HIV: Pregnancy in Serodiscordant Couple

Dr Chow TS
ID Clinic
HPP
Sexual Reproductive Health and Rights

The recognition of the sexual and reproductive health and rights (SRHR) of all individuals and couples affected by HIV, including HIV-serodiscordant couples, requires intervention strategies aimed at

• achieving safe and healthy pregnancies
• preventing undesired pregnancies
• reducing risk of horizontal and vertical transmission
• addressing HIV-related infertility
Safe conception and pregnancy in PLHIV is an achievable goal

Every interaction is an opportunity:

- **ALL women** with HIV in reproductive age group
  - discuss reproductive health desires
    - Preconception
    - Contraception
    - Safe conception
    - Safe pregnancy
Malaysia 2016

Vertical transmission rate – almost 0
<table>
<thead>
<tr>
<th>Section</th>
<th>Description</th>
<th>2016</th>
<th>2015</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1</td>
<td>Percentage of HIV positive pregnant women who received ARV to reduce the risk</td>
<td>78.1%</td>
<td>81%</td>
<td>MOH antenatal surveillance</td>
</tr>
<tr>
<td></td>
<td>of mother-to-child transmission</td>
<td></td>
<td></td>
<td>data and spectrum (EPP)</td>
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<tr>
<td>3.2</td>
<td>Percentage of infants born to HIV positive women receiving a virological</td>
<td>68.5%</td>
<td>62.9%</td>
<td>MOH antenatal surveillance</td>
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<tr>
<td></td>
<td>test for HIV within 2 months of birth</td>
<td></td>
<td></td>
<td>data &amp; estimations (EPP)</td>
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<tr>
<td>3.3</td>
<td>Estimated percentage of child HIV infections from HIV+ women delivering in</td>
<td>5%</td>
<td>4.8%</td>
<td>Spectrum 2016</td>
</tr>
<tr>
<td></td>
<td>the past 12 months</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3.3(a)</td>
<td>Registered percentage of child HIV infection from HIV+ women delivering in</td>
<td>1.3%</td>
<td>0.8%</td>
<td>PMTCT programmatic data</td>
</tr>
<tr>
<td></td>
<td>the past 12 months</td>
<td></td>
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<tr>
<td>3.4</td>
<td>Percentage of pregnant women with known HIV status</td>
<td>100%</td>
<td>100%</td>
<td>PMTCT programmatic data</td>
</tr>
<tr>
<td>3.5</td>
<td>Percentage of pregnant women attending antenatal clinics whose male partners</td>
<td>38%</td>
<td>31%</td>
<td>Survey in selected sites</td>
</tr>
<tr>
<td></td>
<td>were tested for HIV during pregnancy</td>
<td></td>
<td></td>
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<tr>
<td>3.7</td>
<td>Percentage of HIV-exposed infants who initiated HIV prophylaxis</td>
<td>99%</td>
<td>97%</td>
<td>PMTCT programmatic data</td>
</tr>
<tr>
<td>3.9</td>
<td>Percentage of HIV-exposed infants who started on CTX prophylaxis within 2</td>
<td>99%</td>
<td>77%</td>
<td>PMTCT programmatic data</td>
</tr>
<tr>
<td></td>
<td>months of birth</td>
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</table>
Case discussion
Heterosexual HIV-Discordant Couple

- Male partner is HIV infected
- His female partner of 5 yrs is HIV uninfected
- Male 39 yrs of age, CD4+ cell count 750 cells/mm$^3$, HIV-1 RNA 5000 copies/mL, treatment naïve; otherwise healthy
- Female partner 32 yrs of age; healthy
- Used condoms previously but are now planning to start a family
- Asking for advice on strategies to minimize transmission to the uninfected female partner and to conceive with uninfected HIV fetus

Slide credit: clinicaloptions.com
Pregnancy Issue in Serodiscordant Couple

• High proportion of HIV transmissions may occur in stable, long-term partnerships, in which one member is HIV-infected → Serodiscordant couple

- Heterosexual sero-discordant
  ▪ Male +/Female - (sexual transmission risk is higher for female)
  ▪ Male -/Female + (sexual transmission risk is lower for the male)
• As people with HIV live longer, healthier lives, safer conception counseling for HIV-serodiscordant couples is a reproductive right.
  - 20–50% of HIV-infected men and women desire children.
  - **Up to 60% of new infections** occur between stable, heterosexual, serodiscordant couples.
The sexual transmission of HIV patients to their partners is strongly correlated with concentrations of HIV in blood (HIV VL) and in the genital tract.

Persistent intermittent “shedding” of HIV in both male and female genital secretions can be expected even when treatment has reduced the blood plasma viral load (potential risk even with undetectable VL)
So How can we make sexual intercourse safer in sero discordant couple ?
HPTN 052: ART for Prevention of HIV Transmission in Serodiscordant Couples

- International, randomized, controlled trial

Stable, healthy, sexually active, HIV-discordant couples with CD4+ cell count 350-550 cells/mm³ (N = 1763 couples)

Early ART Arm
Initiate ART immediately
(n = 886 couples)

Delayed ART Arm
Initiate ART at CD4+ cell count ≤ 250 cells/mm³ or at development of AIDS-defining illness
(n = 877 couples)

• HPTN 052: Key Results

- N = 46 linked HIV transmissions to HIV-negative partner observed
  - Overall 93% reduction in risk of transmission with early therapy
- N = 8 linked partner infections diagnosed after index partner started ART\[1\]
  - Recently initiated ART (n = 4)
  - Virologic failure (n = 4)
- No linked HIV transmissions where index partner suppressed on ART
- Rate of unlinked infections similar between arms


Slide credit: clinicaloptions.com
KEY MESSAGE

- TREAT HIV POS partner regardless CD4 ASAP in order to control HIV VL
- In the mean time advice condom / abstain from sexual intercourse while waiting for VL to be controlled (first 6 months of ART )
- Stay monogamous – even with HIV POS partner on ART with HIV VL suppressed, if the HIV uninfected partner has outside relationship, risk of HIV transmission is no different from the general population with high risk exposure
FURTHERMORE....

Beneficial effect of early ART
TEMPRANO: immediate ART + 6 mos IPT reduced risk of severe illness vs deferred ART + no IPT in African pts with CD4+ cell count > 500 cells/mm$^3$[1]

HIV-positive, ART-naive adults with CD4+ cell count > 500 cells/mm$^3$ (N = 4685) randomized to ART initiated immediately following randomization or ART deferred until CD4+ cell count ≤ 350 cells/mm$^3$, AIDS, or event requiring ART

Composite primary endpoint: any serious AIDS-related or non-AIDS–related event

HR for primary endpoint (imm/def): 0.43 (95% CI: 0.30-0.62; $P < .001$)[2,3]
- 68% of primary endpoints events occurred in pts with CD4+ cell counts > 500 cells/mm$^3$

First step:
treat HIV pos partner

How to further protect the HIV uninfected?

- Multisite, randomized, double-blind, placebo-controlled trial

HIV-discordant couples from Kenya and Uganda with HIV+ partner not receiving ART (N = 4747 couples)

- TDF QD (n = 1584 couples)
- TDF/FTC QD (n = 1579 couples)
- Placebo (n = 1584 couples)

All couples received standard HIV treatment and prevention services, including risk reduction counseling, free condoms and condom counseling, contraception counseling and provision, screening and treatment for STDs, counseling and referral for other HIV prevention interventions (eg, male circumcision)

Partners PrEP: Efficacy and Resistance Results

- Both PrEP arms significantly reduced HIV acquisition risk; similar efficacy in men and women\(^1\)
  - TDF levels correlated with HIV protection
- No differences in serious AEs, creatinine abnormalities across arms
- Resistance detected in 7.4% (9/121) HIV seroconverters\(^2\)
- Transmission risk within 6 mos of ART initiation by HIV+ partner comparable to pre-ART risk in placebo pts\(^3\)


Slide credit: clinicaloptions.com
The Partners PrEP study showed dramatically that the rate of HIV acquisition was much higher despite condoms and counseling in those in placebo group compared to individuals who got tenofovir or tenofovir/FTC. Tenofovir/FTC was associated with a 75% decreased incidence of HIV. So in the discordant couple, there are 2 potent tools—

- **PrEP for the uninfected partner and**
- **treatment as prevention for the infected partner.**
Partners Demonstration Project: Combining Treatment as Prevention + PrEP in Africa

- High-risk serodiscordant heterosexual couples in Uganda and Kenya (N = 1013 couples)
- Continued oral daily TDF/FTC PrEP in uninfected partner for 6 mos after start of ART in infected partner
- Follow-up through 24 mos
  - 97% of HIV-uninfected partners initiated PrEP
  - 78% of HIV-infected partners initiated ART; of these, 89% experienced viral suppression
- 96% reduction in expected infections ($P < .001$)

<table>
<thead>
<tr>
<th>HIV Incidence, Actual vs Expected</th>
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<tr>
<td>Group</td>
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<tr>
<td>Expected</td>
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<tr>
<td>Actual</td>
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- Both pts with seroconversion had no TFV detectable in plasma at time of seroconversion

Conception counseling for HIV-Discordant Couples

- Multiple safe conception options for HIV discordant couples\[1\]
- 1) ART decreases HIV transmission risk by > 90\%\[2\] but may take up to 6 mos\[3\] to achieve HIV-1 RNA suppression
- 2) PrEP is highly effective if used consistently by the HIV-uninfected partner
- 3) Assisted reproduction can decrease HIV transmission risk
  - IVF and IUI
  - Sperm wash
  - Expensive, may not be necessary if ART and PrEP are used

PrEP in Pregnancy

- PrEP use at conception and during pregnancy by the uninfected partner may offer an additional tool to reduce the risk of sexual HIV acquisition\[1\]
- Data directly related to the safety of PrEP use for a developing fetus are limited
- Potential risks and limited information should be discussed
- TDF and FTC are classified as FDA Pregnancy Category B medications\[2\]


Slide credit: clinicaloptions.com
<table>
<thead>
<tr>
<th>Potential indicators of substantial risk of acquiring HIV infection</th>
<th>Clinically eligible</th>
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<tbody>
<tr>
<td><strong>MSM</strong></td>
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<tr>
<td>▪ HIV-positive sexual partner</td>
<td></td>
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<tr>
<td>▪ Recent bacterial STD</td>
<td></td>
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<tr>
<td>▪ High number of sex partners</td>
<td></td>
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<tr>
<td>▪ History of inconsistent or no condom use</td>
<td></td>
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<tr>
<td>▪ Commercial sex work</td>
<td></td>
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<tr>
<td>▪ Documented negative HIV test result; no signs/symptoms of acute HIV infection</td>
<td></td>
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<tr>
<td>▪ Normal renal function; no contraindicated medications</td>
<td></td>
</tr>
<tr>
<td>▪ Documented hepatitis B virus infection and vaccination status</td>
<td></td>
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<tr>
<td><strong>Heterosexual Women and Men</strong></td>
<td></td>
</tr>
<tr>
<td>▪ HIV-positive sexual partner</td>
<td></td>
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<tr>
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<td></td>
</tr>
<tr>
<td>▪ Commercial sex work</td>
<td></td>
</tr>
<tr>
<td>▪ In high-prevalence area or network</td>
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<tr>
<td><strong>Injection Drug Users</strong></td>
<td></td>
</tr>
<tr>
<td>▪ HIV-positive injecting partner</td>
<td></td>
</tr>
<tr>
<td>▪ Sharing injection equipment</td>
<td></td>
</tr>
<tr>
<td>▪ Recent drug treatment (but currently injecting)</td>
<td></td>
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</tbody>
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For our case

- HIV-serodiscordant couple
- Male 39 yrs of age, HIV-infected, CD4+ count 750 cells/mm³, treatment naive, healthy
- Female 32 yrs of age, not infected with HIV, healthy
- Planning to start a family

- Early initiation of ART is beneficial to HIV-infected people and will make them less infectious to sexual partners
  - Optimal virologic suppression may take up to 6 mos and requires ongoing adherence
- Use of PrEP by the uninfected partner may help reduce the risk of HIV transmission
- PrEP could be stopped once HIV-infected partner is stably virologically suppressed
  - Transmissions can occur outside relationship; PrEP may still be indicated if the HIV-uninfected partner is not monogamous
Efficacy of HIV Prevention Strategies From Randomized Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART for prevention; HPTN 052, Africa, Asia, Americas</td>
<td>96 (73-99)</td>
</tr>
<tr>
<td>PrEP for discordant couples; Partners PrEP, Uganda, Kenya</td>
<td>73 (49-85)</td>
</tr>
<tr>
<td>PrEP for heterosexual men and women; TDF2, Botswana</td>
<td>63 (21-84)</td>
</tr>
<tr>
<td>Medical male circumcision; Orange Farm, Rakai, Kisumu</td>
<td>54 (38-66)</td>
</tr>
<tr>
<td>PrEP for MSMs; iPrEX, Americas, Thailand, South Africa</td>
<td>44 (15-63)</td>
</tr>
<tr>
<td>Sexually transmitted diseases treatment; Mwanza, Tanzania</td>
<td>42 (21-58)</td>
</tr>
<tr>
<td>Microbicide; CAPRISA 004, South Africa</td>
<td>39 (6-60)</td>
</tr>
<tr>
<td>HIV vaccine; RV144, Thailand</td>
<td>31 (1-51)</td>
</tr>
</tbody>
</table>

CDC PrEP
Guidelines for Heterosexually Active Adults at Ongoing, Very High Risk

- Substantial risk categories
  - HIV-positive sexual partner
  - Recent bacterial STI
  - High number of sex partners
  - History of no/inconsistent use of condoms
  - Commercial sex worker
  - In high prevalence network or area
HIV+ ♂ vs. HIV- ♀

- Unprotected sex is considered safe if:
  - The HIV + ♂ on HAART with good adherence
  - Had an undetectable viral load > 6/12
  - STI treated

- Timed intercourse around the time of fertile period

- PrEP for HIV - ♀

- Sperm washing +/-
HIV+ ♀ vs. HIV- ♂

- Unprotected sex is considered safe if:
  - The HIV+ ♀ on HAART with good adherence
  - Had an undetectable viral load > 6/12
  - STI treated

- Timed intercourse during fertile period

- Simple self intra vaginal-insemination can be use

- PrEP to HIV - ♂: A short course ARV pre/post sexual exposure
Case

How would you counsel and manage this couple?

- Counsel and start the husband on HAART.
- Stress on compliance and barrier sex.
- Repeat VL after 6 months.
- Assess husband and wife for any fertility issues.
  - Husband – low sperm count?
  - Wife – irregular menses?
- If VL suppressed, plan for timed unprotected intercourse during fertile period.
- Recommend PrEP
- Early booking if UPT positive
PrEP in sero-discordant couple

- Considerations when the partner is HIV positive.
- An undetectable viral load in the infected partner on ART, is highly effective in preventing transmissions to others.
- However, PrEP can provide additional protection in certain situations:
  - As a bridge when the HIV infected partner has been taking ART for less than 6 months (ART can take 3-6 months to suppress viral load)
  - The uninfected partner is unsure about the HIV status of their partner or whether their viral load is suppressed.
  - PrEP:
    - At least 7 days of PrEP are needed before achieving full protection
    - At least 5 to 7 days of PrEP are needed before achieving full protection for anal intercourse and
    - nearly 20 days of PrEP are needed before achieving full protection for vaginal intercourse (based on preliminary pharmacological study
    - In patients wishing to stop PrEP, can be discontinued 28 days after the last exposure to infected fluid.
Conclusion

• Having a baby for RVD +ve patient - carries a minimal risk of transmission if managed well.

• Should involve multi-disciplinary management.

• Serodiscordant couple – having a child is possible without seronegative partner getting infected.
  - Better protective rate and higher chance to get pregnant
  - Sex without condom limited to peak fertility.
Safe conception and pregnancy is an achievable goal among PLHIV.