

HIV-infected persons on effective antiretroviral therapy (and free of other STDs) are sexually non-infectious

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Having taken into consideration all scientific evidence, the Expert Clinical Commission on HIV/AIDS Treatment of the Federal Office of Public Health, and after great deliberation, the federal committee for issues related to HIV/AIDS has arrived at the following conclusion:

HIV-seropositive individuals on antiretroviral therapy with a fully suppressed HIV viral load (hereafter referred to as "fully suppressive antiretroviral therapy") and no additional sexually transmitted infections do not transmit HIV by sexual means.

This assertion is contingent on the following conditions:

- That the HIV+ individual is under the care of a treating physician and that s/he takes the medication exactly as indicated;
- That the HIV viral load is below the level of detection of common viral load tests ("undetectable") and has been for at least 6 months;
- That the HIV+ individual is not currently experiencing any other sexually transmitted infections.

Introduction

One of the tasks of the Committee consists of making public new information about the infectious nature of HIV+ individuals who are being successfully treated with antiretroviral therapy. The Committee would like to assuage the fears of both HIV+ and HIV- individuals in order to permit as many as possible of the estimated 17,000 HIV+ individuals living in Switzerland to live as close as possible a "normal" life.

Scientific basis and evidence

"Fully suppressive antiretroviral therapy" is defined as antiretroviral therapy (ART) that achieves a stably undetectable (<40 copies/ml) HIV viral load in the blood. "Stable" viral suppression and antiretroviral therapy are defined as having an HIV viral load below the limit of detection for 6 months or greater.

The Committee is cognizant of the fact that, from a strictly scientific point of view, biological and medical principles available to date have been unable to prove that effective antiretroviral therapy can prevent all instances of HIV

infection (in effect, it is simply not possible to prove the non-existence of an improbable but theoretically imaginable event). Be that as it may, it remains the point of view of the Committee and interested organizations that data available to date is sufficient to justify our message. The situation is comparable to that of 1986, when it was publicly communicated that HIV could not be transmitted by a kiss. Even though this assertion could never be irrefutably proven, more than 20 years of experience with HIV have nevertheless permitted us to support its very strong plausibility. Moreover, the facts and scientific criteria supporting the assertion that HIV+ individuals on fully suppressive antiretroviral therapy and not suffering from other sexually transmissible infections do not transmit HIV by sexual routes are clearly more favorable than those of 1986. Therefore, the Committee and interested organizations are of the opinion that currently available data are sufficient to justify this message.

Epidemiologic underpinnings

In the case of serodiscordant couples (one HIV+ and the other HIV-), the risk of HIV transmission depends on the viral load of the HIV+ persons [1] (fig. 1)

A longitudinal study of 393 serodiscordant heterosexual couples has shown that over 14 years of follow-up, none of the HIV- partners was infected by his or her HIV+ partner on a fully suppressive antiretroviral regimen, whereas among couples where the HIV+ sexual partner was not on treatment, the cumulative rate of HIV transmission approached 8.6% [2].

In a second longitudinal study of 93 serodiscordant couples, among whom 41 HIV+ partners commenced antiretroviral therapy, 6 individuals became HIV infected; the 6 sexual partners of HIV+ individuals not on antiretroviral therapy and with a plasma HIV viral load of 1,000 copies/ml or greater [3].

Of the 62 serodiscordant couples that had unprotected sexual relations in order to procreate (HIV+ man on fully suppressive antiretroviral therapy), not one woman became infected [4].

Mother-to-child HIV transmission also depends on the maternal viral load and can be avoided by means of effective antiretroviral therapy [5-8].

According to the San Francisco's Men's Health Study, the incidence of HIV in the homosexual community (men who have sex with men, or MSM) between 1994 and 1996 was 0.12 (infections per couple). Fully suppressive antiretroviral therapy has been available since 1996. From 1996 to 1999, the incidence of HIV fell to 0.0048, even though far from all HIV+ men had been treated with antiretroviral therapy [9].

The HIV transmission rate is clearly more likely during the acute phase of infection ("primary infection"). Several studies have demonstrated that a large percentage of new HIV infections can be linked to a sexual partner who has only recently become HIV-infected [10-12].

Sexually transmissible diseases (STDs) aggravate the risk of HIV transmission (in the absence of fully suppressive antiretroviral therapy). Certain mathematical models, for example, show that in this context, syphilis infection, notably, plays an important role in the epidemiologic picture [13].

Within only a few days or weeks after treatment interruption, HIV viral load rises rapidly. At least one case of HIV transmission has been documented to have occurred under such circumstances [14].

Biological underpinnings

Antiretroviral therapy leads to a diminution of the concentration of HIV RNA in genital secretions to levels below the limit of detection [15-17].

As a general rule, the concentration of HIV RNA detected in vaginal secretions is lower than that detected in the blood; moreover, it is no longer detectable in vaginal secretions once effective antiretroviral therapy has produced its effect. In principle, the HIV viral load in blood plasma rises *before* the viral load in genital secretions [18].

By contrast, HIV DNA in cells of genital secretions can still be detected despite the presence of suppressive antiretroviral therapy [15, 19-21]. This, however, is not indicative of infectious virus in itself. HIV-infected cells in semen fail to incorporate DNA at the long terminal repeat (LTR), signifying that this virus is not actively propagating [22].

The risk of transmission is related to the concentration of HIV RNA in the sperm: when the presence of HIV RNA is undetectable, the risk of transmission is nearly zero [23] (fig. 2). Referring back to the biological underpinnings enumerated above, fully suppressive antiretroviral therapy significantly reduces the risk of transmission by this route.

During primary HIV infection, the level of HIV in genital secretions soars [24], which would explain the heightened risk of transmission during this early phase.

Presence of an additional STD (urethritis, genital ulcers) increase the HIV viral load present in genital secretions (but not in the blood) for several weeks; thereafter, when the STD is effectively treated, the HIV viral load in genital secretions falls [25]. HIV viral load in semen can, nevertheless, slowly rise even if the person experiencing an STD (urethritis) is following an effective antiretroviral regimen. This progression remains very low and is clearly inferior to that which would be the case in the absence of antiretroviral therapy [26].

Conclusion

In the presence of effective antiretroviral therapy, no free virus is detectable in the blood or genital secretions. All epidemiologic and biologic evidence

indicates that the successful use of antiretroviral therapy allows us to rule out any significant risk of HIV transmission.

In the case of full virologic suppression, the relative risk of HIV transmission by sexual contact in the absence of condom use is clearly inferior to 1 in 100,000.

If the relative risk cannot be entirely eliminated from a scientific point of view, the Committee and interested organizations judge this risk to be negligible.

Importance and field of application of the message according to which: "STD-free, successfully antiretroviral treated HIV-positive individuals do not transmit HIV by sexual routes"

Significance for physicians/care providers

This information aimed at treating physicians is designed to help establish whether or not the seropositive patient is at risk transmitting HIV via sexual routes. The patient will not transmit HIV by sexual routes provided that:

- That the HIV+ individual is under the care of a treating physician and that s/he takes the antiretroviral medication exactly as indicated;
- That the HIV viral load is below the level of detection of common viral load tests ("undetectable") and has been for at least 6 months;
- That the HIV+ individual is not currently experiencing any other sexually transmitted infection.

The decision to commence treatment with antiretroviral therapy must still be made according to current treatment guidelines. At this time, it is not expected that the commencement of antiretroviral therapy with the sole goal of preventing transmission: in addition to the costs of such an approach, it is also uncertain that HIV+ individuals not in need of antiretroviral therapy will be sufficiently motivated over the long term to adhere to the strict requirements of such therapy.

Treatment interruptions and misuse run the risk of the development of drug resistant viral strains. For this reason, it would not only raise the possibility of creating a public health threat but also would jeopardize the health of the patient. For this reason, the initiation of antiretroviral therapy for the sole reason of prevention could only be indicated in cases of highly motivated seropositive patients. It is therefore not recommendable to try to convince a patient to initiate antiretroviral therapy solely for reasons of prevention.

Significance for suppressed HIV+ individuals on effective antiretroviral therapy with no concurrent STDs

For HIV+ individuals on fully suppressive antiretroviral therapy who are in a longtime, stable relationship with an HIV- partner and have no other (active)

sexually transmitted diseases, it is important that they know that they do not put their partner in danger of becoming HIV-infected so long as they are strictly adherent to their antiretroviral therapy regimen and are regularly followed by their treating physician. Once having fully understood these conditions and criteria, it is up to the *seronegative* partner to decide whether or not the couple would like to suspend other measures of protection.

Significance for individuals not in a stable relationship

For HIV+ individuals on fully suppressive antiretroviral therapy, it is important that they know that they cannot transmit the virus to their sexual partners so long as they are strictly adherent to their antiretroviral therapy regimen, have no other (active) sexually transmitted diseases, and are regularly followed by their treating physician.

Importance for HIV/AIDS prevention efforts

The message contained here within (that HIV+ individuals with full viral suppression on antiretroviral therapy cannot transmit HIV through sexual acts) in no way changes the HIV prevention strategies in place in Switzerland. In fact, with the exception of monogamous seropositive couples on fully suppressive antiretroviral therapy regimens, the standard measures of protection must be followed at all times. Individuals not in a stable relationship must, above all else, protect themselves: a seronegative individual must never fail to take preventive measures during a sexual encounter. If s/he comforts himself/herself with the oral declaration of his/her partner such as, "I am HIV negative" or "I am HIV positive but have an 'undetectable' viral load," s/he courts the risk of becoming infected with HIV because there is no way (in that moment) of verifying these facts. It is in exactly these types of situations that the responsibility for his or her own health cannot and must not be relegated to altruism.

In the case of stable relationships where one partner is HIV+ and the other HIV- ("Serodiscordant"), the decision whether or not to suspend the use of other protective measures is incumbent on the *seronegative* partner. For it is s/he who, if against all odds becomes infected with HIV, will suffer the consequences.

Importance for jurisprudence

Courts and other legal bodies must take into account that "HIV+ individuals with full viral suppression on antiretroviral therapy cannot transmit HIV through sexual acts" when ruling on cases of the reprehensible aspect of intentional HIV infection. From the point of view of the Committee, a non-protected sexual encounter between an HIV- individual and an HIV+ individual on fully suppressive antiretroviral therapy who is adherent to his/her treatment and not suffering from another STD cannot be said to be willingly attempting to spread a dangerous disease, according to article 231 of the Swiss Penal Code, nor to be willingly inflicting grave bodily harm, according to articles 122, 123 or 125 of the same code.

Medical management of patients on antiretroviral therapy

At the time of the next consult, the treating physician would raise the issue with fully suppressed patients on antiretroviral therapy about the intransmissibility of HIV in HIV+ patients adherent to a fully suppressive antiretroviral therapy regimen, and counsel them according to the current state of their relation. The sexual partner of the patient should be present during this discussion, who must also bear in mind the current legal situation.

The medical interview

Medical discussion with a stable, serodiscordant couple (both partners must be present and participate) should explain in detail the conditions by which a seropositive person is deemed non-infectious:

- The HIV+ persons must consistently adhere to the antiretroviral therapy regimen and the effectiveness of the therapy be monitored at regular intervals by his or her treating physician according to officially accepted guidelines
- The viral load must be below the limit of detection (<40 copies/ml) for a minimum of 6 months
- The HIV+ person must not be suffering from any other sexually transmitted infections

Over the course of the interview, the couple must understand that from the moment they decide to suspend other protective measures against HIV transmission, adherence to the prescribed antiretroviral therapy becomes of utmost importance in their relationship. At the same time, the couple must also understand the importance of avoiding any additional STDs and must establish rules regarding sexual contact outside of their relationship.

Heterosexual couples who decide to suspend protective measures with condoms must additionally think about other means of contraception they might want to employ if they do not wish to conceive. They must therefore consider:

- The possible drug-drug interactions between hormonal contraceptive measures and anti-HIV medications that may risk weakening the effect of the contraceptive medicines;
- The teratogenic potential (possibility of damage to fetus) of some of the antiretroviral medications; specifically, the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz (trade name Sustiva but also one of the constituent components of the increasingly popular once-a-day pill Atripla) should be avoided if the couple wishes to conceive

Artificial insemination via sperm "lavage" (sperm washing) is no longer indicated in the presence of fully suppressive antiretroviral therapy where the only goal is to avoid transmission of HIV.

The medical interview between treating physician and couple should give each of the partners the opportunity to ask follow-up questions. The physician must also understand that it is up to the *HIV-negative partner* (and not the HIV+ partner!) to decide whether or not s/he would like to suspend the use of condoms; the interview should help the couple to define together how they will manage adherence to antiretroviral therapy, sexual contacts outside of the relationship (risk of STDs) and, where appropriate, the desire for a child. The physician should review these agreed upon ground rules and the success or failure at adhering to them at each subsequent clinic visit.

HIV+ individuals on fully suppressive antiretroviral therapy with no other (active) STDs with no stable partner should be informed by their treating physician that they cannot transmit HIV so long as they adhere to their antiretroviral therapy regimen. This could come as a great relief to them. Many studies show that the fear of infecting sexual partners makes the sexual lives of HIV-positive very difficult. In the interest of public health, however, physicians have continued to recommend that HIV+ individuals protect themselves ("safer sex") during occasional and/or anonymous sexual encounters in order to minimize the risk of acquiring other STDs. Depending on the frequency of these contacts, agreed upon regular spot-checking and testing for the possible acquisition of additional STDs might also be reasonable. The parties in question should be sensitized/educated about the presenting symptoms of the various STDs.

Internet sites and brochures are available for treating physicians who would like to seek further advice from AIDS service organizations. The Committee encourages them not to hesitate to take advantage of these resources.

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Figures & illustrations

Figure 1

Viral load and risk of transmission

Quinn et al. New England Journal of Medicine 2000, 342:921-9.

Figure 2

HIV viral load in sperm and the risk of transmission

Chakraborty et al. AIDS 2001, 15:621-7.