

treatment

## information

Does herpes

accelerate

HIV infection?

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by *Meaghan Byers*

Researchers have studied the links between HIV and herpes for more than two decades. Early in the HIV epidemic, a persistent herpes infection was one of the first signs of HIV infection. By the late 1980s, scientists were postulating that somehow these two viruses interact at the cellular level in a way that results in a more efficient transmission of HIV and possibly even an increased rate of HIV replication. The scientific evidence to support this later hypothesis is still accumulating, but enough evidence already exists to cause concern for several reasons.

The herpes virus remains in the body after initial infection. It is incurable and can flare up causing recurrent active disease and symptoms when the body is under stress or the immune system is weakened. For a long time, it was common knowledge that HSV-2, spread through sexual contact, was the culprit behind genital herpes. HSV-1, a far more common form of herpes that is spread through saliva or nasal secretions, was believed to only cause cold sores. As much as 70% of the population has HSV-1, and for most people, the virus remains dormant. Now researchers know that you can get genital herpes from oral sex with a person who is having an episode of cold sores. Similarly,

you can also get a cold sore from performing oral sex on a person who is having an outbreak of genital herpes.

Recent evidence suggests that more than 50% of genital infections among men are caused by HSV-2, while almost half of genital infections among women are caused by HSV-1. For those HIV-positive people who still have a healthy immune system, the frequency of outbreaks is no different than among HIV-negative people with either herpes virus. However, once the immune system becomes compromised by HIV infection, herpes outbreaks are often more painful, more frequent, and seldom clear up spontaneously.

### Herpes and HIV

HSV-2 herpes is the most common sexually transmitted disease (STD) among people with HIV. In fact, in the last few decades, it has increased in prevalence by 30% among the general population. For those people who contracted HIV through sexual activity, the prevalence of HSV-2 is even higher, with 60% to 80% of people with HIV having it. For this reason, the possibility that HSV-2 can interact with HIV and potentially accelerate the progression of HIV is very disturbing.

That herpes outbreaks are more frequent and severe in HIV-positive people is

not a big surprise considering the nature of HIV. The body normally controls herpes outbreaks with the part of the immune system affected by HIV. When HIV weakens the immune system, the dormant herpes viruses are more likely to start causing trouble. When T-cell counts are below 50, recurrences are more severe and prolonged and the ulcers may even develop secondary infections. Infections become more frequent and more painful and the chance of spreading both viruses increases.

### HSV-2 and the transmission of HIV

Convincing evidence demonstrates that HIV is transmitted to someone with herpes more efficiently during an outbreak of genital herpes, possibly as much as 3–5 times more efficiently. Two biological aspects of genital herpes support this hypothesis. First, genital ulcers cause a mucosal disruption, which may allow entry of HIV. Second, genital herpes lesions attract activated CD4 cells that act as target cells for HIV attachment.

Studies also suggest that transmission of HIV is more likely to occur from a person who has genital ulcers, although this route has been harder to study. When HIV and HSV-2 are both present in the body, each herpes sore is chock full of both HSV-2 and HIV particles. Scientists believe this viral boom occurs because the body creates billions of new T-cells when it responds to the herpes outbreak. These T-cells in turn release billions of HIV particles that are manufactured by the body every day. Research shows that HIV shedding from genital herpes lesions is frequent. Therefore, scientists believe that higher levels of HIV virus during a herpes outbreak may make HIV even more infectious during these times. For this reason, HSV-2 appears likely to facilitate transmission of HIV to uninfected sexual partners.

### HSV-2 and the progression of HIV

To make matters even worse, evidence is accumulating to support the hypothesis that recurrent flare-ups of HSV-2 virus somehow cause an increase in HIV replication,

possibly accelerating the progression of HIV. While the scientific studies conducted to date are inconclusive, researchers have good reasons to believe a causal link exists. Several in-vitro laboratory studies have indicated that certain regulatory HSV proteins can increase the rate of HIV replication. In addition, both HSV-2 and HIV can co-infect CD4 cells, suggesting that these viruses may interact frequently in vivo. Several clinical studies have shown that opportunistic infections, or other means of immune activation (such as pneumocystis carinii pneumonia, bacterial pneumonia, tuberculosis, or immunizations) can stimulate HIV replication and, at least transiently, increase viral load. Herpes seems to have a similar effect. Evidence shows that plasma HIV viral load increases in people who have recurrences of genital herpes.

Studies have shown that during acute

lence of herpes is among persons with HIV. Detection and treatment of genital herpes appears to decrease the rates of HIV infection and offers survival benefits to those who are infected with both viruses.

Use of acyclovir, an antiviral medication used to treat herpes, is associated with increased survival in HIV-infected persons. Studies indicate that acyclovir may slow the progression of HIV disease by preventing reactivation of HSV. The suppression is also believed to offer the additional benefit of reducing T-cell activation. Highly active antiretroviral therapy (HAART) medications do not prevent recurring outbreaks of herpes, though outbreaks do appear to be less frequent and severe.

Consensus has not been reached on using antiviral medications to suppress HSV in HIV-positive patients. Routine use of HSV-specific antiviral therapy is not yet

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outbreaks of herpes infection, the amount of HIV RNA increases substantially in the genital lesions. One study, involving analysis of swabs taken from lesions of twelve men co-infected with HSV and HIV, found the herpes sores were loaded with HIV particles as well as HSV. High amounts of HIV RNA were found in people with both high and low plasma HIV RNA levels, meaning that the amount of virus in the lesions was not related to the amount found elsewhere in the body. The amount of HIV RNA remained at high levels until the sores healed. These bursts of HIV virions that accompany genital lesions may also help to explain how a herpes outbreak increases the chance of transmission of HIV.

### Implications

The results of such studies are extremely important for preventing the spread of both herpes and HIV and for protecting the health of people who are already co-infected. The incidence of herpes infections continues to increase and the highest preva-

lence of herpes is among persons with HIV. Detection and treatment of genital herpes appears to decrease the rates of HIV infection and offers survival benefits to those who are infected with both viruses. Use of acyclovir, an antiviral medication used to treat herpes, is associated with increased survival in HIV-infected persons. Studies indicate that acyclovir may slow the progression of HIV disease by preventing reactivation of HSV. The suppression is also believed to offer the additional benefit of reducing T-cell activation. Highly active antiretroviral therapy (HAART) medications do not prevent recurring outbreaks of herpes, though outbreaks do appear to be less frequent and severe. Consensus has not been reached on using antiviral medications to suppress HSV in HIV-positive patients. Routine use of HSV-specific antiviral therapy is not yet recommended as part of the medical regimen of co-infected people. However, it may prove to be warranted to suppress herpes among people with HIV, if evidence of the acceleration of HIV in the presence of herpes continues to accumulate. Given that the vast majority of HSV-2 infections in the US are both unrecognized and untreated, a lot of people not only have an increased risk of getting HIV, but, for those with HIV, herpes is a potentially deadly addition to the mix. ⊕

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