

## Treatment for HIV prevention, one couple at a time

The belief that treatment of HIV infection will reduce the spread of the virus was inspired by a series of observational studies of HIV serodiscordant heterosexual couples, in which HIV transmission was reduced or eliminated if the sexual partner with HIV was given antiretroviral therapy (ART),<sup>1</sup> and by the results of the HPTN 052 multinational randomised controlled trial.<sup>2</sup> However, these studies included few homosexual couples; therefore, the risk of HIV transmission from condomless anal intercourse could not be addressed.

Bavinton and colleagues<sup>3</sup> report on the Opposites Attract study of HIV transmission in serodiscordant homosexual couples living in Australia, Brazil, and Thailand. 343 couples were followed up for 588.4 couple-years. More than 75% of HIV-positive partners had durable suppression of HIV to less than 200 copies per mL with ART. Bavinton and colleagues detected no phylogenetically linked HIV transmission events in 16 800 acts of condomless anal intercourse reported. Three participants acquired HIV from a

sexual partner outside the study. These results confirm the earlier work of Rodger and colleagues<sup>4</sup> who followed up 340 homosexual couples for 439 couple-years and noted no linked HIV transmission events. The published research seems to contain no reliable reports of HIV transmission within couples when HIV replication in the infected partner has been durably suppressed.

The efficacy of HIV treatment to prevent HIV transmission deserves further examination. Although ART suppresses HIV in blood, copies of HIV can routinely be recovered from semen.<sup>5</sup> The success of treatment as prevention suggests that HIV detected in semen (despite treatment) is either not replication competent or does not reach a crucial concentration required for transmission, or that antiviral drugs concentrated in semen inhibit transmission after ejaculation. Development of strategies to eliminate HIV from male and female genital tracts remains important to cure HIV infection.<sup>6</sup>

Treatment as prevention is effective despite frequent sexually transmitted infection (STI) coinfections. In the Opposites Attract study,<sup>3</sup> a third of HIV-positive partners and a quarter of HIV-negative partners acquired STIs during follow-up. In the absence of HIV treatment, STIs amplify transmission of HIV by increasing HIV shedding and lowering the threshold for acquisition;<sup>7</sup> however, ART seems to abrogate these risks. The benefits of ART are also seen when the emtricitabine and tenofovir disoproxil fumarate combination is used as pre-exposure prophylaxis (PrEP). Despite the high incidence of STI coinfections,<sup>8</sup> ART as PrEP reliably prevents HIV acquisition.

A third of HIV-negative partners reported daily use of PrEP during follow-up. Nonetheless, in 232.2 couple-years of follow-up in which condomless anal intercourse was reported and PrEP was not used, no transmission events were detected. It has been argued that serodiscordant couples should use PrEP when ART is initiated<sup>9</sup> because HIV transmission events have been observed during this window of time.<sup>10</sup> Additionally, reliable viral suppression in a HIV-positive individual depends on selection of appropriate agents and patients' adherence to medications. ART delivered through long acting injection agents or implants might have an important role in the management of serodiscordant couples.

Treatment of HIV for prevention has become the mainstay of HIV prevention worldwide, and seems to have decreased HIV incidence in many countries.<sup>11</sup> However, such benefit is realised one couple at a time. The Opposites Attract<sup>3</sup> and PARTNER<sup>4</sup> studies show the benefits of treatment as prevention to homosexual couples and in HIV prevention during condomless anal intercourse. Furthermore, detection and treatment of HIV infection improves quality of life and life expectancy. As shown in this study<sup>3</sup> and other studies,<sup>1,2,4</sup> successful treatment of HIV reduces the risk of sexual transmission to a negligible level. The Undetectable=Untransmittable campaign<sup>12</sup> was launched to inform people with HIV that treatment eliminates contagion, which should reduce stigma.

The findings from Opposites Attract further contribute to our understanding of the prevention of transmission of HIV, and to the wellbeing of people with HIV infection.

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- 1 Muessig KE, Cohen MS. Advances in HIV prevention for serodiscordant couples. *Current HIV/AIDS Reports* 2014; **11**: 434–46.
- 2 Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; **365**: 493–505.
- 3 Bavinton BR, Pinto AN, Phanuphak N, et al. Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. *Lancet* 2018; published online July 16. [http://dx.doi.org/10.1016/S2352-3018\(18\)30132-2](http://dx.doi.org/10.1016/S2352-3018(18)30132-2).
- 4 Rodger AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA* 2016; **316**: 171–81.
- 5 Kalichman SC, Di Berto G, Eaton L. Human immunodeficiency virus viral load in blood plasma and semen: review and implications of empirical findings. *Sex Transm Dis* 2008; **35**: 55–60.
- 6 Gantner P, Ghosn J. Genital reservoir: a barrier to functional cure? *Curr Opin HIV AIDS* 2018; published online May 29. DOI:10.1097/COH.0000000000000486.
- 7 Galvin SR, Cohen MS. The role of sexually transmitted diseases in HIV transmission. *Nat Rev Microbiol* 2004; **2**: 33–42.
- 8 Molina JM, Charreau I, Spire B, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. *Lancet HIV* 2017; **4**: e402–10.
- 9 Baeten JM, Heffron R, Kidoguchi L, et al. Integrated delivery of antiretroviral treatment and pre-exposure prophylaxis to HIV-1-serodiscordant couples: a prospective implementation study in Kenya and Uganda. *PLoS Med* 2016; **13**: e1002099.
- 10 Eshleman SH, Hudelson SE, Redd AD, et al. Treatment as prevention: characterization of partner infections in the HIV Prevention Trials Network 052 Trial. *J Acquir Immune Defic Syndr* 2017; **74**: 112–16.
- 11 UNAIDS. UNAIDS data 2017. Geneva: UNAIDS, 2017.
- 12 The Lancet HIV. U=U taking off in 2017. *Lancet HIV* 2017; **4**: e475.