Review paper

PROBLEMS OF ANOGENITAL HERPES. A DERMATOLOGICAL POINT OF VIEW

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ABSTRACT

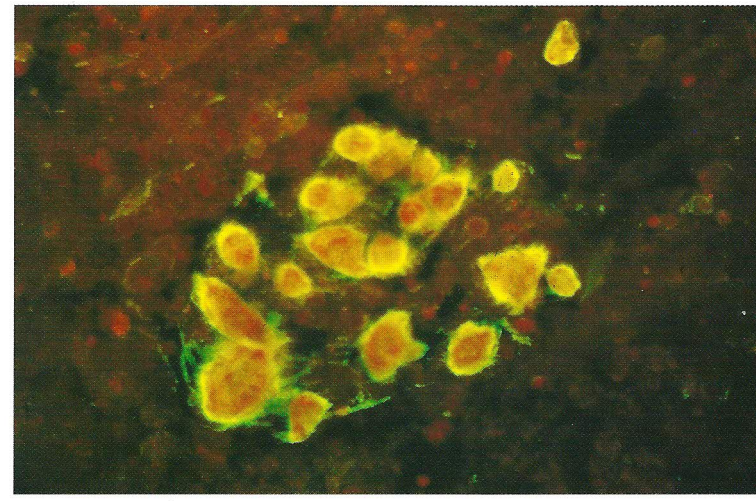
All herpes simplex virus variants of the same serotype (HSV 1/2) cause anogenital infections. Complications such as ulcerations, lymphangitis, urethritis, vaginitis, cervicitis, prostatitis and even sensormotoric disorders can arise during the manifest disease. Additional infections with bacteria or fungi lead to a complicated course of the disease. Eczema herpeticum and postherpetic erythema multiforme are two particular diseases which can develop during the course of a HSV infection. In immunocompromised patients, complications in HSV infections are especially common and always life-threatening. The drug of choice in all HSV-induced diseases is the extremely well tolerated virustatic, acyclovir. If this substance is started early and in dosage and administration appropriate to the clinical picture, it is generally capable of reducing the severity of the disease, substantially shortening its duration and of reliably overcoming complications. Prophylactic oral long-term suppression therapy can successfully prevent complications.

KEY WORDS:
herpes simplex virus, serotypes 1 and 2, anogenital lesions, treatment, acyclovir

INTRODUCTION

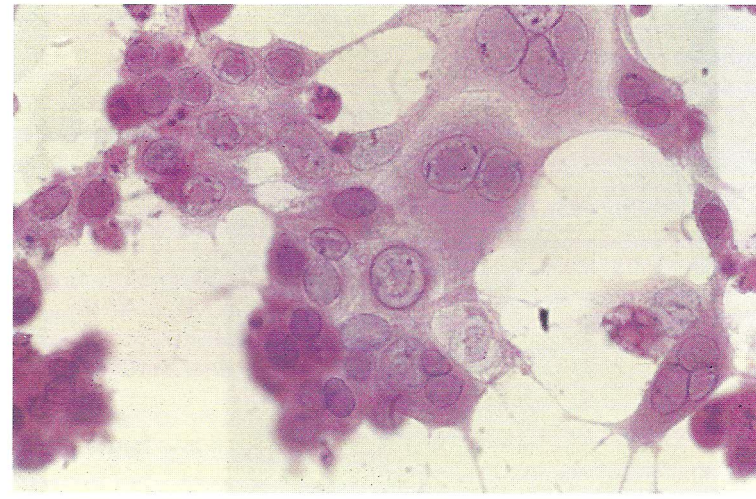
Anogenital herpes is usually caused by the herpes simplex virus 2 (HSV 2), which is transmitted by infected secretions during intimate physical contact. However, transmission of the herpes simplex virus does not necessarily require the presence of clearly visible lesions; sometimes the virus can be shed onto the mucosae before the outbreak of clinical symptoms. For example, herpes simplex virus has been cultivated from tears, saliva, sperm or secretions from the prostate, vagina and urethra in up to 24 % of cases without obvious herpetic lesions (Kaufmann et al. 1967, Jarratt 1983, Yeager 1984, Langenberg et al. 1989).

In the last ten years it has been shown that herpes simplex virus 1 (HVS 1) also plays an increasing role in anogenital infections, probably due to the rise in orogenital sexual practices. HSV 1 has been isolated in up to 60 % of genital lesions (Ozaki et al. 1980, Reeves et al. 1981, Corey et al. 1983). It is interesting to note that reactivations of a genital HSV 1 infection occur less frequently and are considerably less dramatic in their course than lesions caused by HSV 2



Herpes simplex virus infections
Fig. 1. HSV-1 positive cells scrabbed from the base of labial lesion (direct immunofluorescence test).

Herpes simplex virus infections
Fig. 2. HSV-1 negative reaction (tracheal mucous membrane cells).



Herpes simplex virus infections
Fig. 4. Typical CPE caused by HSV-1 (pretreated conjuctival swab inoculated in Vero cells). CPE: cytopathogenic effect

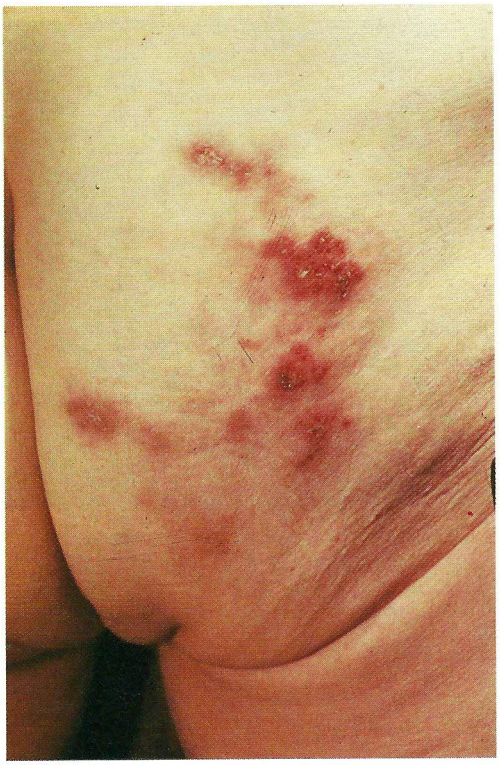


Fig. 1: Zosteriform gluteal HSV 2 primary infection with marked sensomotoric impairment

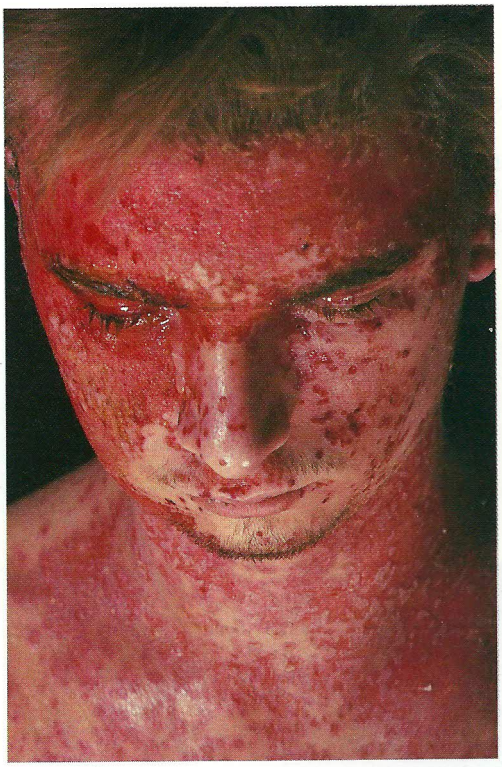


Fig. 2: Eczema herpeticum: onset of generalization in a patient with atopic eczema

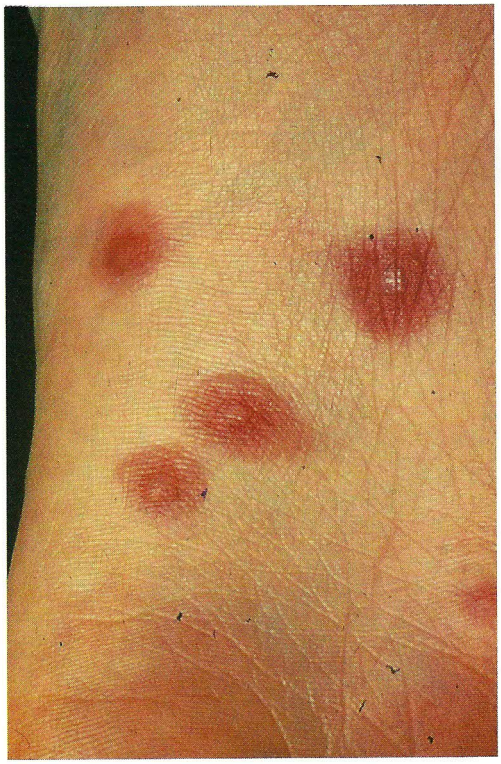


Fig. 3: Post-herpetic erythema multiforme (minor form)

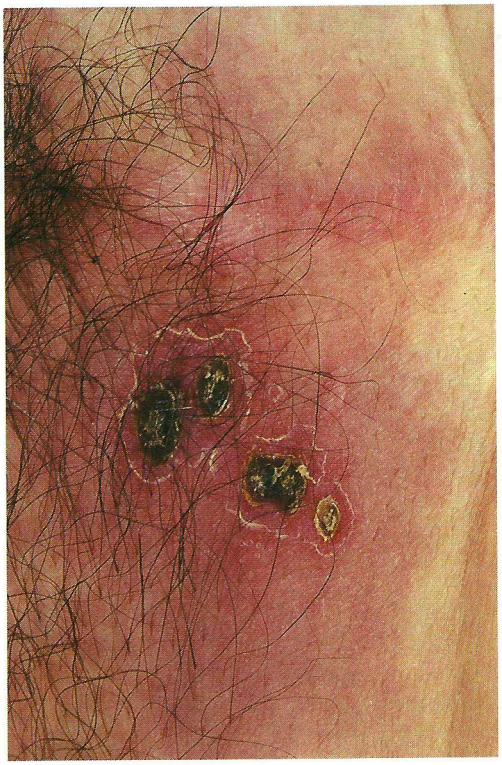


Fig. 6: Persistent ulcerating perianal herpes in AIDS

(Jarratt 1983). This may be due to the fact that HSV 1/2 show intraserotypic variants which have undergone a different location-specific adaptation during their development; in the main, the clinical and morphological changes cannot be related to a particular variant.

COMPLICATIONS

Complications during a clinical herpes simplex virus infection in the anogenital region may arise from time to time in immunocompetent persons, but are naturally more common in immunocompromised patients.

Complications may occur in a HSV 2 primary infection, initial HSV 2 infection, and in a recurrent infection because of severe or unusual clinical symptoms, through possible secondary infections, the development of eczema herpeticum or a post-herpetic erythema multiforme. Occasionally, undesirable reactions occur to local, poorly tolerated medications.

Immunocompromised patients are at particular risk of developing complications.

Since the course of the infection differs, it is logical to differentiate between true HSV 2 primary infections and initial HVS 2 infections. In children, herpes simplex primary infection with HSV 1 predominates. In adolescence (with the start of sexual intercourse), subsequent infection with HSV 2 in the anogenital region is therefore not a true primary infection, but is better described as an initial HSV 2 infection (exogenous HSV second infection) in an existing HSV 1 latency (patients are seropositive). In these cases, the infection runs a far milder course than a true primary infection with HSV 2 (previously HSV-negative). Clinically manifest primary infections with HSV 2 are generally associated with intense symptoms and are not infrequently accompanied by complications (Tab. 1).

A serious complication in a primary infection with HSV 2 often involves vesicular, pustular and occasionally ulcerating lesions lasting 2 - 3 weeks. The changes are mostly localised in the vulva, the vaginal area, perianal region or on the buttocks, as well as the things and on the penis. An accompanying cervicitis can be found in over 80 % of women (Nahmias et al. 1976). In some cases, synechia vulvae and urethral strictures can occur (Walzmann and Wade 1989, De Marco et al. 1987). Occasionally endometritis and salpingitis have been observed in women and prostatitis in men during a primary infection with HSV 2 (Abraham 1974, Lehtinen 1985).

Table 1:

HSV 2 Primary infection
Anogenital ulcerations
Lymphadenopathy
Dysalgia
Dysuria
Cervicitis
Proctitis
Urethritis
Vaginitis

Rectal and perianal HSV 2 primary infections are particularly common in men with homosexual practices. The symptoms include - in addition to weeping and reddening - vesicular or ulcerating lesions sometimes extending as far as the rectum and sigmoid colon (Shab and Scholz 1983) as well as proctalgia, tenesmus, constipation, paraesthesias, urinary retention or even impotence (Goldmeier et al. 1975). Occasionally, extensive dermatome-associated skin changes are found on one half of the buttocks, quite often accompanied by a marked sensomotoric impairment. This is described as a "zosteriform herpes simplex" (Fig. 1).

With all primary infections, initial HSV 2 infections and recurrent diseases, there is always the possibility of additional infection not only with fungi, especially Candida albicans, but also with bacteria. Secondary infections with Treponema pallidum, Haemophilus ducreyi or Chlamydia trachomatis serotype L 1 - 3 are particularly important. Such secondary infections lead to a considerable change in the morphological appearance, which frequently masks the underlying herpes simplex virus infection but which above all requires additional, specific therapy.

A sclerosing lymphangitis (Van der Straak 1977) of the praeputium and labia can develop especially in frequent recurrent genital infections, which are associated with marked and protracted symptoms.

HERPETIC URETHRITIS

After exclusion of other aetiological pathogens corresponding to the particular clinical picture such as Neisseria gonorrhoeae, Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis, Trichomonas vaginalis, the possibility of urethritis caused by herpes simplex should

be considered. The symptoms generally include marked dysuria and localized pain on pressure to the urethra and there is also often painful inguinal lymphadenopathy (Adam 1992). Due to the chronic mucosal irritation and discharge, there is a danger that a papilloma virus (HPV)-induced infection can develop like condyloma acuminatum. The condyloma bed, initially localized at the urethral orifice, can extend as far as the fossa navicularis urethrae.

ECZEMA HERPETICUM

Eczema herpeticum is a disseminated cutaneous herpes simplex infection, more frequently initiated by HSV 1 than by HSV 2 (Fig. 2). The incubation period varies between 2 and 19 days and the disease can run a primary or recurrent course. Various underlying dermatological diseases are generally present, especially atopic eczema, Darier's disease, mycosis fungoides, pemphigus foliaceus, or even ichthyosis. Life-threatening complications with generalization can be accompanied by bronchopneumonia, diarrhoea, keratoconjunctivitis and cerebral symptoms (Segar and Watson 1978). Particularly in atopic eczema, the multiple epithelial defects provide a significant route for HSV penetration. An underlying cellular defect in the T-cell system appears to play a crucial role (Hovmark 1977).

ERYTHEMA MULTIFORME

Erythema multiforme (erythema exsudativum multiforme, EEM) is a disease of the skin and mucous membranes with a characteristic morphological course, which can occur in minor and major forms (tab. 2 and 3).

Table 2:

Erythema multiforme	
Minor form:	target lesions vesicles bullae

Table 3:

Erythema multiforme	
Major form:	Stevens-Johnson Syndrome mucous membranes affected (many orificies) fever bronchopneumonia nephropathy

The commonest causes of erythema multiforme are drugs and microbial agents (Elias, Fritsch 1978). The association of herpes simplex virus infection (HSV 1 more often than HSV 2) and erythema multiforme is well known (Huff 1983). Given an appropriate predisposition, within 1 to 2 weeks of a herpes simplex virus infection, typical target-like efflorescences develop on various parts of the skin (Fig. 3).

Fig. 4: Post-herpetic Stevens-Johnson syndrome

The most severe form of erythema multiforme that can develop is the Stevens-Johnson syndrome (Fig. 4), where the mucosal membranes of many orifices are affected, high fever is present and which is occasionally accompanied by bronchopneumonia and nephropathy. Today it is believed that this is a mucocutaneous hypersensitivity reaction to various antigens, for which the skin and mucous membranes are particular targets (Kazmierowski, Wuepper 1986). On the basis of histological changes in early erythema multiforme lesions, which show infiltration of mononuclear cells, necrosis of keratinocytes and lymphocytic infiltrates, a cellular immune mechanism is believed to be involved in the course of the reaction (Margolin 1983). A HLA-linked genetic predisposition is thought to be responsible for this immune response. An increased risk of developing erythema multiforme could be coupled with HLA-B 15 in two separate investigations (Duvic et al. 1983, Middleton et al. 1983). Post-herpetic erythema multiforme appears even more strongly connected with HLA-DQw3 (Kämpken et al. 1988). According to these results, a DQw3 allel was found in nearly all patients with frequently recurring erythema multiforme, confirming a close connection of erythema multiforme associated with herpes simplex virus (16 out of 18 patients).

HERPES ANOGENITAL INFECTIONS IN PATIENTS WITH IMMUNE DEFICIENCY

Increasingly severe herpes simplex virus infections are

known to arise with the use of immunosuppressants (Hirsch 1981, Stadler 1982). A reactivation of the latent virus infection was found in 82 % of HSV-antibody positive persons among bone marrow recipients. Virus reactivations, with the formation of lesions, were seen within the first 4 weeks of transplantation in 25 to 60 % of renal transplant recipients and this depended on the degree of the reduction in the immune response (Meyers et al. 1982, Walker et al. 1982). Similarly, severe herpes simplex virus infections have been reported in patients with lymphomas and various forms of leukaemia especially during cytostatic treatment (Vonderhaid 1980). In addition to marked ulcerating lesions and necrosis (Fig. 5), spread of a disseminated herpes simplex virus is not uncommon. These patients are also at high risk of developing visceral infection, especially oesophagitis, pneumonia and hepatitis by herpes simplex viruses (Taylor et al. 1981, Walker et al. 1982).

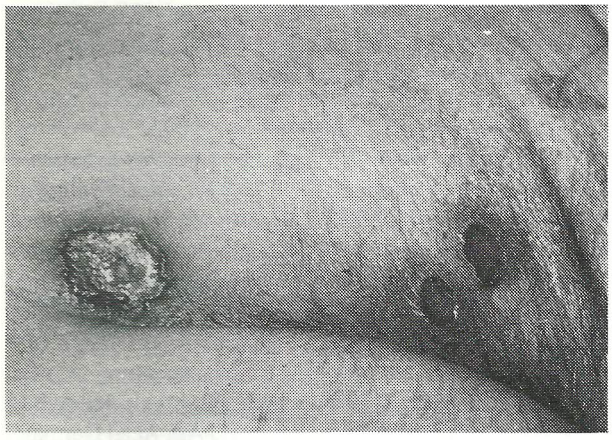


Fig. 5: Disseminated necrotising genital herpes in leukaemia during cytostatic treatment

HERPES SIMPLEX INFECTIONS IN HIV-INDUCED IMMUNE DEFICIENCY SYNDROME

It is known that the incidence of HSV 2 in homosexual and bisexual men is very high; recurring anogenital herpes infections are found relatively frequently. The initially short-lived, circumscribed, spontaneously healing groups of vesicles change with increasing immunodeficiency (Siegal et al. 1981). Thus even in the stage of lymphadenopathy, the clinical manifestations increase in duration and severity, to become, especially in AIDS-related complex and then in full developed AIDS, very painful, punched out, and sometimes necrotic in the form of persistent and ulcerating anal or perianal herpes simplex (Fig. 6). The lesions last for weeks or months, and in advanced stages, lose their tendency towards spontaneous healing. In principle, such severe courses of the disease can arise in all regions of the body, with the risk of developing an interstitial pneumonia, encephalitis, or hepatitis (Goodell et al. 1985).

In the differential diagnosis, the perianal ulcerations occurring in immune deficiency syndrome should be distinguished from primary syphilis infection, chancroid, cytomegalovirus infection, atypical mycobacteriosis and streptococcal-induced ecthyma.

TREATMENT RECOMMENDATIONS IN ANOGENITAL HERPES

A: Non-immunocompromised patients:
HSV 2 primary infection with marked symptoms: acyclovir 5 mg/kg body weight i.v. three times daily for 5 - 7 days.
In less severe cases: acyclovir 200 mg five times daily p.o. for 5 - 7 days.

Initial infection with HSV 2 and marked symptoms:
acyclovir 5 mg/kg i.v. three times daily for 5 - 7 days.
In less severe cases: acyclovir 200 mg five times daily p.o. for 5 - 7 days (Mindel et al. 1982, Nilsen et. al. 1992, Corey et al. 1983, Douglas et al. 1984).

Recurrent anogenital herpes with clear symptoms: acyclovir 200 mg five times daily p.o. for 5 - 7 days (Nilsen et al. 1992, Douglas et. al. 1984).

From our own experiences, oral acyclovir, 400 mg twice daily for 24 weeks, was able to objectively suppress further recurrences in 10 patients with 6-12 episodes of recurrent anogenital herpes in the previous year, without causing any adverse reactions (Engst 1988).

A 3-year suppression study of recurrent genital herpes (more than 6 recurrences per year) confirmed the efficacy of acyclovir 400 mg twice daily (Kaplowitz et al. 1991). The treatment was described as very well tolerated. There were no indications of any clinical resistance to acyclovir.

Erythema multiforme associated with genital herpes:
Prophylactic oral acyclovir can prevent episodes of post-herpetic erythema multiforme (Green et al. 1985). Where there is a known history (HLA DQw3-positive), immediate treatment with 200 mg acyclovir five times daily for 5-7 days should be started at the onset of any recurrence of genital herpes. According to our own experiences, this is an effective way of suppressing episodes of post-herpetic erythema multiforme.

Long term recurrence prophylaxis with 400 mg acyclovir twice daily is recommended in cases of frequent recurrent

anogenital herpes with additional complications such as erythema multiforme

Eczema herpeticum:
Acyclovir 5 mg/kg i.v. three times daily for 5 to 7 days (Beykirch and Kuhlwein 1984).

B: Immunocompromised patients
In primary or recurrent anogenital herpes infections, i.v. acyclovir therapy with 5 to 10 mg/kg three times daily for 7 - 10 days is recommended. The duration of treatment depends on the clinical symptoms and the results of the virus culture tests. Alternatively, in the early stages, acyclovir can be given orally as 200 (400 mg) five times daily for 7 to 10 days (Strauss et al. 1984, Meyer 1985).

According to our own results, patients with leukocytosis caused by leukaemia for example, and with a history of recurrent herpes simplex infections, should be treated prophylactically with oral acyclovir at least 400 mg twice daily before starting, during, and also for 1 week after ending cytostatic treatment, under constant monitoring.

In patients with advanced immunodeficiency syndrome, i.v. acyclovir therapy with at least 10 mg/kg every 8 hours for 8 to 10 days is necessary from the early stage (Mertz et al. 1988, Schöfer 1989). The duration of treatment depends on the clinical symptoms and the results of the virus culture tests.

If started early and in cases where symptoms are limited, oral acyclovir 400 mg five times daily for 10 days was also successful (Conant 1988, Schöfer 1989).

Due to the serious risk that an inadequately high and protracted therapy with acyclovir in patients with immunodeficiency syndrome may lead to the emergence of mutations in the herpes simplex viruses (Engel et al. 1989), high dosage acyclovir treatment, started at an early stage, is absolutely preferable. Low dosage, long-term treatment should never be given in cases of existing efflorescences. If the response is inadequate and the skin lesions fail to show signs of regression, therapy should be switched to continuous acyclovir infusions of 1.5 to 2.0 mg/kg per hour for 7 to 10 days; in cases of resistance, foscarnet should be given as 40 mg/kg i.v. every 8 hours (Engel et al. 1989, Safrin et al. 1989).

After healing is complete, prophylactic treatment with long-term acyclovir against recurrence is recommended. The initial dosage is 200 mg four times daily p.o., reducing to 200 mg three times daily (Mindel et al. 1988) or 400 mg twice daily (Engst 1988) depending on the individual case.

REFERENCES

Abraham AA: Herpesvirus hominis endometritis in a young woman wearing an intrauterine contraceptive device. A.J. Obstet. Gynecol. 1974;131:340-343

Adam E : Herpes simplex virus infections. In: Glaser R, Gotlieb-Stematsky Y (eds) Human herpesvirus infections. Marcel Dekker, New York, Basel 1982 p 1

Beykirch W, Kuhlwein A: Zur Therapie des Ekzema herpeticatum mit Aciclovir (Zovirax^{R}). Wehrmed. Mschr. 1984;7:276-281

Conant MA: Prohphylactic and suppressive treatment with acyclovir and the management of herpes in patients with acquired immunodeficiency syndrome. J Am Acad Dermatol 1988;18:186-188

Corey L, Fife KH, Benedetti JK, Winter CA, Fahnlander A, Connor JD, Hintz MA, Holmes KK: Intravenous acyclovir for the treatment of primary herpes. Ann. Intern. Med 1983;93:914-921

De Marco BJ, Crandall RS, Hreshchyshyn MM: Labial agglutination secondary to herpes simplex II infection. Am J Obstet Gynecol 1987;157:296-297

Douglas JM, Critchlow C, Benedetti J, Mertz GJ, Connor JD, Hintz MA, Fahnlander A, Remington M, Winter C, Corey L: A double-blind study of oral acyclovir for suppression of recurrences of genital herpes simplex virus infections N.Engl. J. Med. 1984;310:1551-1556

Duvic M, Reisner EG, Dawson DV, et al: HLA-B15 association with erythema multiforme. J Am Acad Dermatol 1983;8:493-496

Elias PE, Fritsch PO: Erythema multiforme, in Fitzpatrick TB, et al. (eds). Dermatology in General Medicine, ed 3. New York, McGraw-Hill International Book Co 1987;555-563

Engel J, Englund J, Fletcher C: Successful treatment of severe, Acyclovir-resistant HSV type 2 proctitis in two patients with AIDS. Use of continuous Infusion Acyclovir. Int. Conference on AIDS Montreal. 1989; Abstract, Nr. M.B.P.51

Engst R: Orale Langzeittherapie bei schweren rezidivierenden Herpes simplex Typ 2-Virusinfektion. Hautarzt, Supplement 1989;VIII:299-300

Goldmeier D, Bateman JRM, Rodin P: Urinary and intestinal Obstruction associated with ano-rectal Herpes simplex virus infection. Br.Med.J. 1975;2:425

Goodell SE, Quinn TC, Mckritichian E, Schuffler MD, Holmes KK, Corey L: Herpes simplex virus proctitis in homosexual

men. N. Engl. J. Med. 1985;308:868-871

Green BA, Spruance SL, Wenerstrom G, Piepkorn MW: Post-Herpetic Erythema Multiforme Prevention with Prophylactic Oral Acyclovir. An Int Med 1985;5:632-633

Hirsch MS: Herpes group virus infection in the compromised host. In: Rubin RH; Young L S, eds. Clinical approach to infection in the compromised host. New York and London. Plenum Medical Book Company, 1981;389-415

Hovmark A: An in vitro study of depressed cell-mediated immunity and of T and B lymphocytes in atopic dermatitis. Acta. Dermato. Venerol.. 1977;57:237-242

Huff JC, Krueger GG, Overrall JC Jr, Copeland J, Spruance SL: The histopathologic evolution of recurrent herpes simplex labialis. J. Am. Acad. Dermatol. 1981;5:550-557

Jarratt M: Herpes simplex infection. Arch Dermatol 1983;119:99

Kämpgen E, Burg G, Wank R: Association of Herpes Simplex Virus-Induced Erythema multiforme. With the Leukocyte Antigen DQw3. Arch Dermatol 1988;24:1372-1375

Kaplowitz LG, Baker D, Gelb L et al.: Prolonged Continuous Acyclovir Treatment of Normal Adults with Frequently Recurring Genital Herpes Simplex Virus Infections. JAMA 1991;6:747-751

Kaufmann HE, Brown DC, Ellison EM: Recurrent herpes in the rabbit and man. Science 1967;156:1628-1629

Kazmierowski JA, Wuepper KD: Erythema multiforme. In: Thiers BH, Dobson RL (eds). Pathogenesis of Skin Disease. New York, Churchill Livingstone Inc 1986; pp 305-316

Langenberg A, Benedetti J, Jenkins J, Ashley R, Winter C, Corey L: Development of clinically Recognizable Genital lesions among Women Previously Identified as Having "Asymptomatic" Herpes simplex Virus Type 2 Infection. An Int. Med. 1989;110:882-887

Lehtinen M, Rantala I, Teisala J: Detection of herpes simplex virus in women with acute pelvic inflammatory disease.

J. Infect. Dis. 1985;152:78-81

Margolin RJ, Tonnesen MG, Soter NA, et. al.: Lymphocyte subsets and Langerhans cells/indeterminate cells in erythema multiforme. J Invest Dermatol 1983;83:403-406

Mertz GJ, Jones CC, Mills J: Long-term acyclovir Suppression of frequently recurring genital herpes simplex infection. JAMA 1988;260:201-206

Meyers JD, Wade JC, Mitchell CD, Saral R, Lietman PS, Durack DT, Levin MJ, Segreti AC, Balfour HH: Multicenter collaborative trial of intravenous acyclovir for treatment of mucocutaneous herpes simplex virus infection in the immunocompromised host Am J. Med. 1982; (Suppl. 1A) 73:29-235

Meyers JD: Antiviral Effectiveness of Acyclovir in Immunocompromised Patients. In: Update Acyclovir Proceedings of a symposium conducted during the 24th Interscience conference on Antimicrobial Agents and Chemotherapy 8-10 ct. 1984, Washington D.C.S. 1985;33-41

Middleton D, Hutchinson TH, Lynd J: HLA antigen frequency in erythema multiforme and in recurrent herpes-simplex. Tissue Antigens 1983;21:264-267

Mindel A, Adler MW, Sutherland S, Fiddian AP: Intravenous acyclovir treatment for primary genital herpes. Lancet 1982;1:697-700

Mindel A, Carney O, Freris M et al.: Dosage and Safety of Long-Term Suppressive Acyclovir Therapy for Recurrent Genital Herpes. The Lancet 1988;926-928

Nahmias AJ, Visitine AM: Herpes simplex. In: Infections Diseases of the Fetus and Newborn. Edited by J. Remington and J. Klein. Philadelphia, Saunders, 1976;156-190

Nilsen AE, Aasen T, Halos AM, Klinge BR, Tjotta EAL, Wikström K, Fiddian AP: Efficacy of oral acyclovir in the treatment of initial and recurrent genital herpes. Lancet 1982;11:571-573

Ozaki Y, Ishuguro T, Ohasi M, Kimura EM: Relationship between antigenic type of virus and antibody response in female patients with herpes genitalis. J. Med. Virol 1980;5:249-256

Reeves WC, Corey L, Adams HG, Vontver LA, Holmes KK: Risk of recurrence after first episodes of genital herpes: Relation to HSV type and antibody response. N. Engl. J. Med. 1981;305:315-319

Safrin S, Assaykeen T, Follansbee S, Mills J: Foscarnet treatment of acyclovir (ACV) resistant HSV Infection in 26 AIDS patients. V. Int. Conference on AIDS, Montreal,1989; Abstract Nr. MBP 48

Schöfer H: Herpes-simplex-Infection bei HIV-assoziierter Immundefizienz. In: Hauterkrankungen bei HIV-Infection und AIDS, Schwer, Stuttgart, 1989;65-68

Segar RJ, Watson W: Kaposi's varicelliform eruption in mycosis fungoides. Arch. Dermatol. 1978;114:1067-1069

Shab SJ, Scholz FJ: Anorectal herpes: Radiographic findings. J. Radiol. 1983;147:81-82

Siegal EP, Lopez C, Hammer GS, Brown AE, Kornfeld SJ, Gold J, Hassett J, Hirschman SZ, Cunningham-Rundles CH, Adelsberg BR, Parham DM, Siegal S, Cunningham-Rundles A, Armstrong D: Severe acquired immunodeficiency in male homosexuals manifested by chronic perianal ulcerative herpes

simplex lesions. N. Engl. J. Med. 1982;305:1439-1444

Stadler H: Herpes virus infection: Its spectrum in immunosuppressed patients. In: Infections in Cancer Patients. Edited by. J. Klastersky. New York, Raven Press. 1982;189-191

Straus SE, Seidlin M, Takiff H, Jacobs D, Bowen D, Smith HA: Oral acyclovir to suppress recurring herpes simplex infections in immunodeficient patients. An Intern Med 1984;100:522-524

Taylor RJ, Saul SH, Dowling JN, Hakala TR, Peel RL, Ho M: Primary disseminated herpes simplex infection with fulminating hepatitis following renal transplantation. Arch. Intern. Med.1981;141:1519-1521

Van de Straak WJ: Non-veneral sclerosing lymphangitis of the penis following Herpes progenitalis. Br J Dermatol, 1977;96:679

Vonderheid EC, Milstein HJ, Thompson KD, Wu BC: Chronic herpes simplex infection in cutaneous T-cell lymphomas. Arch. Dermatol. 1980;116:1018-1022

Walker DP, Longson NP, Mallick, Johnson RWG: A prospective study of cytomegalovirus and herpes simplex virus disease in renal transplant recipients. J. Chlin. Pathol. 1985;35:1190-1193

Walzman W, Wade AAH: Labial adhesions after genital herpes infection. Genitourin Med 1989;65:187-188

Yeager AS, Arvin AM: Reasons for the absence of a history of recurrent genital infections in mothers of neonates infected with herpes simplex virus. Pediatrics 1984;73:188-193

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