

## DISCORDANT COUPLES

# HIV-DISCORDANT COUPLES: AN EMERGING ISSUE IN PREVENTION AND TREATMENT

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An increasingly encountered phenomenon in research and clinical management of HIV is HIV discordance, the situation where one member of a sexual partnership is HIV infected, while the other is uninfected. This situation has wide clinical and research implications. In particular, seronegative partners within discordant relationships are a particularly high-risk group for HIV acquisition; a high proportion of new HIV infections in mature generalised epidemics is likely to occur within discordant couples.<sup>1</sup> In this overview we will examine some of the biological and socio-behavioural correlates of discordance. As identification of the joint serostatus of a couple poses particular challenges for counselling and testing, we will describe the model for couples counselling developed by the Centers for Disease Control and Prevention, which we use at our centre, and some of the lessons we have learned in conducting couples counselling since the establishment of a couples counselling centre at the Perinatal HIV Research Unit (PHRU) in April 2004. Lastly, we will also discuss two clinical issues that frequently arise, namely dealing with the desire for children and HIV prevention options.

### THE TSWARISANANG COUPLES CENTRE

South Africa, with one of the highest HIV prevalence rates in the world, has a generalised heterosexual epidemic. Voluntary counselling and testing (VCT) is an important component of HIV prevention strategies. The traditional clinic-based VCT has been more accessible to women. In 2004, the PHRU established a couples HIV counselling centre (Tswarisanang Centre), possibly the first of its kind in South Africa. Between April 2004 and February 2006, 1 425 couples have received couples HIV counselling and testing (CHCT). The mean age of couples entering the service was 30.7 years. Only 238 (17%) of the couples were formally married. Of the couples 452 (32%) were discordant, 671 (47%) were concordant negative, and 302 (21%) were concordant positive. Of the 452 couples who were discordant, the male was positive in 326 cases (72%) and the female in 126 (28%). While these figures may not be representative of the broader Soweto community, given the self-selected nature of the couples presenting for CHCT, they are nonetheless instructive. CD4

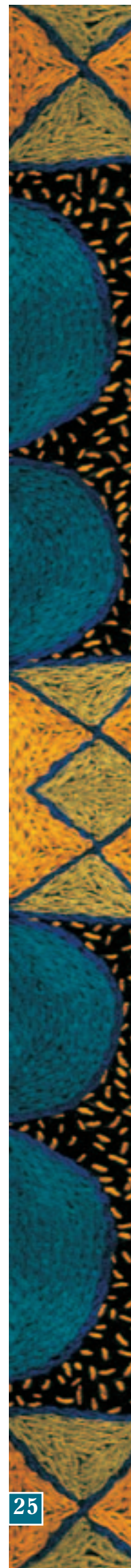
counts were available for the positive partner in 210 of the discordant couples, the median CD4 count being 379/ $\mu$ l (interquartile range 230 – 566/ $\mu$ l). Of the HIV-positive partners in the discordant relationships 185 (87%) were also herpes simplex-2 (HSV-2) positive.

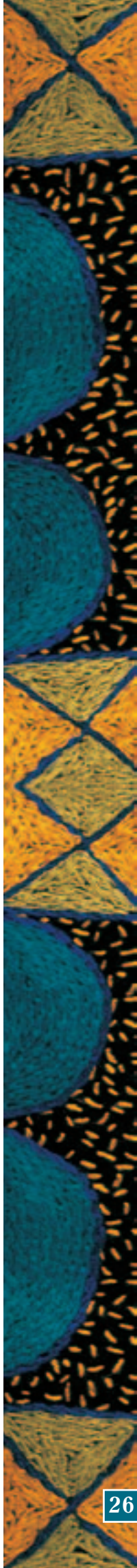
### CORRELATES OF HIV DISCORDANCE

A number of biological factors have been described that appear to modify the chances of transmission within a couple. The chances of transmission have been shown to increase with increasing viral load in several studies.<sup>2-4</sup> The level of HIV in plasma has been noted to be lower in HIV-positive men in discordant relationships compared with men in HIV-concordant relationships.<sup>2</sup> The sex of the uninfected partner may modify the risk of transmission. In prior North American or European studies, the rate of male-to-female transmission has been noted to be greater than that of female-to-male transmission (reviewed in<sup>5</sup>). However, in developing countries this asymmetry is not noted, and the efficiency of female-to-male transmission appears far greater, in some instances exceeding male-to-female transmission.<sup>6</sup> Male susceptibility to infection appears to be attenuated by circumcision, which has been shown to be associated with an approximate halving of the odds of concordance among 221 couples participating in an observational study in four African cities.<sup>7</sup> The finding that circumcision can reduce the risk of male acquisition of HIV has since been confirmed in a randomised controlled trial.<sup>8</sup>

Prior sexually transmitted infections, in particular genital ulcer disease, and serological presence of infection with HSV-2 have also been shown to be highly associated with concordance.<sup>3,9</sup> In the four cities study, HSV-2 status of the couple was the only factor that remained significantly associated with concordance. In couples where both members have serological evidence of HSV-2 infection, the odds of HIV concordance were 8.6-fold that of couples where neither partner was HSV-2 infected.<sup>7</sup>

A wide number of immunological and virological factors have been investigated for their role in efficiency of HIV transmission between partners, including viral subtype, stage





of HIV infection, sharing of human leukocyte antigen or HIV co-receptor gene alleles, and the presence of serum HIV-specific IgA.<sup>3,6,10-14</sup> However, the relative contribution of each of these multiple factors is unclear.

Social or behavioural factors may also influence the concordance of HIV results within couples. These may broadly be divided into factors that affect the transmissibility of HIV between couples per sex act and factors influencing the number of sex acts during which exposure may occur. Examples of the former include use of condoms or other barrier methods and certain sexual behaviours, such as sex during menstruation or 'dry sex' (use of vaginal drying agents). Examples of the latter include the frequency of intercourse and duration of the relationship. Sexual activity outside of the partnership is another critical aspect.

Partnership dynamics that may determine risk behaviour within partnerships include such concepts as emotional closeness, communication, power, duration, and concurrency.<sup>15</sup> The interaction between relationship dynamics and condom use or concurrent partnerships may be complex. Knowledge of HIV status, receipt of voluntary counselling and testing, and fertility desires are further considerations when approaching the social or behavioural aspects of HIV concordance. Condom use within the marriage has been associated with reductions in concordance in several studies.<sup>2,7,16</sup> However, as highlighted by several authors, condom use is unusual prior to HIV testing.<sup>3,17</sup> Importantly, condom use has been noted to increase substantially after CHCT, although correlation of self-reported rates of condom use with biological markers (such as sperm seen on a vaginal smear, pregnancy, or HIV transmission) indicates that substantial underreporting of unprotected intercourse persists.<sup>18,19</sup> Concurrent partnerships raise the chances that one or more members of a couple will be infected with HIV, or that the couple will have concordant positive results.<sup>2,16,20</sup>

### COUPLES HIV COUNSELLING AND TESTING

The majority of South Africans living with HIV/AIDS do not know their status, as rates of testing are still very low owing to limited access. This leads to a common situation where one member of a couple will assume, in the absence of a test result, that their results are the same as their partner, a phenomenon known as 'testing by proxy'.<sup>21</sup> Clearly this position does not recognise the possibility of discordant results. Hence, one of the key features of CHCT is to explore communication around sexual activity by each member of the couple, and that partners support each other during CHCT, a notable difference to individual VCT. A key condition of CHCT is that partners test and receive their results together. All phases of CHCT are conducted with both members of the couple present. This avoids the dilemma faced by individuals learning they are HIV positive in individual VCT and having to disclose these results to a partner who may not be adequately prepared. Owning the results together may help reduce problem situations, blame and possible violence. CHCT also assists the couple to make decisions and to plan adequately for the future.

As a new strategy, CHCT presents its own challenges and advantages. CHCT uses a risk-reduction model, and the presentation of results to the couple together facilitates the introduction and planning of prevention, tailored to the joint serostatus. In South Africa the adoption of CHCT has been a recent event, much assisted by national campaigns such as the emphasis on CHCT by Khomanani (Fig. 1).

Our initial experience indicates that deciding to test together was a mutual decision for the majority of couples.<sup>22</sup> The most common reasons cited for attending CHCT were that the couple are planning a family, want to find out HIV status, or attend as a sign that they support each other. Our impression is that, to some extent, individuals may use CHCT as a means of disclosure of a prior test result to their partners. Our centre has provided training in CHCT to over 100 local counsellors. In that undertaking we have noted that, while couples generally do not express incorrect beliefs regarding discordance at the time of CHCT, dealing with 'myths' regarding discordance is an important aspect of counsellor training. Examples of these 'myths' include the concept of a hidden infection not detectable by HIV tests, that the negative partner may be in the 'window period', the thought that transmission is a consequence of 'rough sex' and that 'gentle sex' will protect HIV-negative partners, belief in protection by God, or simply denial that discordance as a phenomenon exists.<sup>23</sup>

## CLINICAL ISSUES FOR HIV-DISCORDANT COUPLES

### PREVENTION OPTIONS

Coping with discordance includes determining how best to implement prevention of infection of the uninfected partner. Many couples cope well with this stressful and challenging situation and arrive at a solution that best suits their circumstances. Perhaps the most common strategy is condom use.<sup>18,19,23</sup> Some studies have shown remarkable uptake following CHCT, from < 3% before CHCT to over 80% of sex acts afterwards being performed with the use of a condom.<sup>18</sup> The impact also seems to be particularly strong when the male partner is receiving counselling and testing for the first time.<sup>19</sup> Other strategies reported include separation, which seems to be an option adopted in particular by couples with relationships of shorter duration that did not include children, and particularly affects discordant relationships where the HIV-infected partner is a woman.<sup>23,24</sup> Few couples appear to choose abstinence, although abstinence is apparently easier to negotiate if endorsed by an HIV-positive man.<sup>23</sup> The adoption of non-penetrative sex could also be considered as an option. Use of antiretrovirals by the uninfected partner, as either pre- or post-exposure prophylaxis, has not been prospectively evaluated in this setting, so efficacy and safety are undefined.

While still in the realm of clinical investigation, additional interventions are being tested that may provide further options for couples.<sup>25</sup> These include suppression of HIV shedding by the infected partner through treatment with antiretroviral agents. In addition, the antiviral drug acyclovir is being tested for its possible effect on reducing HIV transmission.





Fig. 1. Khomanani Campaign has highlighted the need for couples testing (images courtesy of Khomanani).

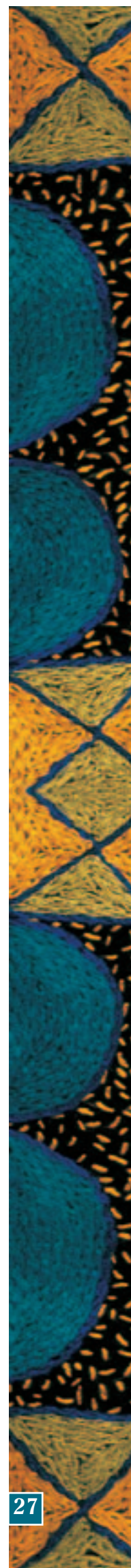
### DESIRE FOR CHILDREN

One of the biggest challenges facing discordant couples is balancing the desire to have children with the risk of HIV transmission. Understanding of the couple's perspective of factors that influence the desire to have a child, as well as maintaining a non-judgemental and culturally sensitive approach by the service provider, can assist the couple in coming to terms with the complexities of HIV discordance and reproductive decision making. Ethical guidelines from professional bodies such as the American College of Obstetrics and Gynecology have noted that assisted reproductive technologies should not be withheld from HIV-infected infertile couples merely on the grounds of HIV serostatus.<sup>26</sup> However, ethical controversies in this area remain.

Adequate preconception counselling to establish the stability of the discordant couple is also important, because many couples separate after childbirth.<sup>27</sup> Fertility care of HIV-discordant couples should be optimised on the basis of the sex of the infected partner; clinical, immunological and virological status of the infected partner; and cost and accessibility of assisted reproductive technologies. The couple should be counselled and informed about risks involved and possible ways of reducing the risk of HIV transmission.

Where the infected partner is male, the main concern is the risk of transmission to the female partner; a range of possible interventions could be considered.<sup>28</sup> None of these have been subjected to clinical trials to fully evaluate the risk-benefit balance for each recommendation. These clinical interactions must therefore be preceded by a detailed discussion about the potential outcomes.

If the couple opt to practise unprotected intercourse, this should take place only during the fertile window period. It is important to adopt a holistic approach to optimise risk reduction and chances of conception. Fertility should be confirmed in both partners. The viral load should be suppressed. It is advisable to document suppression of both blood and seminal viral load when possible, acknowledging that most laboratories may not be equipped to handle genital tract samples.<sup>29</sup> Both partners should be investigated for genital infection and treated appropriately if it is present. All components of risk reduction behaviour counselling should be emphasised. These include unfaithfulness, risky sexual practices (e.g. anal sex, dry sex), use of vaginal irritants, etc. The couple should return to safe sex as soon as the fertile period is over, regardless of pregnancy status. The uninfected partner should also undergo routine HIV testing. Experimental



approaches using pre-exposure chemoprophylaxis to further reduce the susceptibility of the uninfected partner are another consideration. In the event of conception, the couple should continue to practise safe sex to prevent perinatal infection. HIV testing should also be done during pregnancy to detect maternal infection and provide interventions to prevent mother-to-child transmission.

In some specialised centres, semen processing and intrauterine insemination have been adopted. Several techniques are available.<sup>30,31</sup> The first involves 'sperm washing', in which sperm are separated from seminal fluid through repeated cycles of centrifugation and resuspension in fresh medium, with the supernatant being discarded after each round. The 'swim up' technique is similar, but includes an additional step in which the preparation is incubated for a period and the motile sperm swim into the medium, from where they are collected. A third technique uses density gradient purification. These techniques have been available since 1992 but are not widely available even in developed countries; accessibility therefore still remains a problem.<sup>28</sup> Also, the cost of PCR testing of the final sperm aliquot and intensive medical supervision makes it an expensive undertaking, unaffordable to the general population. The procedure might have to be repeated a number of times before pregnancy is achieved, further raising the cost. It is also known that some couples lose patience and try to conceive spontaneously through unprotected intercourse.

Where the infected partner is female, the aim is to reduce the risk of transmission to the uninfected male partner and the unborn child. The comprehensive approach when practising unprotected sex during the fertile period is as described above. The prevalence of pregnancy is generally low among HIV-infected women owing to lower rates of conception and increased rates of pregnancy loss.<sup>32</sup> The couple should be provided with this information at preconception counselling because fertility problems create anxiety and stress even among concordant-negative couples. In these cases, artificial insemination could be considered.

In conclusion, discordant couples need to be encouraged to make informed reproductive decisions. Ideally there should be no coercion; both the infected and the uninfected individuals in the discordant relationship need to be comfortable with the decision to have a child, regardless of the sex of the infected/uninfected partner. The role of the health provider is to provide adequate information and to help guide the whole process, including through the postpartum period if pregnancy is achieved. Existing programmes need to be strengthened in dealing with this, and research programmes and multidisciplinary guidelines to define the safest and most effective therapy possible in South Africa need to be established.

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