

Seroadaptation: *Disclosure, Sero(status)-sorting and Strategic Positioning*

Serosorting involves choosing partners by perceived HIV status. We believe that one of the ways HIV-positive men reduce the risk of new infections is by choosing to have higher-risk sex with other HIV-positive individuals.

When we say “higher-risk,” we are referring to sex that is more likely to transmit HIV, such as anal sex without a condom. “Lower-risk” sex refers to activities that have little or no risk for HIV transmission, such as oral sex or anal sex with a condom.

Strategic positioning is another risk-reduction strategy in which the HIV-positive partner bottoms to an HIV-negative or unknown-status partner during unprotected anal sex (no condom). When the HIV-positive partner is in the receptive position there is less risk for HIV transmission to the HIV-negative partner.

Our study

Positive Partners is a study of HIV superinfection in San Francisco. We looked for evidence of serosorting in a sample of HIV-positive men who have sex with men (MSM) enrolled in this study.

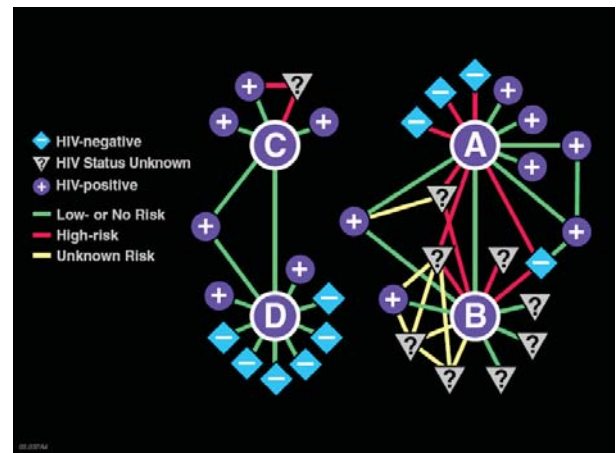
Our study participants report sexual behavior on a partner-by-partner basis. We learn the following:

- 1) Sexual partner’s HIV status
- 2) Specific sexual practices with each partner

In the following diagram, each letter represents an HIV-positive participant from Positive Partners. By asking each participant about his sexual behavior with each of his partners in the last three months and learning each partner’s

HIV status, we were able to create the following categories of partnerships that are illustrated in the diagram by dashed and solid lines:

1. High-risk for HIV transmission (partner was HIV-negative and partnership included unprotected anal sex)
2. Unknown risk for HIV transmission (partnership included unprotected anal sex, but participant did not know his partner’s HIV status)
3. Low- or no risk for HIV transmission (partner was also HIV-positive, or partner was HIV-negative or unknown-status but partnership did not include unprotected anal sex)



Here, we see two pairs of partners and their sexual networks. Participant D is an example of a “perfect” serosorter – someone whose partnerships in the last three months did not include risk of new HIV infection.

Using this method of analysis, the Positive Partners study has been able to identify patterns of serosorting and strategic positioning among our HIV-positive participants.

These risk-reduction strategies may help to reduce the spread of the HIV epidemic in San Francisco.

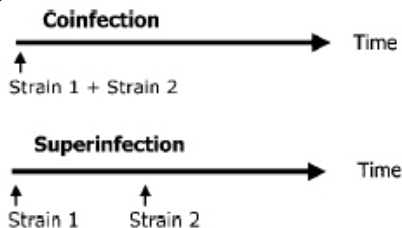
HIV Superinfection

Superinfection is infection with a second strain of HIV-1 after one strain has established infection.

- Superinfection is a concern because 1) it may be a way for someone who is HIV-positive to acquire drug resistance, and 2) it may lead to more rapid disease progression.
- A different strain of the virus is one that can be genetically distinguished from the first in a “family” or phylogenetic tree.

How does superinfection differ from dual infection?

- Dual infection – sometimes called coinfection – can occur when someone is exposed to more than one virus before seroconversion (see figure below from Smith *J Infect Dis* 2005)



- Dual infection that is sequentially expressed could appear to be superinfection.
- It is important for us to identify a source partner in a superinfection case so we can be sure that the second virus was acquired after seroconversion.
- No source partners have been identified in any of the reported superinfection cases.

When does superinfection happen?

- Twenty-eight cases of apparent superinfection have been reported. Twenty of these took place in the first three years after primary infection. (www.gladstone.ucsf.edu/givi/pps)

Is it bad to have more than one virus?

- Two studies have shown more rapid disease progression in dually infected individuals (Gottlieb *Lancet* 2004, Grobler *J Infect Dis* 2004).
- In most of the apparent superinfection cases described in the scientific literature, disease progression accelerated after the second virus appeared. (Smith *J Infect Dis* 2005).

Can superinfection happen later on in infection?

- In one study of chronically infected individuals, there were no superinfection cases detected after 1,072 person-years of observation (Gonzales *J Infect Dis* 2003).
- In another study, no superinfection cases were found among highly-exposed intravenous-drug users after 215 person-years of observation (Tsui *J Virol* 2004).
- In contrast, recently a well-documented case of HIV superinfection with a source partner was reported in two chronically infected gay men in a long term relationship (Blick *J Infect Dis* 2007).

Seroadaptation and Superinfection:

- Serosorting or the use of information about HIV status in the selection of sex partners and the decision about whether to use condoms and other safer sex steps with the partner, has been considered a potentially important measure to reduce HIV transmission [AIDS Alert 2004; 19:55–6., Parsons *AIDS* 2005; 19(Suppl 1):S13–25.]. We believe that existing evidence continues to suggest that superinfection with systemic expression of a second HIV variant is uncommon after the first few years of infection, and this report (Blick *J Infect Dis* 2007) should not lead to the abandonment of serosorting as one strategy to reduce HIV transmission. However, this case is an important cautionary tale that drug-resistant HIV truly can be transmitted to a chronically HIV-infected partner. Prior reports of HIV superinfection have documented transmission of drug-resistant HIV and potential rapid disease progression in early HIV infection [Smith *J Infect Dis* 2005]. Health care providers who counsel HIV-infected patients now need to insure that patients are aware that acquisition of drug-resistant HIV through unprotected sex is possible in chronic HIV infection, although the magnitude of the risk remains uncertain. (Hecht, *J Infect Dis* 2007)

What we still don't know...

- It is unknown whether exposure to different viral strains provides protective immunity against superinfection.
- It is also unknown whether there is a window of susceptibility to superinfection during recent infection as opposed to chronic infection.

Glossary

Acute infection usually occurs two to four weeks after infection with HIV and is often (but not always) accompanied by symptoms that resemble the flu and may last as long as two weeks. A person with acute HIV infection often has a very high viral load and may be particularly infectious to others. This stage of infection ends when seroconversion occurs.

CD4 cells (T cells) are the cells in the immune system that HIV attacks. CD4 cells play an important role in fighting disease. Healthy adults usually have a CD4 count of at least 800 cells per cubic milliliter of blood (about one drop). HIV usually causes CD4 counts to drop; a CD4 count that falls below 200 leaves the body much more vulnerable to other infections and sickness.

Chronic infection refers to the stage of infection after recent infection. At this point, the virus has fully established itself in the body.

Drug resistance occurs when HIV mutates in such a way that HIV medications no longer work to suppress the virus. A person's virus may become resistant to a whole group of drugs so that a new combination of HIV medications is necessary to control it.

Drug-resistance testing (genotyping/phenotyping) can show whether a person's virus is likely to be suppressed by each available HIV medication. A genotypic test looks for genetic mutations that are linked to drug resistance. A phenotypic test assesses which drugs will stop the virus from reproducing in a test tube. A drug-resistance test may not work for someone who is not on HIV medications or has a very low viral load.

Dual infection (or **coinfection**) occurs when a person is infected with two strains of HIV. That person may have acquired both strains simultaneously or one after the other at the time of initial infection.

HIV-1 is the type of HIV that is predominant worldwide. HIV-2 is found primarily in West Africa. Within HIV-1 and HIV-2, there are at least nine genetically distinct subtypes (or clades), including A, B, C, D, F, G, H, J, and K, with subtypes B and C being the most widespread. Sometimes, two viruses of different subtypes can recombine within a person's cells and create a new hybrid virus; for example, subtypes A and B may recombine to become an A/B mixture. Many of these new viral strains do not live for very long, but some survive to infect more than one person.

HIV medications (highly active antiretroviral therapy or HAART) are used to prevent the virus from reproducing inside the body. HAART keeps viral load relatively low, unless the virus becomes resistant to the drugs that person is taking. HAART usually consists of at least three drugs taken in combination and is also sometimes called antiretroviral therapy (ART).

HIV transmission most often occurs through sexual contact, particularly unprotected intercourse. HIV can also be transmitted through injection drug use in which contaminated needles and syringes are used, through transfusions of contaminated blood or blood products, through the placenta from the mother to the fetus, and (rarely) through breastfeeding.

Recent infection usually refers to the first year or two of infection after seroconversion has occurred.

Sequentially expressed dual infection

(SEDI) occurs when a second virus appears after a first has been established. The second virus may have been present at low levels in the body prior to its genetic appearance. On the other hand, the second virus may have been acquired after seroconversion through unprotected sex or other exposure (superinfection).

Seroconcordant refers to a partnership in which the partners have the same HIV status, i.e. both are HIV-positive or both are HIV-negative.

Seroconversion occurs when a person develops antibodies to HIV. This usually happens several weeks after exposure and infection. Most HIV tests are meant to detect antibodies to HIV, so an infected person will not test positive before seroconversion has happened.

Serodiscordant refers to a partnership in which one partner is HIV-positive and the other is HIV-negative.

Seroadaptation is the selection of sexual practices based on the partner's HIV status.

Serosorting is the selection of sexual practices based on the partner's HIV status. We believe that HIV-positive people frequently choose to have unprotected intercourse with other HIV-positive people rather than HIV-negative people or people of unknown HIV status. Over the past decade, men who have sex with men (MSM) in San Francisco have reported having more unprotected intercourse, but the incidence of HIV has not increased. We theorize that serosorting has allowed HIV incidence to remain stable despite this increase in what is usually considered "high-risk" sex.

Serostatus is a person's HIV status, either negative or positive. This refers, in particular, to

whether a person tests negative or positive for HIV antibodies. A seropositive individual is someone who has been infected with and has developed antibodies to HIV.

Superinfection, or reinfection, occurs when someone who is HIV-positive acquires another, possibly drug-resistant strain of HIV after the first virus has already been established (see seroconversion). We know that superinfection occurs in monkeys who are recently infected, but we do not know definitively whether it happens in humans. When it looks like someone has been superinfected because a second virus appears that is genetically different from the first, it is difficult to rule out the possibility that the second virus was there, but undetectable, all along. We hope to develop more sensitive measures as well as identify source partners to more accurately characterize superinfection. If superinfection is rare, or if it only happens in recent infection, it is important to identify the mechanisms that make an HIV-positive person immune to acquiring a second virus. This information may aid in the development of an HIV vaccine.

Viral load is the amount of HIV in an infected person's blood. It is usually reported as the number of copies of virus per milliliter of blood. If a person's viral load is "undetectable," it does not mean that there is no virus present in the blood; rather, it means that there are not enough viral copies for the test to count. A high viral load may indicate that a person's body is not controlling the virus well, and that person may decide to go on antiretroviral therapy (HIV medications). Viral load tests can also be used to diagnose HIV before seroconversion occurs.

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