicolegal purpose and, in HIV-infected individuals, for deciding on suppressive therapy.^[1,2] The most important application of serology is in the diagnosis of asymptomatic infections in transplant recipients and in patients receiving immunosuppressive drugs.^[4] Disadvantages of serological tests include false-negative results (due to delayed appearance of antibody or low sensitivity), false-positive results in low-risk populations, low purity of the recombinant glycoprotein G and the potential for cross-reactivity between glycoproteins G1 and G2 in ELISA, inability to determine the route of HSV acquisition (genital or oral) and difficulty in interpretation of results in HIV and other types of immunosuppressions.^[1] It must be remembered during interpretation of serological results that almost all HSV-2 infections are sexually acquired whereas HSV-1 antibodies indicate either an orolabial or a genital acquisition.^[7]

PRINCIPLES OF THE MANAGEMENT OF GENITAL HERPES

The following goals are to be met during the management of patients with genital herpes:

- Inducing healing of clinical lesions
- Preventing recurrences
- Preventing transmission to others
- Sexual partner management
- Management of the psychological morbidity
- Counseling regarding the natural history of genital herpes, sexual and perinatal transmission and methods to reduce transmission
- Handling of special circumstances like herpes genitalis in HIV, pregnancy and neonatal herpes

Antiviral chemotherapy offers clinical benefits to the majority of symptomatic patients and is the mainstay of management.^[5,8] Palliative measures like loose-fitting

cotton underwears, cold compresses, saline bathing of the affected area, keeping the area dry and clean and topical zinc cream application should be advised.^[1] Systemic antiviral drugs can partially control the signs and symptoms of herpes episodes when used to treat first clinical and recurrent episodes or when used as daily suppressive therapy. However, these drugs do not eradicate the latent virus.^[5,8,9]

Currently, three drugs are approved for the treatment of genital herpes: acyclovir, valacyclovir and famciclovir.^[1] Acyclovir is highly active against HSV-1 but slightly less active against HSV-2.^[4] The antiviral activity of acyclovir is due to the intracellular conversion of acyclovir, by viral thymidine kinase, to the monophosphate, with subsequent conversion by cellular kinases to diphosphate and the active triphosphate. This active form inhibits viral DNA synthesis and replication by inhibiting the herpes virus DNA polymerase enzyme as well as by being incorporated into the viral DNA causing premature DNA chain termination. The whole process is highly selective for infected cells because the initial activation needs viral thymidine kinase and, for the same reason, acyclovir has no activity against latent virus. Compared with acyclovir, penciclovir is 100-160 times less potent in inhibiting viral DNA polymerase but compensates for that by a longer half-life and higher intracellular concentration. Penciclovir inhibits viral DNA synthesis through irreversible and competitive inhibition of DNA polymerase rather than DNA chain termination.^[1] Penciclovir is not indicated for HSV-2 infections.^[10]

Valacyclovir and famciclovir are prodrugs of acyclovir and penciclovir, respectively. They have enhanced absorption after oral administration and higher oral bioavailability, thereby allowing for lower dosage and lesser frequency of administration (oral bioavailability of acyclovir is 10–20% and that for valacyclovir is five times higher^[11]). Topical acyclovir preparations are less useful and are not recommended.^[8] Acyclovir resistance is most commonly due to mutation in the viral thymidine kinase and rarely due to mutation in viral DNA polymerase. In acyclovir resistance, valacyclovir and famciclovir are also ineffective. In spite of reports of treatment failure, resistance has never been a major problem in genital herpes.^[4]

Foscarnet inhibits viral DNA polymerase directly without requiring activation by viral thymidine kinase.^[1] Therefore, it is effective in acyclovir-resistant

HSV infections. Foscarnet resistance is rare. Cidofovir, after activation by cellular kinases, inhibits viral DNA polymerase and is useful in acyclovir- and foscarnet-resistant cases. It is given intravenously (IV) once a week. Topical cidofovir 1% gel is also effective in acyclovir-resistant HSV infections [Figure 1].^[1]

Antivirals may be used in the following ways [Table 1]:

1. Symptomatic management to reduce symptoms and improve healing
2. Episodic (intermittent therapy) to abort or reduce the duration of episodes
3. Continuous suppressive therapy to prevent recurrences

FIRST CLINICAL EPISODE OF GENITAL HERPES

Many persons with first-episode herpes have severe or prolonged symptoms. Therefore, patients with initial genital herpes should receive antiviral therapy.^[8]

ESTABLISHED HSV-2 INFECTION

Antiviral therapy for recurrent genital herpes can be administered either episodically to ameliorate or shorten the duration of lesions or continuously as suppressive therapy to reduce the frequency of recurrences.^[8] The patient should also be counseled regarding the triggering factors and measures to avoid them.^[1]

EPISODIC THERAPY FOR RECURRENT GENITAL HERPES

Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset or during the prodrome that precedes some outbreaks. The maximal viral replication occurs within 24 h of the first prodromal symptom.^[11] Patient-initiated episodic therapy started during the onset of prodromal symptoms, which most patients can be easily taught to identify, is preferred by many clinicians because it takes advantage of the window period between onset of prodromal symptoms and clinically visible lesions of herpes (which is usually 12–24 h).^[11] Episodic treatment with nucleoside analogs is usually given for 3–5 days. However, single-day patient-initiated episodic treatment (e.g., with famciclovir 1000 mg twice daily^[11] or valacyclovir 2000 mg twice daily^[1]) has been found to be a better option, with better compliance and outcomes.^[8,11]

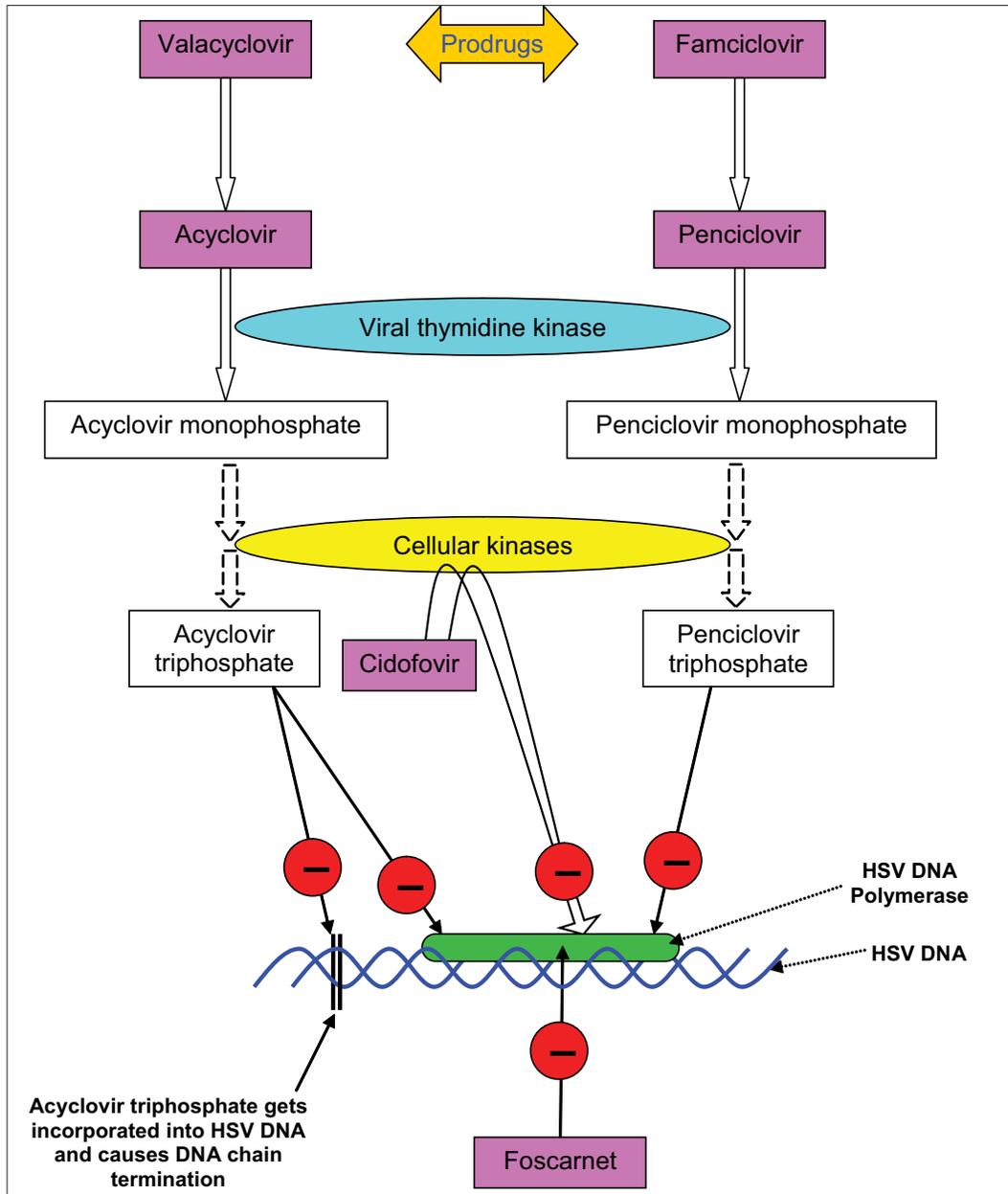


Figure 1: Major mechanisms of action of anti-herpes simplex virus antiviral drugs

SUPPRESSIVE THERAPY FOR RECURRENT GENITAL HERPES

Suppressive therapy is indicated when recurrent genital herpes is frequent (≥ 6 recurrences in 1 year), severe, distressing or associated with distressing prodromes. Other indications are herpetic lesions in the last trimester, patients with psychological and psychosexual problems due to the infection and immunocompromised patients. The risk of transmission of the virus to the sex partner is reduced as suppressive therapy reduces asymptomatic viral shedding.

Long-term antiviral prophylaxis may be started any time and continued for an unspecified duration.^[1] Safety and efficacy have been documented among patients receiving daily therapy with acyclovir for as long as 6 years and with valacyclovir or famciclovir for 1 year. Quality of life of patients with frequent recurrences is better in those who receive suppressive therapy than in those who receive episodic treatment. In a study, 72% of the patients preferred to take suppressive therapy over episodic therapy.^[12] Long-term suppression is reported to reduce clinical outbreaks of genital herpes and subclinical shedding by 80 and 95%, respectively.^[1]

Table 1: Treatment of genital herpes^[8]

Clinical scenario	Immunocompetent individuals	HIV-infected individuals
First clinical episode of genital herpes*	Acyclovir 400 mg orally three times a day for 7–10 days OR Acyclovir 200 mg orally five times a day for 7–10 days OR Famciclovir 250 mg orally three times a day for 7–10 days OR Valacyclovir 1 g orally twice a day for 7–10 days	
Episodic therapy for recurrent genital herpes	Acyclovir 400 mg orally three times a day for 5 days OR Acyclovir 800 mg orally twice a day for 5 days OR Acyclovir 800 mg orally three times a day for 2 days OR Famciclovir 125 mg orally twice daily for 5 days OR Famciclovir 1000 mg orally twice daily for 1 day OR Valacyclovir 500 mg orally twice a day for 3 days OR Valacyclovir 1.0 g orally once a day for 5 days	Acyclovir 400 mg orally three times a day for 5–10 days OR Famciclovir 500 mg orally twice a day for 5–10 days OR Valacyclovir 1.0 g orally twice a day for 5–10 days
Suppressive therapy for recurrent genital herpes	Acyclovir 400 mg orally twice a day OR Famciclovir 250 mg orally twice a day OR Valacyclovir 500 mg orally once a day OR Valacyclovir 1.0 g orally once a day, (for > 10 recurrences per year)	Acyclovir 400–800 mg orally two to three times a day OR Famciclovir 500 mg orally twice a day OR Valacyclovir 500 mg orally twice a day

*Treatment might be extended if healing is incomplete after 10 days of therapy. First clinical episode of genital herpes in HIV is managed with conventional doses of acyclovir, valacyclovir or famciclovir. Treatment is continued until all lesions have crusted or re-epithelialized (generally 5–10 days longer than that in HIV-negative individuals). Higher doses of acyclovir (400 mg 3–5 times a day) have been recommended for severe infection.

The frequency of recurrent genital herpes outbreaks diminishes over time in many patients.^[8]

Breakthrough episodes during therapy should prompt one to look for poor compliance, need to adjust therapy, resistance or a mistaken diagnosis. A minimum of 3 months to 1 year of daily therapy is warranted for any efficacy.^[1] Some patients desire short-term suppression for a duration of 1 month. Annual evaluation is required and cessation of therapy (or drug holiday) should be discussed with patients who are well controlled for a long time.^[1] Some authors recommend that suppressive therapy should be discontinued after 12–24 months in order to assess the ongoing frequency of recurrences.^[10]

Valacyclovir appears to be somewhat better than famciclovir for the suppression of genital herpes and associated shedding.^[9] However, valacyclovir 500 mg once a day may be less effective than other acyclovir or valacyclovir regimens in patients with very frequent (> 10 in a year) recurrences.^[2]

SEVERE DISEASE

IV acyclovir therapy is recommended in patients

who have severe HSV disease or complications that necessitate hospitalization (e.g., disseminated infection, pneumonitis or hepatitis) or CNS complications (e.g., meningitis or encephalitis). The recommended regimen is acyclovir 5–10 mg/kg body weight IV every 8 h for 2–7 days or until clinical improvement is observed, followed by oral antiviral therapy to complete at least 10 days of total therapy.^[8]

HIV INFECTION

Antiretroviral therapy reduces the severity and frequency of symptomatic genital herpes, but frequent subclinical shedding still occurs. Suppressive or episodic therapy with oral antiviral agents is effective in reducing HSV shedding, is safe and well tolerated and may provide additional benefit by decreasing HIV-1 levels in the blood and genital tract. Treatment should be continued till all the lesions heal, which may take a significantly longer duration compared with genital herpes in the immunocompetent individuals. Some specialists suggest that HSV type-specific serology should be offered to HIV-positive persons during their initial evaluation and suppressive antiviral therapy should be considered in those who have HSV-2 infection.^[8,13]

Acyclovir resistance is much higher (3.6–10.9%) in patients with HIV compared with immunocompetent hosts (< 1%). The scenario did not change even after the introduction of HAART.^[10] Cases of thrombotic microangiopathy reported earlier in the literature occurring following valacyclovir therapy in the immunocompromised individuals were related to a high dose of valacyclovir given for a prolonged duration. With the currently recommended dosage, such adverse effects are unlikely (patient on high-dose valacyclovir should, however, be monitored for such adverse effects). Valacyclovir has been FDA approved for use in HSV infections in HIV.^[1]

GENITAL HERPES IN PREGNANCY

The risk of neonatal transmission is low if genital herpes occurs in the first and second trimester.^[1] However, patients with genital herpes after 34 weeks of gestation and those who have not completed at least 4 weeks of acyclovir therapy before delivery are at a high risk of transmitting the infection to the neonates.^[10] Cesarean delivery is indicated for such cases, but it does not completely eliminate the risk. The best policy would be to continue acyclovir till delivery and perform cesarean section at full term.^[10] Elective cesarean delivery is especially indicated if active HSV lesions are present during or within 2 weeks of labour.^[1]

Acyclovir, valacyclovir and famciclovir are Pregnancy Category B drugs.^[7] Safety of these drugs in pregnancy has not been definitively established but available data do not suggest major birth defects due to acyclovir.^[14] The benefits much outweigh the risk.^[7] Acyclovir attains good concentration in the fetus.^[7] Data regarding valacyclovir and famciclovir are limited. However, safety of acyclovir may be extended to valacyclovir as it is a prodrug of acyclovir.^[10]

Antiviral (acyclovir 400 mg tid for 7–14 days or valacyclovir 1 g bid for 7–14 days) therapy is recommended for women with symptomatic primary or first-episode HSV infection during pregnancy.^[7] Symptomatic recurrent HSV should be treated with acyclovir 400 mg tid for 5 days or valacyclovir 500 mg bid for 5 days.^[7] For women with frequent or severe recurrences, especially after the first trimester, daily suppressive therapy (acyclovir 400 mg tid or valacyclovir 500 mg bid) from 36 weeks of gestation till delivery may be indicated.^[7] Andrews *et*

al. reported that administration of valacyclovir (500 mg bd) beginning at 36 weeks gestation till delivery in women with a history of recurrent genital HSV reduced the number of subsequent clinical HSV recurrences.^[15]

Prevention of neonatal herpes involves one or more of the following measures: serology for identifying those women at risk of acquiring new infection, recommendation of abstinence or protective condoms or antiviral prophylaxis in the context of a HSV-2-seropositive man and HSV-2-seronegative woman (seroincompatible), prophylactic antivirals from the 36th week of gestation in pregnant females at a high risk of HSV outbreaks during labour, antiviral treatment of HSV infections during late pregnancy, abstinence from oral sex in HSV-1-seroincompatible couples, thorough evaluation (including speculscopy) for herpetic lesions during labour, avoiding exposure of the infant to herpetic lesions during delivery by performing cesarean section, providing occlusive dressing for nongenital lesions during labour, avoidance of iatrogenic trauma to the fetus and refraining health care workers with visible herpetic lesions from providing postnatal care.^[1,7]

NEONATAL HERPES

Infants suspected to have been exposed to HSV during birth should be followed carefully in consultation with a specialist and cultures of mucosal surfaces would be desirable. Some specialists recommend the use of acyclovir for infants born to women who acquired HSV near term.^[8]

Neonates delivered through an infected birth canal should be screened between 24 and 48 h of age with viral cultures of the eyes, nasopharynx, mouth and rectum.^[15-18] Treatment with systemic acyclovir should be started promptly. The recommended regimen for infants treated for known or suspected neonatal herpes is acyclovir 20 mg/kg body weight IV every 8 h for 21 days for disseminated and CNS disease or for 14 days for disease limited to the skin and mucous membranes.^[8]

DRUG RESISTANCE

If lesions persist or recur in a patient receiving antiviral treatment, HSV resistance should be suspected and a viral isolate should be obtained for

sensitivity testing.^[19] All acyclovir-resistant strains are resistant to valacyclovir and the majority are resistant to famciclovir. In the case of clinical resistance, virological studies with resistance testing should be carried out. This will help a clinician decide whether to give a high dose oral or intravenous acyclovir, if the strain shows complete or intermediate sensitivity, or to switch to an alternative agent like foscarnet.^[10] Foscarnet, 40 mg/kg body weight IV every 8 h until clinical resolution is attained is frequently effective for the treatment of acyclovir-resistant genital herpes. Topical cidofovir gel 1% applied to the lesions once daily for five consecutive days might also be effective.^[8] A combination of multidrug therapy has also been tried in resistant HSV disease.^[1]

MANAGEMENT OF SEX PARTNERS

The sex partners of patients who have genital herpes can benefit from evaluation and counseling. Symptomatic sex partners should be evaluated and treated in the same manner as patients who have genital lesions. Asymptomatic sex partners of patients who have genital herpes should be questioned concerning histories of genital lesions and offered type-specific serologic testing for HSV infection.^[8]

COUNSELING

Counseling of infected persons and their sex partners is critical to the management of genital herpes.^[8] The goal of counseling is to help patients cope with the infection and prevent sexual and perinatal transmission.^[20]

The following recommendations apply to counseling of persons with HSV infection:

- Explain and educate about the nature of genital herpes, the potential for recurrent episodes, asymptomatic viral shedding and the risks of sexual transmission.
- Explain the role of suppressive or episodic therapy in persons experiencing a first episode of genital herpes.
- Encourage to inform the sex partners.
- Explain the need to abstain from sexual activity with uninfected partners when lesions or prodromal symptoms are present.
- Explain that latex condoms reduce the risk for genital herpes transmission.
- Evaluate the sex partners, even in the absence of symptoms, by serology to identify serocompatibility.

- Educate regarding neonatal herpes.
- Seropositive but clinically asymptomatic patients should receive the same counseling message.

In addition, patients should be taught about the clinical manifestations and prodromal symptoms of genital herpes.^[8]

PREVENTION

1. Sexual abstinence is the only method for absolute prevention of genital herpes.
2. Contact should be avoided when active lesions are present. Avoid contact until re-epithelialization has occurred.
3. Use of condoms and spermicidal foams is recommended in patients who have a history of recurrent herpes genitalis.
4. Condoms are effective only if they cover all the lesions and are more effective at protecting susceptible females from HSV transmission than susceptible males.
5. If both partners had genital herpes, protective measures are not necessary if both carry the same virus type and active lesions are not present.
6. Having herpes in one area is not protective against acquiring the infection in another location.

NEW ADVANCES

Vaccines

Vaccination, at least in theory, is the best method for preventing virus spread, but this strategy has been only marginally successful in genital herpes.^[21] The HSV candidate vaccines tested till now were mostly purified subunit vaccines and/or recombinant envelope glycoproteins (such as gB and gD). In many experiments performed in mice, guinea pigs and rabbits, clear-cut protection against acute virus challenge was demonstrated along with the reduction of the extent of latency. The immunotherapeutic effect of herpes vaccines seems less convincing. However, the introduction of new adjuvants, which shift the cytokine production of helper T-cells toward the stimulation of cytotoxic T-cells, reveals a promising development.^[21]

Recently, the results of two controlled trials of an HSV type 2 (HSV-2) glycoprotein D (gD) vaccine revealed that vaccination reduced the rate of acquisition of genital herpes disease, but it did so only among HSV-seronegative women.^[22] The vaccine did not reduce

the risk of disease among men and did not add to the protection provided by a previous HSV-1 infection in women.

Topical immunomodulators

Resiquimod and imiquimod have been tried topically and have been found to decrease the median lesions and the shedding rate without any influence on the recurrence duration.^[10]

FUTURE TRENDS

Helicase–primase inhibitors are new nonnucleoside antivirals that target the helicase–primase complex critically involved in HSV DNA replication. Results from animal studies are encouraging.^[23] They may prove to be the new generation of anti-HSV drugs with improved efficacy, less toxicity, better cost-effectiveness and more convenient administration.^[23] A study using BAY 57-1293, a helicase–primase inhibitor, in animal models of ocular HSV-1 infection showed that it is more effective than valacyclovir with a good safety profile.^[24]

Zhang *et al.* tested a novel needle-free mucosal vaccine containing synthetic peptide epitopes of HSV-2 extended with an agonist of Toll-like receptor 2 (TLR-2) that are abundantly expressed by dendritic and epithelial cells of the vaginal mucosa. After intravaginal inoculation, there was the development of protective immunity (local and systemic CD8+ T cells response) against HSV-2.^[25]

A new microbicide product named VivaGel (containing SPL7013 as the active ingredient) has been showing promising efficacy and safety in initial animal and human studies.^[2]

CONCLUSION

Genital herpes infection is treatable, but not curable. Prolonged suppressive therapy prevents recurrences and reduces asymptomatic viral shedding. Genital herpes in pregnancy, HIV and neonatal herpes pose special problems; however, treatment with standard antiviral drugs appears to be safe and effective in such circumstances. The psychological aspect of genital herpes infection should be addressed and professional help may be sought if required. Partner management is important. Newer therapeutic options appear to be interesting development but what remains challenging is to achieve cure.

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Multiple Choice Questions

- Which of the following tests can be used to confirm recurrent genital herpes?
 - Serology
 - HSV-PCR
 - Viral culture
 - Direct fluorescent antibody test (DFA)
- All are TRUE regarding serological tests in genital herpes EXCEPT
 - False negative results can occur
 - False-positive results can occur
 - Can determine the route of HSV acquisition (genital or oral)
 - Difficulty in interpretation in HIV
- All of the following statements are TRUE EXCEPT
 - Acyclovir is more effective against HSV-1 compared to HSV-2.
 - Penciclovir is as potent as acyclovir in inhibiting viral DNA polymerase.
 - Penciclovir can not be used for HSV-2 infections.
 - Oral bioavailability of valacyclovir is 5 times higher than that for acyclovir.
- In recurrent genital herpes, the maximal viral replication occurs within how many hours of the first prodromal symptom?
 - 6 hours
 - 24 hours
 - 48 hours
 - 72 hours
- Single-day therapy for recurrent genital herpes is
 - Acyclovir 800 mg three times a day
 - Famciclovir 500 mg twice daily
 - Famciclovir 1000 mg once daily
 - Valacyclovir 2000 mg twice daily
- All of the following are TRUE EXCEPT
 - Early initiation of antiviral chemotherapy will prevent development of latent infection
 - Acyclovir resistance is more commonly due to mutation in the viral thymidine kinase
 - In acyclovir resistance, valacyclovir and famciclovir also are ineffective
 - Forcarnet is effective in acyclovir-resistant HSV infections
- Long-term suppressive therapy is generally indicated for
 - More than 4 recurrences of genital herpes in one year
 - More than 6 recurrences of genital herpes in one year
 - More than 9 recurrences of genital herpes in one year
 - More than 10 recurrences of genital herpes in one year
- All of the following are TRUE regarding genital herpes in HIV EXCEPT
 - HSV type-specific serology should be offered to all HIV-positive persons
 - Acyclovir resistance is higher in patients with HIV compared with immunocompetent hosts
 - The incidence of acyclovir resistance in HIV has decreased significantly after the introduction of HAART
 - Thrombotic microangiopathy is unlikely with the usual dose of valacyclovir in HIV
- The risk of neonatal herpes is high if a patient with genital herpes has not completed
 - At least 2 weeks of acyclovir therapy before delivery
 - At least 4 weeks of acyclovir therapy before delivery
 - At least 6 weeks of acyclovir therapy before delivery
 - At least 8 weeks of acyclovir therapy before delivery
- All of the following measures are recommended for reducing the risk of neonatal herpes EXCEPT
 - Abstinence or protective condoms or antiviral prophylaxis in the context of a HSV-2 seropositive man and HSV-2 seronegative woman
 - Prophylactic antivirals from 36th week of gestation in pregnant females at high risk of HSV outbreaks during labour
 - Evaluation for herpetic lesions during labour
 - Vaginal delivery

1. a, 2. c, 3. b, 4. b, 5. d, 6. a, 7. b, 8. c, 9. b, 10. d

Answers