

CLINICAL PRACTICE

Assisted reproduction in the HIV-serodiscordant couple

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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.² 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.⁴ It would therefore be ethically unjustifiable to deny these couples fertility treatment.²

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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.¹⁰ The rate of transfer from man to woman is 0.15% and from woman to man 0.09%.¹¹ The risk is also influenced by viral load, degree of virulence and stage of disease.¹¹ 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.¹² 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.⁴

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.¹² 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.¹²

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.¹² However, with tubal factor infertility, severe male factor and failed inseminations, *in vitro* fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) is necessary.¹²

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 IVF.¹² However, with tubal occlusion and severe male factor infertility, sperm washing coupled with IVF/ICSI should be performed.¹²

Semen preparation – laboratory aspects

Semprini and co-workers originally proposed the semen preparation technique¹² in which HIV-infected leucocytes in the semen are removed from the motile sperm by gradient centrifuga-

tion 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 (Liuzzi *et al.*,¹³ reviewed in Vernazza *et al.*¹⁴), HIV-1 has also been demonstrated within spermatozoa by electron microscopy,¹⁵ and either HIV-1 DNA or RNA in spermatozoan preparations has also been detected.¹⁶ However, these cells have generally been reported to be negative for HIV-1 RNA or proviral DNA.¹⁷⁻¹⁹ In HIV-1-infected men the viral load in semen and blood decreases markedly after the initiation of HAART.^{20,21}

According to Marina *et al.*,²² 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 spermatozoa, even when HIV-RNA reverse transcriptase-polymerase chain reaction (RT-PCR) was used to screen specimens before IUI, Sauer and Chang²³ 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.*¹ 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

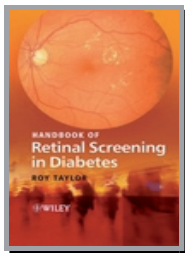
The demand for risk-reduction fertility treatment in HIV-discordant couples is rising. Timed unprotected intercourse is an unacceptable practice. Sperm washing is an ideal treatment option when the male partner is HIV positive.

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.

1. Semprini AE, Vucetich A, Oneta M. Amp intra conjugale: Quelle strategie de prise en charge? L'experience italienne. Communication a la journee: Le desir d'enfant chez les couples VIH serodifferents. Toulouse: 28-29.
2. Dhai A, Noble R. Ethical issues in HIV. *Best Pract Res Clin Obstet Gynecol* 2005; 19(2): 255-267.
3. Kambin SP, Batzer F. Assisted reproductive technology in HIV serodiscordant couples. *Sexuality, Reproduction and Menopause* 2004; 2(2): 92-100.
4. Ajayi R, Ogunmokin A. Infertility treatment for HIV- serodiscordant couples. *Reviews in Gynaecological Practice* 2004; 4: 93-96.
5. European Collaborative Study. Risk factors for mother to child transmission of HIV-1. *Lancet* 1992; 339: 107-111.
6. Semprini AE, Vucetich A, Hollander L. Sperm washing, use of HAART and role of elective caesarean section. *Curr Opin Obstet Gynecol* 2004; 16: 465-470.
7. International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type-1: a meta-analysis of 15 prospective cohort studies. *N Engl J Med* 1994; 331: 1173-1180.
8. American College of Obstetricians and Gynecologists. *Ethics in Obstetrics and Gynecology*. 2nd ed.
9. Anderson DJ. Assisted reproduction for couples infected with HIV-1. *Fertil Steril* 1999; 72: 592-594.
10. Ajayi RA, Melie NA. Assisted reproductive technologies in human immuno-deficiency (HIV) serodiscordant couples: practice, prognosis and future prospects. In: Allahbadisa GN, Das RB, Merchant R, eds. *The Art and Science of Assisted Reproductive Techniques (ART)*. New Delhi: Jaypee Brothers Medical, 2003: 338-342.
11. Gilling-Smith C. Fertility management of HIV-discordant couples. *Curr Obstet Gynecol* 2003; 13: 307-313.
12. Semprini AE, Levi-Setti P, Bozzo M, et al. Insemination of HIV-negative women with processed semen of HIV positive partners. *Lancet* 1992; 340: 1317-1319.
13. Liuzzi G, Bagnarelli P, Chirianni A, et al. Quantitation of HIV-1 genome copy number in semen and saliva. *AIDS* 1995; 9: 651-653.
14. Vernazza P, Eron J, Fiscus S, Cohen M. Sexual transmission of HIV: infectiousness and prevention. *AIDS* 1999; 13: 155-166.
15. Baccetti B, Benedetto A, Burrini AG, et al. HIV particles in spermatozoa of patients with AIDS and their transfer into the oocyte. *J Cell Biol* 1994; 127: 903-914.
16. Dulioust E, Tachet A, De Almeida M, et al. Detection of HIV-1 in seminal plasma and seminal cells of HIV-1 seropositive men. *J Reprod Immunol* 1998; 41: 27-40.
17. Lasheeb AS, King J, Ball JK, et al. Semen characteristics in HIV-1 positive men and the effect of semen washing. *Genitourin Med* 1997; 73: 303-305.
18. Marina S, Marina F, Alcolea R, et al. Pregnancy following intracytoplasmic sperm injection from an HIV-1-seropositive man. *Hum Reprod* 1998a; 13: 3247-3249.
19. Kim LU, Johnson MR, Barton S, et al. Evaluation of sperm washing as a potential method of reducing HIV transmission in HIV-discordant couples wishing to have children. *AIDS* 1999; 13: 645-651.
20. Gupta P, Mellors J, Kingsley L, et al. High viral load in semen of human immunodeficiency virus type 1-infected men at all stages of disease and its reduction by therapy with protease and nonnucleoside reverse transcriptase inhibitors. *J Virol* 1997; 71: 6271-6275.
21. Barroso P, Schechter M, Gupta P, et al. Effect of antiretroviral therapy on HIV shedding in semen. *Ann Intern Med* 2000; 133: 280-284.
22. Marina S, Marina F, Alcolea R, et al. Human immunodeficiency virus type 1-serodiscordant couples can bear healthy children after undergoing intrauterine insemination. *Fertil Steril* 1998b; 70: 35-39.
23. Sauer MV and Chang PL. Posthumous reproduction in a human immunodeficiency virus-discordant couple. *Am J Obstet Gynecol* 2001; 185: 252-253.



Handbook of Retinal Screening in Diabetes

Roy Taylor

Diabetes is the most common cause of blindness in the working age population of developed countries. Retinopathy may be present in over 95% of people who have had type 1 diabetes for 20 years or more. Screening leads to effective treatment and preservation of sight. The organization of effective, efficient screening programmes is vital, as recognised in the National Service Framework for Diabetes in the UK.

This book, a successor to the highly popular Practical Guide to Polaroid Retinal Photography, describes the essential components of a retinopathy screening programme, including the criteria for referral to an ophthalmologist, drawing upon the experience of the Newcastle

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