

Commentary

HIV transmission hunting – the chase for low risk events

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See article by Stürmer and colleagues on pp 729–732 of this issue.

The risk of sexual transmission of HIV by a patient with stable and fully suppressive antiretroviral therapy (ART) is admittedly very low, but the residual risk is difficult to quantify. The infrequency of case reports documenting sexual transmission despite fully suppressive ART is indirect evidence for the very low risk of transmission. Even if the risk is low, however, HIV transmission might still occur under optimal conditions of viral suppression in blood either by cell-associated [1] or compartmentalized [2] virus. Thus, documentation and publication of individual cases are paramount.

In this issue of *Antiviral Therapy*, Stürmer *et al.* [3] report the first case of apparent sexual transmission of HIV despite fully suppressive ART in the index case. Such an investigation demands persistence and much effort for which the investigators should be applauded. However, there are some caveats that need to be discussed and the limitations of this case report should prompt other investigators to maximize every effort to properly document similar suspected cases. In our own experience, all suspected cases of transmission during ART turned out to have another source. A similar observation has been reported by Zhu *et al.* [4].

To document the unlikely event of a sexual transmission under ART, two main conditions must be met. The first is the documentation of stable (>6 months) and fully suppressive (<50 copies/ml) ART during sexual exposure of the partner. The second is the documentation of molecular linkage of the viruses from both partners. The latter is usually performed by comparing the donor's and recipient's virus [5]. Phylogenetic analysis is a mandatory requirement for such a case report. Stürmer *et al.* [3] showed in their case report that the viral pair segregated together in phylogenetic trees and exhibited common amino acid signatures. This finding proves that the two viral strains are closely related and supports direct transmission from the index to the patient; however,

an infection by another epidemiologically linked third individual is only ruled out by sexual history, which is notoriously unreliable (for an instructive – and amusing – discussion of the pitfalls of sexual history taking, see Lewontin [6]).

The first condition, the documentation of a fully suppressive ART during the whole time of the sexual relationship is perhaps even more difficult to ascertain and relies on accurate clinical history and documentation. After interruption of treatment, HIV viral load rises rapidly, often to very high levels similar to those of primary HIV infection with concomitant risk of transmission [7]. Again, absence of interruption of ART can only be ruled out by history. Stürmer *et al.* [3] emphasize that the index case never interrupted ART.

However, the major weakness of their line of evidence is the lack of documentation of the negative test in the partner. The result is based on the patient's recollection of an anonymous HIV test obtained 5 years earlier. As the partner already had sexual relations with the index case during the first weeks of ART, it is possible that the couple had unprotected exposure before the viral load was suppressed.

The recollection of a non-documented HIV antibody test more than 5 years earlier is a considerable weakness of this report. However, the report by Stürmer *et al.* [3] reminds us to carefully continue to collect further information on potential cases of HIV transmission events during fully suppressive ART. Analogous to the situation with oral sex, where individual cases of oral transmission of HIV have been reported, an individual – even well-documented – case of sexual transmission during suppressive ART would not indicate that this practice is associated with a risk of sufficient magnitude to have public health implications. Nevertheless, it is important that each well-documented case is carefully summarized and reported in order to inform the

public about residual risks associated with unprotected sex during fully suppressive therapy.

The limitations of this case report underscore the importance of careful documentation. It is wise to keep a pre-treatment blood sample from all patients for later phylogenetic analysis. In addition, it seems prudent to obtain and document regular (for example, yearly) HIV test results in all partners of HIV-positive patients coupled with a brief intervention to discuss preventive behaviour. According to regular surveys in the Swiss HIV Cohort study, 15–20% of patients have unprotected sex with their steady partner, regardless of treatment status [8].

Disclosure statement

The authors declare no conflicts of interest.

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