Cold Sore Comfort

That pesky herpes-simplex virus may pack an extra punch for HIVers, but knockdown drugs can keep outbreaks at bay -- and may stop a lethal AIDS-related cancer in the bargain. Daniel Wolfe reports.

April 1, 2001 By Daniel Wolfe

Once upon a time, when STI stood for “sexually transmitted infection”—not “strategic treatment interruption”—America became obsessed with a new virus. Slow to act, incurable, spread through sex and linked to immune-system strength, the organism was seen as a threat to both marriage and sexual liberation. Hotlines were established. Support groups sprang up. The afflicted went on television with their faces obscured, while TV crews worried about whether it was safe to touch them. In a 1982 cover story, *Time* carried tales of a dozen viral victims, labeling the disease a “scourge,” “Jerry Falwell’s revenge” and “a full-fledged epidemic.”

The virus in question was not HIV but HSV -- herpes simplex virus, the most famous cause of genital sores -- which makes you appreciate how completely AIDS shattered our notions of sexual risk. Soon, of course, HIV would knock the fear of other sexually transmitted diseases (STDs) off the talk-show circuit. Herpes, though, has shown no need of the spotlight to progress. The Centers for Disease Control and Prevention (CDC) estimates that there are now 1 million new infections each year with HSV-2 (herpes type 2, often referred to as genital herpes), and that 45 million Americans over the age of 12 -- more than one in five -- are infected. Among people with HIV, rates of HSV-2 infection are estimated to be astronomically higher -- up to 80 percent.

Herpes takes its name from the Greek word meaning “to creep,” because HSV crawls along the body’s nerve pathways causing outbreaks and then receding. Transmitted through contact with mucous membranes or small breaks in the skin, herpes, whether type 1 or 2, is usually marked by one or more of the following: read, painful sores on the lips, genitals or anal area; swollen lymph nodes; or flulike symptoms. But the virus can also lie dormant for a lifetime. After the initial outbreak, HSV takes refuge in the ganglia, the mass of nerve tissue at the base of the vertebrae, waiting to re-emerge at a moment of immune stress.

For people with HIV, even a virus-in-waiting can hurt. Some studies suggest that if you aren’t on HAART, each herpes outbreak may boost your HIV levels. Happily, drugs to prevent herpes activity are nontoxic and may also help prevent HIV-related lymphoma, a potentially fatal cancer showing up in more and more healthy HIVers (see “Cancer Rising,” *POZ*, January 2001). If you have had one herpes outbreak, the sad truth is that you will likely have another -- whether you’re on your last CD4 or have a full complement. Outbreaks can recur as rarely as once in a lifetime or as often

as 12 or more times a year. This cycle of suffering predates the Christian era: The Greek historian Herodotus wrote of herpes lesions among the legions, and Emperor Tiberius is said to have tried to stem the sores by banning kissing outright.

As with HIV, the distinction between the strains of HSV means more to researchers than to patients. Type 1 may be termed “oral” and type 2 “genital,” but each causes sores both above and below the belt. “You can get HSV-1 from Aunt Fannie giving you a kiss hello,” says Tom Barrett, MD, of the Howard Brown Health Center in Chicago -- which is why herpes cold sores are a common feature of childhood. And for the erotically active, receiving oral sex from someone with an HSV-1 lip sore may soon mean an outbreak on your genitals. Likewise, HSV-2, passed most commonly through sex, can bloom wherever sores contact skin. People with seriously weakened immune systems face additional complications, including internal outbreaks in the brain, intestine, esophagus or lungs.

Healthy HIVers aren’t in danger of internal lesions, but their external ones tend to be bigger and more painful than those of their HIV negative counterparts. “I kept getting these excruciating blisters on my buttocks and thighs,” says Patty Alvarado, a 49-year-old Los Angelena whose chronic herpes outbreaks qualified her for an AIDS diagnosis. After the first few, outbreaks tend to lessen in severity and duration. But some unlucky souls get hit with the whole spectrum of symptoms every time -- fever, fatigue, sores and pain across the buttocks and down the leg. Doctors need to see or culture a herpes sore to confirm diagnosis. Ken Mayer, director of research at Fenway Community Health, a Boston clinic, says, “People come in and say, ’I had something here three weeks ago, but now it’s gone.’ What do you think it was?’” If you can get an appointment while you still have sores, he says, don’t delay.

Herpes’ most serious medical consequence for HIVers may be sustained increases in HIV viral load, though this matter is still subject to some debate. “As with many infections,” says Howard Brown’s Barrett, “a herpes outbreak causes a sharp surge in the level of HIV.” One 1994 study found that HSV-1 may also expand HIV’s infectious power: In people with HIV who had herpes lesions, researchers saw that HIV had infected keratinocytes, skin cells normally impervious to the virus. Apparently, coinfection opened the door.

Other research suggests that in the case of herpes, those HIV viral spikes -- particularly in the absence of combination therapy -- may have a lasting, cumulative effect. “Though HIV viral load went back down after an HSV outbreak, it didn’t always go down to pre-outbreak levels,” says researcher Larry Mole, PharmD, who coauthored a small 1997 study on the effect of HSV outbreaks on HIV viral load at the Veterans Affairs Palo Alto Health Care System in California. Still, Mole cautions, his study followed patients for only 45 days and was followed shortly by approval of the first protease inhibitors. Combination therapy, of course, frequently keeps HIV at undetectable levels even during herpes outbreaks, leaving largely unanswered the question of whether recurrent sores can edge HIV viral loads higher and higher over time.

For those not on HAART, including those on a drug holiday, the boost herpes gives to HIV may carry risks for not only your immune system but your sex partners. Many studies have found high

concentrations of HIV in herpes sores, and a recent study of 300 women in the Central African Republic found that those with active outbreaks of HSV-2 were more likely to have higher levels of HIV in their vaginal secretions -- theoretically making it far easier for them to transmit the virus.

How to beat back the double trouble of HIV rebound? The best way may be anti-herpes medication, though not all doctors are willing to prescribe it. Three available antivirals -- acyclovir (Zovirax or a generic), valacyclovir (Valtrex) or famciclovir (Famvir) -- help make sores go away faster, prevent outbreaks by suppressing HSV and also suppress one of HSV's most harmful cousins, Epstein Barr virus (EBV; see "Kissing Cousins"). "Study after study confirms the link between EBV and the lymphoma most commonly diagnosed in people with HIV -- a malignancy against which combination therapy has not proven effective," says Larry Bruni, MD. The Washington, DC, HIV specialist has long prescribed therapy to suppress HSV and EBV with acyclovir (800 milligrams, three times daily) and, since its approval in 1997, valacyclovir (500 to 1,000 mg, twice daily) for virtually all of his HIV positive patients. Famciclovir (500 mg, twice daily) has also been shown to work. Federal standards have yet to support suppressive therapy for all HIVers, but Bruni points to the tiny number of his patients who have developed lymphoma over the past 15 years while on the prophylaxis -- fewer than five out of more than 2,000. "You know what the plural of anecdote is?" he asks, only half-joking. "*Data.* Even if you take no other drugs, I'd strongly recommend a daily dose of herpes and EBV prophylaxis for all people with HIV."

While each drug comes with its pros and cons -- acyclovir requires more pills per day, while valacyclovir and famciclovir are more bioavailable but more expensive -- bad side effects do not seem to be among them. For people with 50 or fewer CD4s, or those who have had kidney or bone-marrow transplants, very high doses of valacyclovir -- eight times what Bruni recommends as prophylaxis -- were associated in drug trials with potentially fatal complications. With the lower doses, mild headache or nausea seem to be the most common downside. (If you get these effects with one drug, try the others.) "Compared to most HIV drugs, these medications are extremely effective and not very toxic," Bruni says. Alvarado, who tries to limit her med intake to the absolutely necessary, reports good results from taking the regular prophylactic dose of acyclovir, and then upping the medication when she notices itchiness or pain -- the first signs of an outbreak. Others skip the medication altogether until they feel those telltale signs, or "prodomal symptoms," which may also include lymph swelling or flulike feelings. But Bruni recommends not waiting to feel symptoms before acting to prevent them. A stop-start approach may create herpes resistance to the common anti-HSV drugs, which could leave you with only one treatment: the highly kidney-toxic, intravenously administered foscarnet (Foscavir).

Even for graduates of the HIV school of hard knocks, herpes disclosure can be surprisingly awkward. Herpes Internet chat rooms (Michael Stalker, spokesperson for the American Social Health Association, recommends www.antopia.com) are jammed with people worried about how to tell their partners or agonizing over having been infected unwittingly. Not all of this hand-wringing comes from the HIV negative. "Many of us have been out so long about our HIV that it's a familiar concept," says Gabriel (not his real name), an HIV positive Californian. "But I'm afraid talking about herpes is another question entirely."

Stalker attributes our national silence in part to the absence of high-profile herpetics. “We haven’t had a herpes Rock Hudson or Magic Johnson,” he says. “Unlike HIV, herpes is usually thought of as something one can only discuss in private.”

How private can you keep HSV? As with HIV, there is no hard and fast rule about disclosure. During a visible outbreak, many with herpes prefer to just say no to sex. “When I have an outbreak,” Gabriel says, “I feel so vulnerable -- both to getting an infection and to giving someone else one -- that I prefer the Nancy Reagan strategy.” Others say they are in so much pain that they wouldn’t even consider sex.

More thorny is the question of what to say or do when you are not in outbreak mode. “You are definitely infectious from the time you start having the pain or tingling that warns of an outbreak until scabs form on the sores,” Barrett says. “And while condoms may work if the sores are contained to a single location, they may not cover sores elsewhere in the genital areas, including sores that are too small to see.” Several studies have found clear evidence of asymptomatic shedding of HSV, which researchers say makes transmission possible even when no symptoms at all are present. Other studies found that HSV prophylaxis sharply reduced this asymptomatic shedding and the risk of transmission, though medication has not been shown to reduce transmission during a visible outbreak.

Strategies for coping vary, but many with herpes recommend a familiar combo: condoms, communication and meds to suppress the virus. To remain herpes free, those lucky HIVers *not* infected should look before they lick (or stick) and ask their sexual partner whether he or she is having an outbreak or feeling warning signs.

For some women, diagnosis with genital HSV-1 or -2 means grappling with the additional risk of mother-to-child transmission. HSV is much harder for moms to pass to infants than HIV -- a 1993 study found only a four in 10,000 chance. But neonatal herpes, while treatable, can prove even more dangerous than HIV. Half of all infants infected with HSV experience serious neurological damage, mental retardation or death.

Getting your first herpes infection during pregnancy poses the greatest risk to your baby. Most dangerous is a genital outbreak during the last trimester. “For a woman with an active outbreak at the time of birth, risk of transmission in the birth canal can climb to 50 percent,” says Lynne Mofenson, MD, of the National Institute for Child Health and Human Development. While cases are evaluated individually at the time of delivery, Mofenson says, she often recommends a Caesarean section, which also reduces the risk of HIV transmission. Avoiding use of a fetal scalp monitor -- a device used to monitor fetal stress that can cause tiny breaks in the newborn’s skin -- can add further protection. Experimental use of anti HSV drugs during pregnancy, though not approved by the FDA, has also shown some benefit; docs evaluate their use case by case.

Some researchers say that young women may soon be spared such measures. Last year, a study conducted by University of Utah researchers claimed that an experimental vaccine against HSV-2, while ineffective overall, showed significant protection for young women who had never been

infected with either herpes strain. “We don’t know enough yet to know why it would work for women rather than men, or whether the gender difference came from differences in sample size,” says Karl R. Beutner, MD, PhD, an associate professor of clinical dermatology at the University of California at San Francisco. For now, at least, an effective HSV vaccine remains more holy grail than achievable reality.

More and more AIDS organizations now focus on prevention and care for the whole spectrum of STDs, and herpetic HIVers -- long practiced in wielding the power of the personal -- may yet open the door for discussion of herpes harm reduction. “Talk to a national magazine about my herpes? Why not?” Alvarado asks. "When girls come to me, worried, with a sore, I tell them to get to the doctor and find out, and to ask questions of their sexual partners. I don’t want other people to learn what I learned: that it’s *not* talking that gets you in trouble."

The American Social Health Association (ASHA) offers counseling and info via its national herpes hotline, 919.361.8488, and through 70 herpes support groups. Click on www.ashastd.org.

KISSING COUSINS The family of herpes viruses is busier and pushier than the Bushes. While they may cause illness once or not at all in the immune-healthy, these common viruses can spell trouble ranging from the painful to the fatal in people with low CD4s.

Varicella zoster. This is the cause of that childhood classic chicken pox. In immune-damaged HIVers, the virus can manifest itself as shingles, erupting into a painful rash or sores.

Cytomegalovirus. CMV can cause serious or deadly infections in the eyes, colon or brain of immune-compromised HIVers, though HAART has drastically reduced its incidence.

Epstein Barr virus. Better known as “mono,” EBV infects 95percent of Americans by adulthood -- though far fewer become symptomatic, experiencing swollen glands or fatigue. In people with HIV, EBV causes hairy leukoplakia, a mouth infection, and is associated with HIV-related non-Hodgkin’s lymphoma.

HHV-6. As with CMV, some researchers see in human herpes virus 6 an AIDS cofactor in immune suppression as well as a cause of chronic fatigue and multiple sclerosis.

HHV-8. Human herpes virus 8 causes the best-known HIV-related cancer, Kaposi’s sarcoma, with its flat skin lesions ranging from red-purple to blue-brown; eight times more common in men than women, its incidence has been reduced by HAART.

If you take acyclovir, valacyclovir or famciclovir to suppress herpes outbreaks, you are likely also protecting against shingles and lymphoma. These anti-HSV meds also show potential in early studies against CMV, though gancyclovir is now the standard anti-CMV drug.

SORE LOSERS

Daily medication with antivirals is the best revenge against HSV. Still, some herpetics favor a holistic approach to preventing sores -- and to doing damage control once an outbreak is in

progress.

Shun the sun. Avoid sunburn, which can activate HSV.

Chill out. Tension is also a herpes trigger, so get enough sleep and experiment with meditation or relaxation methods.

Ask about aminos. “High doses of the amino acid L-Lysine --up to 4 grams a day -- seem to help people during outbreaks, while 500to 1000 milligrams daily can help suppress recurrences,” says *POZ* writer Michael Onstott of the AIDS Nutrient Bank in California. Or try a lysine-rich diet: lamb, fish, beans and unskinned potatoes. Also, Onstott says, “avoid seeds, nuts and chocolate,” which are rich in L-arginine, an amino acid that can reactivate herpes.

Soothe the sores. Forget cortisone creams, which can aggravate sores. Instead, try natural remedies: gel from an aloe vera plant, vitamin E oil or an oatmeal bath. Treat “weeping” sores with a blow dryer or a little cornmeal, and wear loose, comfortable clothes.

Keep it clean. You can spread herpes to other parts of your body after scratching a sore. Carefully avoid getting HSV in your eye, which can damage the cornea. Wash your hands regularly, and don’t reuse bath towels.

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http://beta.docker.poz.com/article/Cold-Sore-Comfort-1124-5891