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AIDS 2006, **20**:000–000

HIV-discordant couples and parenthood: how are we dealing with the risk of transmission?

Parenthood is a strong, biologically motivated, instinctive desire. In the past, individuals infected with HIV struggled with the dilemma of a limited life expectancy and the strong wish to reproduce themselves. The risk of viral transmission to uninfected partners and offspring posed an additional barrier to conception. Many couples have practised unprotected intercourse to conceive, despite the risk of HIV transmission. The introduction of antiretroviral therapy with dramatically improved life expectancy has resulted in a resurgence of interest in parenting by HIV-affected couples.

Since its introduction by Semprini *et al.* [1] in 1992, several European antiretroviral therapy clinics have adopted the approach of intrauterine insemination with processed semen and other risk-reduction measures to minimize the risk of HIV transmission in discordant couples with infected male partners. More than 4500 inseminations have been performed without the apparent transmission of HIV to the uninfected female partner (manuscript in preparation). Although semen washing is relatively simple and inexpensive, polymerase chain reaction (PCR) testing of the final sperm aliquot to ensure HIV removal, and intensive medical supervision, render the final costs above the financial means of most HIV-discordant couples. In addition, patients may often need to travel long distances to reach these specialized units.

In Milan and St Gallen, approximately 30% of couples did not start the insemination process after initial counseling. Another 30% subsequently withdrew after a number of failed cycles. A recent survey from the Milan centre involving 500 HIV-discordant couples who participated in the insemination programme found that almost half of the couples who did not conceive with artificial insemination attempted spontaneous conception through unprotected intercourse, and at least one infection occurred. The percentage of spontaneous conception attempts increased up to fivefold in couples residing a long distance from the centre. Finally, reproductive assistance for HIV-discordant couples is not widely available outside of Europe, including regions of the world with the highest HIV prevalence. The number of HIV-discordant couples worldwide practising unprotected sex for the purpose of conception could number in the millions.

The counseling provided to HIV-discordant couples seeking assisted reproduction at these centres includes a discussion of strategies aimed at maximizing protection

from HIV transmission (such as adoption, intrauterine insemination or in-vitro fertilization and intracytoplasmic sperm injection with processed semen), but also includes important information on other risk-reduction measures that draw on recent advances in therapeutics and a scientific understanding of factors underlying HIV transmission. We propose that this information be provided to all HIV-discordant couples seeking reproductive advice. Ideally, counseling should include a discussion of what is known, and the effectiveness of each strategy. Unfortunately, at present, data on the efficacy of most of the risk-reduction strategies listed below are unavailable as there has been no systematic data collection on how often these measures are used and with what outcomes.

The possible HIV risk-reduction measures for HIV-infected men with HIV-uninfected partners can be divided into five categories: (i) Optimization of the chances of conception. Fertility should be confirmed in both partners; couples should be counseled to practise unprotected intercourse only during the fertile window of a woman's cycle, identified by luteinizing hormone peak measurement in the urine when possible. (ii) Suppression of viral load. HIV transmission risk is related to peripheral and seminal HIV viral load. Men with peripheral viral loads greater than 1000 should be treated with antiretroviral therapy to suppress the seminal viral load and transmission risk. Confirmation of undetectable HIV RNA in the seminal plasma is recommended, when possible. (If HIV viral load cannot be suppressed, sperm wash/intrauterine insemination should be recommended.) (iii) The exclusion and treatment of genital tract infections or inflammatory processes in both partners and the avoidance of products and practices that irritate the vaginal epithelium. Bacterial vaginosis and infections with herpes simplex virus 2, *Trichomonas vaginalis*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Treponema pallidum* can increase HIV transmission [2]. Vaginal products that contain nonoxynol-9 or other irritants [3], and the practice of dry sex [4], anal intercourse and other behaviours that lacerate genital mucosal surfaces are other risk factors for HIV transmission and should be avoided. (iv) Experimental approaches to reduce further the susceptibility of the uninfected woman should be discussed, with the proviso that data supporting their potential efficacy are preliminary: (a) Pre-exposure prophylaxis [5,6]. Tenofovir was recently recommended as pre-exposure prophylaxis because of the limited presence of tenofovir resistance,

its rapid mode of action during the pre-integration phase of viral replication and its long intracellular half-life (> 60 h) [7]. Given the rapid uptake of tenofovir, we suggest one tablet of tenofovir taken orally 2 h before the unprotected sex act; (b) The vaginal application of estriol gel during the first 5 days of the menstrual cycle. This method has been shown to protect macaques from vaginal challenge with SIV by increasing the thickness of the vaginal epithelium [8]. The gel has been widely used by postmenopausal women and appears to be non-toxic and not irritating. (v) Immediately discontinue unprotected intercourse should pregnancy occur because seroconversion during pregnancy greatly increases the risk of fetal infection. Also, retest the partner for HIV during pregnancy as the use of antiretroviral drugs reduces the risk of transmission to the baby [9].

The purpose of this commentary is to start a discussion about the appropriateness of such counseling, and to call for a central registry that collects information from physicians worldwide about their individual experience with the reproductive counseling of HIV-discordant couples.

Pietro L. Vernazza^a, Lital Hollander^b, Augusto E. Semprini^{b,c}, Deborah J. Anderson^d and Ann Duerr^e,
^a*Division of Infectious Diseases, Department of Medicine, Cantonal Hospital St Gallen, Switzerland,*
^b*ESMAN Medical Consulting, Milan, Italy,* ^c*Department of Obstetrics and Gynaecology, University of Milan Medical School, Milan, Italy,* ^d*Center for AIDS Research, Harvard Medical School, Boston, MA, USA,*

and ^e*Fred Hutchinson Cancer Research Center, Seattle, WA, USA.*

Received: 28 October 2005; accepted: 17 November 2005.

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