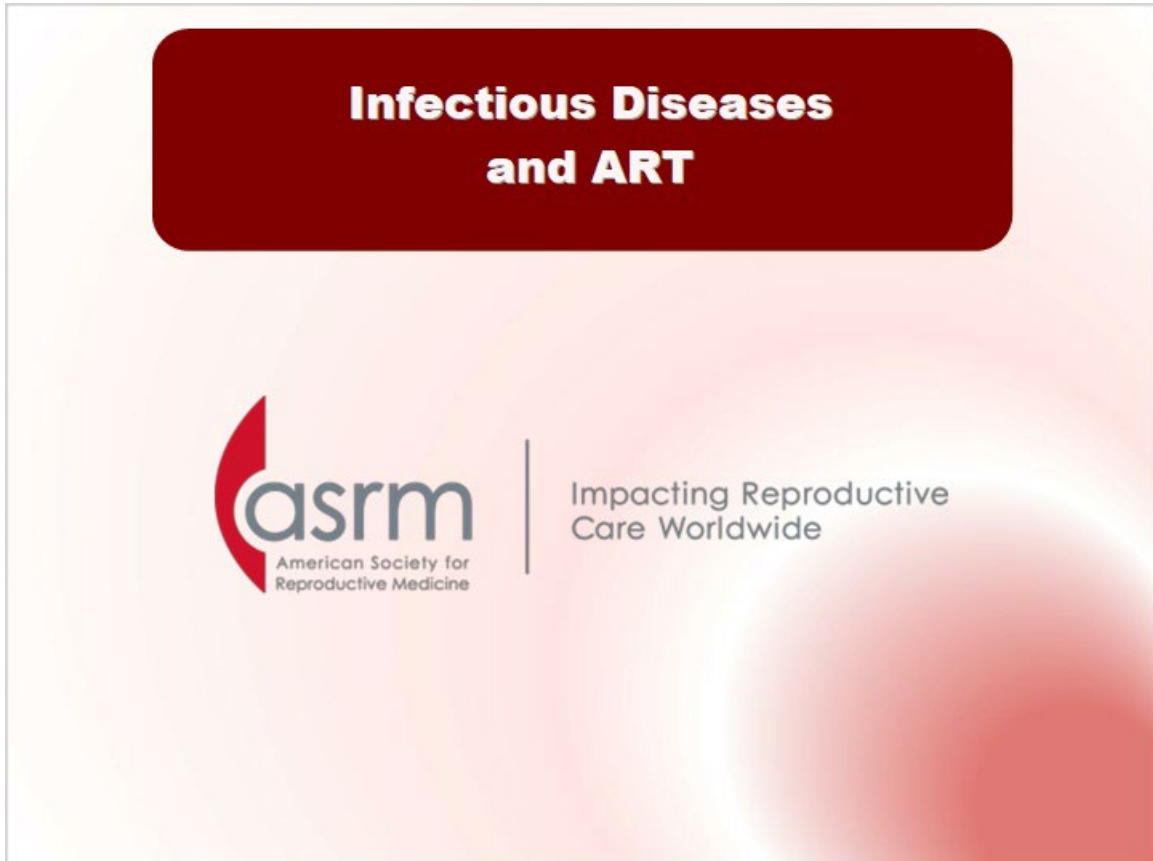


LABCC100 Lesson 30

1.1 Infectious Diseases



Notes:

Welcome to the American Society for Reproductive Medicine's eLearning modules. The subject of this presentation is Infectious Diseases and Assisted Reproductive Technology.

1.2 Learning Objectives

Learning Objectives

At the conclusion of this presentation, participants should be able to:

1. Discuss recommendations for evaluation of, vaccination, and possible treatment for infectious diseases prior to fertility evaluation and treatment.
2. Identify strategies to reduce transmission risks and the benefits of current methods of treating couples using assisted reproductive technology.

Note: This module is not intended to be an exhaustive review of communicable diseases that can be transmitted via sexual contact and/or assisted reproductive technology, but a review of the viral and bacterial pathogens that are of major concern in this field.

Notes:

At the conclusion of this presentation, participants should be able to:

Discuss recommendations for evaluation of, vaccination, and possible treatment for infectious diseases prior to fertility evaluation and treatment.

Identify strategies to reduce transmission risks and the benefits of current methods of treating couples using assisted reproductive technology. Note that this module is not intended to be an exhaustive review of communicable diseases that can be transmitted via sexual contact and/or assisted reproductive technology, but a review of the major viral and bacterial pathogens that are of major concern in this field.

1.3 Abbreviations Used Throughout this Module

Abbreviations Used Throughout this Module

- ART - Assisted Reproductive Technology
- CDC - US Centers for Disease Control and Prevention
- CMV - Cytomegalovirus
- FDA - US Food and Drug Administration
- HIV - Human Immunodeficiency Virus
- HPV - Human Papillomavirus
- HSV - Herpes Simplex Virus
- HTLV - Human T-cell Lymphotropic Virus
- ICSI - Intracytoplasmic Sperm Injection
- IUI - Intrauterine Insemination
- PCR - Polymerase Chain Reaction

Notes:

The abbreviations shown here will be used throughout this module.

ART - Assisted Reproductive Technology

CDC - US Centers for Disease Control and Prevention

CMV - Cytomegalovirus

FDA - US Food and Drug Administration

HIV - Human Immunodeficiency Virus

HPV - Human Papillomavirus

HSV - Herpes Simplex Virus

HTLV - Human T-cell Lymphotropic Virus

ICSI - Intracytoplasmic Sperm Injection

IUI - Intrauterine Insemination

PCR - Polymerase Chain Reaction

1.4 Infectious Diseases and ART

Infectious Diseases and ART

- Standard preconception screening, testing, and counseling
- Viral screening as indicated prior to ART to minimize risk of transmission to partners and offspring
- Sexually transmissible pathogens and tests
 - HIV-1,2 antibody; HIV-1 nucleic acid test (NAT); HIV group O
 - Hepatitis screen (hepatitis B surface antigen (HBsAg); hepatitis B core antibody (HBcAb); hepatitis C (HCV)
 - Cytomegalovirus (CMV)
 - HTLV I, II (at discretion of clinician)
 - Bacteria: *Neisseria gonorrhoeae* (gonorrhea), *Chlamydia trachomatis*, *Treponema pallidum* (syphilis)
- Screen patient for travel consistent with exposure to
 - Zika virus
 - Ebola virus

ASRM Practice Committee, 2013

Notes:

Generally, as part of the workup of an infertile couple prior to assisted reproductive technology (ART), the physician will recommend standard preconception screening, testing, and counseling. Viral screening may be required or indicated to ensure that appropriate precautions are taken to minimize risk of transmission to partners and offspring. Pathogens such as those listed can cause incurable, even fatal, infections in adults or damage to a developing fetus. These can be transmitted via sexual means, but also through insemination procedures, and from infected mothers to the fetus or newborn. Some viruses cause chronic lifelong infections. While there are no cures for some of these viruses, for others, including bacterial infection, there are various treatments and potential cures, thus reducing or even eliminating the risk of sexual or vertical transmission. There is also substantial information on reducing the risk of viral transmission. Sensitive and precise diagnostic tests allow for early detection and monitoring, and new antiviral drugs make it possible to manage chronic viral infections.

1.5 Screening and Testing of ART Patients

Screening and Testing of ART Patients

- Sexually intimate partners are excluded from FDA requirements for screening and testing for viral infections (FDA 21 CFR 1271)
 - Couples proceeding to ART should have appropriate screening and testing to insure appropriate precautions are taken to minimize risk of viral transmission to partner and offspring, and to reduce risk to clinic personnel.
- Anonymous gamete donors must be screened and tested according to FDA regulations (FDA 21 CFR 1271), and would be prohibited from donating gametes if screening or testing is positive.
 - Known or directed gamete donors that screen or test positive for communicable diseases can be used with exception (FDA 21 CFR §1271.65[b]).
 - CMV and HTLV testing not routine for oocyte donors since oocytes not classified as “leukocyte rich”

Notes:

The FDA Code of Federal Regulation (FDA 21 CFR 1271) provides specific information regarding human cells, tissues, or cellular or tissue-based products (HCT/Ps). Although the FDA requires extensive screening and testing of both anonymous and known gamete donors, there is no such requirement for screening and testing of a sexually intimate partner. However, it is preferable to screen and test a couple for the aforementioned communicable diseases to minimize transmission to the partner and offspring, and to reduce risk to clinic personnel.

Anonymous sperm donors must be screened and tested according to FDA regulations, which include cryopreservation and quarantine of specimens for a minimum of 180 days followed by retesting before release for use. There is no requirement for quarantine for known or directed sperm donors, provided that testing is done within 7 days of each collection. Anonymous oocyte donors must meet all screening requirements as for sperm donors, but the testing must be done within 30 days of each egg retrieval. CMV and

HTLV testing are not routine for oocyte donors since oocytes are not classified as "leukocyte rich."

1.6 Vaccination Guidelines

Vaccination Guidelines



- Vaccination before or during pregnancy protects women from serious illnesses, prevents vertical transmission to the fetus and confers passive immunity to the newborn.
- Immunization schedules are best completed before beginning treatment for infertility because some vaccinations should not be administered during pregnancy.
- Measles, mumps, rubella (MMR); influenza; varicella; tetanus, diphtheria, pertussis (Td/Tdap)
- Hepatitis A, B; HPV; Meningococcal

CDC, 2014

ASRM Practice Committee, 2013

Notes:

As with any couple considering family planning, infertile couples should be counseled about vaccinations prior to pregnancy. Ideally, immunization schedules are best completed prior to beginning infertility treatments, so as not to risk harm to the fetus. Recommendations for screening and vaccination include measles, mumps, rubella (MMR); influenza; and tetanus, diphtheria, pertussis (Td/Tdap). A hepatitis vaccine series, HPV and meningococcal vaccines may also be recommended.

1.7 Treatment when One or Both Partners is Positive

Treatment when One or Both Partners is Positive

- Preconception counseling on risks of sexual and vertical transmission of the infection
 - Interventions to reduce transmission risk
 - Condom use
 - Serial diagnostic testing of uninfected partner, mother and infant during first year after birth
 - Other options (adoption, donated gametes)
- Proceeding with treatment
 - Informed consent prior to any ART procedures
- Psychological, medical, obstetrical care by multidisciplinary team

ASRM Practice Committee, 2013

Notes:

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.

1.8 Treatment when One or Both Partners is Positive

Treatment when One or Both Partners is Positive

- 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.

ASRM Ethics Committee, 2010

Notes:

The Ethics Committee of the American Society for Reproductive Medicine 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.

1.9 Specific Pathogens of Concern in ART

Specific Pathogens of Concern in ART

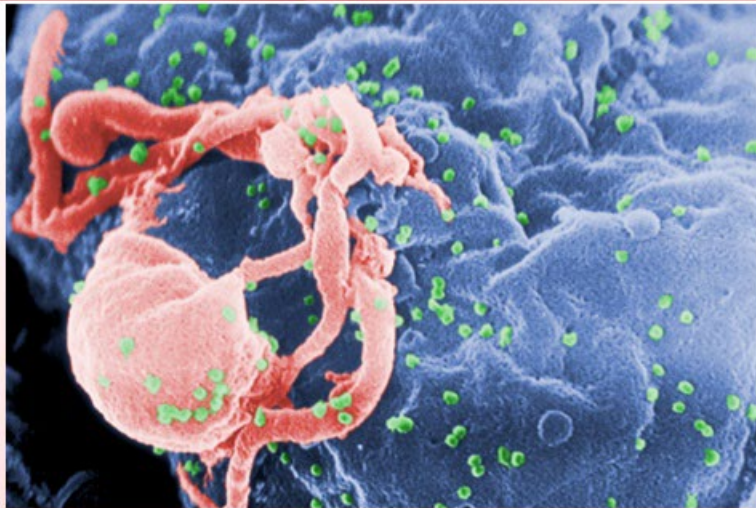


image source, public domain from
<http://upload.wikimedia.org/wikipedia/commons/1/1a/HIV-budding-Color.jpg>

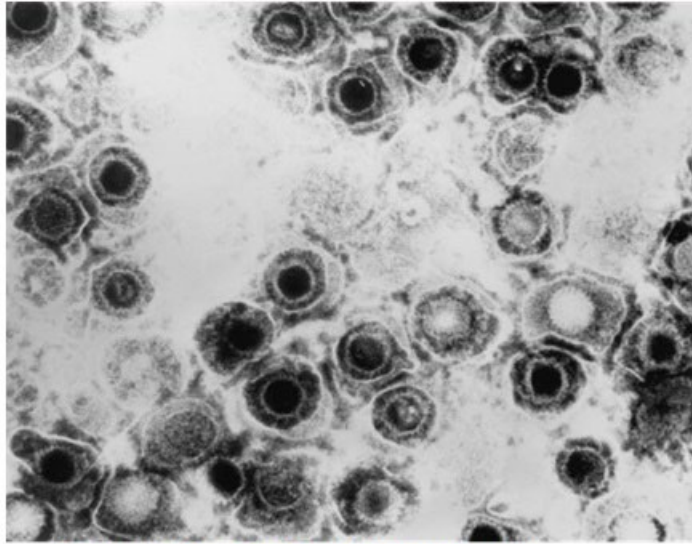
Notes:

This section will address some of the specific pathogens of concern in ART.

1.10 Herpes Viruses

Herpes Viruses

- Alpha
 - Herpes simplex viruses 1 and 2 (HSV-1; HSV-2)
 - Genital herpes
- Beta
 - Include cytomegalovirus (CMV)
 - Replicate slowly
- Gamma
 - Slow-growing lymphotropic viruses
- No cure



http://phil.cdc.gov/PHIL_images/00301990/00014/802-0474_lores.jpg

Notes:

Based on biological differences, the herpes virus family is divided into three subgroups. Alpha herpes viruses are neurotropic and replicate rapidly. Examples included HSV-1 and HSV-2, called the herpes simplex viruses, which cause genital herpes. Beta herpes viruses include cytomegalovirus (CMV). These replicate slowly and have restricted host cell specificities. Gamma types are slow-growing lymphotropic viruses. There is no cure for herpes.

1.11 HSV-1 and HSV-2

HSV-1 and HSV-2

Transmission

- More easily transmitted men → women than the reverse.
- Via contact with open lesion, mucosal surface, genital or oral secretions.
- Sexual contact is a significant mode of transmission for HSV-2 as well as other types of herpes viruses.
- Most herpes viruses have been detected in semen.
- Semen collection for ART should be avoided when a lesion is present.
 - Sperm washing procedures may be effective since HSV-2 appears in semen as free viral particles which can be removed by gradient or swim-up procedures.
 - Treatment with antiviral medication prior to semen collection can reduce HSV-2 shedding.

ASRM Practice Committee, 2013
www.cdc.gov

Notes:

Infections are transmitted through contact with an open lesion, mucosal surface, genital or oral secretions. Herpes infection is more easily transmitted from men to women than the reverse.

Sexual contact is a significant mode of transmission for HSV-2, CMV and the gamma type, HHV-8. If the fetus becomes infected during maternal seroconversion serious complications could arise. Most of the herpes viruses have been detected in semen.

To reduce the risk of HSV-2 transmission, semen collection should be avoided when the male has a visible lesion. Antiviral medications can also reduce HSV-2 shedding. Since HSV-2 normally appears in semen as free viral particles, sperm wash protocols may be an effective method to reduce transmission to the female from herpes positive males during ART procedures. Treatment with antiviral medication prior to semen collection can reduce HSV-2 shedding.

1.12 Cytomegalovirus (CMV)

Cytomegalovirus (CMV)

- Herpes virus family - beta type herpes virus
- Causes cell fusions ("megalo-")
- Present in semen, urine, and saliva
- Approximately half of US population infected; most have no symptoms
- 1/3 women infected during pregnancy pass virus to fetus
- The most common viral infection in newborns
- ~1 to 2 babies/1000 live births will have permanent CMV-related problems (hearing loss, blindness or developmental disabilities)
- Risks limited to women unexposed to CMV prior to pregnancy who contract primary infection at/around time of conception or during pregnancy

www.cdc.gov/cmv

ASRM Practice Committee, 2013

Notes:

CMV is one of the herpes viruses and causes cell fusions, hence the term "megalo-" in the name. The virus is present in semen, urine, and saliva. Approximately half the US population is infected, but most healthy children and adults infected with CMV have never had symptoms. One-third of women infected during pregnancy pass the virus to the developing fetus and it is the most common viral infection in newborns. For every 1000 pregnancies that result in a live birth, approximately 1 to 2 babies will have permanent CMV-related problems, including hearing loss or developmental disabilities. Congenital CMV infection causes more long-term problems and childhood deaths than Down syndrome, fetal alcohol syndrome, and neural tube defects. In the United States, congenital CMV causes one child to become disabled every hour. These risks are almost entirely limited to women who were not exposed to CMV prior to pregnancy and contract a primary CMV infection during pregnancy.

1.13 Cytomegalovirus (CMV) and Insemination

Cytomegalovirus (CMV) and Insemination

- Insemination with semen from a CMV-infected man is acceptable when the female partner is also CMV-positive.
- Female CMV- and male CMV+
 - Sperm washing may reduce the risk of transmission of CMV.

ASRM Practice Committee, 2013

Notes:

Insemination with semen from a CMV-positive man with an active CMV infection is acceptable when the female partner is also CMV positive; that is, prior exposure to CMV as evidenced by a positive CMV IgG test. The risk of newborn CMV infection is approximately 1% with no significant infant infection or abnormality.

In cases of a CMV-positive male, with a negative female partner, sperm washing may reduce the risk of CMV transmission.

1.14 Human Papillomaviruses (HPV)

Human Papillomaviruses (HPV)

- Small DNA viruses that induce epithelial cell proliferation, or papillomas.
- HPV 16, 18, 31, and 45 considered high-risk types due to association **with** genital tract cancers.
- Most common sexually transmitted infection.
- Transmitted primarily through sexual contact, and 50% of sexually active adults have been infected with one or more HPV type.
- HPV detected frequently in semen and urethral swabs from normal men.
- No coherent strategy for donor screening and risk reduction has been developed.
- 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, but this has not been demonstrated conclusively (Foresta et al., 2011)

ASRM Practice Committee, 2013
<http://www.cdc.gov/std/hpv>

Notes:

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. 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 types. 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

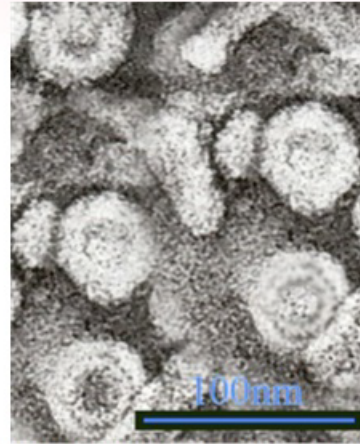
has not been developed. Since HPV appears in semen as cell-free virus and in infected epithelial cells, sperm-wash protocols may reduce the infectiousness of semen from HPV-infected men, but this has not been demonstrated

conclusively.

1.15 Hepatitis B

Hepatitis B

- Discovered in 1969
- Stable virus - remains infectious on dry surfaces for more than a week
- Transmitted by infected body fluids, including saliva and semen
- Acute infection leads to jaundice; resolves within 4 months
- Treatment with antiretroviral drugs and/or interferon sometimes effective



Transmission electron micrograph of Hepatitis B virus particles and surface antigen from blood

Image by permission GrahamColm at en.wikipedia

www.cdc.gov/hepatitis

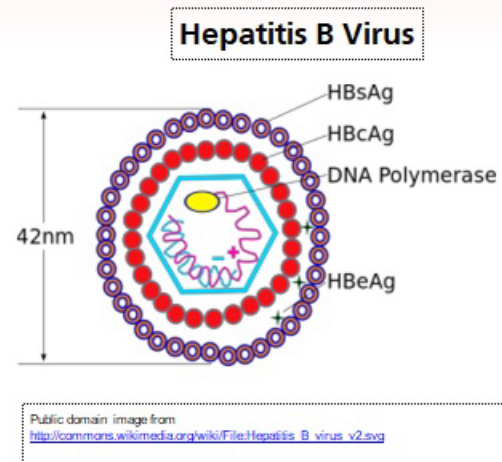
Notes:

The hepatitis B virus is a hepadnavirus and was discovered in 1969. Its genomic DNA is partially double-stranded and is reverse-transcribed from an RNA intermediate in infected cells. It is a stable virus and remains infectious on dry surfaces for more than a week. HBV can be transmitted parenterally, sexually, vertically, and via other routes of mucosal exposure, including saliva and semen. Acute infection leads to jaundice, but usually resolves within four months. Hepatitis infection can become chronic, particularly in children. Treatment with antiretroviral drugs and/or interferon is sometimes effective.

1.16 Hepatitis B Testing

Hepatitis B Testing

- Tests for serum antibodies
 - Hepatitis B surface antigen (Anti-HBsAg)
 - High levels during acute or chronic infection
 - Indicates person is infectious
 - Hepatitis B core antibody (Anti-HBc)
 - Appears at onset of acute hepatitis B and persists for life
 - Indicates previous or ongoing infection
- Tests for viral DNA in serum
 - HBV-DNA: NAT testing
 - Correlates well with infectivity



www.cdc.gov/hepatitis

Notes:

Hepatitis B serologic testing involves measurement of several hepatitis B virus (HBV)-specific antigens and antibodies. Different serologic “markers” or combinations of markers are used to identify different phases of HBV infection and to determine whether a patient has acute or chronic HBV infection, is immune to HBV as a result of prior infection or vaccination, or is susceptible to infection.

1.17 Hepatitis B

Hepatitis B

- Approximately 25% of sexual partners will become seropositive for HBV through sexual contact.
- HBV has been transmitted through artificial insemination.
- HBV discordant couples
 - Vaccinate seronegative partner against HBV prior to fertility treatments.
- Sperm washing to reduce viral load is not required after the female partner is immunized.
- Hepatitis B antigen+ female (actively infectious) during the pregnancy
 - Female and infant should undergo medical treatment.

ASRM Practice Committee, 2013

Notes:

Approximately 25% of regular sexual contacts of HBV-infected persons will become seropositive for HBV through sexual contact. HBV has been transmitted through artificial insemination. In couples who are discordant for HBV infection the negative partner should be vaccinated against HBV. Once the titer is positive, fertility treatments can be initiated. Sperm washing would not be required after the female partner is immunized against HBV. If the female is hepatitis B antigen-positive, and thus actively infectious during the pregnancy, both the female and the infant should undergo medical treatment.

1.18 Hepatitis C

Hepatitis C

- Bloodborne RNA virus
- Transmitted principally by infected blood; detected in saliva, urine, semen, vaginal secretions, and breast milk
- No vaccine against HCV
- Acute infection = Short-term illness occurring within the first 6 months after exposure
 - 70%-80% of acute infections become chronic
 - Long-term health problems including cirrhosis of the liver, liver cancer and even death.
- Chronic hepatitis C infection
 - ~3.2 million persons in the United States
 - Most unknown; often no symptoms

<http://www.cdc.gov/hepatitis/C/cFAQ.htm#overview>
ASRM Practice Committee 2013

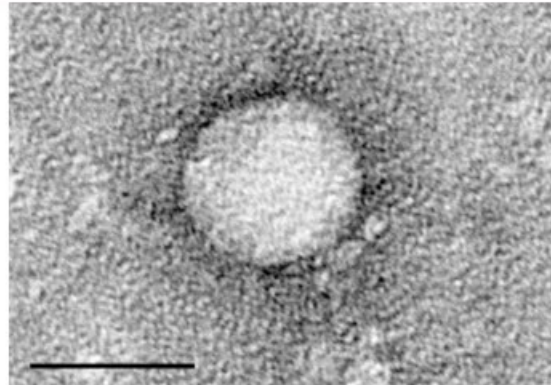
Notes:

Hepatitis C is a bloodborne RNA virus that is transmitted principally by infected blood. 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. The virus remains infectious on dry surfaces for several days. Acute infection is a short-term illness occurring within the first 6 months after exposure. HCV is a highly pathogenic virus. Seventy to 80 percent of acute infections become chronic and a high percentage of those infected with HCV will develop long-term health problems including cirrhosis of the liver, liver cancer, and even death. An estimated 3.2 million persons in the United States have chronic hepatitis C infection. Most do not know they are infected because there are often no symptoms.

1.19 Hepatitis C

Hepatitis C

- Small but measurable risk of HCV transmission via semen
- Sperm washing can reduce the viral load in semen and hence, transmission.
- ICSI also reduces risk of HCV transmission when male partner is seropositive.
- Interferon therapy



Electron micrographs of hepatitis C virus purified from cell culture. Scale bar is 50 nanometers. Courtesy of the Center for the Study of Hepatitis C, The Rockefeller University. Public domain image from http://commons.wikimedia.org/wiki/Category:Hepatitis_C_virus#/media/File:HCV_EM_picture_2.png

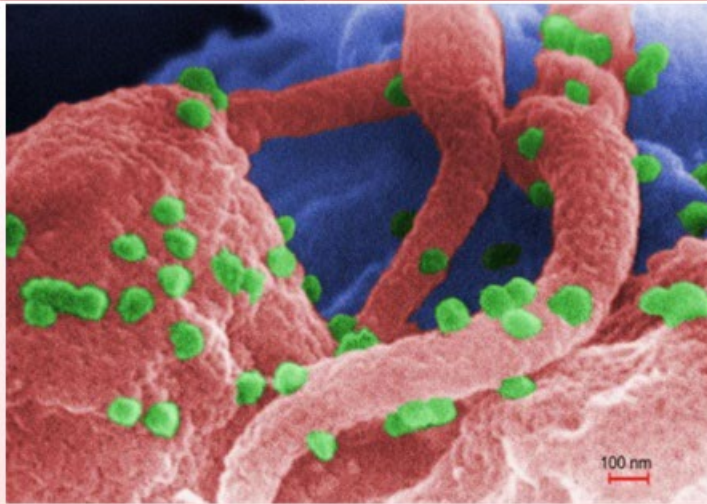
ASRM Practice Committee, 2013
Pasquier et al., 2000
Mencaglia et al., 2005

Notes:

There is a small but measureable risk of HCV transmission with semen. When the male partner is HCV-infected, sperm washing may reduce the viral load in semen, and can reduce the risk of transmission to the female partner. ICSI may also reduce the risk of transmission from an HCV positive male. If either partner is chronically infected with HCV, treatment with interferon should be considered prior to infertility treatment in order to reduce the viral load, and hence the risk of transmission. Since such therapy is initially 48 weeks, pregnancy should be deferred not only during the treatment, but for an additional six months following the conclusion of treatment. The ASRM Practice Committee indicates 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.

1.20 Human Immunodeficiency Virus

Human Immunodeficiency Virus



Scanning electron micrograph of HIV-1 from cdc.gov

Notes:

This section will discuss the human immunodeficiency virus and its implications for ART.

1.21 Human Immunodeficiency Virus (HIV)

Human Immunodeficiency Virus (HIV)

- First recognized as sexually transmitted infection in mid-1980s
- Historical concerns partly responsible for reluctance of fertility clinics in the United States to treat HIV-positive men
- HIV now established as a chronic disease
- Current view
 - Assisted reproduction for HIV-positive men is preventive medicine ¹
 - Reducing the number of infections caused by natural conception involving unprotected intercourse in HIV-discordant couples is a public health issue. ²⁻⁴

1. Sauer et al., 2009	1. Daar & Daar, 2006
2. Frodsham et al., 2005	2. Meikle & Orleans, 2006

Notes:

HIV was first recognized as a sexually transmitted infection in the mid-1980s. The ensuing regulations, together with the Clinical Laboratory Improvement Amendments of 1988, caused a revolution in fertility clinic laboratory science in the early 1990s. In particular, laboratories became vigilant about compliance with federal regulations for the first time. Historical concerns engendered during that era are partly responsible for the reluctance of fertility clinics in the United States to treat HIV-positive men. HIV is now considered a chronic disease and the virus has proven to be much less infective than originally feared. The current view is that assisted reproduction for HIV-positive men is preventive medicine and reducing the number of infections caused by natural conception involving unprotected intercourse in HIV-discordant couples is a public health issue.

1.22 HIV History

HIV History

- CDC recommended against insemination with semen from HIV-infected men
- ART programs developed procedures to assist couples living with HIV disease to safely become parents
- Found primarily in white blood cells and as cell-free virions in semen
- Introduction of “sperm-wash” and other risk-reduction techniques → IUI and IVF with processed sperm from HIV-seropositive men to achieve pregnancy in HIV-seronegative women
- When both partners HIV-infected → techniques to reduce risk of superinfection of female partner with different strains of HIV or drug-resistant HIV

ASRM Practice Committee, 2013

Notes:

The CDC recommendations against unprotected intercourse or insemination with semen from HIV-infected men prompted ART programs to develop procedures to assist couples living with HIV disease to safely become parents.

Because HIV is found primarily in white blood cells and as cell-free virions in semen, “sperm-wash” techniques that separate motile sperm from the round cell and seminal fluid fractions can markedly reduce HIV levels prior to insemination. 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. 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.

1.23 HIV Transmission in ART

HIV Transmission in ART

- 2014 meta-analysis of 24 studies of IUI and IVF with HIV
 - No transmissions in 1,254 seropositive male and seronegative female IVF cycles
 - No transmissions in 8,212 seropositive male and seronegative female IUI cycles
 - Upper 95% confidence limit of 4.5 transmissions per 10,000 seropositive male and seronegative female IUI cycles.

Barnes, et al., 2014

Notes:

A 2014 meta-analysis considered 24 studies of couples undergoing IUI and/or IVF. No transmissions were reported for the 1,254 seropositive male and seronegative female IVF cycles or the 8,212 seropositive male and seronegative female IUI cycles studied. If these reports are accurate, the risk of transmission is estimated at 4.5 infections/10,000 cycles of IUI treatment.

1.24 Is HIV Associated with the Sperm Cell? Controversial

Is HIV Associated with the Sperm Cell? Controversial

- Some authors report no association of HIV with washed, motile sperm using PCR for HIV DNA/RNA ¹⁻²
- Although there are no HIV receptors on the sperm surface, HIV attaches avidly to sperm via sperm surface mannose or heparin sulfate receptors. ³⁻⁷
- HIV may infect morphologically abnormal sperm in semen. ⁸
- Highly motile sperm selected from semen of HIV-infected men usually have undetectable HIV nucleic acid levels. ⁹
- Leukocytes in semen are the main mode of HIV infection. ⁹⁻¹⁰

1. Quayle et al 1997, 1998
2. Kim et al., 1999
3. Baccetti et al., 1991, 1994
4. Barboza et al., 2004
5. Bandivdekar et al., 2003

6. Fanibunda et al., 2008
7. Ceballos et al., 2009
8. Muciaccia, 2007
9. Anderson et al., 2010
10. Nicopoulos et al., 2010

Notes:

Some authors have shown no association of HIV with washed sperm using PCR for HIV DNA/RNA. Sperm do not have the HIV receptors CD4, CXCR4, or CCR5 on their surfaces that are involved in HIV infection of leukocytes, and HIV cannot be detected by sensitive PCR techniques in motile sperm separated by gradient methods from other seminal constituents.

This is a controversial area, and some have shown by electron microscopy and atomic force microscopy that HIV can enter sperm in vivo and that sperm from HIV-positive men harbor HIV particles. Others also showed that sperm transferred HIV particles into human oocytes during fertilization in vitro.

Although missing traditional HIV receptors and co-receptors, sperm are able to attach avidly to HIV particles, apparently via HIV envelope glycoprotein GP120 interactions with sperm surface mannose receptors or heparin sulfate receptors.

HIV-1 DNA has been found to be associated with germinal cells in the testis and with morphologically abnormal sperm in semen of infected men.

Although it is possible that sperm cells may harbor HIV in rare cases, highly motile sperm selected from semen of HIV-infected men usually have

undetectable HIV nucleic acid levels. It is generally accepted that the leukocytes in semen are the main mode of HIV infection.

1.25 HIV and ART Outcomes

HIV and ART Outcomes

- Injection of human eggs with HIV reporter gene constructs revealed robust HIV-driven gene activity → HIV infection at fertilization would probably disrupt embryogenesis¹
- Miscarriage rates appear similar to those for HIV-seronegative subfertile couples for IUI but are higher for ART.²
- HIV+ men with HIV– partners have pregnancy and live-birth rates with ART comparable to seronegative couples.²
- HIV+ females undergoing ART were found to have lower pregnancy rates per cycle.²

1. Kiessling, 1998; 2. Barnes et al., 2014

25

Notes:

Serodiscordant couples with HIV have a reasonable chance of pregnancy through fertility therapy and have pregnancy rates comparable to the general fertility population. In early studies, injection of human eggs with the HIV reporter gene constructs revealed robust HIV-driven gene activity, indicating HIV infection at fertilization would probably disrupt embryogenesis. However, miscarriage rates seem similar to those for HIV-seronegative subfertile couples for IUI but are higher for ART. Seropositive men with unaffected partners have pregnancy and live-birth rates with ART comparable to seronegative couples. However, seropositive females undergoing ART were found to have lower pregnancy rates per cycle. This disparity may have multifactorial origins, and further studies will be needed to address this issue.

1.26 HIV – Mother-to-Child Transmission

HIV - Mother-to-Child Transmission

- Perinatal transmission is most common route of HIV infection in children¹
 - Risk is highest in women with high viral load
 - Can be reduced to <1% if appropriate medical treatment given, virus becomes undetectable, breastfeeding is avoided.
- No reports of HIV-infected fetuses from uninfected mothers²

1. www.cdc.gov/hiv; 2. Sauer et al., 2009;

28

Notes:

Perinatal transmission (from mother to child during pregnancy, labor and delivery, or breastfeeding) is the most common route of HIV infection in children. The risk is highest in women with a high viral load. When HIV is diagnosed before or during pregnancy, perinatal transmission can be reduced to less than 1% if appropriate medical treatment is given, the virus becomes undetectable, and breastfeeding is avoided. Since the mid-1990s, HIV testing and preventive interventions have resulted in more than a 90% decline in the number of children perinatally infected with HIV in the United States. There have been no reports of HIV-infected fetuses from uninfected mothers.

1.27 The Need for More Clinics Treating HIV-Infected Couples

The Need for More Clinics Treating HIV-Infected Couples

- Regulatory agencies and professional societies in the United States have supported reproductive treatment of HIV-positive patients for a decade or more.
- Most fertility clinics do not openly treat these couples.
- Only 10 fertility clinics openly treat HIV-positive men.
 - This was ~3% of the clinics registered with Society for Assisted Reproductive Technology (SART).¹
 - Treatment of serodiscordant couples with sperm washing and IUI is standard of care in most European countries and Canada.²

1. Sauer et al., 2006

Notes:

As has been seen, regulatory agencies and professional societies in the United States have supported reproductive treatment of HIV-positive patients for a decade or more. However, most fertility clinics do not openly treat these couples. It has been estimated that only 10 fertility clinics openly treat HIV-positive men, representing about 3% of the clinics registered with Society for Assisted Reproductive Technology (SART). Since this estimate, there have been two published accounts involving anonymous surveys of fertility clinics. The treatment of serodiscordant couples with sperm washing and IUI is the standard of care in most European countries and Canada.

1.28 Pre-exposure Antiretroviral Therapy (PrEP)

Pre-exposure Antiretroviral Therapy (PrEP)

- Periconception administration of PrEP for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission
- Importance to adhere to daily doses of medication.
 - Daily oral PrEP safe and reduced risk of HIV transmission by 63%-75%.
 - >90% protection results in those whose drug levels showed medication was taken consistently.
 - Long-term safety has not been determined for woman, fetus or infant (breastfeeding)
 - In clinical trials, women taken off PrEP if pregnant
- Assistance of fertility professionals is important.
 - Preconception workup and counseling

<http://www.cdc.gov/hiv/prevention/research/prep/>
http://www.cdc.gov/hiv/pdf/PrEP_GL_Clinician_Factsheet_Pregnancy_English.pdf

Notes:

The CDC provides recommendations for decreasing risk of HIV transmission during conception, pregnancy, and breastfeeding. Periconception administration of antiretroviral pre-exposure prophylaxis (PrEP) for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission. Daily oral PrEP has been shown to be safe and reduce the risk of transmission by an average of 63% to 75% in heterosexually active adults. Higher levels of protection were found among persons whose drug levels in their blood indicated that they had consistently taken the medication. Although no serious health risks were associated with antiretroviral medications, patients have been followed for an average of only 1 to 4 years. In PrEP trials women were taken off medication as soon as pregnancy was detected. No health problems were associated with PrEP use by women in early pregnancy or for their offspring during the trials. However, the long-term safety of PrEP taken by HIV-uninfected women after fetal (during pregnancy) or infant (during breastfeeding) exposure is not yet determined. The assistance of fertility professionals in education and counseling is critical to the preconception workup.

1.29 HIV and ART Treatment Recommendations

HIV and ART Treatment Recommendations

- PrEP of negative partner has not been studied with ART
- Treat any sexually transmitted infections prior to attempting conception
- Limit unprotected intercourse to once per cycle as determined by a reliable ovulation timing method.
- HIV- males with HIV+ female partners
 - Artificial insemination (intravaginal insemination with partner semen) is safest option
 - Use of condoms except during peak fertility times
 - Antiretroviral treatment of HIV-positive female
- HIV+ males with HIV- female partners
 - Antiretroviral therapy recommended before and around time of conception, including around time of ART cycles.
 - Intravaginal or intrauterine insemination or IVF/ICSI, with washed sperm preparation or limit intercourse without a condom to peak fertility times
 - Confirmation of washed specimen as negative for presence of remnant HIV
 - Use of donor insemination is safest option

http://www.cdc.gov/hiv/pdf/PrEP_GL_Clinician_Factsheet_Pregnancy_English.pdf
ASRM Practice Committee, 2013

Notes:

The utility of PrEP of the uninfected partner when the infected partner is receiving ART has not been studied. It is also important to recognize that treatment of the infected partner may not be fully protective against sexual transmission of HIV. The CDC recommends that unprotected intercourse be limited only to once per cycle as determined by a reliable ovulation timing method.

For HIV-negative males with HIV-positive female partners, artificial insemination (intravaginal insemination with partner semen) is the safest option.

To reduce the risk of HIV acquisition by a seronegative woman from an HIV-positive male partner, recommendations include antiretroviral therapy of the positive male to achieve an undetectable viral load, followed by intravaginal or intrauterine insemination of washed sperm, or IVF/ICSI of washed sperm confirmed to have a negative test result for the presence of remnant HIV. Sperm washing, preferably using gradient centrifugation

and/or swim-up methods, reduces the presence of HIV-infected white blood cells and free virus in the inseminate. The CDC also recommends where available, testing of the processed specimen for HIV RNA prior to insemination. Use of donor sperm is the safest option.

1.30 HIV Informed Consent and Counseling

HIV Informed Consent and Counseling

1. Options explained and alternatives encouraged:
 - Use of donor semen, adoption or remaining childless
2. Risks explained (in addition to standard procedure risks):
 - Risk of the woman becoming infected
 - Risk of resulting child being infected
 - Risk of adverse reactions to anti-retroviral therapy if used by the woman for prophylaxis and during pregnancy
 - Risk of cancelled cycle if HIV is detected in inseminate (3%-8%)¹⁻⁴
 - IUI has low pregnancy rate per cycle (10%-15%) vs. IVF/ICSI (30%-40%)
 - Time and finances required per cycle of treatment are both high

1. Persico et al., 2006
2. Gilling-Smith et al., 2006

1. Nicopoulos et al., 2011
2. Vitorino et al., 2011

Notes:

For couples with one or both partners HIV-positive, informed consent and counseling are critical. Options are explained and alternatives encouraged, such as the use of donor semen, adoption, or remaining childless. Risks are also explained, in addition to standard risks of the procedure. These include:
Risk of the woman becoming infected in the case of an HIV-positive male partner
Risk of resulting child being infected
Risk of adverse reactions to HAART if used by the woman for prophylaxis and during pregnancy
Risk of cancelled cycle if PCR is used and HIV is detected in inseminate (3%-8%)

IUI has low pregnancy rate per cycle (10%-15%) vs. IVF/ICSI (30%-40%)
Time and finances required per cycle of treatment

1.31 HIV Informed Consent and Counseling (continued)

HIV Informed Consent and Counseling (continued)

1. Consult with psychologist
 - Experienced in counseling couples for assisted reproduction and for HIV
2. Consult with obstetrician
 - Experienced treating woman with HIV
 - Prenatal counseling
3. Couple signs safe-sex agreement
 - Including agreement to use condoms for every coital act and abstain from any high-risk behavior

Notes:

HIV-positive patients should consult a psychologist with experience in counseling couples for assisted reproduction and for HIV and an obstetrician who is experienced in treating woman with HIV. Prenatal counseling is also recommended. The couple should sign a safe-sex agreement, which includes an agreement to use condoms for every coital act and abstain from any high-risk behavior.

1.32 Work-up for Assisted Reproduction:

Work-up for Assisted Reproduction: The HIV-negative Woman

- Normal Pap smear and no evidence of inflammation or lesions
- Vaginal culture and treatment of infections
- Screening for STIs
- Normal menstrual cycles and documentation of ovulation
- Testing for ovarian reserve, if indicated
- Tubal patency assessed by hysterosalpingography
- Age < 40 years



Notes:

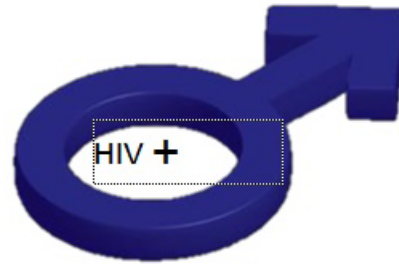
The work-up for assisted reproduction in the HIV-negative woman includes the following:

- Normal PAP test and no evidence of inflammation or lesions
- Vaginal culture and treatment of infections
- Screening for sexually transmitted infections
- Normal menstrual cycles and documentation of ovulation
- Testing for ovarian reserve, if indicated
- Tubal patency assessed by hysterosalpingography
- Age <40 years

1.33 Work-up for Assisted Reproduction:

Work-up for Assisted Reproduction: The HIV-positive Man

- History and physical examination
- Consultation with infectious disease specialist
- Semen analysis
- Semen culture and treatment of infections
- Screening for sexually transmitted infections



Notes:

For the HIV-positive man, the workup includes

- History and physical examination
- Consultation with infectious disease specialist
- Semen analysis
- Semen culture and treatment of infections
- Screening for sexually transmitted infections

1.34 “Sperm Washing” for IUI in HIV-discordant Couples

“Sperm Washing” for IUI in HIV-discordant Couples

- IUI after specialized “sperm washing” for HIV-discordant patients first described in 1992.¹
- Sperm are first separated from leukocytes and seminal plasma by gradient separation followed by a swim-up.
- In this early study: 59 inseminations – no seroconversions of recipients within 6 months; none in the babies followed up to 3 years
- Sperm washing reduces HIV from the sperm suspension to undetectable levels in most specimens.²



1. Semprini et al., 1992
2. Kim et al., 1999

Notes:

The treatment of HIV-discordant patients with IUI after specialized sperm washing was first described in 1992. Sperm are first separated from leukocytes and other seminal constituents by centrifugation over a gradient, and motile sperm are separated from the resulting pellet by a swim-up step in which washed sperm are overlaid with fresh medium into which sperm migrate. In the series of 59 inseminations, there were no seroconversions of recipients within 6 months and none in the babies followed up to 3 years. This washing method has been shown to reduce HIV from the sperm suspension to undetectable levels in most specimens.

1.35 “Sperm Washing” for IUI in HIV-discordant Couples

“Sperm Washing” for IUI in HIV-discordant Couples

- Gradient followed by swim-up
- PCR testing of prepared sperm specimen
 - The final sperm suspension can be stored while testing for HIV is performed by sensitive PCR.
 - Specimens found negative for HIV are then used for IUI.
 - Insemination is not performed if HIV is detected.
 - Processed sperm are held during PCR at room temperature, at 4°C, or are cryopreserved and stored until the day of IUI.

35

Notes:

The final sperm suspension can be stored while testing for HIV is performed by sensitive RT-PCR. Specimens found negative for HIV are then used for IUI. Insemination is not performed if HIV is detected and these cycles are cancelled.

Processed sperm are held during PCR at room temperature, at 4°C, or are cryopreserved and stored until the day of IUI.

1.36 PCR to Detect HIV after Specialized

PCR to Detect HIV after Specialized “Sperm Washing”

- ~3%-8% of washed specimens contain detectable HIV after washing and cannot be used.¹⁻⁴
- As this is within the range of false-positive results for this test, these may represent samples that test positive but contain no HIV.
- Controversial whether this test is required, particularly for men with undetectable viral loads
- PCR requires up to 20 hours, during which processed sperm lose some viability.
- Cryopreservation of the washed sperm is used by some groups so PCR can be done before the day of insemination.⁵
- Strict quality control is required.

1. Persico et al., 2006 2. Gilling-Smith et al., 2006 3. Nicopoulos et al., 2011
4. Vitorino et al., 2011 5. Bujan et al., 2007a

Notes:

Testing of the prepared sperm before IUI with PCR techniques to detect HIV nucleotides is used by many groups. In practice, about 3%-8% of washed specimens contain detectable HIV after washing and cannot be used. However, as this is within the range of false-positive results for this test, these may represent false-positive results in which there is actually no detectable HIV in the specimen. It remains controversial whether this test should be required, particularly for men with undetectable viral loads. The European Centres for Reproductive Assistance Techniques in HIV (CREAThE) requires PCR testing, but there have been no studies validating the requirement for this step.

PCR techniques can take up to 20 hours, during which the processed sperm lose motility and viability. Some have held the processed sperm at 4°C while PCR is performed. More recently, real time PCR methods have reduced the assay time to less than 10 hours.

Cryopreservation of the washed sperm is used by some groups so PCR can be done before the day of insemination. Because it is a clinical test, the PCR requires strict quality control. Cryopreservation also allows for the PCR to be re-run if positive or negative controls fail on the day of testing.

1.37 IVF with ICSI in HIV-discordant Couples

IVF with ICSI in HIV-discordant Couples

- Outside the U.S., ICSI is generally used only in patients with an indication other than HIV status. ¹⁻³
- Some advise against ICSI for HIV-infected men because it could introduce HIV into the oocyte. ²⁻⁴
- Concern about state criminalization of insemination with HIV-positive semen. ⁵⁻⁶
- Largest series of sperm washing for HIV-positive men in the United States using ICSI exclusively. ⁷
- No evidence that ICSI is safer than IUI
- Minimize risks/costs of ART by use of IUI for some couples
- Risk/benefit analysis must consider the higher success rate of IVF/ICSI compared with IUI: each attempt is associated with some risk. ⁸
- Use of testicular biopsy retrieved sperm in an HIV-positive man, followed by ICSI recently reported. ⁹

1. Ohl et al., 2003 2. Gilling-Smith et al., 2006 3. Savasi et al., 2007 4. Bujan et al., 2006, 2008
5. Pena et al., 2003 6. Sauer, 2008 7. Sauer et al., 2009 8. Vitorino et al., 2011 9. Garrido et al., 2009

Notes:

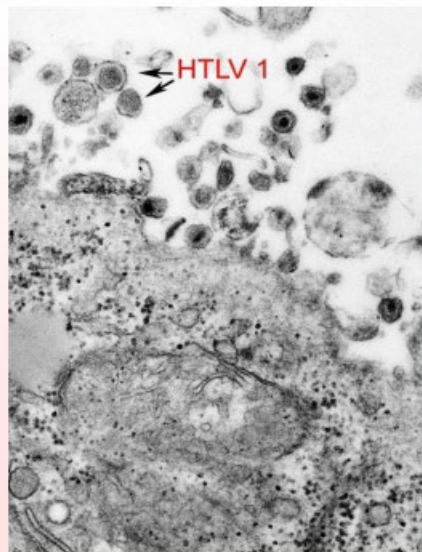
In Europe, ICSI is generally used only in those patients with an indication other than HIV status (e.g., low sperm count, failure of IUI, blocked fallopian tubes), and there has been some controversy about the exclusive use of ICSI for all cases of HIV-discordant assisted reproduction. Some advise against universal use of ICSI for HIV-discordant patients because it could introduce HIV into the oocyte. However, in the United States, concern about state regulations criminalizing insemination using semen from HIV-positive men has limited the options of fertility clinics treating HIV-discordant men. U.S. researchers have reported the largest series of sperm washing for HIV-discordant couples using IVF with ICSI exclusively.

There is no evidence that ICSI is safer than IUI with appropriate washing and pre-testing of sperm. ART is associated with risks and costs that can be minimized by the use of IUI for some couples. However, the risk/benefit analysis must consider the higher success rate of IVF/ICSI compared with IUI. More IUI cycles will be required for conception, and each attempt is

associated with some risk of infection. Testicular sperm extraction (TESE) in an HIV-positive man, followed by ICSI, was recently reported.

1.38 Human T-cell Lymphotropic Viruses I and II

Human T-cell Lymphotropic Viruses I and II (HTLV I and II)



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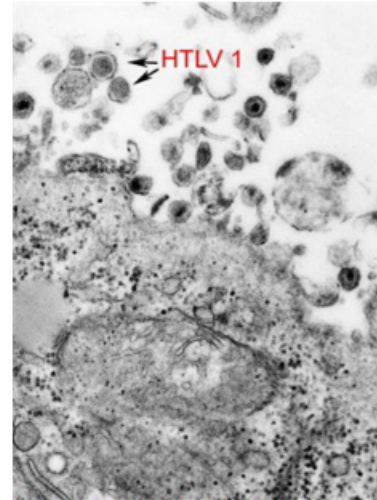
Notes:

This section will address Human T-cell Lymphotropic Viruses I and II. These viruses appear to be ancient retroviruses that establish permanent infections, but have low potential to cause human disease. They are present in leukocyte-rich cells and tissues. Because HTLV-I and -II have several properties in common with HIV, risk reduction protocols devised for HIV-discordant couples could be applied in cases where semen from directed donors infected with HTLV-I and -II will be used to inseminate an uninfected partner.

1.39 HTLV I and II

HTLV I and II

- Present in leukocyte-rich cells/tissues
- HTLV I infects CD4 T-cells
 - Cause of adult T-cell leukemia and HTLV I associated myelopathy (spastic paraparesis)
- HTLV II infects CD8 T-cells
 - Links to neurological disorders suspected
- Distribution in United States differs from other areas
 - Low endemic rate in Caribbean and tropical Africa black persons, Native Americans, natives of southern Japan and northern Oceania



With permission from phil.cdc.gov/phil

ASRM Practice Committee, 2013

Notes:

HTLV I infects human CD4-positive cells and is the cause of adult T-cell leukemia and HTLV I-associated myelopathy or spastic paraparesis in 1%-4% of infected individuals. HTLV II infects CD8-positive T-cells, and is suspected as a cause of neurological disorders but this has not been proven. 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.

1.40 HTLV I and II

HTLV I and II

- Is propagated through
 - Sexual contact
 - Contaminated needles in drug users
 - Transmission from mother to child
- Seminal fluid enhances replication of HTLV-1 in peripheral blood cells in culture.
- Effect of HTLV-I/II on semen parameters is unknown.
- HTLV-I/II-infected males are counseled to use condoms to avoid transmission to uninfected sex partners.

www.cdc.gov
ASRM Practice Committee, 2013

Notes:

In endemically infected populations, the virus is propagated through sexual contact and by transmission from mother to child. It is also spread through sharing of contaminated needles by drug users; secondary sexual transmission in this population has introduced these viruses at low levels into the general population and blood donors. There is also transmission from mother to child.

Seminal fluid was shown to enhance the replication of HTLV-1 in peripheral blood cells in culture. The effect of HTLV-I/II on semen parameters is unknown. HTLV-I/II-infected males are counseled to use condoms to avoid transmission to uninfected sex partners.

1.41 HTLV I and II

HTLV I and II

- Semen donors are tested for HTLV I and II because semen is considered leukocyte rich.
- Egg donors generally are not screened for HTLV I and II.
- Procedures that separate white blood cells and free virus from sperm (sperm-washing gradient and swim-up procedures) could be applied when using a directed or known sperm donor.

FDA 21 CFR 1271
ASRM Practice Committee, 2013

Notes:

Semen donors are tested for HTLV due to the fact that semen is leukocyte rich and this virus primarily infects white blood cells. There is, thus, potential for transmission through insemination procedures. As with HIV-discordant couples, methods that separate white blood cells from motile sperm, such as sperm washing gradient centrifugation and swim-up procedures, should be applied when known positive semen is used to inseminate an uninfected partner.

1.42 Semen Bacteria

Semen Bacteria



Notes:

Other pathogens that are of concern in assisted reproductive technology include semen bacteria.

1.43 Semen Bacteria – Leukocytosis

Semen Bacteria - Leukocytosis

- Long thought to be associated with poor semen parameters.
- Infertile men with leukocytospermia have significant reductions in total motile sperm counts¹
- ≥ 1 million leukocytes per mL of ejaculate^{2,3}
- Infertile men have more seminal leukocytes than fertile controls⁴
- Infertile men with leukocytospermia have significant reduction in total motile sperm counts¹
- Antibiotic treatment
- Sperm washing (gradient centrifugation and/or swim-up) to reduce or eliminate white blood cells and bacteria

1. Wolff H, et al., 1990; 2. Cornhaire F, et al., 1980; 3. WHO Manual, 2010; 4. El-Demiry, et al., 1985

Notes:

The presence of bacteria in semen has long been thought to be associated with poor semen parameters as well as infertility. Leukocytospermia, (increased white blood cells in semen) is thought to reflect an infection in one of the semen-producing male accessory sex glands. Generally, there is concern when the round cell concentration is greater than 1 million leukocytes/mL of semen, or greater than 4 round cells per high power field. With initial evaluation of the infertile male, the physician, usually the urologist, can evaluate for the presence of bacteria, or empirically treat the male with antibiotics to reduce or eliminate the elevated white blood cell count. Sperm washing and insemination are also reliable procedures to reduce the white blood cell and bacteria content for insemination.

1.44 Semen Bacteria – *Neisseria Gonorrhoeae*

Semen Bacteria - *Neisseria Gonorrhoeae*

- *N. gonorrhoeae*
 - 10% of affected men are asymptomatic
 - If involves epididymis or testis, may result in testicular damage or ductal obstruction
 - Men with a history of *N. gonorrhoeae* infection have increased seminal leukocytes compared with men without a history of this infection
- Can be cured with the appropriate medication
- Untreated gonorrhea can cause serious health problems



With permission from
<http://phil.cdc.gov/phil/>

Handsfield HH, et al., 1974

<http://www.cdc.gov/std/gonorrhea/default.htm>

<http://www.cdc.gov/std/Gonorrhea/treatment.htm>

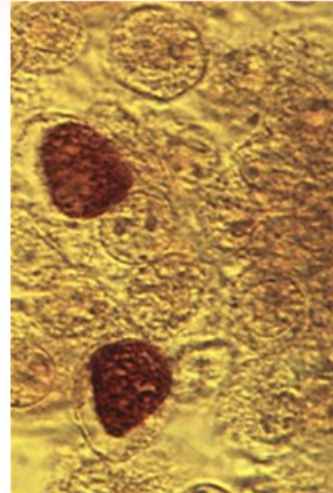
Notes:

Ten percent of men with *Neisseria gonorrhoeae* are asymptomatic. Infection involving the epididymis or testis may result in testicular damage or ductal obstruction. Men with a history of the infection have increased seminal leukocytes compared with men without a history of this infection. It is important to note that gonorrhea can be cured with the appropriate medication.

1.45 Semen Bacteria – *Chlamydia Trachomatis*

Semen Bacteria - *Chlamydia Trachomatis*

- Most common sexually transmitted infection in industrial nations¹
 - Intracellular organism; can cause infertility due to direct cell damage and ductal obstruction in the male, and tubal damage in the female²
 - 10%-25% of infected men may be asymptomatic³
 - Antibiotic treatment clears infection^{4,5}



McCoy cell monolayers with *Chlamydia trachomatis* inclusion bodies. From cdc.gov

1. Nagler & Litvin, 1992;
2. Paavonen J et al., 1999
3. Karam GH, et al., 1986

4. <http://www.cdc.gov/std/treatment/2010/chlamydial-infections.htm>
5. <http://www.cdc.gov/std/chlamydia/treatment.htm>

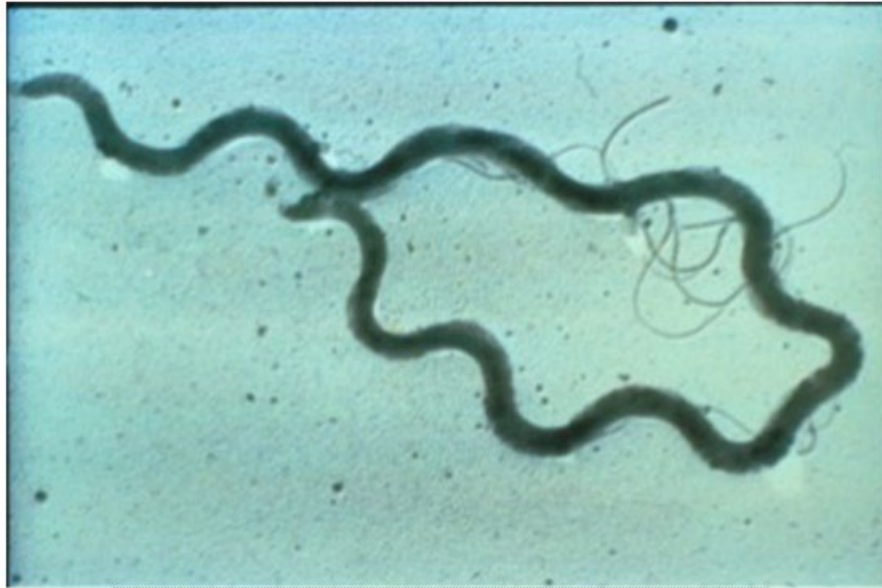
Notes:

Chlamydia trachomatis is the most common sexually transmitted infection in industrial nations. Chlamydia is an intracellular organism that can cause infertility due to direct cell damage. It is known to cause ductal obstruction in the male, and tubal damage resulting in blocked fallopian tubes in the female.

Approximately 10%-25% of infected men are asymptomatic. Chlamydia is easily treated with antibiotics and if treated early, the infection does not cause long-term damage. But untreated, significant impact can occur.

1.46 Semen Bacteria – *Treponema Pallidum* (Syphilis)

Semen Bacteria - *Treponema Pallidum* (Syphilis)



Electron photomicrograph, 36,000 x

Source: CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides

Notes:

Treponema pallidum, commonly known as syphilis, is a corkscrew-shaped, motile bacterium that cannot be cultured in vitro and cannot be viewed by normal light microscopy. It enters the body via skin and mucous membranes through abrasions during sexual contact and can be transmitted transplacentally from mother to fetus during pregnancy. It travels through the circulatory system and invasion of the central nervous system can occur during any stage of syphilis.

1.47 Facts about Syphilis

Facts about Syphilis

- Transmission is sexual and vertical; from infected mother to unborn baby
- Most contagious to sex partners during the primary and secondary stages
- No commercially available assays for *T. pallidum* DNA, but antibody tests are available
- Difficult to prove infection has been cleared in seropositive men
- Initial infection is a relatively painless lesion, usually in the genital area -may go unnoticed
- Once lesion heals, may be no clinical symptoms for many years
- Syphilis is easily treated with appropriate antibiotics, but antibiotics will not repair damage that has already occurred.

<http://www.cdc.gov/std/syphilis/STDFact-Syphilis.htm>

Notes:

Syphilis transmission is sexual and vertical and is most contagious to sex partners during the primary and secondary stages. *T. pallidum* cannot be cultured in the laboratory and there are no commercially available assays for *T. pallidum* DNA; however, antibody tests are available. There have been no reported surveys of *T. pallidum* DNA in semen of infected men and it is difficult to prove infection has been cleared in seropositive men. The initial infection is a relatively painless lesion, usually in the genital area and thus may go unnoticed. Once the lesion heals, there may be no clinical symptoms for many years.

1.48 Congenital Syphilis

Congenital Syphilis

- Occurs when *T. pallidum* transmitted from pregnant woman to fetus
- May lead to stillbirth, neonatal death, and infant disorders such as deafness, neurologic impairment, and bone deformities. Half of children infected with syphilis in utero die shortly before or after birth.
- Transmission can occur during any stage of syphilis; risk is much higher during primary and secondary syphilis
- Fetal infection can occur during any trimester of pregnancy
- Wide spectrum of severity exists; only severe cases are clinically apparent at birth
 - Early lesions (most common): Infants <2 years old; usually inflammatory
 - Late lesions: Children >2 years old; tend to be immunologic and destructive

www.cdc.gov/std

Notes:

Congenital syphilis occurs when *T. pallidum* is transmitted from a pregnant woman to her fetus. It may lead to stillbirth, neonatal death, and infant disorders such as deafness, neurologic impairment, and bone deformities. Transmission can occur during any stage of syphilis but the risk is much higher during primary and secondary syphilis. Fetal infection can occur during any trimester of pregnancy. A wide spectrum of severity exists but only severe cases are clinically apparent at birth. Early lesions seen in infants younger than 2 years old, are most common and are usually inflammatory. Late lesions, in children older than 2 years of age tend to be immunologic and destructive.

1.49 Summary

Summary

- Infertile couples should be advised that viral transmission in assisted reproduction is possible, but the magnitude of the risk is unknown.
- Although viral screening of intimate partners prior to ART is not required, screening can help to ensure appropriate precautions can be taken, and methods utilized to minimize risk of transmission to uninfected partners and offspring.
- Periconception administration of antiretroviral pre-exposure prophylaxis for HIV-uninfected partners may reduce the risk of sexual transmission
- ART procedures have been shown to reduce the risk of semen transmission of infectious diseases.
- “Sperm washing” has been reported to eliminate pathogens (e.g. CMV, HIV) from all but about 8%-12% of specimens.
- Fertility services should not be withheld from individuals with chronic viral infections or treatable sexually transmitted infections if the center has the resources to provide such care. Otherwise, referral to a fertility center capable of treating such individuals is appropriate.

Notes:

In summary, infertile couples should be advised that viral transmission in assisted reproduction is possible, but the magnitude of the risk is unknown. Although viral screening of intimate partners prior to ART is not required, screening can help to ensure appropriate precautions can be taken, and methods utilized to minimize risk of transmission to uninfected partners and offspring. Periconception administration of antiretroviral pre-exposure prophylaxis for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission. The use of ART procedures reduces the risk of semen transmission of infectious diseases. “Sperm washing” has been reported to eliminate pathogens (e.g. CMV, HIV) from all but about 8% to 12% of specimens.

Fertility services should not be withheld from individuals with chronic viral infections or treatable sexually transmitted infections if the center has the resources to provide such care. Otherwise, referral to a fertility center capable of treating such individuals is appropriate.

1.50 Thank you!



Notes:

Thank you for participating in this educational activity.