

# Genital herpes and human immunodeficiency virus: double trouble

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**Abstract** The synergistic relationship between herpes simplex virus type 2 (HSV-2) and transmission of human immunodeficiency virus (HIV) can be substantial in developing countries that have high prevalences of both viral infections. Genital herpes, most frequently caused by HSV-2, has become the leading cause of genital ulcer disease worldwide. This review of recent research on genital herpes and enhanced susceptibility to, and transmission of, HIV is part of the "Advances in HIV/AIDS research series" which endeavours to form a bridge between the research into HIV and acquired immunodeficiency syndrome (AIDS) and the practice of HIV/AIDS prevention, care and support in developing countries. Research findings have shown that being seropositive for HSV-2 can increase the risk of HIV acquisition among high-risk HIV-negative people exposed to HIV and, likewise, the infectiousness of individuals co-infected with HIV-1 and HSV-2 can increase during periods of HSV-2 reactivation. These observations have led to the initiation of several intervention trials and could ultimately lead to the setting of new priorities in public health and clinical practice. WHO has recently issued new guidelines for the syndromic management of genital ulcer disease that include antiviral treatment for lesions consistent with genital herpes. The United States Centers for Disease Control and Prevention issued updated *Sexually Transmitted Diseases Treatment Guidelines* in 2002 that recommended the use of type-specific serological tests for diagnosing HSV-2. Recently launched proof-of-concept, HSV-2 intervention trials in several countries will help to determine the proportion of new HIV infections that could be prevented by suppression of HSV-2, and the findings from these studies will inform those involved in setting prevention and treatment priorities and strategies in developing countries.

**Keywords** Herpes genitalis/epidemiology/diagnosis/therapy; HIV infections/transmission; Acquired immunodeficiency syndrome/etiology; Herpesvirus 2, Human/pathogenicity; HIV-1/pathogenicity; Comorbidity; Disease susceptibility; Review literature (source: MeSH, NLM).

**Mots clés** Herpès génital/épidémiologie/diagnostic/thérapeutique; HIV, Infection/transmission; SIDA/étiologie; Herpèsvirus 2 humain/pathogénicité; VIH-1/pathogénicité; Morbidité associée; Sensibilité à maladie; Revue de la littérature (source: MeSH, INSERM).

**Palabras clave** Herpes genital/epidemiología/diagnóstico/terapia; Infecciones por VIH/transmisión; Síndrome de inmunodeficiencia adquirida/etiología; Herpesvirus 2 humano/patogenicidad; VIH-1/patogenicidad; Comorbilidad; Susceptibilidad a enfermedades; Literatura de revisión (fuente: DeCS, BIREME).

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Voir page 451 le résumé en français. En la página 451 figura un resumen en español.

## Introduction

Herpes simplex virus type 2 (HSV-2), is a sexually transmitted infection (STI) that is chronic, widespread, and infectious during both its symptomatic and asymptomatic periods. This infection is a significant factor for increased risk of acquisition and transmission of HIV. A meta-analysis of studies on HSV-2 found that infection with HSV-2 doubled the risk of becoming infected with HIV through transmission during sexual activity (1). Furthermore, HSV-2 is the leading cause of genital ulcer disease worldwide. New prevention strategies are urgently needed to reduce the contribution of HSV-2 to HIV transmission, particularly in developing countries that have high prevalence of both HSV-2 and HIV.

The existence of a synergistic relationship between HSV-2 and transmission of HIV has been indicated by many observational and biological studies in which HSV-2 has been implicated as a cofactor in the acquisition and transmission of HIV. HSV-2 causes ulcers and micro-ulcerations, which are often asymptomatic and thus unrecognized; these breaks in the mucosa and in the genital area create portals for the entry of HIV. HSV-2 lesions contain substantial numbers of CD4+ lymphocytes, which are target cells for HIV. Laboratory studies have shown that these CD4+ lymphocytes are likely to facilitate the acquisition of HIV in HIV-negative, HSV-2-positive individuals when they are exposed to HIV. Episodes of reactivation of HSV-2 are associated with increased shedding of HIV from lesions and genital mucosa.

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Researchers who have conducted epidemiological and clinical studies on HSV and HIV have proposed that interventions that target HSV-2 infection would provide a way to intervene in transmission of both HIV and HSV-2. Until very recently, most sexually transmitted disease (STD) interventions have focused on bacterial STIs, which are easier to diagnose and treat than genital herpes. As a result, little attention has been paid to the diagnosis of genital herpes and there has been a lack of prevention interventions; consequently, the epidemics of HSV-2 and HIV continue to fuel each other. In some parts of sub-Saharan Africa, where HIV is of great concern, the prevalence of HSV-2 among women is as high as 75% (2).

Recently, large-scale, proof-of-concept, intervention trials have been launched at several sites to determine whether susceptibility to and infectiousness of HIV can be reduced either by treating HSV-2 episodically or by suppressing HSV-2 reactivation. Although there is no cure for genital herpes, the drugs acyclovir, valacyclovir and famciclovir can shorten initial or recurrent episodes ("episodic" therapy). These drugs may also be taken daily for suppression of herpes, which dramatically reduces the frequency and severity of recurrences of HSV-2 ("suppressive" therapy). Support for the concept that antiviral suppression can interrupt transmission of HSV-2 was provided by the results of a recent multi-country, randomized, double-blind study by Corey et al. who found that suppressive therapy with valacyclovir reduced transmission of HSV-2 by 50% for both men and women in heterosexual HSV-2-discordant couples (3).

It is not yet clear which strategy for the diagnosis and management of HSV-2 will be the most feasible and effective in developing countries. The options range from widespread screening for HSV-2 and suppressive antiviral therapy, to other strategies that may have benefits in reducing HSV-2 transmission as well as in HIV prevention. Studies currently being conducted will provide more data on which policy-makers can base their decisions as to the most feasible and cost-effective approaches. Additionally, WHO has incorporated empirical treatment for HSV-2 into its management recommendations for the syndromic management of genital ulcer disease (4). The impetus for such a significant change in treatment approaches has come from the accumulation of recent research findings and the high prevalence of HSV-2 in many countries.

## Methods

This paper provides an overview of the research on HSV-2 and HIV published since 2000. We (CC and AW) identified articles, reports and abstracts published during or after 2000. An online MEDLINE search for articles published in English during or after 2000 was also conducted.

## Current state of research

### The relationship of HSV-2 to acquisition and transmission of HIV

The majority of epidemiological studies have assessed the role of HSV-2 in increasing the risk of HIV acquisition, because of the difficulty of conducting studies of sexual transmission of HIV. Substantial biological data from *in vivo* and *in vitro* studies support the hypothesis that HSV-2 increases HIV infectiousness.

### Genital herpes and enhanced susceptibility to HIV

In a meta-analysis of the epidemiological literature related to HSV-2 and the risk of HIV infection, Wald & Link (1) found that people infected with HSV-2 had a risk of becoming infected with HIV twice as high as that in those who were not infected with HSV-2. The meta-analysis was based on the most rigorous studies that documented HSV-2 infection that had occurred prior to infection with HIV.

Rodríguez et al. conducted a nested case-control study in the Mwanza region of the United Republic of Tanzania to explore the relationship and time sequence between prevalent and incident HSV-2 infection and HIV seroconversion among 127 men and women (5). They discovered a strong association between HSV-2 status and HIV seroconversion among the 70 male study subjects, and reported that 60 of these HIV seroconversions occurred in men with HSV-2 infection. The adjusted odds ratio for HIV incidence in HSV-2-positive men was higher for the male subjects who seroconverted to HSV-2 during the 2-year follow-up period than for those who were HSV-2-seropositive at baseline, suggesting that the severity and more frequent reactivation of new HSV-2 infections plays an important role in increasing the risk of HIV acquisition. The findings from female study subjects were not statistically significant.

In a cross-sectional study of 1507 subjects aged 14–24 years in the mining district of Carletonville, South Africa, Auvet et al. determined that HSV-2 seropositivity was a risk factor for HIV infection (6). Nine per cent of the young men and 34% of the young women in the study area were infected with HIV, and HSV-2 seroprevalence was almost twice as high (17% among men and 53% among women). HSV-2 seropositivity was strongly associated with HIV infection: men who were seropositive for HSV-2 were seven times more likely to be HIV-positive than men who were seronegative for HSV-2. Among the individuals infected with HIV, 91% of the women and 65% of the men were co-infected with HSV-2.

Buvé et al. (7) explored the factors that influence the differences in HIV prevalence in four cities in Africa, two with a high prevalence of HIV: Kasumi, Kenya, and Ndola, Zambia, and two in which the prevalence of HIV is relatively low: Cotonou, Benin, and Yaoundé, Cameroon. They reported that higher prevalences of HSV-2 in men and women, and of trichomoniasis in women and the lower prevalence of circumcision of males in the two cities that had a high prevalence of HIV played a greater role than sexual behaviour in explaining the differences in HIV prevalence between the four cities studied. Given the high HSV-2 seroprevalence in Kisumu and Ndola, Buvé and colleagues hypothesized that as the prevalence of HIV and HSV-2 increased in these cities, the two viruses fuelled transmission of one another by increasing susceptibility and infectiousness. Weiss et al. (8) looked more specifically at the role of HSV-2 in this study and found that in three of the four cities studied by Buvé et al., the prevalence rates of HSV-2 were higher than 50% in women and 25% in men. In all four cities, the prevalences of HSV-2 and HIV were strongly correlated.

### Genital herpes and enhanced transmission of HIV

In a prospective study of 12 HSV-2-seropositive, HIV-positive men, Schacker et al. (9), detected HIV-1 RNA in lesions in 25 out of 26 episodes (i.e. periodic reactivations) of genital herpes, with a modestly higher quantity of HIV in genital lesions than in blood, suggesting that HSV reactivation could increase infectiousness of HIV in people co-infected with HIV and HSV.

In the Rakai community-randomized trial of mass STD treatment, researchers looked at factors that increased the risk of HIV transmission in HIV-discordant, monogamous couples, including HSV-2 serostatus, HIV viral load in the HIV-positive partner and sexual activity. Gray et al. (10) estimated the probability of HIV-1 transmission per sex act by studying 174 monogamous HIV-discordant couples identified retrospectively, among whom 38 of the HIV-negative partners seroconverted to HIV-positive. Recent genital ulcers and higher levels of HIV in blood significantly increased the likelihood of transmission of HIV in these HIV-discordant couples (10, 11). Gray et al. (10) found that the probability of transmission of HIV-1 was approximately four times higher for those study subjects with genital ulcers than for those without.

The prevalence of HSV-2 is one factor that may explain the different outcomes in the STD intervention trials conducted in Mwanza, the United Republic of Tanzania, Masaka, Uganda and Rakai, Uganda. Three rounds of mass treatment for bacterial STIs were given every 10 months in 56 communities in the rural Rakai district of Uganda from 1994 to 1997. The intervention trial resulted in a modest decrease in the prevalence of syphilis but no reduction in the incidence of HIV-1 (12). In the same setting, HSV-2 was identified as the cause of 45% of the genital ulcers that were tested and that had a confirmed etiology (12). Also, the HIV-1 epidemic in the Rakai district was at a mature stage, with a much higher prevalence of HIV-1 and a higher incidence of HIV-1 than that in the Mwanza region in the United Republic of Tanzania, where strengthened syndromic management of STDs reduced HIV incidence by 40% (12). In mature epidemics, a larger proportion of the population is infected with HIV-1. People who are co-infected with HIV and HSV-2 may experience more frequent episodes of genital herpes with symptomatic lesions and ulcers than people who are HIV-negative, which may also increase their risk of transmitting HIV-1 to others. Kamali et al. (13) found that behavioural interventions and improved syndromic management of STI had little effect on the incidence of HIV-1 in the Masaka district of Uganda, a region where there is a mature HIV-1 epidemic and a significant prevalence of HSV-2.

To assess the outcomes of these three STI intervention trials that focused on different strategies to control bacterial STDs, Orroth and colleagues compared sexual behaviours and STD prevalence in the three populations studied and determined that in subjects aged 15–29 years, the adjusted prevalence of HSV-2 in Rakai was 43% in women and 21% in men; in Mwanza, 47% in women and 13% in men; and in Masaka, 44% in women and 17% in men (14). The high prevalence of HSV-2 in all three sites of these community-randomized STD intervention trials indicates that genital herpes may be an important factor in explaining the different outcomes of the trials. Infection with HSV-2 was much more prevalent than all other bacterial STDs combined. This underscores the need for further trials to characterize the relationship that exists between HSV-2 and HIV transmission and to identify effective interventions.

### **Shedding of HSV-2 in asymptomatic people and risk of transmission**

In the 1990s more sensitive diagnostic tests, such as the polymerase chain reaction (PCR) assay, allowed researchers to better characterize the pattern and frequency with which asymptomatic people infected with HSV-2 shed virus; at such times asymptotically infected individuals could unknowingly transmit

HSV-2 to their sexual partners. Wald et al. (15) measured the frequency of HSV shedding in HSV-2-seropositive women using both the sensitive HSV PCR assay and the standard viral isolation culture method. In this study, the HSV-2 detection rate using the PCR assay was 3.5 times higher than that using the culture method; viral shedding was detected on 28% of the days tested. Wald et al. (16) compared genital shedding in 53 HSV-2-seropositive subjects who had no history of genital herpes with that in 90 HSV-2-seropositive subjects who had symptomatic disease. Interestingly, after patient education about genital herpes, 46 of the 53 asymptomatic persons did report lesions or other symptoms. The rate of subclinical shedding was similar in both groups, consistent with infection with genital herpes. HSV-2 was detected in the genital secretions of 44 of the 53 individuals in the group of HSV-2 seropositive subjects who did not report a history of genital herpes. In general, the recurrent episodes in these subjects were shorter and less frequent than those reported in the group of 90 patients with known symptomatic disease. Krone et al. (17) studied the frequency of viral shedding in HSV-2-seropositive, HIV-negative men who had sex with men, and found that shedding of HSV occurred on 5.5% of the days on which cultures were obtained. Shedding of HSV-2 was found to occur primarily in the anal and rectal region, and on almost half of the days on which HSV-2 was detected, no lesions were present.

The frequency of viral shedding has substantial implications for counselling patients about the natural history and risk of transmission of HSV-2 even when no lesions are recognized (i.e. subclinical shedding).

### **Diagnosis and treatment of HSV-2**

New type-specific serological assays and PCR have dramatically improved the ability to identify and diagnose HSV-2, and have increased the feasibility of large-scale HSV-2 vaccine trials and of HSV-2 intervention trials. As yet there are not enough data available to establish which diagnostic and treatment strategies, whether alone or in combination, will prove effective in reducing the prevalence of HSV-2 in developing countries. To date HSV-2 vaccine trials have not demonstrated substantial efficacy. HSV-2 intervention trials exploring episodic and suppressive therapy with acyclovir in developing countries are just beginning and will raise as many questions as they answer about the feasibility and implementation of programmes in countries with varying resources. New WHO guidelines for the syndromic management of genital ulcer disease are likely to result in more people being diagnosed with and treated for HSV-2, although the overall impact on prevalence of HSV-2 and on HSV-2 and HIV transmission will not be evident for several years (4).

### **Testing for herpes simplex virus**

Serological screening for genital herpes will be an essential “cornerstone” of prevention strategies as most people infected with HSV-2 are unaware of their infection. For the minority of people who present with genital lesions, clinical diagnosis is unreliable because of the diverse and subtle symptoms of HSV-2 infection. Herpes ulcers often mimic other causes of genital ulcers, such as chancroid, another STI, and may be misdiagnosed even by experienced clinicians (18).

Type-specific serological assays, which were developed in the 1990s and are now commercially available, enable the detection of HSV-2 in asymptomatic individuals. Before these tests became available, no commercially available HSV antibody

tests were able to differentiate between infection with HSV-1 (a related herpesvirus, most commonly associated with cold sores on the mouth) and HSV-2. These new assays have acceptably high sensitivity and specificity for use in many settings, particularly in those with a high prevalence of infection (18). The HSV Western blot differentiates between antibodies to HSV-1 and HSV-2 and was developed more than a decade ago at the University of Washington, USA, but is not commercially available. Although regarded as the gold standard for such tests, its high cost (US\$ 95), the technical skill and experience required to conduct it, and the time needed for its performance prohibit its widespread use in developing countries (18). All serological assays have a time lag before antibodies are detectable after initial acquisition of HSV-2, the duration of which can range from several weeks up to several months (18).

### Vaccines against HSV-2

A recombinant subunit vaccine to prevent the acquisition of HSV-2 has been tested in clinical trials. The vaccine showed significant efficacy in reducing symptomatic genital herpes among women who did not also have HSV-1 antibodies, but very little efficacy in protecting women from HSV-2 infection (19). This vaccine is undergoing further evaluation and other candidate HSV-2 vaccines are at earlier stages of testing.

### Syndromic management of HSV-2

WHO has incorporated empirical antiviral treatment for HSV-2 into the syndromic management of genital ulcer disease based on clinical appearance (vesicles or ulcers), history of recurrent lesions and prevalence of HSV-2 in the population (4). Traditionally, syndromic management has focused attention on chancroid and syphilis, two bacterial STIs that also cause genital ulcer disease, but that have declined in prevalence over the past decade. In areas such as sub-Saharan Africa, where the prevalence of HSV-2 is high, such approaches result in a lack of treatment for the most common cause of genital ulcer disease, i.e. HSV-2. The effect of HSV-2 therapy for the treatment of genital ulcer disease on people infected with HIV warrants study of HIV shedding during HSV-2 reactivation compared with that during suppression in relation to potential infectiousness.

### HSV-2 intervention trials

Future interventions may focus on HSV-2 prevention and treatment as an HIV prevention strategy. Several studies, including one funded by the US National Institutes of Health (NIH), are evaluating the efficacy of acyclovir in preventing the acquisition of HIV in HSV-2-infected individuals. For the NIH trial, HIV-negative HSV-2-seropositive heterosexual women in South Africa, Zambia and Zimbabwe and homosexual men in Peru and the USA are being enrolled. The trial will provide data on the effect of twice-daily acyclovir suppressive therapy in preventing acquisition of HIV and data on adherence to suppressive acyclovir. The cost of implementing widespread suppressive therapy is difficult to justify in many developing countries. If the trial of suppressive HSV-2 therapy demonstrates reduced acquisition of HIV, suppressive therapy for people infected with HSV-2 could be targeted to those who are at high risk for HIV infection. The Bill and Melinda Gates Foundation has funded a trial of acyclovir suppressive therapy to reduce transmission of HIV in HIV-discordant couples in which the HIV-infected partner also has HSV-2 infection at a number of sites in Africa and India.

## Discussion

The diagnosis and management of genital herpes presents a challenge for public health programmes and for clinicians in developing countries. The approach needed may differ between areas depending on the stage of the HIV epidemic, the prevalence of HSV-2 in high-risk populations, and on the cost and availability of diagnostic tests and treatment. In middle-income countries with a lower prevalence of HSV-2, such as Latin America, a tailored approach of serological testing in specific high-risk populations might be feasible. In countries in sub-Saharan Africa, where the prevalence of HSV-2 is extremely high, the provision of acyclovir for persons with genital ulcers who are being treated syndromically at clinics may be useful. There are as yet too few data to determine which strategies will be most effective in which settings.

If the trials of HSV-2 suppressive therapy show a reduction in the acquisition of HIV, the transmission of HIV, or both, such therapy may contribute to reducing both genital herpes and HIV. The cost-effectiveness of providing HSV-2 suppressive therapy may be an important consideration; as with any intervention, the cost-effectiveness would be improved if it were possible to identify those individuals who would benefit most from HSV-2 suppression and to target suppressive therapy to them.

The cost and availability of generic acyclovir, particularly in settings where resources are limited, may affect the feasibility of HSV-2 suppressive therapies. The question of resistance to acyclovir developing as a result of its widespread use has been raised. However the mathematical model of Gershengorn et al. (20) suggests that even if there were to be widespread use of acyclovir, the level of drug-resistant HSV-2 in immunocompetent populations after 25 years would be very low. Also, the effect of episodic treatment of HSV-2 may not considerably shorten the duration of symptoms or HIV infectiousness in people co-infected with HIV and HSV, as there are often delays in seeking care and because treatment with antivirals results only in modest reductions in the duration of symptoms. For these reasons, other strategies such as suppressive HSV-2 therapy, are actively being explored to reduce HIV infectiousness.

The US Centers for Disease Control and Prevention (CDC) Division of Sexually Transmitted Diseases have also considered the management of genital herpes. While data were accumulating on the prevalence of HSV-2 infection and the role of HSV-2 in HIV acquisition and transmission, CDC did not have in place any recommendations or programmes specific to the prevention of genital herpes, apart from the standard STI treatment guidelines. In May 1998, CDC hosted a meeting of HSV-2 experts to define programmes to which it will be important to devote resources and to identify research priorities for CDC with regard to genital herpes (21). Some important points emerged from this meeting.

- The participants did not reach consensus on the suggestion that CDC recommend that all people infected with HIV be evaluated for genital herpes using type-specific serological testing (those that questioned this recommendation proposed more scientific, operational and behavioural research).
- The participants agreed that CDC should immediately begin education campaigns to raise the level of awareness about genital herpes among health-care providers and the public.
- There was broad consensus that CDC should specifically recommend the use of type-specific tests when HSV serological tests are used.

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- With a view to promoting standards of care in STD clinics, there was broad consensus that CDC should recommend that patients be told if they are not being tested for genital herpes as part of clinical evaluation, that type-specific serological tests should be available if testing is requested by patients, and that tests to detect HSV-2 should be routinely used when diagnosing genital ulcers.

In 2002, CDC issued a set of *Sexually Transmitted Diseases Treatment Guidelines* (22) that contained new information regarding the management of genital herpes. In these updated guidelines, CDC strongly recommended the use of laboratory tests for confirming the diagnosis of genital herpes and the use of accurate type-specific serological tests.

## Conclusion

Worldwide, HSV-2 infection has reached epidemic proportions. Infection with HSV-2, even among people who do not have recognized herpes lesions, increases susceptibility to HIV, as documented by numerous observational studies. HSV-2 also increases the risk of transmission of HIV, most likely through micro-ulcerations and an increased amount of HIV in genital secretions during HSV-2 reactivation. In countries where there are large numbers of people infected with HSV-2 and HIV, suitable public health approaches for the diagnosis and management of genital herpes must be identified. Currently, there are no easy answers. Effective vaccines against HSV-2 have yet to

be identified, and episodic and suppressive therapy approaches are often too expensive to be implemented in developing countries on a large scale. Although the epidemic of HSV-2 and the synergy between HSV-2 and HIV infection has been recognized by international public health experts, more research is needed to identify effective programmatic and clinical strategies for diagnosing and managing genital herpes worldwide. ■

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## Résumé

### Herpès génital et virus de l'immunodéficience humaine : un double problème

La relation synergique entre le virus de l'herpès humain type 2 (HSV-2) et la transmission du virus de l'immunodéficience humaine (VIH) peut prendre une importance notable dans les pays en développement où la prévalence de ces deux infections virales est élevée. L'herpès génital, fréquemment dû au HSV-2, est devenu la cause majeure d'ulcérations génitales dans le monde entier. La présente revue des recherches récentes sur le lien entre l'herpès génital et l'augmentation de la sensibilité au VIH et de sa transmission fait partie de la série « Advances in HIV/AIDS research series » qui a pour objectif de favoriser le lien entre la recherche sur le VIH et le syndrome d'immunodéficience acquise (SIDA) et la pratique en matière de prévention du VIH/SIDA, de soins et de soutien aux malades dans les pays en développement. Les résultats des travaux de recherche ont montré que la séropositivité pour le HSV-2 peut augmenter le risque d'infection par le VIH chez les personnes VIH-négatives à haut risque exposées au VIH et que, de même, l'infectiosité des personnes co-infectées par le VIH-1 et le HSV-2 peut augmenter pendant les périodes de réactivation du HSV-2. Ces observations ont conduit à la mise en route de

plusieurs essais d'intervention et pourraient en fin de compte aboutir à l'établissement de nouvelles priorités en santé publique et en pratique clinique. L'OMS a récemment publié de nouvelles directives pour la prise en charge syndromique des ulcérations génitales, comportant un traitement antiviral des lésions compatibles avec un diagnostic d'herpès génital. Aux Etats-Unis d'Amérique, les Centers for Disease Control and Prevention ont publié en 2002 une mise à jour des directives sur le traitement des maladies sexuellement transmissibles (*Sexually Transmitted Diseases Treatment Guidelines*), recommandant l'utilisation de tests sérologiques spécifiques de type pour le diagnostic du HSV-2. Des essais d'intervention contre le HSV-2 ont été récemment lancés à titre de validation dans plusieurs pays pour tenter de déterminer la proportion des nouveaux cas d'infection par le VIH qu'il serait possible d'éviter par la suppression du HSV-2 ; les résultats de ces essais seront utiles lors de l'établissement des priorités et des stratégies de prévention et de traitement dans les pays en développement.

## Resumen

### Herpes genital y virus de la inmunodeficiencia humana: un doble problema

La sinergia entre el virus herpes simple tipo 2 (VHS-2) y la transmisión del virus de la inmunodeficiencia humana (VIH) puede ser considerable en los países en desarrollo donde hay una alta prevalencia de esas dos infecciones víricas. El herpes genital, causado la mayoría de las veces por el VHS-2, se ha convertido en la principal causa de ulceración genital a nivel

mundial. La presente revisión de las más recientes investigaciones sobre el herpes genital, la mayor vulnerabilidad al VIH y la mayor transmisión del virus forma parte de la serie «Advances in HIV/AIDS research series», que aspira a tender puentes entre las investigaciones sobre el VIH/SIDA y las prácticas de prevención, atención y apoyo relacionadas con esa infección en los países en

desarrollo. Los resultados de las investigaciones han demostrado que el hecho de ser seropositivo para el VHS-2 puede aumentar el riesgo de contagio por el VIH entre las personas de alto riesgo VIH-negativas expuestas al VIH, y que, análogamente, la infecciosidad de los individuos coinfectados por el VIH-1 y el VHS-2 puede aumentar durante los periodos de reactivación del VHS 2. Estas observaciones han llevado a iniciar varios ensayos de intervención y en último término podrían conducir al establecimiento de nuevas prioridades en el terreno de la salud pública y la práctica clínica. La OMS ha publicado recientemente unas nuevas directrices para el manejo sindrómico de las úlceras genitales, que incluyen tratamiento antiviral para las lesiones compatibles con herpes

genital. Los Centros de Control y Prevención de Enfermedades de los Estados Unidos publicaron en 2002 unas directrices actualizadas para el tratamiento de las enfermedades de transmisión sexual en las que se recomendaba el uso de pruebas serológicas específicas de tipos para diagnosticar la infección por VHS-2. Los ensayos de intervención contra el VHS-2 emprendidos a modo de demostración práctica en varios países ayudarán a determinar la proporción de nuevas infecciones por VIH que podrían prevenirse eliminando el VHS-2, y los resultados de estos estudios facilitarán la adopción de medidas informadas por todos aquellos implicados en establecer prioridades y estrategias de prevención y tratamiento en los países en desarrollo.

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