

# what do we know about HIV superinfection?

### what is dual infection, co-infection, superinfection?

Dual infection is when a person is infected with two or more strains of HIV. That person may have acquired both strains simultaneously from a dually infected partner or from multiple partners. A different strain of the virus is one that can be genetically distinguished from the first in a "family" or phylogenetic tree.

Acquisition of different HIV strains from multiple partners is often called co-infection if all the virus strains were acquired prior to seroconversion, that is, very early before any HIV infection is recognized.

Acquisition of different HIV strains from multiple partners is called superinfection if the second virus is acquired after seroconversion when the first virus strain already has been established. Superinfection and re-infection mean the same thing.

Dual infections can be sequentially expressed, which can make co-infection look like superinfection. Sequentially Expressed Dual Infections (SEDI) may occur because immune responses against the predominant virus may allow other virus strains in the body to be expressed. Random shifts in evolving virus populations can also occur, which could look like superinfection even though dual infection was present from the beginning.

#### why does superinfection matter?

Superinfection is a concern because it may be a way for someone who is HIV+ to acquire drug resistance, and it may lead to more rapid disease progression.<sup>2,3</sup> Research on when superinfection may or may not occur could identify types of immune responses that may protect against infection. This could guide the development of HIV vaccines.

People who are HIV+ and have HIV+ partners often ask about superinfection. Public health officials need information about superinfection in order to craft messages that help people understand the possible risks of unprotected sexual intercourse among HIV+ persons, without creating undue anxiety that could undermine rewarding relationships between HIV+ persons and disclosure of HIV status with prospective new partners.

#### does superinfection occur?

Many scientists believe that superinfection can occur. Research in monkeys has indicated that superinfection with viruses like HIV can occur.<sup>4,5</sup> Sixteen people with SEDI (apparent superinfection) have been reported in the scientific literature, including injection drug users in Asia, women in Africa, and men in Europe and the US. Laboratory analysis in some of these reports suggested that the second virus that appeared in these individuals was not present earlier in the course of infection, which suggests superinfection. The sensitivity of these laboratory assays is limited, and source partners have not been identified, so there is no way to know for sure when the second virus was acquired.

#### who is at highest risk?

Ninety-five percent of apparent superinfection cases have occurred during the first three years of infection. Studies have found evidence of superinfection in 2 to 5% of persons in the first year of infection. 6-9 Intermittent treatment in acute or recent HIV infection may prolong superinfection susceptibility. 10,11

In contrast, studies in persons with longer term infection have found no evidence of superinfection. One study found no cases after 1,072 person-years of observation. <sup>12</sup> Another found none after 215 person-years of observation among intravenous drug users. <sup>13</sup> A third found none after 233 person-years and 20,859 exposures through unprotected sex. <sup>14</sup>

It is possible that people with very low viral load in their blood may be more susceptible to superinfection. Low viral load in the blood can occur during combination antiretroviral therapy or in "healthy non-progressors." Antiviral immune responses and viral interference is lower in persons with low viral load, so superinfection may occur more frequently. More research is needed to know for sure.

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## Says who?

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#### is it bad to have more than one virus?

Dual infection can have a harmful effect on the health of HIV+ persons. Superinfected individuals may have higher viral loads and lower CD4 counts, which causes more rapid disease progression.<sup>2,3</sup> Disease progression can accelerate after a second virus appears.<sup>1</sup>

Superinfection may also affect treatment of HIV, as it increases the likelihood of drug resistance. <sup>16</sup> HIV+ persons with dual infection may not respond as well to available antiretroviral medication due to resistant strains.

#### what don't we know?

There is a lot we still do not know about superinfection. First of all, we need to be more sure whether superinfection actually occurs between HIV+ persons. A definitive case of superinfection has not been documented, which would require that the timing of the second infection be traced to initiation of a relationship with a new sexual partner.

Second, we need to understand how and when superinfection occurs. Among researchers some consensus is developing about the idea that HIV+ persons in early infection--and particularly the first year of infection--may be at higher risk for superinfection than HIV+ persons with chronic infection.<sup>17</sup> We also should determine whether persons with suppressed viral load on treatment are susceptible to superinfection.

Third, we need to know how to protect against superinfection. If superinfection is rare, or if it only happens in recent infection, it is important to determine what mechanisms make an HIV+ person immune to acquiring a second virus. It would be important to know if exposure to different viral strains may provide protective immunity against superinfection.<sup>18</sup>

Lastly, we must continue to provide up-to-date scientific data on superinfection, its causes and consequences to HIV+ persons and healthcare professionals who work with them.

#### what can we recommend right now?

Counseling about superinfection should be based on understanding the individual's sexual relationships. Before providing advice about superinfection, the counselor should know whether the individual is in a continuing relationship with another HIV+ partner, whether the person routinely seeks out other HIV+ partners for unprotected sex, and whether there is disclosure of HIV status with prospective partners. This background should inform the discussion about the risks and benefits of sex among HIV+ partners. If the counselor does not have time to consider these personal issues, it would probably be best to simply say that "There is not enough information available about superinfection. If superinfection occurs at all, it probably occurs in the first few years after infection. After that, it may be rare."

Even less is known about superinfection as a result of sharing needles, although it is reasonable to expect that the same pattern of initial high risk followed by low risk during chronic infection may occur. However, because intravenous drug users are at high risk of hepatitis C infections from sharing needles, efforts to obtain clean needles through needle exchange should always be emphasized.

Interested persons should be referred to on-going research studies so that important gaps in information can be filled.<sup>19</sup>

People with multiple sexual partners, or partners with multiple partners, should be counseled regarding the risks of other sexually transmitted infections. Vaccination for hepatitis B and periodic testing for syphilis is warranted.

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