GENITAL HERPES: Clinical Features, Psychological Aspects and Therapeutic Options

P. M. Abdul Gaffoor, DV, DDV, FAMS
Department of Dermatology,
Hamad Medical Corporation

Genital herpes is a sexually transmitted disease affecting millions of people worldwide. It is caused by herpes simplex virus (HSV) a member of the large herpesvirus family which includes Herpes zoster virus, Cytomegalovirus and the Epstein-Barr virus. The HSV contains a core of double-stranded DNA which, together with the nucleocapsid, is surrounded by an envelope of lipid and glycoprotein.

Many of the herpes viruses cause persistent or latent infections in man which can be activated or reactivated by various stimuli. So far it has proved extremely difficult, and usually impossible, to eliminate these latent infections which consequently are then present life-long.

The task is made more difficult as there are hundreds of thousands of different strains of HSV1 and HSV2. Nearly every person has his or her strain of HSV[1]. The virus also can infect a wide range of hosts and many tissue culture cell lines derived from vertebrates[2].

The disappointment caused by failure to eliminate the latent infection and the frequency of recurrence, especially following sexual activity, has a profound psychological effect upon the patient. It is the intention of this communication to emphasise this aspect of the treatment of HSV infection and to discuss the possible long-term use of acyclovir in improving the quality of life for the patient. Should long-term suppression therapy with acyclovir be used or not?

Correspondence to:
Dr. P. M. Abdul Gaffoor,
Department of Dermatology
Hamad Medical Corporation,
P.O. Box 3050, Doha, Qatar.

Transmission of HSV

Infection is usually transmitted genitally or orogenitally through abrasions of the mucosae following sexual trauma. The virus enters by a process of fusion and replicates within the epidermal and dermal cells. Transmission may be asymptomatic if only one of the partners is infected with HSV. Auto-in oculation is possible to adjacent epithelial surfaces, eyes, oropharynx and fingers[3] but infection through fomites or aerosols has not been documented. Male to female transmission is more common than the reverse[6].

Clinical Course.

The initial infection may be symptomatic or asymptomatic, with the asymptomatic carrier still having the ability to infect the partner. Usually following transmission by sexual intercourse the incubation period is five to ten days but it can be as short as 24 hours or as long as 26 days. The first episode varies in severity in different individuals but tends to be more severe in females than in males.

Primary genital herpes is characterised by multiple vesicular lesions which rupture to form ulcers. These primary lesions are usually severe, painful and of long duration with the patient complaining of itching, soreness and a "burning" sensation even before eruption. There may also be myalgia, fever, headache and photophobia. Complications include retention of urine, constipation and transient impotence.

In a person not previously infected with HSV1, primary infection with HSV2 virus can result in a clinically severe attack with complications[5].

Recurrent genital herpes: Recurrence is a feature of herpes virus infections due to endogenous reactivation of latent infection by physical or psychological stress, ultra-violet rays, menstruation or sexual trauma. There is a prodromal syndrome of itching or tingling for a few hours or even a few days before the appearance of the lesions. These

are usually unilateral, milder, smaller and of shorter duration than those of the primary attack. Recurrence can take place five or more times a year. Asymptomatic genital HSV shedding at the onset of labor because of subclinical genital primary HSV infection is associated with preterm delivery[4].

Psychological distress

Many patients with recurrent genital herpes are distressed. Anxiety and depression are serious psychological problems that arise from the stigma of the disease, the frequency of recurrence, a feeling of isolation, helplessness and "victimisation" and an apparent inability to obtain effective treatment. Their distress is increased by their lack of control over the symptoms, an inability to identify the contributory factors and a feeling of insecurity as to when the disease is contagious[7].

Luby and Gillespie emphasise that herpes can pose remarkably painful and difficult adaptational problems[7] especially in younger age groups at a time of psychological development when they are trying to develop lasting relationships. "Initial shock" and "emotional numbing" occurs in many patients when they know the diagnosis of herpes[8].

The morale of these patients are low and there is a reluctance to engage in social activities or form friendships with the opposite sex because of the fear of spreading the disease. The results are an aversion to sex, and reduced sexual pleasure. The psychological stress may be manifested in the form of diminished self esteem, anxiety, isolation and reluctance to initiate close relationships with opposite sex[7]. There is psychological morbidity associated with genetal herpes[10]. There are also moral problems[9].

Diagnosis

Using light microscopy multinucleated giant cells and intracellular inclusions can be seen in Giemsa-stained scrapings from the genital lesions. Virus particles can be detected by electron microscopy. In cell cultures HSV antigen or DNA can be detected within 16 - 48 hours although the DNA might need amplification by the polymerase chain reaction (PCR).

Treatment

Patients with genital herpes will seek medical attention with either primary or recurrent lesions. Many will be distressed following frequent recurrences and they might even have heard that there is no permanent cure. Although this is true, they need to be reassured that the condition can be alleviated with treatment.

The most important objective of any antiviral therapy is to minimise the effects and shorten the duration of the disease without producing further complications. A secondary objective is to prevent a recurrence. In the case of HSV infection this secondary objective is not attainable because the latent infection cannot be eliminated from the body (Fig.1).

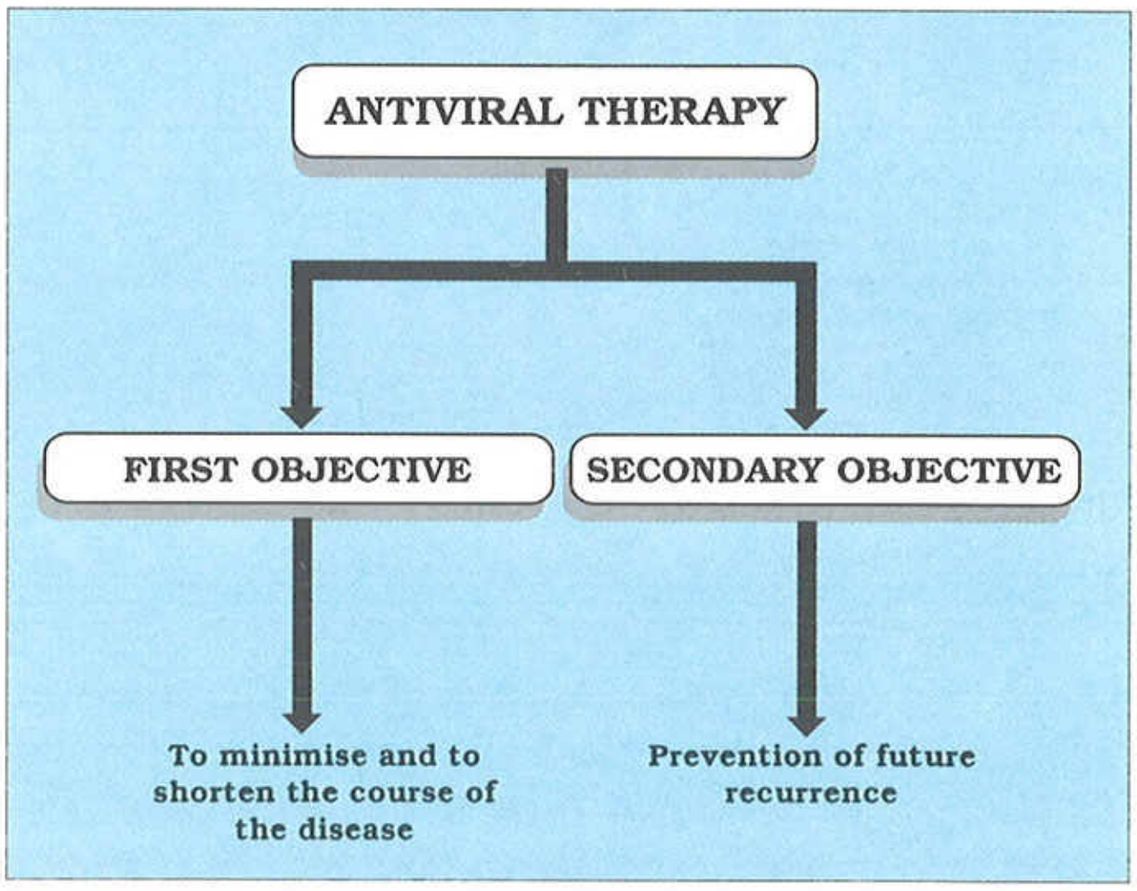

Fig. 1:

Acyclovir is a potent inhibitor of herpes virus replication and is thus an excellent choice for the treatment of genital herpes. Acyclovir becomes antiviral only after phosphorilation and activation in the infected cells in which it becomes more concentrated (Fig.2).

The usual regimen for primary genital herpes is acyclovir 200 mg orally every five hours for 5-7 days together with topical application of acyclovir cream 5% four or five times daily.

Long term suppressive therapy with acyclovir improves psychological wellbeing[10] but it should

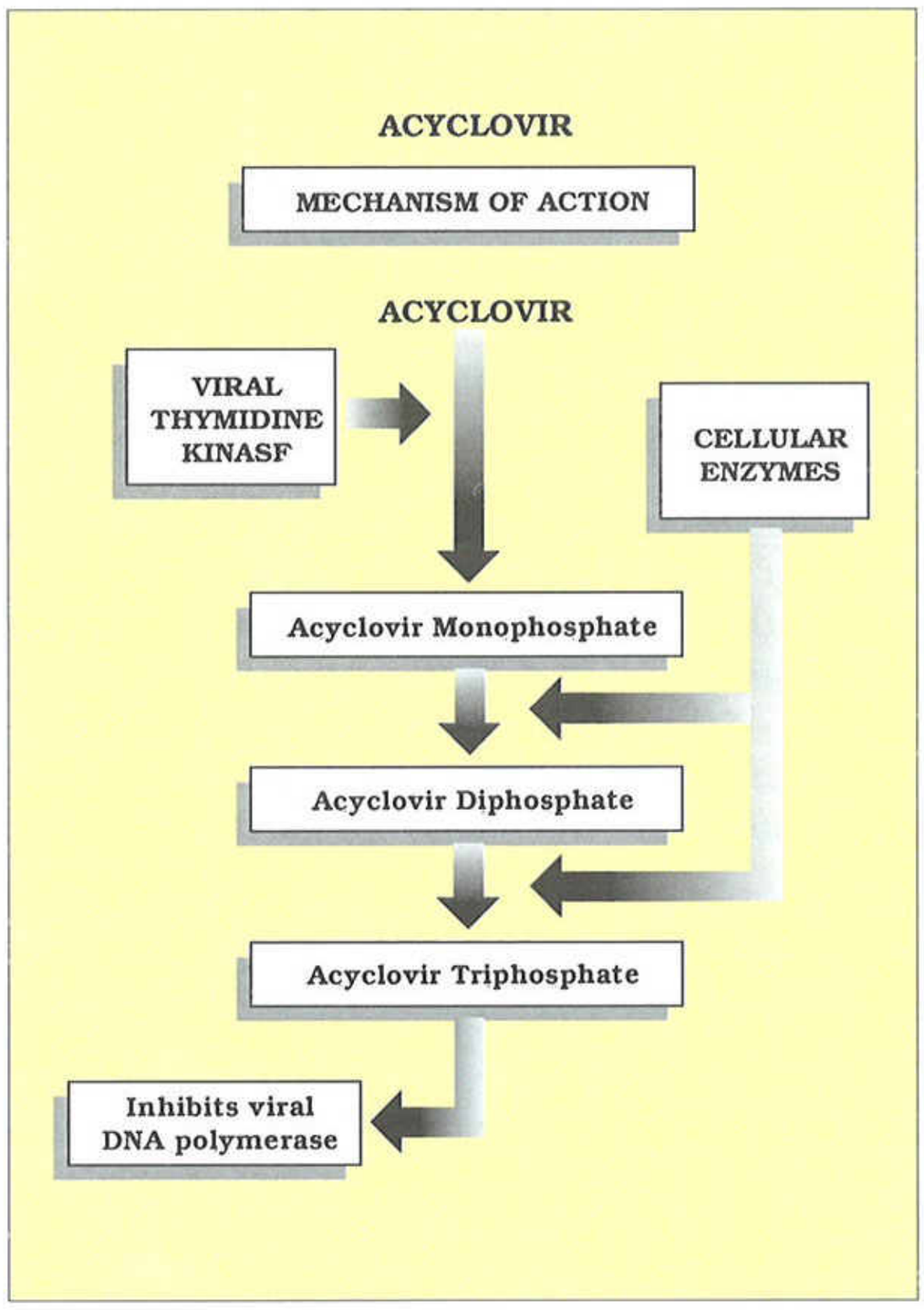

Fig.2:

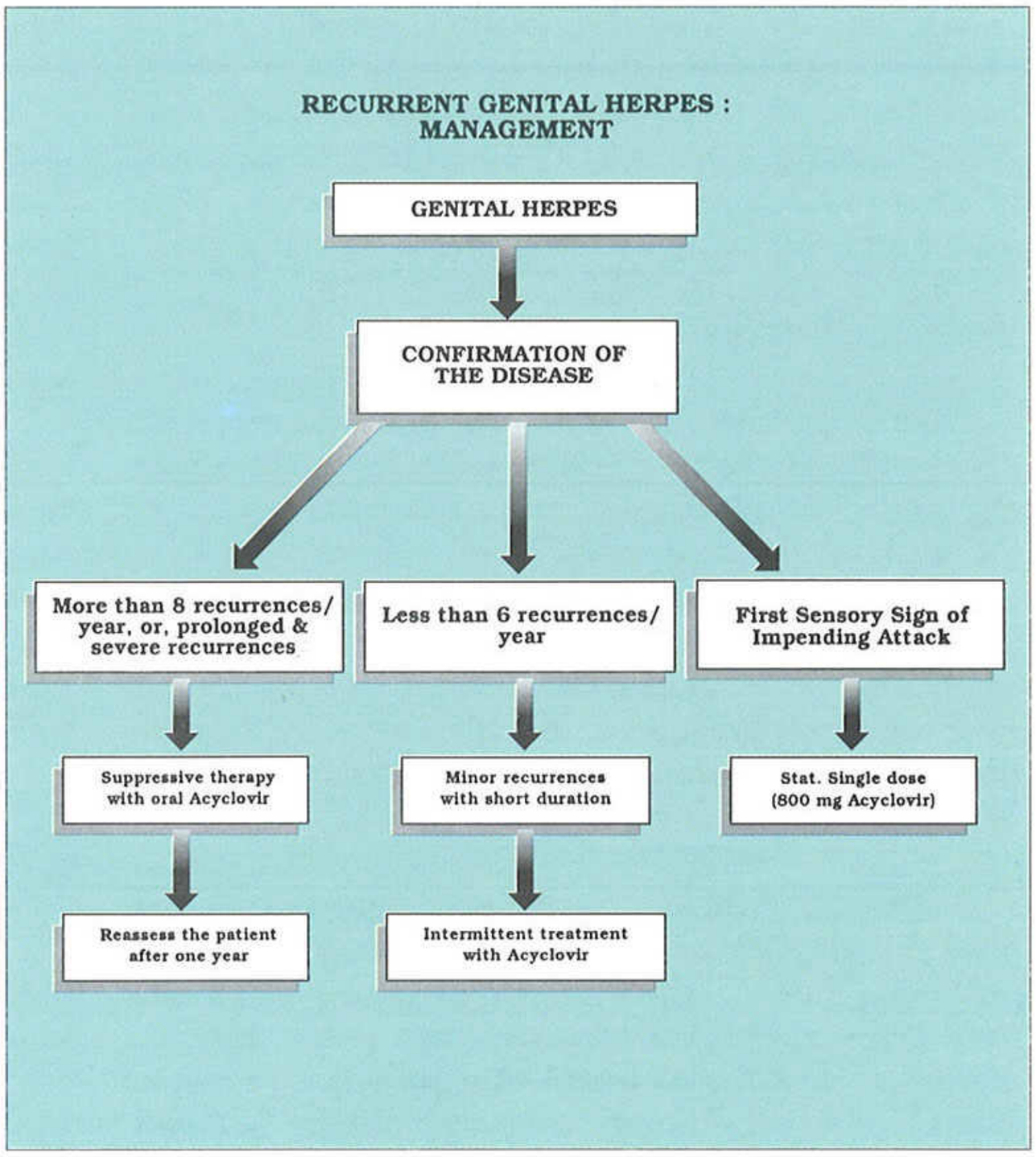

Fig. 3:

not be used as routine.. The decision to use it should be made on an individual basis taking into account the psychological and social needs of the patient. It is indicated in patients with more frequent recurrences, eight times or more per year, and with greater severity of lesions. It is also indicated in patients unable to cope with the situation because of the frequent recurrences, or with neuralgia, and also in patients presenting a risk of transmission (Fig.3).

The regimen for suppressive therapy is oral acyclovir 400 mg twice daily, or 200mg four times a day, continued for 6 - 12 months. All patients should be reassessed after 12 months of treatment but the treatment can be continued for years depending upon individual needs.

Suppressive therapy will reduce the prodrome and also reduce the risk of transmission of infection. The benefit of such prophylaxis is far greater than that achieved by treating individual episodes of reactivation with the same drug[5]. Although prophylactic treatment suppresses the disease, the infection is not eliminated and the clinically free carrier can still infect a sexual partner.

The five year course of therapy for recurrent genital herpes using oral acyclovir 400mg twice daily has been successful in either reducing severity and frequency of recurrence or in maintaining the patient free of disease[11].

Suppressive therapy can also be used during stressful periods when patients might otherwise suffer outbreaks of genital herpes[12]. The patients should avoid sexual intercourse during the prodromal period or when genital lesions are present. If the patient is in doubt about the prodrome a condom should be used for protection during sexual intercourse.

Once the decision for long term suppressive therapy is made, the timing for the commencement of treatment is important. It is best to start immediately following a recurrence or during a period of no recurrence[10]. Patients who started a course of oral acyclovir 200 mg four times daily were significantly less likely to have a recurrence than those on 400 mg twice daily[13]. More frequent doses appear to be more effective.

A cost effective alternative to long term therapy is a single "stat" dose of 800 mg oral acyclovir taken at the first sensory sign of either oral or genital herpes. This regularly prevented lesions[14].

Patients receiving long term acyclovir suppressive therapy experienced a dramatic drop in the recurrence rate in the first year followed by a further gradual improvement in their therapeutic response over the remaining years of observation[15]. The safety of long term acyclovir was excellent[15] but the daily dose should be reduced as soon as possible. The treatment should also be interrupted every twelve months so that the need for continuing suppression can be assessed[16]. In genital herpes the use of long term oral acyclovir will suppress the virus into latency and greatly improve the quality of life for the patient[5].

Acyclovir is the first antiviral to decrease significantly the duration and severity of genital herpes. However, acyclovir does not eliminate the latent virus from the nerve ganglia. Even though some patients may appear free of the disease, asymptomatic shedding of virus can take place and they may still be capable of infecting their partners.

The effectiveness of acyclovir treatment may depend upon the dosage and frequency, patient compliance, uninterrupted dosage, malabsorption and resistance. Acyclovir is assumed to be absorbed over the entire length of the small intestine and the possibility of malabsorption should be borne in mind especially in patients that have undergone abdominal surgery[17].

Adverse effects

The most frequent reactions to oral acyclovir are headache, nausea, diarrhoea and vomiting. The most frequent adverse effect of intravenous acyclovir is inflammation and phlebitis at the injection site. The two most serious adverse effects that may occur are encephalopathic changes with abnormal electro-encephalograms, tremor, confusion and seizures, and renal precipitation of the drug due to rapid bolus parenteral administration[18].

Acyclovir is a safe drug. It is not a carcinogen or a mutagen and it does not impair fertility[18]. Acyclovir has a very specific action primarily on the thymidine kinase and deoxyribonucleic acid polymerase; it does not act upon cellular processes to damage normal cells[19].

Resistance of HSV to acyclovir is of some concern and patients with concurrent infection with human immunodeficiency virus (HIV) may require treatment with intravenous Foscarnet[16].

The management and pharmacological therapy of genital herpes in pregnancy is controversial and studies of oral acyclovir in late pregnancy are currently under way[16]. Suppressive therapy with acyclovir has reduced the need for caesarean section for recurrent herpes in women whose first clinical episode of genital HSV occurred during pregnancy[20]. Suppressive therapy has also reduced asymptomatic shedding of virus from these patients.

Genital herpes infection should be borne in mind when screening for human papilloma virus (HPV). It has been observed that female partners of men with both HPV and HSVhave a greater risk of presenting with high grade cervical lesions[21].

The strong relationship between HSV type 2 and sexual life style suggests that the presence of antibody to the virus may be used as an objective, serological marker pattern of sexual behaviour in different populations[22]. Herpes infection has been identified as a significant co-factor in the transmission of Human Immunodeficiency virus infection[23] (HIV), hence accurate diagnosis and treatment are necessary to avoid such problems. Women with HIV infection, especially those with low CD4 cell counts, shed HSV2 from the vulva and cervix more commonly than those not infected with HIV[24].

Conclusion

One of the most important areas of the body concerned with self-image and self esteem is the genital and those with skin disorders of the genitalia may be manifestly depressed[25]. Acyclovir therapy offers the opportunity to reduce the prodromal symptoms, the frequent recurrence and the neuralgia. Suppressing the genital herpes reduces the anxiety and depression of the patient which in turn improves his or her emotional status and self esteem leading to a considerably improved quality of life.

REFERENCE

1. Lawrence Corey. The diagnosis and treatment of genital herpes. JAMA 1982 248 (9) 1041-48.

2. Lawrence Corey, Patricia G. Spear. Infection with herpes simplex viruses. The New England J of Med. 1986 314 (11) 686 - 691.

3. King Horn GR. Genital herpes: Natural history and Treatment of Acute episodes 1993. J. Med. Virol. Supplement 1993. 1: 33-38.

4. Brown ZA, Beneditte J, Selke S. et al. Assymptomatic maternal shedding of herpes simplex virus at the onset of labor: Relationship to preterm labor. Obst-Gynecol. 1996 87 (4) 483-8.

5. Griffiths P.D., Review - Progress in the clinical management of herpes virus infections antiviral chemistry & chemotherapy 1995. 6 (4) 191-209.

6. Metz G.J., Benedetti J, Ashley R et al. Risk factors for the sexual transmission of genital herpes. Ann Intern Med 1992. 116: 197-202.

7. Elliot D. Luby, Valerie Klinge. Genital herpes. A pervasive psychosocial disorder. Arch. Dermatol 1985. 121: 494 - 497.

8. Luby ED, Gillespie O. Psychological responses to genital herpes. The Helper 1981. 3(4) 2-3.

9. Peter J. Lynch. Psychiatric, legal and moral issues of herpes simplex infections. J. Am Acad Dermatol 1988; 18: 173-5.

10. Mindel A. Longterm clinical and psychological management of genital herpes. J. Med. virol supplement 1993. 1: 39-44.

11. Goldberg LH, Kaufman RH, Kurtz TO, et al. Continuous five-year treatment of patients with frequently recurring genital herpes simplex virus infection with acyclovir. J. Med. Virol Supplement 1993. 1: 45-50.

12. Conant M. Managing the patients with genital herpes and the patient's partner. I.H.M.F. Focus 1994. 20-21.

13. Mindel A, Carney O, Freiris M., et al. Dosage and safety of long term suppressive acyclovir therapy for recurrent genital herpes. Lancet 1988 1: 926-928.

14. Walter B Shelley, E. Dorinda Shelley. "Stat" single dose of acyclovir for prevention of herpes simplex. Cutis 1996 57. 453.

15. Leonard H Goldberg, Raymond Kaufman, Terrance O. Kurtz, et al. Long-term suppression of recurrent genital herpes with acyclovir. A 5-year Benchmark. Arch Dermatol 1993. 129-582-587.

16. De-Ruiter A, Thin RN. Genital herpes. A guide to Pharmacological therapy Drugs. 1994 47 (2): 297-304.

17. Mindel A, Carney O. Acyclovir malabsorption. B.M.J. 1988. 296: 1605.

18. Kenneth A. Arndt. Adverse reactions to acyclovir: topical, oral and intravenous. J. Am Acad Dermatol 1988. 18: 188-90.

19. Kenneth A. Arndt, Marcus A Conant, Clyde S. Crumpacker, et al. Questions & Answers. J. Am Acad Dermatol. 1988 18: 196-7.

20. Scott LL, Sanchez PJ, Jackson JL, et al. Acyclovir suppression to prevent cesarean delivery after first - episode genital herpes. Obst Gynecol. 1996 - 87 (1) 69-73.

21. Ayanaudo O, Bijaoui G, Ionesco M, et al. Genital herpes simplex virus infection among men screened for genital papillomavirus. Ann Dermatol Venereol 1994. 121 (5): 376-81.

22. Cowan FM, Johnson AM, Ashley R, et al. Antibody to herpes simplex virus type 2 as serological marker of sexual lifestyle in populations. BMJ. 1994. 309 (6965) 1325-9.

23. Lavoie SR, Kaplowitz LG. Management of genital herpes infection. Semin Dermatol. 1994. 13 (4): 248-55.

24. Augenbraun M, Feldman J, Chirgwin K, et al. Increased genital shedding of herpes simplex virus type 2 in HIV - seropositive women. Ann. Intern. Med. 1995 1: 123 (11) 845 - 7.

25. Cotterill J.A. Psychiatry & the skin . Br. J. Hosp. Med. 1989. 42. 401-4.