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Human immunodeficiency virus and infertility treatment

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Human immunodeficiency virus (HIV) has infected people of all ages. The fact that the largest group affected (86%) are persons of active reproductive age (15–44 years) underscores the risk of viral transmission to sexual partners and offspring. Because women make up approximately 20% of cases and because HIV has become more prevalent among heterosexual couples than in the past, some infected persons will probably ask their health care providers for advice about and assistance with having children who are free of the virus.

In 1994, the Ethics Committee of the American Society for Reproductive Medicine set forth guidelines concerning patients with HIV who may request or need reproductive assistance (1). The Committee expressed concern about potential transmission of the virus to an uninfected partner or to the couple's offspring. It also addressed potential problems for the child related to the shortened life span of one or both infected parents. On the basis of these concerns, the Committee recommended that testing for the presence of the virus be offered to all couples requesting reproductive assistance. The Committee also recommended that institutions establish their own written policies on infertility treatment for people infected with HIV. It suggested that physicians counsel couples about the consequences of using potentially infected sperm and discuss the options of donor sperm, adoption, or not having children.

When these guidelines were published in 1994, HIV infection was considered a serious contraindication to establishment of a healthy pregnancy. Since then, understanding and treatment of HIV-infected persons and laboratory techniques for the preparation of virus-free sperm for reproductive assistance have changed substantially (2–5). With more effective treatment regimens, the death rate has decreased dramatically among persons who become infected.

Several methods of limiting the risk for HIV transmission to partner and offspring have also been developed. For example, zidovudine has reduced the vertical transmission of infection from 16%–24% to 5%–8% when given to HIV-positive pregnant women during the second and third trimesters and to their newborns for 6 weeks (4, 6–9).

A meta-analysis of studies conducted in North America and Europe concluded that elective (planned) cesarean section added to antiviral treatment would decrease the vertical transmission rate to 2% compared with 7.6% in children of treated women who deliver vaginally. Subsequent studies have found that cesarean section is not needed to lower the risk of transmission if viral levels in the pregnant woman are undetectable (10–12).

Lack of apparent transmission of HIV to partner or child with intrauterine insemination and IVF with ICSI has been reported for discordant (male-positive) couples. Highly active antiretroviral therapy can lessen the viral burden in a person's serum and semen. Testing of sperm by using a polymerase chain reaction assay has improved the ability to determine whether the virus is present in the washed sperm preparation (4, 5, 13–15).

In light of these changes in the treatment and reproductive consequences for men and women who are HIV positive, the Ethics Committee re-examined its earlier guidelines. This paper addresses ethical issues concerning [1] infertility treatment when one partner is HIV positive, [2] infertility treatment when both partners are positive, [3] knowingly conceiving a child who may be born with HIV, [4] HIV

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testing for couples seeking fertility assistance, and [5] potential risks to the caregivers of patients who are HIV positive.

INFERTILITY TREATMENT WHEN ONE PARTNER IS HIV POSITIVE

The presence of HIV may not affect the reproductive potential of a seropositive person unless he or she is ill owing to an opportunistic infection. The HIV transmission rate to an uninfected partner is estimated to be approximately 1 in 500 to 1,000 episodes of unprotected intercourse (16). The risk of viral transmission increases dramatically if the HIV-positive partner's viral load is high or if the HIV-negative partner has a concomitant genital infection, inflammation, or abrasions.

If a woman is HIV positive and her male partner is HIV negative, transmission of infection to the male partner can be avoided by using homologous insemination with the partner's sperm. The resulting pregnancy may still pose some risk to the HIV-positive woman and her child, because opportunistic infections occurring during pregnancy can be devastating to the woman and fetus. An HIV-positive woman may require certain medications in the early stages of pregnancy that could have adverse effects on a developing fetus. Amniocentesis, a procedure commonly recommended to women older than 35 years of age, carries the risk of viral transmission to the fetus as the needle is passed through the HIV-positive woman's abdominal cavity into the amniotic sac.

If an HIV-positive pregnant woman is not actively treated with antiviral drugs, the risk of HIV transmission to the infant is greater than 20% regardless of the viral load. Administration of zidovudine to pregnant women and newborns during the first 6 weeks of life can substantially reduce the risk of HIV transmission to 5%–8%. Delivery by cesarean section and avoidance of breast-feeding may further reduce the chance of infection to approximately 2%.

If a man is HIV positive and his female partner is HIV negative, the risk of transmitting the virus to the female partner appears to be reduced but not eliminated by using condoms during sexual activity, except during ovulation. The seroconversion rate was 4.3% in one study of 92 HIV-negative women with HIV-positive partners trying to establish pregnancies through timed intercourse. Two of the women in this study seroconverted during pregnancy, and another two converted in the postpartum period. These four women reported inconsistent condom use by their partners (14). Even though some HIV-discordant couples have established pregnancies through timed unprotected intercourse without infecting the negative partner or child, this practice is unsafe and is not recommended.

Recent reports have described specific methods for sperm preparation and testing that can substantially reduce the chance of HIV transmission to the female partner and child. In 1998, Semprini et al. (4) reported using a density gradient and swim-up technique to obtain sperm, which were then tested by PCR assays for the presence of HIV. If the final sperm sample tests negative on these assays, it is used for insemination. With this technique, $<1\%$ (6 of 623) of the samples tested positive for the virus and were not used. Semprini et al. reported almost 1,600 inseminations of 513 HIV-negative women, from which 228 pregnancies resulted. A follow-up of 97.5% of the women at 3 months and 92% at 1 year revealed that all children older than 3 months of age and all mothers tested were HIV negative (4).

In 1998, Marina et al. reported similar results in 63 women using a similar method of sperm processing (14). More sensitive methods to isolate noninfected sperm are currently being tested for clinical use (3).

The statistics noted above are reassuring, but as previously stated, the seroconversion rate with unprotected intercourse is low. More data are needed to demonstrate the complete efficacy of these sperm preparation techniques. Until then, couples must still be cautioned about the potential risk of HIV transmission to the uninfected partner and to their offspring. Couples seeking the safest methods to prevent transmission of the virus when the male partner is HIV positive should be counseled about using donor sperm, considering adoption, or not having children.

When male-positive discordant couples want to have their own genetically related children, they should be informed of available risk-reduction techniques and encouraged to seek assistance at institutions that can provide the most effective methods of sperm preparation as well as the rigorous testing and treatment necessary to minimize the chance of HIV transmission to partner and offspring. To determine the true efficacy of the chosen method of treatment, these centers should use strict study protocols with proper informed consent and thorough follow-up of patients, partners, and offspring.

INFERTILITY TREATMENT WHEN BOTH PARTNERS ARE HIV POSITIVE

As with any couple presenting for evaluation and treatment, both persons may have normal fertility potential or one or both may have impaired fertility. If an HIV-positive couple asks for medical advice regarding pregnancy, they must be informed about the risks to the pregnant woman and the risk that a child could become infected. If the viral load can be suppressed to undetectable levels in both partners, the couple may have a child who is free of HIV. Aggressive drug therapy with protease inhibitors and other antiretroviral therapy can extend life and improve health in HIV-positive persons; however, it is unknown whether they will ultimately have a normal or near-normal life expectancy. The child may

lose one or both parents to AIDS before he or she reaches adulthood.

ETHICAL ISSUES RAISED BY KNOWINGLY RISKING THE BIRTH OF A CHILD WITH HIV

The risk of HIV transmission to offspring can be greatly reduced but not eliminated. This risk raises ethical issues concerning the scope of freedom to reproduce, what can be considered harm sufficient to justify restricting that freedom, and the responsibilities of health care professionals faced with a request to provide services to HIV-infected patients.

Does a couple's desire to have genetic offspring justify the risk of transmitting a serious disease to their child? Although the risk can be reduced in many ways, it cannot be completely avoided. Those who assess the ethics of assisting such patients to have children must address the question of whether offspring born with HIV are harmed despite the preventive steps taken. They must consider that some risk remains that the child will be born with HIV. Until sperm preparation techniques prove completely effective, there may be no way, short of refraining from reproduction altogether, to completely prevent some cases of HIV transmission.

In situations in which a child could be born with a serious disease, one can argue that individuals are not acting unethically in proceeding with reproduction if they have taken all reasonable precautions to prevent disease transmission and are prepared to love and support the child, regardless of the child's medical condition. Similarly, one can argue that health care providers are not acting unethically if they have taken all reasonable precautions to limit the risk of transmitting HIV to offspring or to an uninfected partner. It would not, however, be ethically acceptable for a physician, clinic, or institution to proceed with reproductive assistance if they lacked the clinical and laboratory resources needed to effectively care for HIV-positive couples who wish to have a child. In such instances, the medical care provider should refer couples to a center that has these resources.

The ethical issues raised here are similar in some respects to those in couples who know that they are carriers of an autosomal recessive disease, such as Tay-Sachs disease, sickle-cell anemia, or cystic fibrosis. Such couples may choose to take the risk of having an affected child rather than forgo parenthood; adopt; use a gamete donor; or, if a test result is positive, terminate the pregnancy. The risk of transmitting an autosomal recessive genetic disease cannot be reduced below 25%, whereas the risk of HIV transmission can be reduced to a substantially lower number—in some cases, to less than 2%. Health care workers who are willing to provide reproductive assistance to couples whose offspring are irreducibly at risk for a serious genetic disease should find it ethically acceptable to treat HIV-positive individuals or couples who are willing to take reasonable steps to minimize the risks of transmission.

TESTING INFERTILE COUPLES FOR HIV

The Centers for Disease Control and Prevention estimate that approximately 200,000 persons in the United States have undiagnosed HIV (17). Because most of these persons are of reproductive age, the question arises as to whether practitioners should require HIV testing for all couples seeking medical or surgical reproductive assistance.

Testing for HIV and other sexually communicable diseases is ethically justified for gamete donors to protect the health of the gamete recipients. The Centers for Disease Control and Prevention, the U.S. Food and Drug Administration, American Association of Tissue Banks, and the American Medical Association all strongly recommend HIV testing for every gamete donor. Agencies may mandate testing in the near future. The American Society for Reproductive Medicine practice guidelines recommend that all gamete donors and recipients be tested for HIV and other sexually transmitted diseases and that testing also be offered to the recipients' partners (18). Testing donors and recipients for potentially transmittable infectious conditions can be reassuring to all parties involved in assisted reproductive technology and should be strongly encouraged.

It is especially important to test persons who are considered at high risk for HIV infection, such as those who have a history of repeated sexually transmitted diseases, multiple sexual partners without barrier protection, bisexual behavior, or i.v. drug use. Knowing the HIV status of the at-risk individual or couple before establishment of a pregnancy could enable health care providers to better assist their patients in making safer reproductive choices.

It is ethically appropriate for practitioners to encourage HIV testing for all couples who want to have children, not just those who request infertility treatment. To mandate that people be tested solely because they request medical assistance in having a child would infringe on their personal liberty and introduce a dubious distinction between those who seek treatment for infertility and those who do not.

On the other hand, it may be appropriate to recommend HIV testing as good medical practice since there are means to significantly lessen the chance for HIV transmission to an uninfected partner and to offspring. An analogy is the common practice of recommending that women seeking to become pregnant be tested for rubella immunity because infection during pregnancy could have dire consequences for the fetus. For couples in which the man has unexplained obstructive azoospermia or congenital absence of one or both vas deferens, it is becoming standard practice to recommend testing for mutations of the cystic fibrosis trans-

membrane conductor gene to evaluate the risk of having a child with cystic fibrosis. Few people refuse these tests.

Couples should consider HIV testing as part of responsible parenting. Often associated with testing is the presumed stigma of some past sexual or drug-related misbehavior. Clinicians have a responsibility to educate their patients about the possible means by which infections can be acquired and the advantages of knowing the test results before a pregnancy is established.

HIV AND THE HEALTH PROFESSIONAL

Health professionals care for patients with serious and potentially contagious diseases, knowing that they themselves could become infected. Knowledge of diseases, combined with careful hygienic practices, has allowed caregivers to lessen that risk. In the late 1990s, the Centers for Disease Control and Prevention identified only 56 persons who had documented occupational transmission of HIV and another 134 people with possible occupational transmission (19). Most were nurses and laboratory technicians who accidentally inoculated themselves with a patient's blood by a needlestick or were splashed with bloody fluid and had significant mucocutaneous exposure. If standard universal precautions to prevent infectious disease transmission are taken, the risk of virus transmission to medical caregivers is very small and, in itself, is not a sufficient reason to deny reproductive services to HIV-infected individuals and couples. Clinicians have the same obligation to care for those infected with HIV as to care for patients with other chronic diseases. Concern about the public's perception of a clinic or provider that cares for HIV-positive patients is insufficient cause to deny services.

Clinicians faced with requests for reproductive assistance from persons who are HIV positive should be aware of the 1998 United States Supreme Court decision in Bragdon vs. Abbott (20). The Court ruled that a person with HIV is considered "disabled" and therefore protected under the Americans with Disabilities Act (21, 22). According to that decision, persons who are HIV positive are entitled to medical services unless a physician can demonstrate "by objective scientific evidence" that treatment would pose "a significant risk" of infection. The Court determined that having HIV was a disability because it interfered with the "major life activity" of reproduction due to the risk of transmitting HIV to offspring. Unless health care workers can show that they lack the skill and facilities to treat HIV-positive patients safely or that the patient refused reasonable testing and treatment, they may be legally as well as ethically obligated to provide requested reproductive assistance.

SUMMARY

Human immunodeficiency virus infection is classified as a chronic disease. It is treatable but not yet curable. Significant advances in HIV treatment appear to have delayed the onset of AIDS and its consequences in many, but not all, infected persons. The potential for HIV-positive persons to have uninfected children and not transmit the virus to their partners has been substantially enhanced, but success cannot be guaranteed. Health care providers and HIV-infected persons together share responsibility for the safety of the uninfected partner and potential offspring. When an affected couple requests assistance to have their own genetically related child, they are best advised to seek care at institutions with the facilities that can provide the most effective evaluation, treatment, and follow-up. Alternatively, they may be advised to look to other options and consider donor sperm, adoption, or not having children.

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