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Repetitive Mucosal Exposure to Human Herpesvirus-8 and Protection against Its Penile-Vaginal Transmission

To the Editor—The article by Atkinson et al. [1], “Seroprevalence of Human Herpesvirus 8 among Injection Drug Users in San Francisco,” reports that the risk of human herpesvirus (HHV)-8 infection among women is inversely related to the number of their recent male sex partners and that this relationship is highly statistically significant (P = .02). Such an unanticipated relationship was not seen among either women who have sex with women or men who have sex with men. It contrasts sharply with HHV-8 transmission characteristics for male injection drug users, in whom number of years of drug use was associated with HHV-8 seropositivity.

Atkinson et al. found no evidence of confounding variables in their multivariate analysis, yet they suggest the possibility that the inverse relationship is a “chance finding,” since it is unlikely that women are protected against HHV-8 by continued exposure to multiple sex partners [1]. I propose an alternative hypothesis.

Several groups have suggested that, in some women, promiscuity, with repetitive and consistent cervicovaginal exposure to human immunodeficiency virus (HIV)-1, can lead to protection against sexual acquisition of HIV-1 [2–6]. These groups’ studies involved cohorts of female commercial sex workers (CSWs) from Africa, East Asia, and India [2–6]. The mechanism of this phenomenon, the highly exposed persistently seronegative (HEPS) state, is unknown. In half of HEPS women in the Nairobi, Kenya, cohort, HEPS was correlated with cytolytic T cell reactivity against uncommonly recognized HIV Gag epitopes [7]. In women in whom this response was present, it declined rapidly after even a brief (≥2 months) cessation of sex work and the consequent interruption of pathogen exposure; in many CSWs who had ceased performing sex work for a period, HIV-1 was promptly acquired when sex work was resumed [7]. It is also conceivable that nonimmune but virus-specific mechanisms—such as blockade of local infection by competition for receptors on vaginal mucosa, between infectious virus and the vast excess of either defective virions or soluble HIV-1 envelope glycoprotein gp120 characteristic of an HIV infection—play a role [8].

I have recently extended the concept of HEPS to another sexually transmitted viral pathogen, human papillomavirus (HPV) [8], using data from 2 large studies of women. The first, a case-controlled study of 187 female CSWs from Copenhagen, Denmark, found that the incidence of HPV acquisition declined as the length and number of sexual exposures increased [9]. Similarly, women with a history of gonorhrea, which is used as an index of high-risk sexual exposures, had a significantly decreased risk for HPV infection [9]. In agreement with the Danish study, the second study, a longitudinal investigation of HPV in 1860 women in Brazil, with examinations at 4-month intervals, found resistance to HPV in a subset, with an inverse relationship between HPV acquisition and the age and number of sexual partners [10]. Here, host mucosal factors—immunologic or otherwise—are likely to be involved, since the phenomenon of either shed viral envelope or defective virions serving as receptor blockers, raised in the context of HIV, would not apply to HPV.

This finding does not mean that having multiple sex partners is a reasonable way to protect against sexual acquisition of HHV-8, HIV-1, or HPV. These observations prompt the question of why the HEPS CSWs failed to become infected by HIV before a protective mech-
anism had been induced. Given the rapidity with which resistance to HIV-1 appears to have been lost after brief interruptions of sex work by the Nairobi cohort [7], initial protection against infection was most likely stochastic. A similar phenomenon may apply to cohorts of HPV-negative and HHV-8–negative women with multiple sex partners. But, perhaps, as a result of the good fortunes of the women in the Nairobi cohort who did not become infected, we will be able to learn something applicable to the development of vaccines against certain sexually transmitted diseases.

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References


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Norwalk Virus Infection and Disease Is Associated with ABO Histo–Blood Group Type

To the Editor—Hutson et al. [1] report an association, in voluntary subjects experimentally infected under laboratory conditions, between ABO phenotype and the risk of symptomatic Norwalk virus infection. We have found a similar association in an outbreak of Norwalk-like virus (NLV) infection that affected British troops.

During May 2002, a British military field hospital located in Bagram, Afghanistan, experienced an outbreak of incapacitating illness, which eventually proved to be the result of NLV infection [2]. The infection was introduced by an index-case subject and, subsequently, rapidly spread through the medical unit. No virological investigations were available in Afghanistan, but NLV was identified by electron microscopy, polymerase chain reaction, and a novel antigen-detection ELISA, in all 8 of the patients who were evacuated to Europe by aircraft equipped with medical devices. The unit represented a small, closed community, and the movement of personnel in and out of the unit was restricted until the outbreak had been controlled. Thirty-five (45.5%) of 77 hospital staff developed symptoms that fulfilled the clinical-case definition. Because all British soldiers have their blood group recorded on their medical records, we were able to calculate odds ratios for symptomatic infection, in relation to blood group. The relationship between ABO group and symptomatic disease is reported in table 1. Because of both the close living conditions within the field hospital and the high number of symptomatic individuals, which is particularly important since restriction of movement had been invoked, it is reasonable to assume that all personnel were exposed to an infecting dose of NLV during the outbreak.

Similar to Hutson et al. [1], we found that individuals of blood group B appeared to have reduced susceptibility to symptomatic NLV infection, although statistical significance was not reached. The severity of the disease, ascertained from hospital records and questionnaires, appeared to be heightened in individuals of blood group O. Two individuals suffered from incapacitating illness that appeared to be life threatening during the early stages and required artificial ventilation. Both individuals were of blood group O.

Our findings are the results of a reactive-outbreak investigation performed in adverse field conditions. To have been able

<table>
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<tr>
<th>ABO group</th>
<th>No. of individuals</th>
<th>OR (95% CI)*</th>
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<tbody>
<tr>
<td>O</td>
<td>18</td>
<td>18</td>
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* CI, confidence interval; OR, odds ratio.