reactivation of virus after transplantation has been shown [7, 8].

In our population, KS also occurred, but at a slower rate, among those who were infected with HHV-8 before acquiring HIV-1, which suggests that reactivation in this population probably also has occurred. Thus, we do not believe that the results of the studies conflict. It will be interesting to compare disease rates among patients undergoing transplantation who are HHV-8 seroprevalent versus those who newly acquire HHV-8. However, this type of cohort study (whether prospective or retrospective) may have to be conducted in a nonendemic population.

It is possible that the timing of reactivation and the HHV-8 viremia produced as a result of reactivation was quite different between the 2 populations. In an endemic population, HHV-8 reactivation due to immunosuppression may be quicker and may result in higher virus loads, compared with primary HHV-8 infection. As we discussed [1], the development of KS may be dependent on the level of HHV-8 virus load, which may be dependent on the level of immunosuppression, as well as on the primary infection. Because the literature on the association of other herpetic infections and the development of disease after immunosuppression indicates that infection during immunosuppression is related to a quicker and more severe outcome, a different mechanism for HHV-8 would be inconsistent for this family of viruses. However, researchers are still in the early stages of understanding the natural history of HHV-8 infection, and we concur that additional research is required to determine the precise role of immunosuppression, including severity and duration, and its interaction with HHV-8 virus load in the development of Kaposi’s sarcoma.

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References


Sensitization to Human Immunodeficiency Virus in Seronegative Exposed Partners

To the Editor—Mazzoli et al. [1] recently presented evidence for the existence of a mucosal immune response in conventionally seronegative sex partners (ELISA/Western blot) of human immunodeficiency virus (HIV)-infected persons [1]. The presence of pathogen-specific IgA in the absence of IgG antibodies is an unprecedented finding in infectious diseases, and underlying mechanisms are obscure. However, the finding suggests the transmission of viral components and is supported by findings of a cellular immune response in partners, health care workers, and vertically exposed persons. Our understanding of this phenomenon will probably depend on future studies of the cellular immune response in exposed subjects. To date, the bulk of evidence for sensitization has been provided by the demonstration of proliferative T cell response to HIV antigens or by studies examining the cytolytic activity of CD8 cells against HIV-infected target cells in exposed partners [2, 3]. Technical sophistication of these classical assays for measuring cellular immunity has, thus far, prevented the widespread study of the phenomenon. Here we report the results of a newly developed flow cytometric method for the detection of HIV-specific CD4 cells in exposed partners [4].

Whole-blood samples from noninfected heterosexual partners were stimulated for 6 h with recombinant HIV p55 gag and anti-CD28 costimulator. We added brefeldin during the last 5 h. After intracellular staining of interferon-γ and CD69, gated CD4 lymphocytes positive for both stimulation markers were calculated and were compared with unstimulated controls in a multiparameter flow cytometric detection system. The assay was evaluated in HIV-infected long-term nonprogressors with undetectable HIV RNA (<20 copies/mL) and blood donors. Cytomegalovirus was used as a positive control.

Eight HIV-seronegative heterosexual partners with a >3-month history of sexual exposure were tested. HIV-specific CD4 cells were found in 2 partners at a frequency of 3.4% and 1.4%, compared with 0.5% spontaneously activated CD4 cells in nonstimulated cultures. Both persons had continuous unprotected sex-
ual exposure with the HIV-infected index partner; all other partners had stopped their risky behavior \( \geq 3 \) months before the assessment.

To our knowledge, this is the first demonstration that this rapid technology can be used in exposed persons to detect HIV-specific CD4 cells. The feasibility of the rapid detection method for this purpose will allow for further study of the sensitization observed in exposed persons.

Theoretical considerations suggest that a cellular immune response without a full antibody response, as described by Mazzoli et al. [1], would occur in cases in which HIV is only present intracellularly and not shed in the extracellular compartment. As a consequence, B lymphocytes would be unable to recognize the antigen. T cells, on the other hand, are specialized to detect intracellular antigens on antigen-presenting cells. The observation of a local IgA production in the mucosa in the absence of a systemic humoral immune response might indicate that the viral antigen is confined to the mucosal compartment by a strong cellular immune response. To support this hypothesis, the presence of viral components should be investigated in mucosa-associated lymphatic tissue. The property of this antigenic viral component is not clear but is not necessarily infectious. The lack of a cellular immunity in persons with only remote exposure to HIV, as described in our partner study, speaks against a true cellular immunity in persons with only remote exposure to HIV—although the presence of viral components is not clear but is not necessarily infectious. The lack of a cellular immunity in persons with only remote exposure to HIV, as described in our partner study, speaks against a true cellular immunity in persons with only remote exposure to HIV—although the presence of viral components is not clear but is not necessarily infectious.

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