lation may affect the generalizability of the study findings: 85% of the patients were African American or African Caribbean, and the number of individuals with complicating hepatitis B or C was not indicated. Renal disease is more prevalent in HIV-infected black people than white people, particularly with respect to HIV-associated nephropathy. Chronic viral hepatitis may also cause secondary renal disease, likely secondary to an immunocomplex-associated inflammatory process. Regardless of these caveats, the authors’ conclusion is very much warranted: “surveillance of quantitative proteinuria with imaging and chemical indicators of renal dysfunction is very much warranted” for children with HIV infection.

Semen-Derived Amyloid Fibrils Drastically Enhance HIV Infection

Seminal Plasma Reduces the Effectiveness of Topical Polyanionic Microbicides

PURPOSE OF THE STUDIES. Heterosexual intercourse is the major route of HIV transmission throughout the world. A variety of factors have been identified that are associated with increased transmission, including virus load, lack of circumcision, and the presence of sexually transmitted diseases. One approach to the reduction of male-to-female transmission has been the use of microbicides, and a major effort has been put forth to identify a safe and effective topical microbicide. The purpose of the Münch et al study was to identify factors in semen that might enhance HIV transmission, and the purpose of the Patel et al study was to examine why one of the most promising microbicides tested has failed thus far to reduce transmission in a large controlled trial.

STUDY POPULATION. Normal human seminal plasma was studied.

METHODS AND RESULTS. In the Münch et al study, investigators screened a complex peptide/protein library derived from human seminal fluid. The authors looked for novel inhibitors and enhancers of HIV infection. They identified fragments of prostatic acidic phosphatase that drastically enhanced HIV infection. Functional and structural analysis showed that these peptides formed amyloid fibrils that captured HIV particles and strongly enhanced the number of productively infected cells in vitro by promoting virion-cell attachment. The authors termed this product “semen-derived enhancer of virus infection” (SEVI). Rats transgenically expressing human CD4 and chemokine receptor 5 (CCR5) are susceptible to HIV infection. In this model, SEVI significantly enhanced the infectivity of HIV in vivo. In the Patel et al study, seminal plasma was shown to dramatically reduce the activity of polyanionic microbicides to reduce infectivity of herpes simplex virus type 2. Further study demonstrated that fibronectin 1 and lactoferrin were the specific factors in seminal plasma that were responsible for this process. In a murine model, this interference in vitro translated to a loss of protection in vivo.

CONCLUSIONS. Components of seminal plasma increase HIV infectivity and reduce the effectiveness of topical polyanionic microbicides.

REVIEWER COMMENTS. That host factors are involved in HIV replication and transmission is not surprising. However, that amyloid fibrils associated with seminal plasma dramatically increase HIV infectivity was not expected. An increased understanding of the mechanism of this enhancement might assist in overcoming the obstacles noted by Patel et al. An extraordinary effort was put forth to identify a safe and effective microbicide that would prevent transmission of HIV. In vitro and in vivo models indicated that the compound, PRO 2000, would dramatically reduce HIV transmission in vivo. The failure of this approach and the finding that seminal plasma directly interferes with this function dramatically illustrate the need to evaluate seminal plasma as a potential interfering agent in the search for effective microbicides.
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Joseph A. Church
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