Introduction

The primary goal of this research is to test the hypothesis that a person with an established HIV-1 infection can be re-infected with a second variant of HIV-1 (i.e. superinfection). A case of HIV-1 superinfection after seroconversion has never been documented in the peer-reviewed literature.

Additionally, the Positive Partners study will assess broader virological and epidemiological implications of unprotected sex between partners already infected with HIV. This will eventually inform including HIV-infected transmission of other viral STDs, and an assessment of how unprotected sex among partners both positive for HIV affects choices about high-risk sex with partners of negative or unknown status.

Specific Objectives for the UARP IDEA Award

1. To develop and evaluate methods of recruitment and retention of anti-HIV-1 seropositive seroconcordant couples who have unprotected intercourse prior to study enrollment and during a one-year follow-up period.
2. To seek evidence of prior superinfection in pilot couples at baseline which could be manifested as dual infection with divergent variants of HIV-1.
3. To determine if HIV-1 superinfection occurs in a small group of sexually exposed couples followed over a 12-month period.
4. To evaluate community interest and support for this research question and support the possible effects that the theoretical risk of HIV superinfection has had on the sexual choices of HIV-positive individuals enrolling in the study.

Background

1. Evidence of co-infection with multiple HIV-1 subtypes and recombinant HIV-1 viruses in humans and monkeys has been taken as de facto evidence of superinfection. However, when transmission has been documented, dual infections have resulted from concomitant exposure. Dual infection after sequential exposure has not been reported.
2. Nonhuman primates can be superinfected only in a short window of susceptibility during primary infection, and when immune responses are not fully developed. Published longitudinal studies of viral evolution in humans have not provided evidence of superinfection.
3. The possibility of superinfection with a drug resistant form of the virus and that successful HAART therapy could contribute to susceptibility has heightened the importance of the question.
4. The possibility of HIV-1 superinfection is assumed in prevention messages to defer infected individuals from a course of high-risk sexual intercourse. Little data exists, however, to support the belief that superinfection among heterosexuals is associated with superinfection and sexual choices.

Research Plan

Study Design. This is a one-year prospective feasibility investigation of the occurrence of HIV-1 superinfection among 50 couples of any gender mix. Recruitment for the pilot study was done primarily through the Positive Partners Community Advisory Board, local ASOs, and HIV clinics. Couples are deemed eligible through an independent telephone screening of partners. Enrollment and follow-up study visits include interviews and biological specimen collection (blood and semen). Retention strategies include providing clinical test results, follow-up telephone contact every three months, and interim interviews/testing in cases of treatment breakthrough.

Inclusion Criteria:

1. HIV-1 seropositive concordant couples.
2. Both partners on HAART, or are on STI.
3. The couple practices unprotected anal or vaginal intercourse.
4. One partner did not infect the other.

Primary Behavioral Measures:

1. Sexual networks’ characteristics and density including sexual exposure to primary and other partners (past three months).
2. Knowledge, attitudes, and beliefs about superinfection.

Virological Measures:

2. Baseline assays to distinguish partner’s viruses, and follow up analysis to look for evidence of superinfection, include plasma RNA RT-PR sequencing and cellular DNA env V3 and tat Heteroduplex Mobility Assays, env V3, gag p17, and tat cloning and sequencing.

Virological Measures:

1. Sexual networks’ characteristics and density including sexual exposure to primary and other partners (past three months).
2. Knowledge, attitudes, and beliefs about superinfection.

Preliminary Results

Analysis of preliminary data focused on whether a reasonably diverse sample representing the epidemic in San Francisco enrolled, how appropriate (at risk) enrolling couples were for superinfection research, and what effect participating participants’ beliefs about superinfection had on their sexual choices, if any.

Concern about superinfection was associated with sexual practices:

1. Participants who believed superinfection poses a “serious problem” were less likely to use oral contraceptives more likely to practice early withdrawal, and tried to protect themselves from superinfection.
2. Those who tried to protect themselves from superinfection had more outside partners who were HIV-negative or of unknown status.

Conclusion

1. Community reaction to the study, including our Community Advisory Board, was quite positive and supportive. Couples approached the investigation of HIV superinfection were willing to enroll in the study. A few couples have separated during the follow-up period, but no individuals are known to have left the study.
2. The telephone screening procedure effectively identified couples that had genetically distinguishable viruses at baseline in about 75% of cases. Superinfection, if it occurs during follow-up, is likely to be detected in these couples.
3. No evidence of prior superinfection (dual infections or recombinant viruses) has been found in the baseline analysis of 12 pilot couples.
4. Beliefs about superinfection apparently fostered harm reduction strategies that may have reduced the risk of superinfection for all partners (i.e. withdrawal), or shifted risk to partners willing to practice more frequent receptive intercourse and to protect themselves from superinfection. Concerns about superinfection may disrupt primary relationships and increase risk of new HIV infections.

Acknowledgments

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References

1. Boedeker, Anna.
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3. Dr. Linda Rasulo, UCSF.
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5. UCSC Positive Health Program.