Recommendations for reducing the risk of viral transmission during fertility treatment with the use of autologous gametes: a committee opinion

The Practice Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

This document provides strategies, based on scientific principles and clinical experience, to reduce the risk of viral transmission in couples seeking treatment for infertility using their own gametes. This document replaces the ASRM Practice Committee document, "*Guidelines for reducing the risk of viral transmission during fertility treatment*," last published in Fertil Steril 2008;90(5 Suppl):S156-62. (Fertil Steril® 2013;99: 340–6. ©2013 by American Society for Reproductive Medicine.)

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Sexually transmitted infections (STIs) are of major concern to reproductive specialists. Heading the list are human immunodeficiency virus (HIV) types 1 and 2 and hepatitis B (HBV) and C (HCV) viruses. These pathogens, which may cause incurable, often fatal, infections, can be transmitted through insemination procedures and from infected mothers to the fetus or newborn. Other sexually transmissible viruses include hepatitis A virus (HAV), human T-cell lymphotropic viruses (HTLV) I and II, human papilloma viruses (HPV), and several members of the herpes virus family: Epstein-Barr virus (EBV), cytomegalovirus (CMV), herpes simplex virus 2 (HSV-2), and human herpes viruses (HHV) types 6 and 8.

Sexually transmitted viruses can cause chronic lifelong infections. Whereas the past two decades of intensive virus research have not provided cures, they have produced a substantial body of information on mechanisms and risk factors underlying STI transmission, suggesting risk-reduction strategies. Furthermore, sensitive and precise diagnostic tests allow the early detection and monitoring of viral infections, and new antiviral drugs make it possible to manage many chronic viral infections. HIV-infected individuals, in particular, are now living healthier, longer lives and, in ever increasing numbers, are choosing to have children. Many are seeking fertility services to maximize reproductive potential and/or minimize the transmission risk to their partners and children.

The Ethics Committee of the American Society for Reproductive Medicine (ASRM) has stated that fertility services cannot be withheld ethically from individuals with chronic viral infections, including HIV, if a center has the resources to provide care. Centers that do not have the resources or facilities to provide care should assist in referral to a center with protocols in place to manage such patients (1). The guidelines in this document provide strategies, based on scientific principles and clinical experience, for reducing the risk of virus transmission in couples seeking treatment from fertility clinics. Recommendations are aimed at the following: 1) reducing viral load in infected partner(s); 2) reducing exposure and susceptibility of a non-infected partner; and 3) promoting frank, detailed discussions with patients about available scientific evidence and risk-reduction strategies to provide a basis for informed consent. Some clinics in Europe and North America have incorporated these principles into practice with encouraging results (2, 3). The Centers for Disease Control and

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Prevention (CDC) are monitoring these developments closely, but have not yet endorsed specific risk-reduction strategies because the number of informed patients is still insufficient to determine the strategies' efficacy (4).

EXISTING SCREENING/TESTING GUIDELINES

Sexually intimate partners are excluded from United States Food and Drug Administration (FDA)-mandated screening and testing for viral infections (5). However, couples proceeding to assisted reproductive technology (ART) will need viral screening. Such screening can help to ensure that appropriate precautions are taken to minimize risk of viral transmission to partners and offspring. Intimate couples in which one or both partners are positive for HIV, HBV, or HCV should be treated by fertility centers which are equipped to care for such couples (1). Also, screening in accordance with the 2007 FDA guidelines would exclude all men as donors who have had any sexual contact with other men during the preceding five years, but would not necessarily exclude heterosexual men who engage in casual sexual relations frequently with different female partners (5).

REQUIREMENTS FOR TREATMENT

Couples in which one or both partners are infected with a sexually transmissible pathogenic virus should receive in-depth preconceptional counseling on the risks of sexual and vertical transmission of their infections. Adoption and, in circumstances involving an infected man and uninfected woman, donor insemination should be presented as the safest options. Couples who decide to proceed with partner-intrauterine insemination (IUI) or other fertility treatment must agree to reasonable interventions aimed at reducing the transmission risk.

Counseling and education concerning safe sex practices should be provided and emphasized. In cases where the male, but not the female, partner is infected, the couple should understand the merits of using condoms throughout fertility treatment, pregnancy, and the postpartum period. Serial diagnostic testing of the uninfected partner is recommended throughout treatment and pregnancy and for both mother and infant during the first year after birth. Informed consent should be explicit and as thorough as possible, emphasizing that risk of transmission cannot be completely eliminated even when specific risk reduction strategies are employed. In-depth psychological, medical, and obstetrical care ideally should be provided by a multidisciplinary medical team.

FACILITIES

Contamination with HIV, HBV, and HCV has been documented in ART clinics (6) and blood banks (7). Although there is no documentation of cross contamination of stored human tissue, it is highly recommended that samples from viral carriers be processed in a separate laboratory or designated space within the main laboratory, utilizing a dedicated storage tank, to minimize the risk of cross contamination. HIV, HCV, HBV, and possibly other viruses can survive in liquid nitrogen, making it possible to cross contaminate samples in liquid nitrogen storage tanks. To protect cryopreserved specimens from potential cross contamination, it is advised that HIV-, HBV-, and HCV-infected specimens be stored in separate tanks. The following measures have been proposed to further reduce the risks of cross contamination of samples in liquid nitrogen storage:

1. The use of specimen containers guaranteed by the manufacturer to withstand freezing temperatures and thawing cycles
2. The use of "double bagging" or sealing techniques to prevent the direct contact of cryocontainers with liquid nitrogen
3. The storage of samples in liquid nitrogen vapor instead of in liquid nitrogen itself. Recent studies have demonstrated that the use of vapor storage of both oocytes and sperm may be a viable alternative to storage of gametes and/or embryos in liquid nitrogen alone, which has the theoretical potential of becoming contaminated (8, 9)
4. The use of "sperm-washing" techniques to decrease the viral load before freezing semen samples (10).

SPERM-WASH METHODS

Sperm-wash procedures involving density gradient centrifugation followed by a sperm swim-up step have been used to separate motile sperm from free HIV virus and HIV-infected somatic cells (11–13). Quantitative assessment of HIV in semen before and after the sperm-wash procedure indicates that >99% of HIV is removed (12). Virologic testing of the sperm fraction for the presence of residual detectable HIV prior to its use for insemination can provide an added measure of safety, as up to 5% to 10% of samples may contain residual virus after this procedure (13). Similar sperm preparation techniques have been used to separate HCV from sperm (14) and may be useful for other viral infections where the majority of virus is found in free form or associated with semen somatic cells (i.e., white blood cells, epithelial cells). Some centers also have adopted routine testing of the washed semen product for HIV and/or HCV with a polymerase chain reaction technique to prevent infection of the inseminated woman.

VIRUS-SPECIFIC RISK REDUCTION STRATEGIES

HIV

HIV-1 and HIV-2 are retroviruses that primarily infect T lymphocytes and other immune cells. HIV-1 and HIV-2 have the same modes of transmission and are associated with similar opportunistic infections and acquired immunodeficiency syndrome (AIDS). Infection with HIV-1 leads to AIDS and death in most untreated individuals. Immunodeficiency associated with HIV-2 infection may be less severe and develop more slowly. Early in the course of infection, individuals infected with HIV-2 are less infectious than those infected with HIV-1.

HIV/AIDS is endemic in sub-Saharan Africa and Southeast Asia and is prevalent throughout the world in high-risk groups, including users of unscreened blood products, intravenous drug users, sex workers, and homosexual men. HIV is found in blood, semen, and vaginal secretions of infected individuals and is transmitted sexually and vertically. The

rate of HIV heterosexual transmission is relatively low (approximately one per 1,000 acts of unprotected intercourse) (15). Risk factors for HIV transmission include genital tract infections and ulceration, sexual practices that induce trauma or bleeding, and lack of male circumcision (16). The rate of HIV transmission is associated highly with peripheral blood viral load and is lowest in individuals with peripheral viral loads <10,000 copies/mL (17). The seminal HIV viral load roughly correlates with plasma viral load (18) but is much more variable. Individuals with undetectable circulating viral loads still can have infectious HIV in their semen, especially if they have a coexisting STI or genital tract inflammation (19, 20). Therefore, it is difficult to predict whether a man will be infectious based on either his plasma viral load or a previous seminal viral load.

The CDC estimated that between eight and 141 women were infected through donor insemination between 1980 and 1984 before strict donor screening and semen quarantine practices were implemented (21). Because HIV is found primarily in white blood cells and as cell-free virions in semen (22), sperm-wash techniques that separate motile sperm from the round cell and seminal fluid fractions, including density gradient centrifugation and swim-up methods, can markedly reduce HIV levels prior to insemination (12). Several European and North American fertility centers have used "sperm-wash" and other risk-reduction techniques for HIV-discordant couples desiring children. Since 1987, several thousand attempts at IUI and in vitro fertilization (IVF) have been reported in which processed sperm from HIV-seropositive men were used to achieve pregnancy in HIV-seronegative women, without HIV infection occurring in uninfected partners or offspring (3, 23, 24). Risk-reduction techniques also have been used for couples where both partners are HIV-infected to reduce the risk of superinfection of the female partner with different strains of HIV or drug-resistant HIV.

Both partners should undergo a sexual health screen. Bacterial vaginosis and infections with HSV-2, Trichomonas vaginalis, Chlamydia trachomatis, Neisseria gonorrhea and Treponema pallidum can increase HIV-1 transmission (25) and should be treated. The use of condoms during sex should be reinforced. Practices and behaviors that lacerate mucosal surfaces are other risk factors for HIV transmission and should be avoided (26). Both partners should undergo a fertility assessment so that the number of exposures is minimized. Ovulation induction, IVF, or intracytoplasmic sperm injection (ICSI) should be applied as indicated.

HIV viremia should be minimized in the infected partner (peripheral blood viral load less than 10,000 copies/mL) through use of highly active antiretroviral therapy (HAART) to reduce levels of HIV in semen. A "sperm-wash" protocol should be used to enrich motile sperm and to reduce or eliminate HIV-infected white blood cells and free virus in the fraction isolated for insemination. The most widely used sperm-wash procedure for HIV reduction involves the use of gradient centrifugation followed by a sperm swim-up procedure (11). Where available, testing of the processed sample for HIV ribonucleic acid (RNA) prior to insemination may further reduce risk. Trauma to the cervix or uterus during the IUI procedure must be minimized.

Experimental approaches such as pre-exposure prophylaxis (PREP) with antiretroviral drugs (27–29) and locally applied vaginal estrogen gels (28) may reduce further the susceptibility of the uninfected female partner. Data suggesting the potential benefit of PREP using tenofovir, a rapidly acting antiretroviral drug with a long half life, are preliminary but may be discussed with couples (30).

A recent Cochran review demonstrated that the reduction of HIV transmission in discordant couples was greatest with the use of antiretroviral therapy (31). This review included 7 observational studies involving a total of 6792 participants in which 436 episodes of HIV transmission were identified: 71 in couples in whom the affected partner was being treated with antiretroviral therapy and 365 among untreated couples. However, if the HIV seropositive partner had >350 CD4 cells/μL, the conversion of the seronegative partner was 0 in the antiretroviral-treated group compared to 61 in the non-treated group with a conversion rate of 0.02. Although many centers have demonstrated low risk of HIV seroconversion, the risk is still possible, but appears to be much better when antiretroviral therapy for the infected partner is utilized and the seropositive partner has a higher CD4 cell count >350 cells/μL.

The uninfected partner in a discordant couple should be tested for HIV serology and viral load at three-month intervals during treatment and pregnancy. If HIV infection is detected in the female partner during pregnancy, she should be referred to an obstetrical service experienced in managing HIV-infected women. Use of antiretroviral drugs during pregnancy and/or labor, use of cesarean section, and avoidance of breastfeeding can reduce the risk of vertical transmission of HIV to less than 2% (32).

Hepatitis B

HBV, a double-stranded DNA virus, is a major cause of acute and chronic hepatitis, cirrhosis, and hepatocellular cancer. HBV is one of the most common infectious diseases in the world; it has been estimated that 350 million people worldwide are HBV carriers (33–35). HBV can be transmitted parenterally, sexually, vertically, and via other routes of mucosal exposure. Approximately 25% of regular sexual contacts of HBV-infected persons will become seropositive for HBV (34), and HBV has been transmitted through artificial insemination (35). Healthcare workers ran a high occupational risk of HBV infection before universal precautions and HBV immunization were introduced in the workplace. Universal safety precautions and vaccination with HBV vaccine, available since 1982, are the most effective ways to reduce the risk of HBV infection (36).

HBV-infected individuals run a high risk of co-infection or superinfection with hepatitis D virus (HDV), a circular replication-defective RNA virus that requires the presence of HBV for replication (37). Approximately 25% of chronic HBV carriers are co-infected with HDV, which increases their risk of cirrhosis from 15% to 80%. Vertical transmission of HDV has been documented. Since HBV is needed for HDV replication, measures to prevent the transmission of HBV, such as

vaccination of uninfected partners and newborns, will prevent the transmission of HDV.

In couples who are discordant for HBV infection, the partner who is seronegative should be vaccinated against HBV. Fertility treatments may be initiated once the vaccinated partner's anti-hepatitis B surface antibody titer (HBsAB) is positive. Modified sperm washing to reduce viral load is not required after the female partner is immunized against HBV. If the female is the infected partner and is HBsAg-positive, her newborn should receive immunoprophylaxis within 12 hours after birth. Immunoprophylaxis consists of both HBV vaccine and immunoglobulin, followed by two more injections of HBV vaccine in the first six months of life. Breastfeeding is not contraindicated in women chronically infected with HBV (38).

Hepatitis C

HCV is a blood-borne RNA virus that is transmitted primarily through parenteral exposure (blood products, shared needles, needle stick injuries). HCV also has been detected in saliva, urine, semen, vaginal secretions, and breast milk, and sexual and vertical transmission are probable secondary modes of transmission (39).

HCV infects over 1% of the world's population. Based on prenatal testing, the seroprevalence of HCV in the United States is between 2.3% and 4.5%. Groups at highest risk are intravenous drug users, hemophiliacs, homosexual men, sexual partners of HCV-infected individuals, and sex workers (40). HCV is a highly pathogenic virus: 80% of patients infected with HCV will develop chronic liver disease, 35% will develop cirrhosis, and 5% will progress to hepatocellular carcinoma (41). Unlike HBV, there is no vaccine for HCV. Therefore, it is essential to employ risk-reduction measures during assisted reproduction.

There is a small, but measurable, risk of HCV transmission via semen. All patients with viral hepatitis C should be counseled about the risks of transmission to their partner, children, and their healthcare team. When the male partner is HCV-infected, sperm washing can reduce the viral load in semen and is recommended to reduce the risk of transmission to his partner (14). Using IVF with intracytoplasmic sperm injection has also been demonstrated to reduce the risk of transmission of HCV when the male is seropositive (42).

If either partner is chronically infected with HCV (HCVRNA positive), treatment with peginterferon alfa and ribavirin should be considered prior to fertility treatment in order to reduce the infected partner's viral load (43). The goal of therapy is to achieve a sustained virologic response, and the recommended duration of the initial course of therapy is 48 weeks. In addition, pregnancy should be deferred for an additional six months after conclusion of therapy, regardless of which partner is undergoing treatment. Although peginterferon alfa is listed as a pregnancy category C drug, ribavirin is a category X medication and has proven teratogenic and embryocidal properties in all animal species. Ribavirin is contraindicated in the male partner of a pregnant female and in pregnancy. Because the drug is believed to cause new mutations, it is recommended that: two forms of contraception be used during therapy; pregnancy testing be performed monthly; and pregnancy be avoided for the first six months after discontinuation of therapy in either partner.

Although few women have been studied, there does not appear to be an increase in adverse pregnancy outcomes in HCV-infected pregnant women. The risk of vertical transmission correlates with maternal viral burden. In HCV-positive women who decline therapy, or in those who fail to achieve a sustained virologic response to therapy, the risk of vertical transmission is greatest when maternal viral levels exceed 106 copies/mL. There is no vaccine available to treat infants born to HCV-infected women; breastfeeding is allowed.

Hepatitis A Virus

HAV, a small RNA virus, is a major cause of acute hepatitis in the United States. Infection usually produces immunity that limits the duration of infection and prevents symptomatic recurrence (36). Chronic infection is rare in immunocompetent individuals. As a result, HAV accounts for less than 10% of all cases of fulminant hepatitis, and the mortality in acute symptomatic HAV infection is less than 0.1%. HAV is spread primarily by fecal-oral transmission. The virus also can be found in semen, and epidemiologic studies indicate that it is sexually transmitted in high-risk groups such as sex workers and homosexual men. Hepatitis A vaccines are available for persons at increased risk of HAV infection, and immune globulin is used to protect against illness associated with HAV infection.

Human T-cell Lymphotropic Viruses I and II

HTLV-I and II appear to be ancient retroviruses of humans that establish permanent infections but have low potential to cause human disease (44). HTLV-1 infects primarily CD4 T-cells and is the cause of adult T-cell leukemia (ATL) and HTLV-I–associated myelopathy (HAM), also known as spastic paraparesis. Only 1% to 4% of infected individuals will develop either ATL or HAM. HTLV-II infects CD8 T-cells. Although HTLV-II has no proven connection to human disease, links to neurologic disorders are suspected. The distributions of HTLV-I and -II in the United States differ from those elsewhere in the world. HTLV-I has a low endemic rate (slightly greater than 1%) in blacks of the Caribbean basin and tropical Africa; black immigrants to the southeastern United States; native Americans in North and South America; and natives of southern Japan and northern Oceania. HTLV-II has a low endemic rate in native North Americans and worldwide among intravenous drug users and their partners. In endemically infected populations, the virus is propagated through sexual contact and by transmission from mother to child. Recently, injection-drug users in the United States and Europe have become infected with HTLV-I and –II through needle sharing, and secondary sexual transmission has introduced these viruses at low levels into the general population and blood donors. Semen donors are screened for HTLV-I and -II because of the potential for transmission through ART procedures. Because HTLV-I and -II have several properties in common with HIV, risk reduction protocols

devised for HIV-discordant couples that separate infected white blood cells and free virus from sperm (i.e., sperm washing before insemination) could be applied in cases where semen from directed donors infected with HTLV-I and -II will be used to inseminate an uninfected partner.

Human Papilloma Viruses

Papilloma viruses are a family of small DNA viruses that primarily induce epithelial cell proliferation, or papillomas. To date, more than 100 HPV genotypes have been identified, of which approximately 50 infect the genital tract (45). These viruses have been grouped into high- and low-risk types based on the potential of the infected cells to progress to carcinoma. HPV 16, 18, 31, and 45 are among those that are considered high-risk types because they have been associated with invasive squamous cell cancers of the genital tract and anus. Squamous intraepithelial lesions (SILs) of the cervix, vagina, vulva, penis and anus have been associated with these and other HPV types. Genital HPV infections are transmitted primarily through sexual contact, and 50% of sexually active adults have been infected with one or more HPV type. HPV is detected frequently in semen and urethral swabs from normal men. Because these viruses are so prevalent, a coherent strategy for donor screening and risk reduction has not been developed. Since HPV appears in semen as cell-free virus and in infected epithelial cells, sperm-wash protocols may reduce the infectiousness of semen from HPV-infected men.

The Food and Drug Administration (FDA) first approved a quadrivalent vaccine for HPV 6/11/16/18 in 2006 (46). This vaccine, approved for administration in girls ages 9 to 26 years, offers protection against cervical dysplasias, cervical cancers, vulvar/vaginal dysplasias, and genital warts. In 2009 this vaccine was also FDA approved for prevention of genital warts due to HPV types 6 and 11 in boys and men ages 9 through 26. A bivalent HPV vaccine has also been approved for girls between the ages 10 to 25 years for the prevention of cervical cancer and cervical dysplasia.

Herpes Viruses

Viruses of the *Herpes viridae* family can be divided into three subgroups based on biologic differences (47). Alpha herpes viruses are neurotropic and replicate rapidly; examples include HSV-1 and HSV-2. Beta herpes viruses, including CMV, HHV-6, and HHV-7, replicate slowly and have restricted host cell specificity. Gamma herpes viruses, which include EBV and HHV-8, are slow-growing lymphotropic viruses. Human herpes virus infections are endemic and cause wide-ranging pathology. Certain herpes viruses encode proteins that override normal controls on cell division, leading to malignant transformation. EBV has been implicated as a causal factor in a number of malignancies, including Burkitt's lymphoma, Hodgkin's lymphoma, and nasopharyngeal carcinoma. HHV-8 has been associated with Kaposi's sarcoma, and CMV has been associated with several malignancies, including prostate carcinoma, cervical carcinoma, and adenocarcinoma, although causal relationships have not been established. HHV-6 infection can cause roseola infantum, hepatitis, and pneumonitis. HSV-1 and 2 can cause painful ulcerative diseases including gingivostomatitis, herpes labialis, keratoconjunctivitis, genital and neonatal herpes, and also encephalitis and meningitis. HSV-2 and CMV infections can produce serious brain damage in the newborn. Most of the herpes viruses have been detected in semen, and sexual contact is a significant mode of transmission for HSV-2, CMV, and HHV-8 (46).

HSV-2 can cause serious complications if the fetus becomes infected during maternal viremia (48). To reduce the risk of HSV-2 transmission, semen collection should be avoided when a lesion is present, and infected male partners may be treated with a nucleoside analog against HSV-2 (i.e., acyclovir or valacyclovir) to reduce HSV-2 shedding (48). Sperm-wash protocols also may be effective because HSV-2 normally appears in semen as free viral particles. Women infected with HSV-2 are treated with acyclovir during pregnancy to reduce the risk of vertical virus transmission. Acyclovir is a category B drug during pregnancy.

Semen donors are screened for CMV because the virus can be transmitted via IUI (49), and primary infection during early pregnancy may have serious complications in the fetus and neonate (50). CMV is the most significant cause of congenital viral infection in the United States. Generalized infection can result in neonatal death or long-term complications such as mental retardation, hearing loss, and blindness. These risks are almost entirely limited to women who were unexposed to CMV prior to pregnancy and contract a primary infection during pregnancy. However, two-thirds of the infants born to women with primary CMV infection during pregnancy do not become infected and only 10% to 15% of the remaining third exhibit symptoms at the time of birth (51). The risk of CMV-related neonatal complications for women infected at least six months before conception appears very low (51). Because CMV is so common, insemination with semen from a CMV-infected man is permissible when the female partner is also CMV seropositive. Although the practice is not entirely without risk, because there are many strains of CMV and superinfection is possible, the associated risk of newborn CMV infection is approximately 1%, and such infants appear to have no significant illness or other abnormality (51). In cases of known-donor directed insemination, when the donor is CMV infected and the partner is uninfected, sperm wash may reduce the risk of transmission of CMV to the partner.

SUMMARY

- Infertile couples should be advised that transmission of viral hepatitis and HIV in assisted reproduction is possible, but the magnitude of the risk is unknown.
- Viral screening of intimate partners undergoing fertility treatment is not required, but can help to ensure that appropriate precautions are taken to minimize risk of transmission to uninfected partners and offspring.

CONCLUSIONS

- Good clinical practice dictates that fertility services should not be withheld from individuals with chronic viral

infections, including HIV, if the center has the necessary resources to provide care. Referral to a center having such capabilities is also appropriate.

- There is good evidence to support the recommendation that antiretroviral drugs should be used in the HIV-infected partner to reduce HIV viremia.
- While there is insufficient evidence to endorse the practice, it makes sense that semen and embryos from patients infected with HIV, HCV, and/or HBV should be stored in separate HIV- HCV- or HBV- designated storage tanks because of theoretic risk of transmission.
- There is good evidence to support the recommendation that, if the male partner is infected with HIV, sperm-wash methods should be used to reduce the levels of HIV-infected white blood cells and free virus in the insemination fraction of IUI specimens. In addition, the uninfected partner should be monitored periodically for HIV during treatment and pregnancy.
- There is good evidence to support the recommendation that if one partner is infected with HBV, the seronegative partner should be vaccinated against HBV. Once the female partner has been immunized against HBV, sperm washing solely to reduce HBV viral load in the male partner is unnecessary.
- There is good evidence to support the recommendation that infants born to mothers who are HBsAg-positive should receive both hepatitis B immune globulin and the hepatitis B vaccine within 12 hours after birth. Breastfeeding of newborns is not contraindicated after immunoprophylaxis.
- There is good evidence to support the recommendation that women who are HCV-positive should be counseled about the risk of transmission of HCV to their fetus with increasing viral loads and positive HIV status. Breastfeeding is not contraindicated.
- There is good evidence that when the male partner is HCV-infected, sperm washing can reduce viral loads in the insemination specimen.
- There is good evidence to support the recommendation that HCV-infected partners be treated with peginterferon alfa (pregnancy category C) and ribavirin (pregnancy category X) to induce a sustained virologic response. Because ribavirin is a category X medication, it is contraindicated during pregnancy. Attempts to conceive should be deferred for six months after completion of treatment in either partner.
- There is good evidence that in women infected with HSV-2 acyclovir decreases the risk of vertical viral transmission.
- Sperm washing may reduce the risk of transmission of HSV and CMV when the male partner is infected. However, as CMV is so common, insemination with semen from a CMV-infected man is permissible when the female partner is also CMV seropositive.

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