SHORT TITLE: HIV and infertility treatment

FULL TITLE: Human immunodeficiency virus (HIV) and infertility treatment: an Ethics Committee opinion

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CAPSULE: Human immunodeficiency virus (HIV) is a serious but manageable chronic disease that affects persons of reproductive age, many of whom express a desire for biological parenthood.

ABSTRACT: Human immunodeficiency virus (HIV) is a serious but manageable chronic disease that affects persons of reproductive age, many of whom express a desire for biological parenthood. This document is a revision of the original document of the same name, last published in 2015 (Fertil Steril 2015;104:e1–8).

Key Words: Serodiscordant, reproduction, infection, transmission, fetus, ethics

KEY POINTS

- Human immunodeficiency virus (HIV) is a serious but manageable chronic disease that affects persons of reproductive age, many of whom express a desire for biological parenthood.
- Current treatments for HIV can limit the risk of viral transmission to partner and offspring. Recent studies show that in HIV-infected women, the use of antiretroviral therapy, and avoidance of breastfeeding may reduce the chance of newborn infection to less than 2%.
- In couples in which the man is infected with HIV, both circumcision and the use of sperm preparation techniques coupled with either intrauterine insemination (IUI) or in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI) have proven to be highly effective in avoiding seroconversion of uninfected women and offspring.
- In serodiscordant couples, pre-exposure prophylaxis (PrEP) with antiretroviral drugs may reduce further the risk of HIV transmission to the HIV-negative female partner.
- There are no reports of HIV infection of laboratory personnel resulting from processing the gametes or embryos of serodiscordant couples using current laboratory protocols. Cross-contamination of the gametes or embryos of other couples in the same laboratory has also not been reported.
- For the above reasons, there is no ethical reason to withhold fertility services at clinics with the necessary resources to provide care to HIV-infected individuals and couples who are willing to use recommended risk-reducing therapies. Clinics without sufficient resources or knowledge to offer care should assist in making referrals to providers who are equipped to manage such patients.
- In third-party reproduction, disclosure of an intended parent’s HIV status to gamete donors or
gestational carriers should be commensurate with principles of informed consent.

Human immunodeficiency virus (HIV) can infect people of all ages, but the largest group affected (86%) contains persons of reproductive age (15–44 years old). Globally, it is reported that 20-50% of persons living with HIV desire children (Beyeza-Kashesya 2010, Mantell 2014). This highlights the importance of minimizing the risk of viral transmission to sexual partners and offspring and providing these patients with access to fertility care. It is important that providers have the available information and technology to minimize the risk of viral transmission to an uninfected partner and offspring.

In 1994, the Ethics Committee of the American Society for Reproductive Medicine (ASRM) set forth ethical guidelines concerning patients with HIV who may request or need reproductive assistance (ASRM 1994). 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 one or both parents having a chronic medical condition. On the basis of these concerns, the Committee recommended that testing for the presence of HIV 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, strategies to minimize transmission risk, and discussing the options of donor sperm, adoption, or not having children.

When these guidelines were published in 1994, HIV infection was considered to be a serious risk to the establishment of a healthy pregnancy. Since then, treatment of HIV-infected persons and laboratory techniques for the preparation of virus-free sperm for reproductive assistance have both improved substantially (Anderson 1999, Politch 2002, Sauer 2005, HHS Panel webpage). In addition, with the use of modern antiretroviral therapy, people living with HIV now have life expectancies equivalent to that of HIV-negative persons (INSIGHT 2015).

Clinical protocols for minimizing the risk of HIV transmission to partner and offspring have also been developed. Initial studies showed that zidovudine reduced the vertical transmission of infection from 16%–24% to 5%–8% when given to HIV-infected pregnant women during the second and third trimesters and to their newborns for 6 weeks (HHS Panel webpage, Connor 1994, Graham 1999, Lindegren 1999). More recent data demonstrate that combination antiretroviral treatment given to HIV-infected women antenatally further reduces transmission to offspring to less than 2% (CDC 2005 p 592-7, Brooks 2017 MMWR, Kawwass 2017 MMWR, Kawwass 2018).

For serodiscordant couples in which the male partner is HIV-positive, male treatment with antiretrovirals to reduce serum and semen viral load and female partner pre-exposure prophylaxis
HIV and infertility treatment

PrEP (PrEP) have been shown to minimize female risk (HHS Panel webpage, ASRM PC 2020, Del Romero 2016, Givens 2018). When assisted reproductive technologies are used, both sperm washing with IUI, and IVF with ICSI have been shown to minimize the risk of seroconversion in the female partner and offspring.

A meta-analysis of studies conducted in North America and Europe concluded that elective (planned) cesarean section added to antiretroviral 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 for those on potent antiretroviral therapy, cesarean section is not needed to lower the risk of transmission if viral levels in the pregnant woman are undetectable (International Perinatal HIV group 1999, van Vliet 1997, Stringer 1999).

In light of these changes in the treatment and reproductive consequences for HIV-infected men and women, the Ethics Committee reexamined and periodically continues to review its earlier guidelines. This report addresses ethical issues concerning: 1) infertility treatment when one partner is infected with HIV; 2) infertility treatment when both partners are infected; 3) knowingly conceiving a child who may be born with HIV; 4) HIV testing for couples seeking fertility assistance; 5) potential risks to the health-care providers of HIV-infected patients; 6) improving access to infertility care for HIV-infected individuals; and 7) providing third-party assisted reproductive services to individuals and couples in which one or both intended parents are infected with HIV.

INFERTILITY TREATMENT WHEN ONE PARTNER IS INFECTED WITH HIV

It is recommended that individuals with HIV delay pregnancy attempts until their HIV-RNA is suppressed or at least after 6 months of antiretroviral therapy (Mujugira 2016). Once couples are ready to pursue reproduction, the presence of HIV may affect the reproductive potential of a seropositive person. For females, the virus may increase their susceptibility to pelvic infections and may also affect ovarian reserve (Irwin 2000, Clark 2001). For infected males, HIV and possibly antiretroviral therapy may be associated with semen abnormalities including low sperm count, low motility, and low volume (HHS Panel website, Garrido 2005, Duliust 2992, Croda-Maya 2009, Frapsauce 2015). In addition, antiretroviral therapy has been shown to affect sperm DNA integrity in HIV infected males, which may be associated with lower natural and assisted pregnancy rates and higher miscarriage rates (Savasi 2018). For others, the virus will have no impact on reproductive functioning unless the person is ill due to an opportunistic infection.

Providing PrEP to HIV-uninfected adults in serodiscordant relationships has been associated with a 95% reduction in HIV-transmission risk, with an observed HIV incidence of <0.5% per year compared to an expected incidence of >5% per year (Baeten 2016). The risk of viral transmission increases...
dramatically if the HIV-infected partner's viral load is high, or if the HIV-uninfected partner has a concomitant genital infection, inflammation, or abrasions. However, HIV shedding into the seminal plasma has been seen in up to 5.3% of HIV infected men, even when on efficient antiretroviral therapy (Pasquier 2017). Even in men with fully suppressed plasma viral loads, viral shedding in the semen is possible (Liuzzi 1996). As outlined below there are a variety of ways in which conception can occur while either eliminating or minimizing the risk of HIV transmission between partners.

Female Partner HIV-infected, Male Partner HIV-uninfected:

If a woman is infected with HIV and her male partner is uninfected, transmission of infection to the male partner can be avoided by performing self-insemination with the partner's sperm at the time of ovulation. The process is known as homologous insemination (Agboghorama 2012). There are also considerable data showing that the risk of transmission can be minimized by using timed intercourse if the woman's viral load is suppressed to undetectable levels on antiretroviral therapy and/or the uninfected male is taking antiretroviral therapy as PrEP (HHS Panel website). While clinicians would need to emphasize that this option may not be as safe as homologous insemination, it does represent an alternative option. No head to head comparative studies have been performed comparing homologous insemination with timed intercourse on antiretroviral therapy.

Regardless of the method used for insemination, the resulting pregnancy may still pose some risk to the HIV-infected woman and her child, because opportunistic infections occurring during pregnancy can be devastating to the woman and fetus. An HIV-infected woman may require medications in the early stages of pregnancy that could adversely affect the developing fetus. In addition, amniocentesis and chorionic villus sampling may also risk viral transmission to the fetus. The U.S. Department of Health and Human Services states that amniocentesis should be performed on women with HIV only after initiation of an effective ART regimen when HIV RNA levels are undetectable and should be done in conjunction with an HIV expert (NIH-Aids info). A small risk of fetal transmission cannot be eliminated. In addition, there is variable risk of transmission to the newborn in utero, during delivery, and with breastfeeding. If an HIV-infected pregnant woman is not actively treated with antiretroviral drugs, the risk of HIV transmission to the infant is >20% regardless of the viral load (Connor 1994). As noted, administration of zidovudine to pregnant women and to newborns during the first 6 weeks of life can substantially reduce the risk of HIV transmission to 5%–8%. Administration of combination antiretroviral therapy and avoidance of breastfeeding may further reduce the chance of infection to approximately 2% (HHS Panel website, Connor 1994, Graham 1999, Lindegren 1999, CDC 2005 p 592-7). However, there are reports of adverse fetal and offspring outcomes among infants exposed to antiretroviral therapy although this is not a consistent finding (Mofenson 2017, Nachega 2017).
Per the U. S. Department of Health and Human Services, breastfeeding is not recommended for women living with HIV in the United States, because most antiretroviral therapy reduces but does not eliminate the risk of HIV transmission via breast milk. In addition, safe and affordable infant feeding alternatives are available and there is a relative paucity of safety data on most modern antiretroviral medications during breastfeeding (AIDSinfo-Breastfeeding).

**Male Partner HIV-infected, Female Partner HIV-uninfected:**

Limiting condomless sex days to the peak fertility window appears to decrease, but not eliminate, the risk of HIV transmission (Liao 2015 IJAS). In one older study, the seroconversion rate was 4.3% of 92 HIV-uninfected women with HIV-infected partners trying to establish pregnancies through timed intercourse, 21/92 men were on antiretroviral therapy at the time of conception, and all of those that converted reported inconsistent condom use (Mandelbrot 1997). In addition, circumcision has also been shown to decrease the risk of HIV transmission (Mills 2008). Other studies show the risk of transmission through unprotected intercourse can be substantially reduced by the use of antiretroviral therapy in the infected partner (Cohen 2011). A prospective study of 453 HIV serodiscordant couples reported no transmission in cases where the infected partner had plasma viral loads less than 1000 copies/ml (Quinn 2000). Even though some HIV-discordant couples have established pregnancies through timed unprotected intercourse without infecting the uninfected partner or child, this practice is not recommended.

For clinics working with couples in which the male is HIV-infected and the female is HIV-uninfected, it is suggested that the male partner viral loads be undetectable. Patients with chronically detectable viral loads should be encouraged to seek fertility treatment through assisted reproductive techniques. In general, viral load < 200 copies for the preceding 6-month period are generally considered acceptable limits for assisted reproduction (Jindal 2016).

In addition to the HIV-positive male partner being actively treated with antiretrovirals, there is accumulating evidence supporting the efficacy of PrEP, in which the uninfected partner is treated with antiretroviral therapy around conception attempts. In one study of 46 serodiscordant couples in which the female was treated with oral tenofovir, none of the women became infected with HIV and pregnancy rates reached 75% after 12 attempts (PHS-PrEP prophylaxis). The U. S. Food and Drug Administration (FDA) states that the risks and benefits of PrEP should be discussed with HIV-discordant couples as one of several options to protect the uninfected partner during conception and pregnancy, so that an informed decision can be made regarding its use (NHS-2017 update). The only medication regimen approved by the FDA and recommended for PrEP with all populations is daily tenofovir 300 mg with emtricitabine 200 mg. REIs should work in collaboration with experts in infectious disease to ensure that patients are adequately counseled regarding the risks and benefits of this therapy and
HIV and infertility treatment

should discuss available alternatives for safer conception.

For HIV serodiscordant couples where the male is living with HIV, sperm preparation and testing can substantially reduce the chance of HIV transmission to the female partner and child. This involves sperm washing to isolate sperm without HIV from seminal plasma and leukocytes (Liao 2015 JIAS), which can then be used for IUI, IVF or ICSI. This is based on the observation that HIV is present in the seminal fluid, but is not capable of attaching to, or infecting, sperm (Agboghoroma 2012). When semen samples devoid of the HIV virus are used for insemination, there have been no reports of mothers or offspring testing positive for HIV (Kambin 2004, Bujan 2007). Of note, many recent protocols have made slight protocol modifications, including triple gradient sperm selection with extended centrifugations (Zamora 2016), or continuous density gradient with swim up (Inoue 2017). A 2016 meta-analysis found no cases of HIV transmission following exposure to washed semen among 3,994 women undergoing 11,585 cycles of assisted reproduction. Similarly, these authors found that in studies that provided data on mother-to-child HIV transmission, there were no cases of vertical transmission among 1,026 newborns, either at birth or at the follow-up evaluations (Zafer 2016). These are highly reassuring data, and these findings have been confirmed in other studies.

Based on these highly reassuring data, in 2017 the Centers for Disease Control and Prevention (CDC) stated that “The risk for transmission from an HIV-infected male partner to an HIV-uninfected female partner is low if appropriate risk-reduction strategies are implemented” (CDC-MMWR-Strategies for preventing HIV). Likewise, in 2018 the U. S. Department of Health and Human Services issued the “Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States”, the contents of which are largely summarized above (AIDSinfo-Recs for use of antiretrovirals).

In addition, some centers will test the washed sperm using polymerase chain reaction (PCR) assay to determine whether the virus is present in the washed sperm preparation, but the utility and effectiveness of this added step has been questioned by other centers that have eliminated PCR from their protocols (Sauer 2005, HHS Panel website, Kambin 2004, Sauer 2009, Peckham 2000).

Data on the use of IVF with ICSI in terms of avoiding transmission to uninfected women are promising. In a 10-year retrospective review of a program offering ART to HIV-discordant couples, 181 couples underwent treatment with IVF with ICSI. There were 116 deliveries of 170 neonates, with no female seroconversions and no infections in any of the offspring (Sauer 2009). Likewise, a 2016 meta-analysis looking at infected male partners with seronegative female partners undergoing IVF/ICSI found no cases of HIV transmission, even among the subset of HIV-infected men without viral suppression at the time of semen washing. Similarly, there were no reported cases of vertical transmission (Zafer 2016).
Data on reproductive outcomes in serodiscordant couples is limited and conflicting. One recent case-control study looking at HIV seropositive men with negative partners undergoing a 3-step sperm-washing procedure with ICSI found slightly lower fertilization rates in HIV males, but otherwise no differences in the number of embryos transferred, cleavage or implantation rates, pregnancy rates per cycle, miscarriage, or live birth rates (Cito 2019). However, a different study looking at HIV seropositive women versus seronegative controls undergoing IVF or ICSI found lower clinical pregnancy rates per transfer (12% versus 32%), implantation rates (10% versus 21%) and live-birth rates (7% versus 19%) in seropositive women (Stora 2016).

While standardized global guidelines are lacking, in high-risk countries, preventative measures do seem to be effective. When a comprehensive safer conception package for HIV-serodiscordant couples was provided (consisting of antiretroviral therapy for HIV-positive partners, oral PrEP for HIV-negative partners, daily fertility and sexual behavior tracking, counselling on self-insemination, voluntary male circumcision and fertility care), the 6 and 12-month cumulative pregnancy rates were 45.3% and 61.9% respectively. No cases of seroconversion were observed (Heffron 2019).

These statistics are reassuring, but the complete efficacy of these techniques is difficult to guarantee. Couples must still be cautioned about the potential risk of HIV transmission to the uninfected partner and to their offspring. It is not possible to guarantee that the female partner will not be infected when using sperm from a HIV-positive male. Options such as donor sperm, adoption (which can be more difficult for HIV-infected prospective parents), or not having children, should be discussed as part of complete counseling. While federal law prevents discrimination of prospective adoptive parents by adoption agencies, the HIV-status of these prospective parents may impact which couple a birth mother selects. 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 skilled in sperm preparation, as well as appropriate testing and treatment necessary to minimize the chance of HIV transmission to partner and offspring. Most recently, a new law will make HIV PrEP and PEP available without a prescription starting in January 2019 in California, thus providing further opportunity to minimize transmission risks (SB-159).

INFERTILITY TREATMENT WHEN BOTH PARTNERS ARE INFECTED WITH HIV

As with any couple presenting for evaluation and treatment, both members of an HIV-infected couple may have normal fertility potential, or one or both may have impaired fertility. Recent data have found that HIV-positive seroconcordant individuals have higher plasma viral loads, with women having higher genital viral loads than their HIV-positive counterparts in discordant relationships, which may translate to faster disease progression and a larger viral reservoir (Jaumdally 2019). Reproductive data
HIV and infertility treatment

on couples in which both are HIV-positive is limited. A single publication has looked at IVF outcomes in seropositive couples. The authors found that outcomes were severely reduced, with only 1 birth after 33 cycles (Vanker Kem 2017). If an HIV-infected couple asks for medical advice regarding pregnancy, they must be encouraged to adopt protocols that have been demonstrated to be safe and effective in Institutional Review Board (IRB)-approved research studies. This will also allow for collection of data on pregnancy and seroconversion outcomes. There have been reports of couples in which both partners' viral loads were suppressed to undetectable levels, who conceived children free of HIV (Vernazza 2011).

While HIV-seroconcordant couples do not have the same concerns of transmission to an uninfected partner described for those serodiscordant, it is important to at least discuss with the couple the possibility of HIV superinfection. While data are imperfect, there are increasing reports that one HIV-infected partner can transmit their unique strain of HIV to another infected partner (Redd 2013). The risk of such events is expected to be very low in the setting where both partners have fully suppressed viral loads on effective antiretroviral therapy, which would be the best way to minimize this risk while optimizing outcomes for the couple and their offspring.

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

The risk of HIV transmission to offspring when one or both parents are seropositive can be greatly reduced but not completely eliminated. According to the American College of Obstetricians and Gynecologists (ACOG), treatment of HIV-infected pregnant women with combined antiretroviral therapy can achieve a 1-2% (or lower) risk of mother-to-child transmission if maternal viral loads of 1000 copies/mL have been sustained, independent of delivery route or duration of ruptured membranes prior to delivery (ACOG 751). Vaginal delivery is appropriate for HIV-infected pregnant women who have been maintained on combined antiretroviral therapy and who have viral loads of 1000 copies/mL or less at the time of delivery (ACOG 751). Vaginal delivery is appropriate for HIV-infected pregnant women who have been maintained on combined antiretroviral therapy and who have viral loads of 1000 copies/mL or less at the time of delivery (ACOG 751). HIV-positive women whose viral loads are more than 1000 copies/mL at the time of delivery should be offered a scheduled pre-labor cesarean delivery (ACOG 751), with intravenous and oral antiretroviral drugs given to infants for 6 weeks post-partum to reduce perinatal transmission rates (Jindal 2016). However, this risk is never completely eliminated.

Does a couple's desire to have genetically related offspring justify the risk of transmitting a serious disease to their child? Although the risk can be significantly reduced, and recent data show no instances of vertical transmission using sperm-prepared IUI or IVF with ICSI, theoretically the risk cannot be completely eliminated. Assessing the ethics of assisting such patients to have children includes addressing the question of whether offspring born with HIV are harmed despite the preventive steps taken. 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-infected couples who wish to have a child. In such instances, the medical care provider should refer couples to a center that has these resources.

There is scant data looking at how young adults living with perinatally acquired HIV fare as they transition into parenthood. The one study that has been conducted was composed of structured interviews of young adults living with perinatally acquired HIV (Fair 2017). Participants expressed concerns about not "being there" for their children due to sickness and worries that their children would experience HIV-related discrimination once the parent’s HIV status was disclosed. Participants reported the importance of emotional support offered by providers and other social services. Those participants who intended to have another child were motivated by a strong desire to create a family of their own as a way to deal with HIV-related losses and stigma. As young adults with perinatally acquired HIV continue to mature, it is important to be aware of the unique needs of families living in the context of intergenerational HIV infection.

TESTING INFERTILE COUPLES FOR HIV

At the end of 2016, the CDC estimated that approximately 162,500 persons in the United States had undiagnosed HIV (CDC-Estimated HIV incidence). Because most of these persons are of reproductive age, the question arises whether or not practitioners should require HIV testing for all couples seeking medical or surgical reproductive assistance. In 2013 the US Preventive Services Task Force recommended that clinicians screen for HIV infection in all adolescents and adults aged 15–65 years (USPSTF 2013). The ACOG (ACOG 752) and the CDC (Branson 2006) have issued similar recommendations.

In the case of gamete donors, testing for HIV and other sexually communicable diseases is ethically justified to protect the health of the gamete recipients. The FDA mandates that all gamete donors be screened for high-risk factors and undergo testing for HIV and other viral infections (FDA final rule). The ASRM Practice Committee recommends that all gamete donors and recipients be tested for HIV and other sexually transmitted diseases and that testing be offered also to the recipients’ partners (ASRM PC 2013-Recs for gamete and embryo donation). Testing donors and recipients for potentially transmittable infectious conditions can be reassuring to all parties involved in ART and should be strongly encouraged.
While new guidelines recommend testing all individuals, repeated testing is recommended for those with ongoing risk for HIV infection, such as those who have a history of repeated sexually transmitted infections, a known HIV-infected sexually intimate partner, multiple sexual partners without barrier protection, bisexual or homosexual behavior, or intravenous 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.

Given the clear data showing that early identification and treatment of HIV-positive pregnant women is the best way to prevent partner seroconversion and neonatal infection, the ACOG recommends that all pregnant women be routinely screened for HIV, unless they decline (opt-out screening), as early as possible in the pregnancy (and even pre-pregnancy). This approach is currently permitted in every American jurisdiction. Repeat HIV testing in the third trimester, is recommended for pregnant women with initial negative HIV antibody tests who are known to be at high risk of acquiring HIV infection. Rapid screening during labor and delivery or during the immediate postpartum period using the opt-out approach should be done for women who were not tested earlier in pregnancy or whose HIV status is otherwise unknown. If a rapid HIV test result during labor is reactive, antiretroviral prophylaxis should be immediately initiated while waiting for supplemental test results (ACOG 752).

Couples should consider HIV testing as part of responsible parenting. National guidelines recommending testing for all adolescents and adults should allay prior concerns that testing is related to suspicions about 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
Knowledge of HIV pathophysiology, combined with careful hygienic practices, has allowed health professionals to minimize the risk of HIV transmission. In the late 1990s, the CDC identified 56 persons who had documented occupational transmission of HIV and another 138 people with possible occupational transmission (CDC HIV/AIDS Surveillance report). Most were nurses and laboratory technicians with accidental infected needle sticks or mucocutaneous exposure. None of these cases of HIV transmission occurred in the context of current ART (Kambin 2004). If standard universal precautions are taken, the risk of viral transmission to medical caregivers is very small and is not a sufficient reason to deny reproductive services to HIV-infected individuals and couples.

Clinicians faced with requests for reproductive assistance from persons who are infected with HIV should be aware of the 1998 United States Supreme Court decision in Bragdon v. Abbott (Bragdon v abbot 1998). The Court ruled that a person with HIV is considered to be “disabled” and therefore
According to that decision, HIV-infected persons are entitled to medical services unless a physician can demonstrate “by objective scientific evidence” that treatment would pose “a significant risk” to the health or safety of others. In the context of ART care, “others” could include health-care workers, patients receiving care at the same clinic, and embryos or gametes stored within proximity to those of HIV-infected patients.

To date, the lack of any occupational transmissions to ART health-care providers or bystander patients in a treating clinic suggests that the risk to these individuals from providing ART care to an HIV-infected patient is minimal. Theoretically, the risk to gametes and embryos could arise through cross-contamination in the laboratory setting although there is no documentation of contamination of stored human tissue. If an HIV-positive female is planning to undergo IVF or ICSI, ICSI is generally recommended over IVF to reduce the number of granulosa and cumulus cells in culture, since these may harbor HIV (Jindal 2016). To avoid even the possibility of cross-contamination, the ASRM Practice Committee recommends that samples from a viral carrier be processed in a separate laboratory or designated space within the main laboratory, utilizing a dedicated storage tank (ASRM PC-viral transmission 2019). Additional measures utilized may include the use of “double bagging” or sealing techniques to prevent the direct contact of cryocontainers with liquid nitrogen, or the storage of samples in liquid nitrogen vapor instead of in liquid nitrogen itself (Agboghoroma, 2012). Unless health-care workers can show that they lack the skill and facilities to treat HIV-infected 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. A comprehensive article discussing guidelines for risk reduction when handling gametes from HIV infected individuals was published in 2016 with detailed and specific instructions for handling semen specimens, eggs, and embryos from HIV-positive patients (Jindal 2016).

IMPROVING ACCESS TO CARE FOR HIV-INFECTED INDIVIDUALS

A recent systemic review found that many individuals in HIV-discordant relationships have fertility desires and intentions, with younger age and a fewer number of living children being associated with increased fertility desires and intentions (Martins 2019). Specifically, a patient survey from a publicly-funded American HIV clinic found that nearly 1/3 of respondents expressed fertility desires (Thomson 2018). Interestingly, in a high-HIV prevalence area, the initiation of antiretroviral therapy in HIV-positive women was found to correlate with the desire to have a child (adjusted OR 2.47), suggesting that improved treatments may impact the desire for children (Mekonnen 2017).

Despite improved outcomes in the use of sperm washing combined with IUI, and IVF with ICSI, and the advent of prophylactic treatment of uninfected partners to virtually eliminate the risk of vertical and
horizontal transmission of HIV, access to these reproductive technologies for seropositive individuals is limited. Fewer than 3% of U.S. ART practices registered with the Society for Assisted Reproductive Technology (SART) provide services to couples in whom one or both partners are infected with HIV (Sauer 2006). Providers are strongly encouraged to reduce barriers to care in order to make infertility treatment available to HIV-infected individuals. The desire for access to reproductive care for HIV-positive individuals has also been voiced by the HIV community. A 2017 article from the Journal of the International AIDS Society states “We strongly believe that fertility care intervention should be the first line treatment, when affordably accessible, over natural conception for HIV serodiscordant couples to achieve pregnancy in a safe and efficacious manner.” The authors later state that “Laboratory assisted fertility methods, including IUI, IVF, and ICSI with semen washing should be the first line treatment recommendation for HIV serodiscordant couples desiring pregnancy...” (Zakarin 2017).

As noted above, to date there have been no reported cases of occupational transmission to ART personnel or contamination of gametes or embryos in the clinic setting that would support denial of service to HIV-infected individuals or couples. The few centers that do provide care report seeing happy and grateful families, many of whom travel a great distance for access to the safest method of reproduction currently available. A 2018 study was performed in which “secret shopper” phone calls were made to SART-designated infertility clinics in which the caller was identified as either a physician (calling on behalf of a HIV-positive patient) or patient, inquiring about ART for HIV-positive patients. The authors found that 40% (for patient callers) to 63% (for physician callers) of clinics offered these services, showing progress with respect to access to reproductive care for persons living with HIV (Leech 2018).

Similar data have been found from the Canadian literature. A study comparing access for HIV-positive persons to Canadian fertility clinics and services in 2007 and 2014 found that 50% of clinics offered a full range of ART services (defined as including IVF). Compared to 2007, more clinics had implemented separate facilities to treat HIV-infected individuals (p = 0.028), offered IVF for HIV-infected female partners (p = 0.013), sperm washing for HIV-infected male partners (p = 0.033), and risk reduction techniques to couples with HIV-infected men and women (p = 0.006) (Lo 2017). While access to fertility services for people with HIV has improved over time, it remains limited, highlighting the need for continued efforts to optimize access to comprehensive services.

THIRD-PARTY ASSISTED REPRODUCTION FOR HIV-INFECTED INTENDED PARENTS

The presence of HIV infection can be a factor for individuals or couples who engage in third-party reproduction by enlisting assistance from a gamete donor or gestational carrier. In the case of an HIV-infected gamete donor or gestational carrier, state laws, federal regulations, and professional guidelines counsel against, and under certain circumstances prohibit, engagement of such individuals (ASRM PC 2013- Recs for gamete and embryo donation, ASRM PC 2015-Recs for practices using gest carriers). In the case where one or both intended parents are infected with HIV, questions arise as to the scope of
disclosure that should be provided to third parties who are enlisted to assist in a reproductive plan. The principle of informed consent can be instructive in this circumstance.

Informed consent in the medical setting requires that physicians disclose any information that would be material to a person’s decision to undergo or refuse treatment. Gamete donors and gestational surrogates do undergo medical treatment and thus are entitled to be fully informed of the risks and benefits of treatments prior to giving consent. In the case of an HIV-infected intended parent who plans to use his or her own gametes in third-party reproduction, for example an HIV-infected male who wishes to retain the services of an egg donor and gestational carrier, what duties of disclosure arise? In terms of medical risk, the egg donor and gestational carrier are not similarly situated because only the woman receiving the gametes is in a position of potential exposure to the virus. Therefore, disclosure of the intended parent’s HIV status would be material to the gestational carrier’s treatment decision as part of the risks/benefits calculus required by informed consent. Full disclosure of the sperm provider’s HIV status must be provided in that case. A gestational carrier who is willing to provide service to an HIV-infected gamete provider/intended parent is entitled to be fully informed of the potential risks to her health, just as an HIV-infected male’s female partner should be informed about potential risks associated with reproductive activity using the male partner’s sperm. In some jurisdictions, recipients of gametes from HIV-infected donors must sign a specialized written waiver acknowledging the medical risks associated with such a transfer (Cal Health and Safety Code).

In the case of an HIV-infected intended parent who does not plan to use his or her gametes, the disclosure analysis is more complex. For example, in the case of a same-sex male couple in which one or both of the partners is infected with HIV but the couple does not plan to use either partner’s sperm, does the physician (or any other professional actor such as an agency) have a duty to disclose the HIV status of the infected partner(s) to the egg donor or gestational carrier? Neither the egg donor nor the gestational carrier faces any medical risk by participating in this couple’s assisted reproduction. The doctrine of informed consent has been interpreted to include nonmedical information that is considered material to a patient’s decision making, but typically only when that information has a potential impact on the patient’s treatment choices and medical outcomes (Moore v Regents of UC 1990). An intended parent’s serostatus would not be included in this category.

Arguments exist that a gamete donor or gestational carrier should be informed of an intended parent’s HIV infection as part of the specialized informed consent process that accompanies third-party reproduction. Since the donor/carrier is providing a service that results in the birth of a child, factors in addition to the medical risks associated with treatment may be relevant to any prospective third-party participant. These factors might include the presence of a chronic medical condition, of which HIV is one of many, in an intended parent. The ASRM Ethics Committee has addressed disclosure of nonmedical
information to gamete donors in the context of informing egg donors about whether their donation resulted in a pregnancy or birth of a child (ASRM EC 2019-Interests in gamete donation). The Committee notes that revelation of such information may interfere with a recipient’s privacy rights and thus encourages clinics to develop written policies regarding revelation of intended parent(s)’ course of treatment to donors. We conclude that programs should clearly inform intended parents, gamete donors, and gestational carriers, before their participation, about what, if any, non-risk posing health information about the intended parents will be shared. To the extent a clinic policy requires or forbids disclosure of an intended parent’s health status to a gamete donor or gestational carrier, HIV infection should be regarded the same as any chronic health condition.

CONCLUSION

Human immunodeficiency virus infection is classified as a chronic disease. It is treatable, but not yet curable. With the use of modern antiretroviral therapy, most people living with HIV now have life expectancies equivalent to those of HIV-negative persons. The potential for HIV-infected persons to live long and healthy lives, have uninfected children, and not transmit the virus to their partners has resulted in increasing numbers of individuals seeking out optimal means for creating biological families. 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 personnel and facilities that can provide the most effective evaluation, treatment, and follow-up. ART clinics with the necessary resources to provide care should offer services to HIV-infected individuals and couples who are willing to use recommended risk-reducing therapies. Clinics without sufficient resources to offer care should assist in referral to providers equipped to manage such patients. In third-party reproduction, disclosure of an intended parent’s HIV status should be commensurate with principles of informed consent. When an intended parent’s HIV status poses no medical risk to gamete donors or gestational carriers, clinics should follow written policies that clearly define what information, if any, will be provided to each party prior to the commencement of any treatment. To the extent a clinic policy requires or forbids disclosure of an intended parent’s health status to a gamete donor or gestational carrier, HIV infection should be regarded the same as any chronic health condition.

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