EDITORIAL COMMENT

Antiretrovirals for safer conception for HIV-negative women and their HIV-1-infected male partners: how safe and how available?

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We have entered a new era in which antiretroviral agents have been demonstrated to be highly effective in preventing HIV-1 infection, especially in serodiscordant couples. The HPTN-052 randomized, controlled trial (RCT) of early versus delayed antiretroviral therapy (ART) for the HIV-1-infected persons in sexual partnerships with HIV-negative persons demonstrated at least a 96% reduction in HIV-1 transmission in the 1763 couples studied in Africa, Asia and South America [1]. The Partners PrEP RCT, conducted among 4758 HIV-1-serodiscordant couples in Kenya and Uganda, showed that when used as preexposure prophylaxis (PrEP) by the HIV-negative partner, daily tenofovir disoproxil fumarate (TDF) and daily TDF/emtricitabine (FTC) were 62 and 73% effective, respectively, in preventing HIV-1 acquisition [2]. These robust effectiveness findings provide a strong basis for the use of antiretroviral agents for prevention, both to reduce the infectiousness of HIV-1-infected persons and to reduce the susceptibility of HIV-negative persons.

In this issue of *AIDS*, Vernazza et al. [3] described their work with HIV-negative women and their HIV-1-infected male partners who attempted to conceive through intercourse scheduled at the time of maximum fertility, determined by luteinizing hormone measurement. To reduce the risk of HIV-1 transmission during sex, men were treated with ART that led to undetectable HIV RNA in plasma (<50 copies/ml) for at least 6 months and there were no active genital infections. Women were provided two doses of PrEP (either TDF or TDF/FTC) to take 12 and 36 h before intercourse. Couples in this cohort could have multiple episodes of timed intercourse per attempted conception. Altogether, 53 partnerships (including seven couples twice) had 244 documented episodes of vaginal intercourse without barrier methods; no woman became HIV-1-infected. Overall, the successful conception rate was 75%, including 26% for the first attempt and 66% after five attempts. Older women were less likely to conceive.

Antiretroviral therapy has rendered HIV a treatable condition and people on effective therapy can have a life expectancy that approaches that of HIV-uninfected people [4,5]. Not surprisingly, an increasing number of people in HIV-1-discordant partnerships desire conception [6–8]. The current study by Vernazza et al. raises several important issues, two that are especially critical. First, how safe is this method of timed intercourse, employing ART and PrEP to prevent HIV infection; and second, how can these findings be translated to allow safe conception for the growing number of HIV-negative women in the world with HIV-1-infected partners?

The precise risk of HIV-1 acquisition associated with conception under these conditions remains impossible to quantify. However, the 96% reduction in HIV-1 transmission documented in the HPTN 052 RCT provides a strong rationale for this approach [1]. It is important to...
note that the only HIV-1 transmission event that occurred in HPTN 052 while the index partner was on ART occurred soon after the initiation of ART, before there was complete viral suppression [9]. The Partners PrEP findings of 62 and 73% reductions in HIV acquisition on antiretroviral PrEP strengthen the basis for this approach [2], although the optimal PrEP regimen for safer conception remains to be established. Taken together, these results are reassuring and should give HIVdiscordant couples worldwide new options for safer conception.

We must, however, approach this opportunity with transparency and caution. Vernazza et al. [3] described a conception algorithm, not a clinical trial result. As the author indicates, all we can do is provide couples with the best available risk estimations under idealized conditions. Whereas this approach may render conception safer, ongoing intercourse during pregnancy by the female partner or a partner outside the relationship holds considerable risk. Pregnant women appear to have increased susceptibility to HIV-1 [10] and HIV-1 acquisition outside of the primary relationship occurred commonly in other studies of discordant couples [1,11]. Moreover, the suppression of HIV-1 in the male genital tract is incomplete even when blood viral levels are below detection [12]; the importance of such residual virus to HIV transmission is unknown. And finally, it will be very difficult to prove that neither partner has acquired a genital infection during the conception cycle; other sexually transmitted infections increase the risk for HIV-1 transmission [13,14]. Our obligation is to provide this information to discordant couples in a clear and transparent way and to provide counseling and clinical support to allow couples to decide whether or not to use these new tools to make conception as safe as possible.

The current study was conducted in the richly resourced setting of Switzerland [3]. Many challenges must be considered when attempting to translate this approach to the resource-limited countries where the vast majority of HIV-1-discordant couples live. Few clinical settings in such countries, especially in Africa, are currently prepared to provide the support necessary to minimize HIV-1 transmission risk during conception. Meanwhile, clinicians globally require management guidelines that will allow appropriate intervention for HIVdiscordant couples [15,16]. In South Africa, fertility guidelines have been developed by the HIV Clinicians Society to assist clinicians in low and medium-resourced settings [17]. Whereas ART and PrEP are promising tools for safer conception for HIV-serodiscordant couples provides yet another good reason for people to learn their HIV status and, if HIV-infected, access prevention, care and treatment programs.

The era of antiretroviral agents for prevention offers great hope for our ability to limit HIV transmission and end the pandemic [18]. Safe conception is the desire and dream of many women in communities affected by HIV including those in known discordant partnerships. ARTand PrEP can contribute greatly to safer conception; however, we have much to do to learn how best to employ these powerful tools and strengthen the systems in resource-limited settings to allow women and couples to benefit maximally.

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Conflicts of interest
There are no conflicts of interest.

References