(HA)ART Making
ART Possible

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Activity Planning Committee

- **Medical Review Committee**
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  - Victoria Harris, Ed.D. Director of Education, TN AIDS Education & Training Center, Vanderbilt Comprehensive Care Clinic

- **Project Administrative Coordination:**
  - Katherine Leopard, CHOICES Community Partners Coordinator
‘I’m not really into having kids. Maybe we could have a robot?’
Learning Objectives

After this presentation, the learner will:

1. Competently address the reproductive life planning needs of HIV positive patients, without judgment and affording the patient every respect.

2. Describe fertility options for individuals living with HIV and increase competence to make knowledgeable recommendations for serodiscordant women/couples wanting to conceive, including use of assisted reproductive technology [ART] procedures available.

3. Identify resources in literature for clinical guidance in care and expected outcomes of fertility programs offering services to individuals living with HIV
Why Parallel Paths?

- Women have sexual and reproductive health needs related to HIV testing and prevention
  - Routine HIV Testing
  - Prevention Counseling
  - Linkages to HIV Care, if Infected

- Women Living with HIV have sexual and reproductive health needs
  - Pregnancy Prevention
  - Pregnancy Planning
  - Basic GYN Care
  - STI Testing and Treatment
  - Prenatal Care
  - Abortion

Over 30 Years of HIV
HIV and Fertility

1990 MMWR
1991 British Medical Journal
1993 ACOG
1994: Ethics Committee of American Fertility Society [ASRM]
1997 FIGO:
1998 New York State Task Force on Life and the Law

Reproductive Desire

- 1440 HIV patients
- 29% of both women and men desired children
- 69% of women and 59% of men realistically expected to have 1 or more children

700 Women
227 had been pregnant
39% had children
48% “never asked by provider if they were pregnant or thinking about getting pregnant”
57% never discussed appropriate treatment before becoming pregnant
61% personally believed they could have children with appropriate medical care
59% felt society strongly urges them not to have children
First Steps: Memphis TGA HIV + Women Reproductive Needs Survey

- 31 Question Survey
- Publication
- Results
- Success:
  - St. Jude Children’s Research Hospital, HIV Care Clinic
  - Ryan White Community Needs Assessment: 3 Questions added
  - Goal 2014: 3+3 for total of 6 Questions

McGowan, Marshall, Gettings, Capece, Rinsdale. (2014)
[Procreation] is central to personal identity, to dignity and to the meaning of one’s life.
~ Robertson (1994)
Augusto E. Semprini, Italy, 1992

- 85 couples, male HIV +, female HIV –
- 29 women suitable for timed insemination
- 15 women, 17 pregnancies

Semprini’s Theory
HIV Testing of Final Spermatozoa
0.9% Failure Rate

<table>
<thead>
<tr>
<th>Patient</th>
<th>Treatment</th>
<th>No of insemination Attempts</th>
<th>Pregnancy Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>hCG</td>
<td>1</td>
<td>Singleton 39 weeks</td>
</tr>
<tr>
<td>B</td>
<td>hCG</td>
<td>1</td>
<td>Singleton 39 weeks</td>
</tr>
<tr>
<td>C</td>
<td>FSH, hMG, hCG</td>
<td>1</td>
<td>Twins 35 weeks</td>
</tr>
<tr>
<td>D</td>
<td>FSH, hMG, hCG</td>
<td>1</td>
<td>Singleton 37 weeks</td>
</tr>
<tr>
<td>E*</td>
<td>FSH, hCG/FSH, hMG, hCG</td>
<td>4/1</td>
<td>Preclinical miscarriage/triplets 37 weeks</td>
</tr>
<tr>
<td>F</td>
<td>FSH, hMG, hCG</td>
<td>1</td>
<td>Singleton 40 weeks</td>
</tr>
<tr>
<td>G</td>
<td>FSH, hMG, hCG</td>
<td>1</td>
<td>Singleton, 39 weeks</td>
</tr>
<tr>
<td>H</td>
<td>FSH, hCG</td>
<td>2</td>
<td>Singleton, ongoing 35</td>
</tr>
<tr>
<td>I</td>
<td>FSH, hMG, hCG</td>
<td>5</td>
<td>Ongoing, 32 weeks</td>
</tr>
<tr>
<td>J</td>
<td>hCG</td>
<td>2</td>
<td>Ongoing, 21 weeks</td>
</tr>
<tr>
<td>K*</td>
<td>FSH, hCG/FSH, hCG</td>
<td>1/1</td>
<td>Preclinical miscarriage/ongoing 21 weeks</td>
</tr>
<tr>
<td>L</td>
<td>hMG, hCG</td>
<td>3</td>
<td>Twins ongoing 25 weeks</td>
</tr>
<tr>
<td>M</td>
<td>hCG</td>
<td>3</td>
<td>Miscarriage 7 weeks</td>
</tr>
<tr>
<td>N</td>
<td>hCG</td>
<td>4</td>
<td>Miscarriage 7 weeks</td>
</tr>
<tr>
<td>O</td>
<td>hMG, hCG</td>
<td>1</td>
<td>Preclinical miscarriage</td>
</tr>
</tbody>
</table>
PCR Testing of all final spermatazoa fraction showed no HIV infected cells
50 + inseminations
No partner seroconversion
All 10 babies born HIV FREE

Mandelbrot et al 1997

- 92 HIV serodiscordant couples (male HIV +)
- Unprotected intercourse only at ovulation
- Protected intercourse at all other times
- 104 pregnancies
- 4 maternal seroconversions (4.3%)
For any couple with one or both partners infected with HIV abstain from engaging in sexual activities or consistently use condoms
1:500 to 1:1000 for each single act of intercourse
Bioethics

- **Ethical Concerns**
  - Creation of child infected with HIV
  - Premature death of parents
  - Transmission of virus: Medical staff, partner, other couples

- **Principals of Bioethics**
  - Autonomy
  - Beneficence
  - Justice

## Medical Ethical Concerns

<table>
<thead>
<tr>
<th>Risks</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Potential transmission to uninfected partner</td>
<td>• Risk of transmission to partner can be lowered</td>
</tr>
<tr>
<td>• Potential transmission to couple’s child(ren)</td>
<td>• Risk of vertical transmission with appropriate medical care is 0-2%</td>
</tr>
<tr>
<td>• Shortened life span of one or both parents</td>
<td>• Couples experiencing fertility difficulties can achieve conception</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1994</th>
<th>June 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>• All individuals seeking fertility assistance should be tested for HIV</td>
<td>• HIV is a chronic, manageable disease and expected life span can be near normal</td>
</tr>
<tr>
<td>• If individual is HIV +, couple should be counseled on donor sperm, adoption, or not having children.</td>
<td>• If individual is HIV +, couple should be counseled on ways to plan a pregnancy while significantly decreasing risk of HIV transmission to HIV – partner and/or child(ren).</td>
</tr>
<tr>
<td>1993</td>
<td>December 2010</td>
</tr>
<tr>
<td>---------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Women seeking pregnancy should weigh her desire for childbearing against the potential harm to an infected child</td>
<td>Physicians should be prepared to have detailed discussions about how to plan a pregnancy to avoid HIV transmission</td>
</tr>
<tr>
<td>Physicians should weigh the moral appropriateness of any medical treatment</td>
<td>Artificial insemination, although not guaranteed to have no risk, is endorsed as a way to avoid transmission</td>
</tr>
</tbody>
</table>

The Committee on Ethics of the American College of Obstetricians and Gynecologists (1993).

The Committee on Ethics of the American College of Obstetricians and Gynecologists (2010).
<table>
<thead>
<tr>
<th><strong>1985</strong></th>
<th><strong>2001</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Physicians encouraged to advise HIV positive women to defer pregnancy because of poor outcomes associated with pregnancy and childbirth while positive</td>
<td>Physicians are instructed to inform HIV positive clients about all their reproductive options with counseling that is non-directive and supportive of client’s decision</td>
</tr>
</tbody>
</table>

PREP: 2012 and 2014
Thanks to the work of Semprini and others, there has been a large shift in fertility options for HIV affected couples and the biomedical ethics around this issue.
Preconception Care

- No smoking
- Avoidance of STD’s
- Avoid substance abuse
- Increase folic acid
- Vaccines for hepatitis A & B
- Pneumococcal and influenza
- Sustiva/efavirenz: pregnancy category D
- Prep for delivery

Eligibility for ART Programs

Two Key Goals of HIV Treatment

- Low Viral load
- High CD4 cell count

### HIV Care Specifics Evaluation

<table>
<thead>
<tr>
<th>Viral Load</th>
<th>CD-4 Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Undetectable</td>
<td>• &gt; 250</td>
</tr>
<tr>
<td>• &lt; 20,000</td>
<td>• Prefer &gt; 400</td>
</tr>
<tr>
<td>• Stable x 6 months</td>
<td>• Stable x 6 months</td>
</tr>
</tbody>
</table>

Cesarean delivery  
Breastfeeding  
Newborn prophylactic care  

### Fertility Work Up

#### Male Work Up
- STD Testing
  - GC/CT
  - RPR
  - HSV I & II
  - Trichomoniasis
  - Hepatitis B & C
- Sperm Analysis
- General Physical

#### Female Work Up
- STD Testing
  - GC/CT
  - RPR
  - HSV I & II
  - Trichomoniasis
  - Hepatitis B & C
- FSH, LH, and Progesterone
  - Day 3 & Day 21
- Lipid Panel
- Follicular Development Evaluation
- Hysterosalpingogram (HSG)

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## HIV and Infertility

**Male**
- Asymptomatic HIV infected No decreased fertility
- Hypogonadism
- Advanced HIV
  - Reduction in sperm concentration
  - Decreased total sperm count
  - Increased abnormal forms
- Zidovudine therapy improves sperm analysis regardless of CD4 counts

**Female**
- No clear evidence of decreased fertility
- No menstrual irregularity
- Possible increase in tubal factor infertility

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Bendikson, Anderson and Hornstein, (2002)
Pregnancy Planning for HIV

Pregnancy Planning Options: HIV+

- Timed, unprotected intercourse
- Timed insemination at home
- Artificial Reproductive Technologies [ART]
  - Sperm Donor with insemination
  - Sperm Washing
  - Intracytoplasmic sperm injection with attempted implantation
- Role of PrEP
- Guidelines
  - American College of Obstetricians and Gynecologists [ACOG]: No. 117, Dec. 2010
  - The Practice Committee of American Society for Reproductive Medicine [ASRM]: Fertility and Sterility Vol 90, Supp 3, November 2008

Serodiscordant: HIV+ Female/HIV- Male

- Timed, unprotected intercourse at time of ovulation, 4.3% seroconversion rate, ACOG and ASRM
- Insemination with partner’s sperm at ovulation
  - Home Insemination (avoids potential exposure to HIV for male)
  - Office Insemination
    - Unwashed: Intra-cervical insemination
    - Washed: intrauterine, only when indicated by male infertility, ASRM
- Donor sperm, ACOG
- In-vitro Fertilization, ACOG, ASRM
- Intracytoplasmic sperm injection, ACOG, ASRM*
- PrEP

Serodiscordant: HIV+ Male/HIV- Female

- Timed, unprotected intercourse around ovulation: 4.3% seroconversion rate, ASRM, ACOG
- Insemination: ACOG, ASRM
  - Home insemination without wash (avoids intercourse)
  - Sperm washing (ASRM: 3 step and AGOC) followed by insemination via intrauterine insemination or intracytoplasmic sperm injection
- Donor Sperm, ACOG
- PrEP

Non-Discordant Couple: HIV+/HIV+: ASRM Only

- Timed, unprotected intercourse around ovulation
- Insemination
  - Home insemination without wash (avoids intercourse)
  - Sperm washing followed by insemination via intrauterine insemination or intracytoplasmic sperm injection
- Donor Sperm
- PrEP: Not applicable
Patient Options

ADVANTAGES: LOW COST
DISADVANTAGES: KNOWLEDGE, COMFORT, EXPOSURE
Teaching Timed Intercourse and the Menstrual Cycle
Teaching: Home Insemination

- Male ejaculates in clean, dry container (glass jar, sterile urine cup)
- Fresh sperm is drawn up into syringe (no needle)
- Place syringe into vagina and depress plunger or place sperm in cervical cap or diaphragm and place in vagina
- Recommendations regarding timing: Based on ovulation (every other day starting at cycle day 5 until menses or + pregnancy test)
- Syringe is re-useable but should be cleaned and dried thoroughly
Teaching: Role of PrEP

- Truvada Daily: 300 mg/200 mg
- Hepatitis B Vaccine/evaluate immunity
- HIV Negative confirmed
- Routine access to healthcare provider and health resources for ongoing evaluation
  - Creatinine Clearance >60 ml per minute
  - HIV evaluation q 3 months
  - STI evaluation and treatment as indicated
  - Pregnancy
    - Safety to continue PrEP during pregnancy

World Health Organization, (July 2012); Centers for Disease Control (August 2012).
Options: Donor Sperm
Options: Adoption

WELL SOMEONE’S GOING TO HAVE TO TELL HIM HE’S ADOPTED
“My husband and I had to try 70 times before I got pregnant — that was one weekend I’ll never forget!”
ART: Assisted Reproductive Technologies

ADVANTAGES: TECHNOLOGY
DISADVANTAGES: ACCESS, COST, RISKS
ART

Sperm Washing:

3 Step process for either intrauterine insemination or intracytoplasmic sperm injection + PCR DNA Testing of Final Spermatazoa

3 Step Preparation
Intrauterine Insemination (IUI)
“...[U]NLESS HEALTH CARE WORKERS CAN SHOW THAT THEY LACK THE SKILL AND FACILITIES TO TREAT HIV-POSITIVE PATIENTS SAFELY OR THAT THE PATIENT REFUSED REASONABLE TESTING AND TREATMENT, THEY MAY BE LEGALLY AS WELL AS ETHICALLY OBLIGATED TO PROVIDE REQUESTED REPRODUCTIVE ASSISTANCE.

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE: ETHICS COMMITTEE, 2004
American clinicians remain slow to embrace the reproductive needs of patients living with HIV.

- Myths
- Lack of Policy
- Training
- Resources
- Equipment
- Facilities
- < 5% of US Reproductive Facilities

Frodshom, et al., 2005; Sauer, M. 2006; Daar & Daar, 2006
Low cost options: Higher risk

Effectiveness rates of ART

Risks of complications

Access to Fertility Services for HIV

Kalu, Wood, Vourliotis, and Gilling-Smith, 2010
Knowingly exposing HIV negative individual to potential infection

Crime for HIV + male to provide sperm for insemination

Liability Concerns for negative partner or fetal infection

UK: Regulatory body [HFEA]

USA: Regulations vary from state to state and strong support for individual provider policy

HIV + Pregnancy Options: Programs

- Columbia University, New York
- Bedford Laboratory, Boston?
- Dr. Ringler?
- United Kingdom
- Semprini
- Valenciaona de Microbiologia, Valencia, Spain
- University of Milan, Milan, Italy
- CHOICES, Memphis Center for Reproductive Health
Resources

- www.memphischoices.org
- www.gardenoffertility.com
- www.creathe.org
- www.cyclebeads.com
- www.thewellproject.org
- www.hivcenternyc.org
- www.studiosemprini.com
- www.thebody.com
References

References, continued


References, continued

- Melo, M., et a. (2008). Human immunodeficiency type-1 virus (HIV-1) infection in serodiscordant couples (SDCs) does not have an impact on embryo quality or intracytoplasmic sperm injection (ICSI) outcome. Fertility and Sterility; 89 (1): 141-150.


Questions?

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