

Fertility, Conception,

The subject of HIV/AIDS as it relates to fertility and conception has begun to generate interest among biological and sociobehavioral researchers. As a result, a better understanding of the fertility-related intentions and desires of HIV positive individuals, as well as advancing knowledge regarding reproductive technologies, now offer the hope of parenthood to childless couples.

Shari Margolese



and HIV

A Desire for Children

Significant numbers of people with HIV intend to have children. “Fertility Desires and Intentions of HIV Positive Men and Women,” a study published in 2001 in *Family Planning Perspectives*, concluded that 29% of HIV positive women and 28% of HIV positive heterosexual or bisexual men who received medical care in the U.S. desired children in the future. Yet while many women and men with HIV desire children, fertility and conception issues may complicate the realization of this dream. Indeed, of those desiring children among the total sample of 1,421 subjects aged 20–44 mentioned above, 31% of women and 41% of men did not expect to have any.

Fertility

One effect of HIV/AIDS on individual women and society at large is a change in fertility levels, which is influenced in part through altered behavior. In studies done in sub-Saharan Africa, behaviors that have been largely influenced by AIDS education, such as increased condom use, delayed onset of sexual relations, older age at first union, and fewer premarital sexual relations, have driven down fertility rates. Within the same population, lower rates of remarriage after an AIDS-related death of a partner due to stigma associated with the surviving partner may also diminish fertility levels.

Behavioral influences may also lead to higher fertility rates. The number of sub-Saharan African couples who reconcile following marital infidelity has increased; these couples tend to go on to have more children. In societies with high HIV/AIDS rates, some couples may desire larger

families to ensure survival of children, though others limit family size due to concerns about leaving orphans behind after an early death. In countries where HIV/AIDS treatment is widely available, positive parenting is on the rise. The risk of mother-to-child transmission is as low as 2% in these areas, and treatment has prolonged life expectancy for many potential parents with HIV.

Biological mechanisms also influence fertility rates in HIV positive women and men. Research has shown that women with HIV may find it more difficult to conceive than their HIV negative counterparts. HIV infected women experience reduced pregnancy rates and higher rates of both planned abortion and miscarriage. HIV/AIDS may induce sterility, increase fetal mortality, decrease production of spermatozoa, and sometimes decrease frequency of sexual intercourse, all contributing to declining fertility.

A look at three studies in HIV positive women shows some of the effects of HIV infection on pregnancy.

Amanda Ross of the Swiss Tropical Institute in Basel and colleagues studied a cohort of 191 women (92 HIV positive and 99 HIV negative at enrollment), aged 15–49, in southwest Uganda between 1990 and 2001 to better understand the association between HIV disease progression and the incidence of pregnancy. Among the women with HIV, sexual intercourse became less frequent as HIV disease progressed. In their analysis, Ross’ team found that “fertility is reduced from the earliest asymptomatic stage of HIV infection resulting from both a reduced incidence of recognized pregnancy and increased fetal loss. The greatest reduction in fertility was observed following progression to AIDS when there was a very low incidence of recognized pregnancies.” (A recognized pregnancy refers to the implantation and survival of an embryo in the lining of the

uterus.) These data were published in the March 26, 2004 issue of *AIDS*.

An earlier study of 412 HIV positive women in Paris and southeastern France from 1988 to 1993 by Isabelle De Vincenzi of Saint-Maurice National Hospital and colleagues found that the incidence of pregnancy decreased by more than half, from 20.4 per 100 person-years before HIV diagnosis to 7.9 per 100 person-years after HIV diagnosis. (A person-year a shorthand term used by epidemiologists to make comparisons.) The study also showed that the proportion of pregnancies voluntarily interrupted more than doubled from 29% to 63% after HIV diagnosis. The percentage of miscarriages and ectopic (outside the womb) pregnancies increased significantly from 8.3% to 25.4% of those conceived before and after HIV diagnosis, respectively. Also, the proportion of women who were sexually inactive rose four-fold, from 5% before to 20% after HIV diagnosis. These data were published in the March 11, 1997 issue of *AIDS*.

Carla D'Ubaldo of Lazzaro Spallanzani Hospital in Rome and colleagues studied a cohort of 272 women from 12 Italian cities in the 1990s and found that 63% of the women with HIV had an intentional abortion, compared with a lower proportion (45%) of the HIV negative women. These data were published in the June 18, 1998 edition of *AIDS*.

The Role of HIV

Little data are available to clarify the specific role of HIV in fertility. Researchers hypothesize that the virus not only plays a direct role in reduced fertility among HIV positive people, but also has an indirect impact for positive women and men.

Directly, HIV infection may influence women to voluntarily terminate a pregnancy out of fear of leaving an orphan or transmitting HIV to the child. D'Ubaldo's team offered possible explanations for increased spontaneous abortion (miscarriage) in HIV positive women. They suggested that HIV affects the placenta by interfering with the transfer of important nutrients to the fetus, or that the virus causes abnormal development of the embryo. Other theories include a direct relationship between HIV and the fetal thymus gland, as well as an increased risk of infection due to the weakened immune system of the mother. HIV may also directly influence the ability of HIV positive men to produce healthy sperm.

Indirectly, women with HIV may experience infertility due to coinfection with another sexually transmitted disease. Complications of HIV, such as increased risk of cervical abnormalities, early menopause, pelvic inflammatory disease (which can cause scarring of the Fallopian tubes), and severe wasting may also contribute to infertility in women.

Conception

Conception, or becoming pregnant, is of particular concern for serodiscordant couples (those in which only one partner is HIV positive). Safer sex is recommended, which usually prevents pregnancy. However, assisted reproductive technologies may aid serodiscordant couples in achieving pregnancy while at the same time minimizing the risk of HIV transmission to the uninfected partner.

Several European fertility clinics, as well as a few American facilities, have experience in providing both intrauterine (within the uterus) insemination and *in vitro* (test tube) fertilization to serodiscordant couples without seroconversion of uninfected female partners. To reduce the risk of HIV transmission, sperm must be isolated from the semen and "washed." Sperm washing must be done in a laboratory. Unfortunately, it is not possible to remove all viral particles from washed sperm, contributing to the controversial nature of this procedure. Yet studies involving washed sperm show that seroconversion rates are low and that many couples are willing to take the risk to become parents.

"[HIV]-serodiscordant couples are actively seeking reproductive assistance and often consider or practice unsafe measures to achieve pregnancy. Reproductive issues and concerns unique to these couples need to be addressed before [fertility] treatment," concluded Jeffrey Klein, MD, of Columbia-Presbyterian Medical Center in New York City and colleagues in the May 2003 edition of *Obstetrics and Gynecology*. These researchers found that some HIV-serodiscordant couples are willing to go to great lengths, and consequently to great risk or expense, to conceive.

Fifty serodiscordant couples interested in undergoing assisted reproduction to avoid HIV transmission were questioned by Klein and his team concerning their attitudes about starting a family. By design, the men were HIV positive, aged 26–51, and asymptomatic. The women were HIV negative, aged 24–45. Most couples (44 of 50) were married or in long-term relationships. Before study enrollment, nine of the 50 couples had conceived and delivered a child. Previous timed intercourse (unprotected intercourse during peak fertile periods) occurred in 8% of the couples. Six individuals stated that they would risk HIV infection and proceed with timed intercourse if no other alternative existed. Forty-eight percent said they would prefer artificial insemination with donor sperm if assisted reproduction failed or were unavailable. Forty-three percent would pursue posthumous (after the death of one partner) conception if cryopreserved (frozen) sperm or embryos were available in the event of the partner's death. Most couples discussed the possibility of single parenting (90%) or the possibility for adoptive parenting (58%). All couples were aware of HIV transmission risk to the female partner, and 92% understood that their child might contract HIV.

Jeanine Ohl, MD, of the Centre d'AMP in Strasbourg and colleagues published their observations of assisted reproduction techniques for serodiscordant couples over 18 months in the June 2003 edition of *Human Reproduction*. Ohl's team concluded that assisted reproductive technology, particularly injection of an egg with a single sperm (intracytoplasmic sperm injection, or ICSI), provided HIV positive men with a safe and highly effective means of fathering children. Among 57 serodiscordant couples, 12 of 39 in which the male was infected produced a total of 14 children. Seroconversion was not observed in any partners of HIV positive men. ICSI was the most successful assisted reproductive technique, resulting in pregnancies in 49% of all transferred embryos. *In vitro* fertilization was less successful, and eight attempts at intrauterine insemination (IUI) did not result in any pregnancies. Of the ten HIV positive women treated, only one became pregnant; Ohl attributed this low rate to possible premature ovarian failure (loss of ovarian function in women under 40).

Further evidence of favorable outcomes using assisted reproduction technologies is found in the August 20, 2003 edition of the *American Journal of Perinatology* as reported by Jane Cleary-Goldman, MD, and colleagues from New York Presbyterian Medical Center. In this study, 25 serodiscordant couples underwent *in vitro* fertilization and embryo transfer (IVF-ET) with ICSI. During this procedure, mature eggs are removed from a woman's ovaries and fertilized with washed sperm in a laboratory. The fertilized eggs are then transferred back into the woman's uterus where, it is hoped, a pregnancy will occur. Investigators reviewed outcomes of HIV negative women after IVF-ET with ICSI from January 1, 1997, to June 1, 2002. Twenty-seven pregnancies were successfully conceived, delivering 40 babies (16 singletons, nine sets of twins, and two sets of triplets). The mean (average) gestational age at delivery was 37 weeks, and the mean birth weight was 2,646 g (about 5.8 lbs). Caesarean sections (C-sections) were performed in 70% of births. Preterm delivery (under 37 weeks) occurred in seven pregnancies, and low birth weight (below 2,500 g or about 5.5 lbs) was observed in eight pregnancies. No HIV seroconversions were detected at delivery, and all of the mothers and their offspring remained HIV negative beyond three months postpartum.

Access

Guidelines for providing infertility treatment to HIV positive people vary across the world. Several countries allow assisted reproductive therapies for HIV positive men, but few allow it for women with HIV. In the February 2002 edition of *Fertility and Sterility*, the Ethics Committee of the American Society for Reproductive Medicine published new guidelines on treating infertility in HIV positive individuals. According to the committee, physicians practicing reproductive medicine should not deny treatment to

anyone with HIV. Ethically as well as legally, providers have the same obligation to treat HIV positive patients as those suffering from any other chronic disease. The committee further recommends that when a clinic lacks the skills and facilities to manage people with HIV, the individuals should be referred to a clinic with adequate resources. The guidelines also outline acceptable procedures for conception, including artificial insemination with the partner's sperm if the female partner is HIV positive; artificial insemination using sperm-washing techniques and testing of the washed sperm for virus if the male partner is HIV positive; and *in vitro* fertilization and ICSI.

HIV positive couples who require the assistance of reproductive technologies to conceive are very limited in their access to care. Until recently, the Special Program of Assisted Reproduction (SPAR), a program of the U.S. Centers for Disease Control and Prevention (CDC), permitted only *in vitro* fertilization using washed sperm. The procedure is expensive, costing about US\$7,000 per ovulation cycle. In 2002 the recommendations were updated to include the *in utero* (in the uterus) method of insemination. A few other countries, such as France and Canada, may offer sperm washing and other technologies on a limited basis to HIV positive or serodiscordant couples.

Conclusion

HIV positive couples are not limited to conventional childbearing methods. Other avenues to parenthood include adoption and sperm donation from a known donor or sperm bank. While stigma continues to be a barrier for couples seeking to become parents by these means, many have been successful. For those seeking unconventional methods of parenting, such as surrogacy (when another woman carries the child), little information is available specific to HIV positive couples. However, it is likely that similar rules would apply regarding implantation of potentially infected tissue into an HIV negative woman.

As more HIV positive couples consider parenthood, it is likely that fertility services will slowly become more available to suit their needs. And it is also likely that ongoing advocacy and education will be required to ensure affordable, timely, and stigma-free access for all couples seeking to become parents.

Shari Margolese is an HIV positive advocate living in Canada. She was recently awarded the Golden Jubilee Medal of Queen Elizabeth II for significant service to her community.

Selected sources

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