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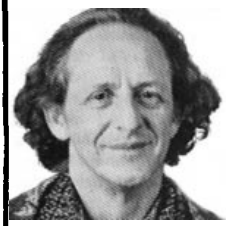

Current Comments

Herpes Simplex Virus Infections. Part 2. Sexually Transmitted Diseases without a Cure

Number 26 June 29, 1981

In the first part of this essay, I described how widespread herpes simplex virus (HSV) infections are in the population today.[1-4] I also explained that genital herpes poses a serious health threat to women in particular. Many researchers believe HSV2 is the "missing link" that explains the observed association between sexual intercourse and cervical cancer.[5,6] In addition, pregnant women with active genital herpes infections at the time of delivery have a 50-50 chance of passing it on to their babies. The American Academy of Pediatrics says that 60 percent of those babies born with HSV infections will die, and half of the survivors will suffer severe damage to the brain, nervous system, and eyes.[7]

Unlike other sexually transmitted diseases (STDs)—gonorrhea, syphilis, and nongonococcal urethritis—herpes infections *cannot* be cured. In fact, many of the drugs used to treat herpes infections may *not* be effective in reducing the severity or the duration of symptoms. In this essay, I'll discuss the variety of drugs recommended for herpes infections and their effectiveness in the opinion of medical researchers. I'll also identify information sources that help keep the public aware of new advances in medical understanding of this disease. While a successful cure or treatment is being developed, we can at least learn from these sources how to limit the spread of herpes infections.

Genital and labial herpes are very difficult to cure because they are *viral* infections. Viruses invade healthy cells, and rely on their "hosts" to provide everything they need for replication.[3] That is, they take advantage of normal host cell functions to make more virus particles. Thus, any treatment that interferes with the manufacture of viruses also runs the risk of altering normal cell functions: the treatment may be worse than the disease!

But herpes differs from most other viruses in an important feature. Nanna Ayisi, University of Saskatchewan, Canada, explains that the genetic code of herpesviruses provides for some of their *own* enzymes, which are needed for replication, instead of relying completely on what the host cell has to offer.[8] Luckily, the viral enzymes are structurally different from the host cell's enzymes.[8] Thus, it is possible to develop antiviral drugs that interfere *specifically* with virus enzymes without affecting host cell enzymes.[8]

The effectiveness of any antiviral drug for treating herpes infections can be measured in two ways. First, the drug should diminish the number or size of the blister-like sores.[9] Second, the drug should decrease the rate of recurrence of herpes infections.[9] As I explained in part one of this essay, herpesvirus "hibernates" in nerve tissue after the symptoms of the infection disappear—HSV1 stays in the trigeminal ganglion in

the cheek and HSV2 remains in the paravertebral ganglia at the base of the spine.[3,10,11] Periodically, the virus is "activated"—that is, the virus moves from the "latent" phase of hibernation to an active phase of infection, causing sores and other symptoms to recur. Several factors can reactivate the virus—sunlight, fever, illness, menstruation, surgery on the nerves in the cheek, and so on. All the factors seem to involve physical or psychological stress.[3] A drug can be considered effective if it extends the period between recurrences of herpes infections, or stops recurrences altogether.[9]

Hope for herpes patients increased when scientists investigated several antiviral drugs available today. Many of them are "nucleoside analogues," drugs that interfere with the formation of DNA and RNA molecules. The nucleoside analogues are in an inactive form when they are given to the patient.[12] H.J. Field, University of Cambridge, explains that they are activated by an enzyme called thymidine kinase.[13] This enzyme is present in virus infected cells much more than it is in normal cells. However, T. Hovi, University of Helsinki, Finland, says nucleoside analogues may cause cancers and birth defects.[14] Thomas Maugh, writing in *Science*, points out that many common drugs, like aspirin, also may cause birth defects.[15] The risk of birth defects can be avoided if these drugs aren't taken during pregnancy.[15]

Michael Jarratt, Baylor College of Medicine, says 5-iododeoxyuridine (IDU), one of the nucleoside analogues, is effective only against herpes infections of the eyes.[9] When it is applied to skin sores, no significant effect is noticed.[9] IDU can't be injected into the body because it has too many undesirable side effects.[15] Charles Alford, University of Alabama, explains that IDU couldn't be used to treat internal infections like herpes encephalitis or the widespread form of infection in newborns, for example.[16] Jarratt describes another drawback to IDU therapy—the drug interferes with normal cell functions.[9]

Hovi observes that adenine arabinoside (ara-A) blocks the formation of viral DNA but it doesn't affect the normal cell.[14] Like IDU, ara-A isn't effective against skin sores caused by HSV1 or HSV2.[9,14,15,17,18] But there are no side effects when ara-A is injected internally.[9] Thus, it is effective against internal herpes infections—it reduces mortality and neurologic damage.[9,14] But ara-A has its drawbacks, too. For example, ara-A is *inactivated* by an enzyme that is normally present in the body.[14] Also, ara-A doesn't dissolve quickly, so high dosages of the drug are required.[14]

Acyclovir (acycloguanosine) is another nucleoside analogue that blocks construction of viral DNA. No side effects are noticed when acyclovir is applied to the skin or injected.[14,18] It *appears* to quicken the healing of sores[14] and limit the spread of infection.[19,20] But William Check, writing in the *Journal of the American Medical Association*, says that controlled, double-blind studies show that acyclovir is ineffective.[21] It doesn't limit the duration of pain or the time between recurrences, and it doesn't shorten the time it takes for sores to heal.[21]

Three other antiviral drugs that aren't nucleoside analogues also are available. Phosphonoformic acid (PFA) appears to work against recurrent HSV1 infections.[18] It quickens the time of healing when applied to sores on the skin surface.[14] However, PFA can't be used internally because it accumulates in the bones.[14]

2-deoxy-D-glucose (2DG) is a glucose analogue that prevents the assembly of the entire viral particle.[3] The nucleoside analogues discussed above interfere only with the formation of the virus' DNA. According to Herbert Blough, Universi-

ty of Pennsylvania School of Medicine, 2DG prevents the formation of large molecules used to build the envelope surrounding HSV.[22] The envelope protects the virus from the body's defenses during "fusion," when the virus spreads from cell to cell. Without this protection, the virus is less infective.[3] In preliminary tests on women with genital herpes, Blough observed that 2DG lessened the number of sores and shortened the duration of symptoms.[23,24] During a two year period, the drug *cured* 45 percent of those patients with recurrent herpes—that is, the disease did not flare up again.[23,24] But 2DG was most effective in treating patients who had herpes for the first time—of these patients, 89 percent had *no* recurrence of symptoms two years after treatment.[23,24] Blough says that many points must still be clarified, and larger groups of patients should be studied before any conclusions are drawn about 2DG as a cure for herpes.[24]

Interferon has attracted a lot of attention as a possible cure for herpes infections. Interferon is an antiviral substance that is produced naturally by the body. When a virus invades a cell, the cell releases interferon so that neighboring cells can fight off the virus.[3] In 1975, Lucy Rasmussen and Linda Farley, Louisiana State University School of Medicine, Shreveport, demonstrated that interferon inhibited the replication of HSV1 in a laboratory cell culture.[25] A number of double-blind, placebo-controlled studies of interferon's effect on patients have been reported.

For example, Thomas Merigan, Stanford University School of Medicine, tested interferon on cancer patients with herpes varicella-zoster infections. He concluded that interferon diminished the severity of the infection by limiting its spread to other organs or over the skin.[26] Barrie Jones, Moorfields Eye Hospital, London, noted that interferon reduced the rate of recurrences by about half in patients with HSV infections of the eyes.[27] George Pazin, University of Pittsburgh School of Medicine, said that interferon reduced the rate of HSV1 recurrences by about half in patients a few days after surgery on the trigeminal ganglion in the cheek.[28] This type of surgery usually causes labial herpes to flare up. However, a follow-up study of the same patients three weeks later showed *no* difference in recurrences between interferon-treated patients and placebo-treated patients.[29] Sarah Cheeseman, Harvard Medical School, found that interferon only had a *modest* effect on herpes simplex virus infections in patients who had kidney transplants.[30] But interferon had a *significant* effect on another type of herpesvirus infection (cytomegalovirus) in these same patients.[30] Unfortunately, interferon is a very expensive drug to test on people with herpes infections.[3] Hopefully, its cost will be reduced soon through genetic engineering.

As an interesting side note to my essay on ulcers,[31] herpesvirus infections are implicated in the occurrence of peptic ulcers. I. Borg, Malmö General Hospital, Sweden, reviewed the "striking similarity" between peptic ulcers and herpes infections.[32] Lesions from ulcers and herpes infections recur at the same site, and both types occur in an area between two kinds of tissue. Also, certain herpes infections are more common in men than women, and the same is true for peptic ulcers. In addition, peptic ulcers and herpes infections are more common in spring and autumn, and both are more common in people with O-group blood.[32] B.F. Vestergaard, University of Copenhagen, Denmark, observed that patients with duodenal ulcers have higher levels of HSV1 antibodies than a control group who had HSV1 antibodies but no ulcers.[33] In fact, the levels of HSV1 antibodies in ulcer patients parallel those in patients with recurring cold sores of

the lip. Vestergaard concludes, "Herpesvirus should be considered as a possible [cause] in some of the many duodenal-ulcer patients."[33]

While researchers continue their search for a truly effective drug to treat or cure herpes diseases, there are practical ways to handle HSV infections and, more important, limit their spread. Richard Hamilton, a San Francisco physician, points out that herpes sores are most infectious when they are in the blister-like stage, and they are less infectious in the crusting or scab stage.[3] Thus, the best thing to do is treat herpes sores with a drying agent. Ether was a popular drying agent until double-blind studies showed that it may *prolong* the duration of lesions![3] Also, Jarratt says that ether is a very flammable liquid to keep around the house.[9] Betadine and tincture of benzoin are safe drying agents which also limit infections of the open sore by other viruses or bacteria.[3,6,9]

But herpes sores are infectious even in the "prodromal" stage, when you feel an itching or tingling before sores actually appear. The best thing to do is avoid direct contact with another person even at this early stage—the only way to transmit herpes is by direct contact.[3] This is the same "treatment" prescribed by the Roman Emperor Tiberius about 2,000 years ago! In order to limit an epidemic of labial herpes, Tiberius outlawed kissing at rituals and public ceremonies.[3] However, the infection can be passed by individuals who show no signs of active infection. The use of a condom might help prevent inadvertent transmission of the disease by individuals who are unaware of their infection, but even condoms are not foolproof against herpes.[5]

At present, the best hope for herpes victims is awareness of the problem. The American Social Health Association (ASHA) publishes a quarterly newsletter on herpes called *The Helper*. They also publish *VD News* four times a year, which covers all venereal diseases including herpes. The newsletters discuss research breakthroughs, epidemiological statistics, how to cope with venereal disease, and federal funding for venereal disease research. They also list addresses of local chapters of ASHA, and the dates and locations of seminars on HSV and other STDs. A one year's subscription to *The Helper* costs $8.00. *VD News* is available to members of ASHA. You can join ASHA for $10 per year in the US, $15 abroad, and organizations can sign up for $50. You can get more information on ASHA publications and membership by writing to: American Social Health Association, 260 Sheridan Avenue, Palo Alto, California 94306. ASHA also staffs a volunteer national hotline to answer questions from people who may be too embarrassed to talk with their friends or physicians. The VD National Hotline's toll-free number is (800) 227-8922.

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Figure 1: Herpesvirus research fronts highlighted in ISI/BIOMED™, 1980. Smaller research "pockets" are identified by author, title, or citation based searches.

HERPES
ANTIVIRAL CHEMOTHERAPY against HERPES and other VIRAL INFECTIONS 1980-2275

HERPES-SIMPLEX
Transfer of HERPES-SIMPLEX TYPE-1 GENE for THYMIDINE-KINASE by RECOMBINANT PLASMIDS 1980-2084

HERPES-SIMPLEX-VIRUS
HERPES-SIMPLEX-VIRUS GLYCOPROTEINS 1980-1642
HERPES-SIMPLEX-VIRUS HOST-CELL interactions 1980-1193
Structure and ISOMERIZATION of the HERPES-SIMPLEX-VIRUS GENOMES 1980-0965

HERPES-VIRUS
ANTIVIRAL drugs effective against HERPES-VIRUS 1980-0252
IMMUNE-RESPONSE to HERPES-VIRUS INFECTION 1980-0333
NEUROLOGIC and DERMATOLOGIC HERPES-VIRUS INFECTIONS 1980-2090
PATHOGENESIS of acute, LATENT, and REACTIVATED HERPES-VIRUS INFECTIONS 1980-0347

ISI/BIOMED™ data base[34] by research front specialty searching. Figure 1 lists nine highly active herpesvirus research fronts identified by ISI/BIOMED. *ASCATOPICS*® alerts subscribers to new articles on specific topics appearing in publications that ISI processed within the previous *week*.[35] The annual cost is currently $125 per year in the US, $150 abroad. Figure 2 presents a sample of an *ASCATOPICS* report on human herpes infections.

Figure 2: Sample of *ASCATOPICS*® report on human herpes infections.

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HUMAN HERPES INFECTIONS

REPORT FOR 27 FEB 81 PAGE 14

VARICELLA ZOSTER/ CELL-MEDIATED-IMMUNITY TO VARICELLA-ZOSTER VIRUS AS ASSESSED BY THE MIGRATION-INHIBITION TEST
TRLIFAJO.J SVEJCAR J SVANDOVA E RYBA M PEKAREK J
ACT VIROLOG 24(6): 406-414,1980 12 REFS
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J TRLIFAJOVA, INST HYG & EPIDEMIOL,
CS-10042 PRAGUE 10, CZECHOSLOVAKIA

HERPES// ISOLATION OF 5 STRAINS OF HERPESVIRUSES FROM 2 SPECIES OF FREE-LIVING SMALL RODENTS (LETTER)
BLASKOVI.D STANCEKO.M SVOBODOV.J MISTRIKO.J
ACT VIROLOG 24(6): 468,1980 4 REFS
-----> CHECK TO ORDER TEAR SHEETS ------>( ) #LA409
D BLASKOVIC, JA KOMENSKY UNIV,FAC NAT SCI,CHAIR GEN & APPL VIROL,
CS-80939 BRATISLAVA, CZECHOSLOVAKIA

HERPES// STUDIES ON CROSS-REACTIVE ANTIGENS IN THE HERPESVIRUSES
YEO J KILLINGT,RA WATSON DH POWELL KL
VIROLOGY 108(2): 256-266,1981 21 REFS
-----> CHECK TO ORDER TEAR SHEETS ------>( ) #LA372
J YEO, UNIV LEEDS,DEPT MICROBIOL,
LEEDS LS2 9JT, W YORKSHIRE, ENGLAND

HERPES// ASSOCIATION OF THE HERPES SIMPLEX-1 VIRAL GENE FOR THYMIDINE KINASE WITH THE HUMAN-GENE FOR ADENYLATE KINASE-1 IN BIOCHEMICALLY TRANSFORMED-CELLS
WILSON DE MCKINLAY MA STACZEK J WHITKOP C HARRISON B POVEY S
BIOCHEM GEN 19(9-10): 981-1001,1980 45 REFS
-----> CHECK TO ORDER TEAR SHEETS ------>( ) #LA448
DE WILSON, RENSSELAER POLYTECH INST,DEPT BIOL,
TROY, NY 12181

HERPES// PARTIAL-PURIFICATION AND CHARACTERIZATION OF THE RIBONUCLEOTIDE REDUCTASE INDUCED BY HERPES-SIMPLEX VIRUS-INFECTION OF MAMMALIAN-CELLS
HUSZAR D BACCHETT,S
J VIROLOGY 37(2): 580-588,1981 34 REFS
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Science journalists are beginning to pick up on the problem of herpes. Several balanced and reasonable reports have appeared in the popular press.[12,36-42] These efforts are valuable because an informed public can have impact on the spread of herpesvirus infections. The hardest problem to solve may turn out to be the social embarrassment of admitting you have an STD. Science journalists and the people at ASHA are doing their share in lessening the stigma attached to HSV and other STDs. I hope this essay has at least convinced readers that herpes is a common infection and, precisely because it is so common, that herpes should be discussed openly and without embarrassment.

* * * * *

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