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HIV Transmission During Condomless Sex With a Seropositive Partner With Suppressed Infection

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To the Editor

The PARTNER (Partners of People on ART—A New Evaluation of the Risks) study[1] reported no documented cases of human immunodeficiency virus (HIV) transmission during condomless sex from stable sexual partners whose HIV infection was suppressed with antiretroviral therapy (ART). In more than 40000 condomless sex acts during 1238 couple-years of follow-up, 11 incident HIV infections occurred, but none was linked by phylogenetic analysis to the index partner. Rather, these 11 incident HIV infections were transmitted from outside the sexual partnership. We suggest that a more detailed analysis of HIV transmission linkage is necessary.

HIV evolves rapidly within a host, owing to the error-prone nature of the HIV replication process and immune pressure. Determination of the similarity between partners' HIV genetic sequences compared with other HIV sequences from regional infections is commonly used to confirm or refute epidemiologically linked HIV transmissions. Previous HIV prevention trials that enrolled initially HIV serodiscordant couples[2,3] showed that minority viral variants demonstrated linkage when the majority variants were not clearly linked.[4,5]

The PARTNER study omitted important information to determine whether HIV was transmitted within the sexual partnership; specifically, analysis of minority variants that might provide evidence of linkage and detailed analyses of the *env* sequences. Prior results for linked specimens in the HIV *env*generegion[4] showed genetic distances similar to those of the unlinked specimens presented in the PARTNER study. Further more, imputed time from seroconversion to collection of the specimen sequenced was not reported, which is required to contextualize the genetic similarity, given the rapid evolution of HIV. It is crucial to more

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robustly exclude transmission linkage, especially in the 4 couples with closely related HIV sequences (ie, couples 7, 8, 10, and 11).

In long-term HIV-serodiscordant partnerships, the risk of HIV transmission is very low when the HIV-seropositive partner's HIV replication is suppressed by antiretrovirals. However, we contend that the evaluation of viral sequences presented was too limited to establish if the point estimates of HIV transmission risk were indeed zero in the PARTNERS study. Clinicians translating this analysis and the upper 95% CI of the risk estimate into patient-centered language face a problem in counseling at-risk individuals. Misinterpretation of these study results could lead to sexual disinhibition and exacerbate the HIV pandemic.

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