HIV, PREP AND PREGNANCY IN SERO-DISCORDANT RELATIONSHIPS

LaShonda Spencer, MD
MCA Clinic
LAC+USC Medical Center

Disclosures

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Background

- Serodiscordant couple refers to an intimate partnership in which one person is HIV+ and the other is HIV negative.
  - In sub-Saharan Africa, up to half of those living with HIV report a serodiscordant partnership.
  - In lower prevalent areas, may be as high as 75%
- One US study (Houston): 212 HIV+ pregnant women
  - 40% serodiscordant partner
  - 34% partner with unknown HIV status
- 20-50% of HIV-infected men and women desire children
- Childbearing desires can lead to unprotected sex and/or nondisclosure of HIV status
- Up to 60% of new infections occur between stable, heterosexual, discordant couples in countries in sub-Saharan Africa, including Kenya
- HIV transmission risk is up to 2x greater among discordant couples who conceive, compared to those who do not

References:
### Reproductive rights and counseling

- With treatment, men and women with HIV are living longer, healthier lives, and can expect to see their children grow into adulthood.
- Safer conception counseling for HIV discordant couples is a reproductive right and should be included as a public health strategy to reduce HIV incidence among men, women, and their children.
- Ethically:
  - The ethical dilemma in providing safer conception strategies to HIV affected couples includes the possibility of mother-to-child HIV transmission and the risk of HIV transmission to an uninfected partner.
  - Some have argued that it would be unethical to withhold proven HIV prevention strategies to HIV-affected couples who desire pregnancy.

### Summary of relevant Trials

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Design</th>
<th>Medication</th>
<th>Key Findings</th>
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<tbody>
<tr>
<td><strong>TDF2</strong></td>
<td>- Phase 2B randomized, double-blind, placebo-controlled study &lt;br&gt; - 5019 heterosexual women &lt;br&gt; - 25% age 25-29</td>
<td>TDF, TDF/FTC, or TDF topical gel vs Placebo</td>
<td>- TDF only detected in 30% of TDF group vs 29% in TDF/FTC group &lt;br&gt; - Adherence was 93% in both arms of study</td>
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<tr>
<td><strong>HPTN 052</strong></td>
<td>- Randomized clinical trial designed to evaluate ART by HIV-infected individuals to prevent sexual transmission of HIV among serodiscordant couples &lt;br&gt; - 1763 heterosexual couples</td>
<td>cART - immediate or delayed immediate cART led to a 96% reduction in transmission of HIV to the uninfected partner</td>
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MCA Case

- 28 year old HIV+ male referred to MCA for preconception counseling. CD4 415, Viral load 285 on cART for 5 years. Wife is 23 years old, married for 1 year. Last tested negative two months ago. Couple has inconsistent condom use and desires to have a baby.

Reproductive Health Services for Serodiscordant Couples

- Preconception counseling
- PMTCT services
- Assisted reproductive services
  - Sperm washing
  - IUI/IVF
- Biomedical approaches
  - TasP
  - Prep and Prep-C
  - STI testing and treatment

Guidelines on Safer Conception

- US Public Health Service PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014 A CLINICAL PRACTICE GUIDELINE
  - PrEP use periconception and during pregnancy by the uninfected partner may offer an additional tool to reduce the risk of sexual HIV acquisition.
  - Both the FDA labeling information¹ and the perinatal antiretroviral treatment guidelines² permit this use.
  - However, data directly related to the safety of PrEP use for a developing fetus are limited

Safer Conception

<table>
<thead>
<tr>
<th>HIV Transmission/goal</th>
<th>Method</th>
<th>Risk Reduction</th>
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<tbody>
<tr>
<td>Female HIV positiveGoal: decrease perinatal transmission (MTCT)</td>
<td>ARV in the motherARV to child after birth</td>
<td>95-98%</td>
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<tr>
<td>Female HIV positiveGoal: decrease female to male transmission</td>
<td>Non-intercourse vaginal insemination Voluntary medical male circumcision</td>
<td>Unknown (100%) 66%</td>
</tr>
<tr>
<td>Male positive Goal: decrease male to female transmission</td>
<td>Sperm washing + Intrauterine insemination or IVF</td>
<td>100%</td>
</tr>
<tr>
<td>Either partner positive Goal: decrease transmission to negative partner</td>
<td>Sex without condoms limited to peak fertilityART for infected partnerPrEP (oral, daily FTC/TDF)Treatment of STIs</td>
<td>Unknown 96% 63-73% 40%</td>
</tr>
</tbody>
</table>

Conception Options for mixed-status couples

- Having a HIV-negative baby is possible with careful planning.
- Your conception options will vary depending on which partner is HIV-positive.
- Preconception counseling is crucial
  - Preparing and planning for a healthy pregnancy before you are pregnant
- Optimal health should be obtained before attempting conception
  - Use contraception until healthy
  - Manage underlying medical conditions: DM, HTN
  - Stop smoking

Preconception Counseling

- Assess HIV status
  - Which partner is infected?
  - Is the HIV+ partner on ARVs? Adherence?
  - What is the HIV+ partners viral load? CD4?
  - Has there been disclosure to the HIV neg partner?
  - Partner HIV testing
  - How often do you and your partner use condoms?
Preconception Counseling (contd)

- HIV positive individual: Attempting to get pregnant or being pregnant may increase the risk of passing HIV to the uninfected partner.

- HIV negative individual: attempting to get pregnant or are already pregnant may put you at high risk of getting HIV from your infected partner.
  - If female - risk of transmitting to baby is very high if seroconvert during pregnancy.

Preconception strategies: Reducing risk of HIV Transmission

- ARV therapy (TasP)
  - Goal of sustained, undetectable viral load
  - CD4 count above 350

- Prep
  - Are healthy
  - No opportunistic infections
  - Not using drugs or alcohol
  - Screen for STI
  - Safest options for becoming pregnant
    - Avoid or limit condomless sex

- **No options** have been shown to be 100% effective, but some can greatly reduce the chance of transmission.

TasP

- HIV-infected partner should be receiving cART and demonstrated sustained suppression of viral load.

- Use of cART reduces but may not completely eliminate the risk of HIV sexual transmission in couples who conceive through unprotected intercourse.

  - Effective cART that decreases plasma viral load to undetectable levels is also associated with decreased concentration of virus in genital secretions.

  - Discordance between plasma and genital viral loads has been reported, and individuals with an undetectable plasma viral load may have detectable genital tract virus.

  - Antiretroviral (ARV) drugs vary in their ability to penetrate the genital tract.

HIV Discordance: Female is HIV positive/ male HIV negative

- Safest:
  - Artificial insemination
    - Artificial insemination protects the male partner from HIV-infected bodily fluids. His sperm is inserted into the woman's vagina using a syringe.
    - Artificial insemination is most effective when a woman is ovulating (releasing an egg). Ovulation occurs about 14 days after a woman's period starts.
  - Home insemination
    - Man ejaculates into a condom (w/o spermicide).
    - Use non-needle syringe or baster to deposit the semen deep inside the vagina
    - Condom use advised at all times.

HIV Discordance: Male is HIV positive and Female is HIV negative

Safest:
- Donor sperm from an uninfected HIV man with artificial insemination
- Sperm washing
  - HIV-infected semen cannot infect your baby, but can infect your partner
  - Sperm washing is a procedure that separates HIV-free sperm from the HIV-infected seminal fluid
  - HIV-free sperm can be inserted into the woman’s vagina by artificial insemination – eliminating any risk of HIV infection
  - Washed sperm can also be used to fertilize the woman’s egg by in vitro fertilization (IVF)
- Access to sperm washing and IVF can be limited in some settings.
  - $10,000–20,000

What about couples that do not have access to these reproductive services?
HIV treatment and planned unprotected sex

- Both types of mixed-status couples could take HIV treatment and conceive naturally with comprehensive counseling.

TIMED, PERIOVULATORY UNPROTECTED INTERCOURSE AFTER:

- Undetectable viral load for 6 months
- The HIV-negative partner can take PrEP prior to unprotected sex in some cases (however, the risk of HIV infection still exists).
- PrEP is one of several options to protect the uninfected partner during conception and pregnancy.
- Adherence to treatment is essential
- No sexually transmitted infections (STIs)
- Semen analysis to evaluate for low sperm count, low motility, low semen volume
- Avoid unnecessary exposure for prolonged periods when likelihood of conceiving is low or nonexistent

Ovulation: Fertile Period

- Calendar Days
- Cervical Mucus
- LH Testing
- Basal Body Temperature
- US

Timed Intercourse with Prep-C

- Switzerland study:
  - Males on cART with undetectable viral load
  - One dose of TDF at peak LH and 2nd dose 24 hours later.
  - No HIV infections
  - High rate of pregnancy: 75% after 12 attempts
- Further studies are needed.
Prep-C

- TDF/FTC is FDA approved for only daily dosing
  - Guidelines: “option for serodiscordant couples during conception and pregnancy”
- Adherence is critical
- The exact time to optimal protection using daily doses of TDF/FTC is not known.
  - maximum intracellular concentrations are reached in cervicovaginal tissues at approximately 20 days
  - rectal tissue at approximately 7 days

Prep-C

- HIV-negative women:
  - Referral to clinical site offering comprehensive care including prevention of MTCT.
    - Risk of HIV transmission increases during pregnancy
    - Risk of transmission to infant increases if mother infected during pregnancy or breastfeeding.
    - Regular counseling regarding consistent condom use
    - Counseling regarding symptoms of acute HIV.
  - ART to positive male partner to achieve undetectable viral load
  - Daily dosing of TDF/FTC beginning one month before conception attempt, continue for 1 month after conception (or longer).
  - Condomless sex limited to peak fertility time identified by lab tests for ovulation.

Prep-C

- Monitoring HIV neg pregnant patient
  - HIV testing: 4th generation/ plasma HIV RNA VL
    - Routine prenatal lab and during 2nd and 3rd trimester
    - Depending on ability to negotiate condom use, we test more frequently.
  - Assess adherence: Pharmacy/SW
  - Frequent counseling on risk of sero-conversion
    - Risk reduction counseling
  - Monitoring of partners HIV VL
  - Discussion on plans for breastfeeding
    - Low vs High risk for seroconversion
PreP- C Risk

- Pregnancy and breastfeeding are not contraindications to PreP
  - Long term safety during pregnancy or during breastfeeding is not yet determined
  - No increased risk of birth defects found in infants exposed to HIV positive mothers taken as part of treatment.
    - One study showed increased risk of preterm birth, unclear if related to TDF/FTC.
- Partner Prep study: IAS 2013
  - 288 pregnancies
  - Babies conceived when the mother was taking either TDF or TDF/FTC.
    - No differences in: miscarriages; stillbirths; preterm delivery; birth weight; congenital abnormalities; Infant growth

EMBRACE MTN 016

- Observational study to learn whether HIV prevention products containing ARVs can affect a woman’s pregnancy outcome or her baby’s general growth and development.
  - CROI presentation 2016
    - 27 women at substantial risk for HIV infection in SF/Bronx.
      - 18 identified when already pregnant
      - 8 identified pre-conception
      - 1 post-partum
      - All but one had HIV positive partner; remaining women had partner that also had sex with men.
        - 72% were on ART
        - 42% had documented viral suppression
        - 39% had known detectable virus
    - Of the 24 women offered PreP
      - 67% (16) chose to use it; median length of time - 30 wks.
      - 33% chose to use condoms
      - Over half relied on their partners TasP
      - No Prep related pregnancy complications
      - Half on Prep chose to breast feed.
      - One seroconversion in women not taking Prep.

Research: Much to learn

Long acting PreP
- Maraviroc (MVC)
- Rilpivirine (RPV)
- Integrase Inhibitors
- Tenofovir alafenamide (TAF) subdermal implant

PreP vaginal rings
- Dapivirine
- Maraviroc (MVC)

HIV vaccine
Financial Considerations

- Most private and employee-sponsored health plans cover TDF/FTC
- Medicaid and Medicare typically cover PreP
- Public insurance may vary
- Medication assistance programs
- Cost: $1300/month

Resources

- MCA Clinic: Prep referral
  - Call or text: 323 455-9454
  - Email MCAclinic@usc-mca.org

- Offering PrEP in Family Planning Clinics
  Mon, October 31, 2016, 9:00 AM – 10:00 AM
  www.hiveonline.org