Infertility treatment for HIV-infected serodiscordant infertile couples is controversial and has ethical implications. Eighty-six per cent of all HIV-infected individuals fall into the age group 15 - 44 years.1

Fifteen years ago HIV/AIDS was associated with short survival. However, the advent and effective use of highly active antiretroviral therapy (HAART) has led to a dramatic improvement in the health and life expectancy of HIV-infected individuals. Currently the life expectancy of such an individual is estimated at 20 years from the time of diagnosis.2

In developed countries HIV-infected people can therefore lead relatively normal lives. However, in developing countries such as South Africa the disease is still often fatal due to poverty, ignorance and lack of access to antiretroviral drugs.

As the prevalence of HIV increases, gynaecologists will more often be faced with the issue of infertility treatment for HIV-serodiscordant couples.

**Background**

In 1990 the Centers for Disease Control (CDC) issued recommendations against reproductive assistance in HIV-serodiscordant couples.3 In February 2002 the American Society of Reproductive Medicine (ASRM) published revised guidelines stating that HIV-serodiscordant couples may seek reproductive assistance.4 However, to date there are no definite guidelines on infertility treatment when both partners are infected with HIV. In these cases, the couple should be thoroughly counselled and treatment should be individualised.4

In the period 1990 - 2002, European physicians performed 3 000 inseminations in HIV-discordant couples without a single case of seroconversion.3 A review of world data on assisted reproduction techniques in HIV-serodiscordant couples showed that 1 370 patients had undergone 3 397 cycles of treatment without a single case of infection.3 Assisted reproduction techniques could therefore definitely be indicated in HIV-serodiscordant couples.

**HIV and infertility**

HIV infection per se can impact on both the female and male partner, thus affecting fertility. The HIV-positive woman can present with menstrual irregularities (in 20% of cases), an increased incidence of sexually transmitted infections and pelvic inflammatory disease, and a decreased pregnancy rate.5 The HIV-positive man can present with hypogonadism, testicular germ cell loss, testicular atrophy and reduced semen parameters.5

**Ethical concerns**

The four basic principles of ethics, namely autonomy, beneficence, non-maleficence and justice, must always be adhered to when dealing with HIV-discordant couples.6 However, these principles often need to be addressed individually and not in combination. Pre-conceptual counselling is vital and informed consent mandatory at all times.

Two major ethical concerns are the welfare of the offspring and the avoidance of seroconversion of the uninfected partner.2

**The welfare of the offspring**

The risk of mother-to-child transmission is of utmost importance. Without any intervention the risk of transmission is 13 - 30%.7 HAART during pregnancy and labour, elective caesarean section, no breastfeeding and administration of antiretroviral drugs to the neonate reduces the risk of vertical transmission to less than 2%.8 Zidovudine (AZT) on its own during pregnancy or labour has been found to lower transmission rates by 5%.9

In HIV-infected individuals the issue of uncertain prognosis always needs to be kept in mind.7 When a pregnancy is being considered, the concern is whether it would be in the best interests of the child to be born to a parent, or parents, who may not be available for long-term childrearing.4 However, advances in medical management have resulted in an improvement in life expectancy and quality of life of infected individuals.3 It would therefore be ethically unjustifiable to deny these couples fertility treatment.2
Infertility treatment of the HIV-serodiscordant couple

The rate of HIV transmission has been estimated to be 1 in 500 - 1 000 acts of unprotected intercourse. The rate of transfer from man to woman is 0.15% and from woman to man 0.09%. The risk is also influenced by viral load, degree of virulence and stage of disease. Unprotected sexual intercourse should be avoided at all times.

Pre-conceptual counselling is mandatory when treating HIV-serodiscordant couples. It aims at discussing all the reproductive options available to them, HAART therapy and its benefits, treatment failure, risk of vertical transmission, their long-term health outcome and the support network that should be in place. However, no treatment option is 100% risk free, and this should be emphasised during pre-conceptual counselling. Alternative options available are adoption or, in the case of an HIV-positive man, the use of donor sperm. These options should also be discussed with the couple. A multidisciplinary team approach will further facilitate the management of these couples.

Treatment should be individualised depending on which partner is infected with HIV and the underlying cause of the infertility. Both partners should undergo full sexual health screening to ensure that any coexisting infections are diagnosed and treated before fertility treatment commences. All appropriate laboratory investigations should be performed during this health screen. A male and female fertility screen should be done, as the findings will impact on the type of fertility treatment to be performed.

Two scenarios are possible with regard to HIV status in a discordant couple: positive female partner and negative male partner and negative female partner and positive male partner.

In the case of a positive female partner and a negative male partner, two treatment options are available. With anovulation, moderate male factor infertility and unexplained infertility, intrauterine insemination (IUI) should be performed. However, with tubal factor infertility, severe male factor and failed inseminations, in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) is necessary.

In the case of a positive male partner and a negative female partner, two treatment options are available. If there is no tubal pathology and the results of semen analysis are normal, sperm washing should be done with IUI or IVE. However, with tubal occlusion and severe male factor infertility, sperm washing coupled with IVF/ICSI should be performed.

Semen preparation – laboratory aspects

Semprini and co-workers originally proposed the semen preparation technique in which HIV-infected leucocytes in the semen are removed from the motile sperm by gradient centrifugation in combination with ‘swim-up’. In short, the semen is centrifuged (15 - 18 minutes at 400 g) through a three-layer (45% - 70% - 90%) discontinuous colloidal silica density gradient. The clean sperm pellet at the bottom of the tube is carefully removed, resuspended in fresh sperm washing medium and centrifuged (10 minutes at 400 g) twice more. After the second wash the supernatant is carefully removed and 0.5 ml fresh sperm washing medium is placed on the pellet. The live sperm are allowed to swim out of the pellet for approximately 1 hour. After this the supernatant with the live sperm is removed and used for IUI.

Although most research has confirmed the existence of HIV-1 in association with cell-free seminal plasma (Luzzà et al., reviewed in Vernazza et al.), HIV-1 has also been demonstrated within spermatooza by electron microscopy, and either HIV-1 DNA or RNA in spermatoozoan preparations has also been detected. However, these cells have generally been reported to be negative for HIV-1 RNA or proviral DNA. In HIV-1-infected men the viral load in semen and blood decreases markedly after the initiation of HAART.

According to Marina et al., the possibility that the sample will contain detectable HIV after processing through a discontinuous gradient and a subsequent swim-up is extremely low, and the risk of HIV-1 transmission is therefore negligible. Although the virus has rarely been directly detected on spermatooza, even when HIV-RNA reverse transcriptase-polymerase chain reaction (RT-PCR) was used to screen specimens before IUI, Sauer and Chang found that small numbers of virus particles might go undetected. It is therefore imperative that couples be informed that although the infection risk may be reduced with assisted reproductive technologies, it cannot be excluded altogether.

Using the above technique of semen preparation for serodiscordant couples, Semprini et al. reported over 2 000 intrauterine inseminations and more than 100 ICSI/IVF-ET cycles without seroconversion of the partner or infection of the baby.

Occupational exposure and cross-contamination

Strict universal precautions should be practised in all infertility laboratories. A separate laboratory area for HIV-infected patients would be ideal, but owing to financial constraints this is not always feasible. However, it is essential that all physicians and clinics treating seropositive patients have adequate knowledge and resources to deal with these circumstances.

Conclusion

The demand for risk-reduction fertility treatment in HIV-discordant couples is rising. Timed unprotected intercourse is an unacceptable practice. Sperm washing is an ideal treatment option when the male partner is HIV positive.

Pre-conceptual counselling and informed consent are essential. Ethical aspects should always be individualised. HAART...
and elective caesarean section decrease the rate of vertical transmission. However, the safe interventions available today mean that it is mandatory to provide infertility treatment when the HIV-discordant couple requests it.

2. Dhai A, Noble R. Ethical issues in HIV.
7. International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission. However, the safe interventions available today mean that it is mandatory to provide infertility treatment when the HIV-discordant couple requests it.