LETTER

Sex, microbial translocation, and the African HIV epidemic

Redd et al. (1) suggest that microbial translocation is not an important contributor to HIV disease progression in Africa, in contrast to its possible role in HIV pathogenesis in North American cohorts (2–4). They further postulate that this discrepancy may relate to mode of HIV transmission, because the Ugandan cohort in which they base their study is composed of heterosexual men and women, whereas North American cohorts typically contain more men who have sex with men and injection drug users. These conclusions are based on a study in which they prospectively examined whether plasma markers of microbial translocation correlated with HIV progression and found that they did not. However, we suggest that these data are not sufficient to conclude that microbial translocation is not an important contributor to HIV disease in Africa.

First, significant levels of bacterial endotoxin [lipopolysaccharide (LPS)] were demonstrated in HIV infected subjects but were not directly compared with levels in uninfected subjects. Theoretically, the endotoxemia they observed could have been related to HIV infection itself, or potentially to unevaluated factors such as endemic gastrointestinal infections. However, we recently found that plasma endotoxin levels were significantly increased in HIV-infected Kenyan female commercial sex workers compared to uninfected women within the same Nairobi cohort(5). Whereas some participants did have detectable levels of plasma LPS in the absence of HIV infection, only HIV status significantly predicted endotoxemia. Therefore, HIV-associated endotoxemia appears to exist in this context of the heterosexual epidemic in Africa.

Redd et al. (1) showed that the rate of HIV disease progression, as indicated by CD4 T cell decline or death, was not related to changing plasma levels of microbial translocation markers. In our cross sectional study (5), we also found that plasma endotoxin levels were not associated with CD4 counts. However, such markers need not increase as disease progresses in order to play a role in disease progression. For instance, it is possible that it is not the degree of microbial translocation but the nature of the host response that determines disease progression. We found that the inflammatory response to endotoxin was highly variable among subjects, suggesting that the host response to endotoxin may be important in determining the effects of microbial translocation on HIV disease. Assessing circulating biomarkers may miss important functional immune differences and/or compartmentalized immune associations. In addition, quantifying disease progression by the lack of CD4 decline alone may miss important HIV-associated clinical endpoints related to increased bacterial translocation and associated innate immune activation, such as cardiovascular disease and cognitive dysfunction.

The fact that subclinical endotoxemia was associated with heterosexually acquired HIV infection in Nairobi suggests that Redd et al. may not be able to extrapolate the research findings from their Ugandan cohort to the HIV epidemic across a very diverse continent. However, their results certainly highlight the need for further investigation into the phenomenon of HIV-associated bacterial translocation in the African context, and to better define its causes and consequences.

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