Reproductive Health for HIV+ Women.. And Men!

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National Perinatal HIV Hotline and Clinicians’ Network

I have no financial conflicts of interest.

Objectives
- To understand the basic principles of preconception counseling for HIV+ men and women
- To describe safe conception methods for serodifferent, HIV-affected couples
- To understand the pros and cons of various contraceptive options for HIV-affected couples

Let’s be in touch!
- National Perinatal HIV Hotline & Clinicians Network
  1-888-448-8765
  24 hour/day coverage
- Reproductive Infectious Disease pager (24/7)
  415-443-8726
- ReproID_HIV listserv: sweber@nccc.ucsf.edu
What are reproductive rights?

- The basic right of all couples and individuals to decide freely and responsibly the number, spacing and timing of their children and to have the information and means to do so, and the right to attain the highest standard of sexual and reproductive health.

World Health Organization

Email survey of 4831 US adults

*Few Americans believe that HIV+ women should have children.*

HIV+ women internalize stigma around conception

- Women Living Positive Survey
- n=700 HIV+ women on ARVs for 3+ yrs
- 59-61% believed could have children if appropriate care
- 59% believed society strongly urges not to have children
  - Caucasian (67%) vs. Hispanic (53%), (p < 0.05)
  - South (66%) vs. Northeast (52%) or Midwest (55%) (p < 0.05)
  - ID (62%) vs. FP/GP (62%) vs. NP or PA care (48%) (p < 0.05)

Squires et al. AIDS PATIENT CARE and STDs 2011

Are HIV providers discussing reproductive desires?

- Women Living Positive Survey (n=700, ARVs for 3+ yr)
  - 48% previously pregnant or considering pregnancy never asked about pregnancy intentions
  - 57% currently/previously pregnant or considering pregnancy had not discussed treatment options
- Baltimore cohort (n=181)
  - 67% reported a general discussion about pregnancy and HIV
  - 80% satisfaction with primary HIV-provider communication
  - 31% reported a personalized discussion about fertility desires/intentions (64% patient-initiated)

Squires AIDS Patient Care STDs 2011, Finocchiaro-Kessler AIDS Patient Care STDs 2010
Reproductive health = primary care

- If we succeed at integrating preconception and family planning into primary care model
- Every HIV-exposed pregnancy will be planned and well-timed
- There will be no HIV transmission to infants or to uninfected partners
- The health of all HIV-affected parents and infants will be optimized

Every interaction is an opportunity.

- To discuss HIV status and testing of partners
- To discuss reproductive health desires
  - Preconception
  - Contraception
  - Safer conception

Establish reproductive desires

- WHO?
  - Every reproductive-aged woman
  - Don’t forget to ask men too!
  - Even if amenorrhea, not in a current heterosexual relationship
- WHEN?
  - Early and Often
    - Puts the issue “on the map”
    - New life circumstances/partners, new medications (drug-drug interactions), new developments in HIV
  - Start the conversation. Stay open. Repeat

Reduce stigma, normalize desires
Preconception Management

Goals of preconception care in the context of HIV infection

- Prevent unintended pregnancy
- Prevent HIV transmission to partner
- Viral suppression
- Optimize maternal & paternal health
- Vaccination, OI prophylaxis, smoking cessation, etc.
- Improve maternal and fetal outcomes
- Prevent perinatal HIV transmission

ACOG Practice Bulletin No 117; December, 2010

Take advantage of the desire to get pregnant/conceive as an opportunity to optimize health and encourage other forward-thinking behavior.

Fertility desires among HIV+

<table>
<thead>
<tr>
<th>US reproductive-aged women</th>
<th>35%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-sectional, n=118</td>
<td>Rochester 20% yes, 15% unsure 12% tubal regret (4% tubal regret in US)</td>
</tr>
<tr>
<td>Cross-sectional, n=182</td>
<td>British Columbia 25.8%</td>
</tr>
<tr>
<td>Cross-sectional, n=181</td>
<td>Baltimore 59%</td>
</tr>
<tr>
<td>HCSUS probability sample, n=1421</td>
<td>US, HCSUS 29% women 28% men</td>
</tr>
</tbody>
</table>

“Being infected with HIV dampens but does not come close to eliminating individuals’ desires and intentions to have children.”

Chen et al. Family Planning Perspectives, 2001

WE want to get pregnant!

Case #1
- "Julia" is 31, HIV+, diagnosed 2 years ago after ending a relationship with an HIV-infected partner
- No history of HIV-related illness
- ARV-naïve
- CD4 count 650
- Viral load 65,000
- New male partner HIV-

You ask Julia if she wants to have another child.
- She says, “Yes.”
- You ask, “When?”
- She says, “Now.”

How do you counsel her?
How do YOU feel about her desire to get pregnant?
(There is no right answer!)

1. Angry
2. Annoyed
3. Ambivalent
4. Cautiously supportive
5. Enthusiastic

How do YOU feel about her desire to get pregnant?
(There is no right answer!)

1. Angry
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In 2012:

- Perinatal transmission is <<1%
- Men and women with HIV can expect to live to see their children grow into adulthood

HIV Heterosexual Serodifference

- HIV + WOMEN
- HIV + MEN

HIV Cost and Services Utilization Study (1996)

- Probability sample, n=1421 (35k♀, 53k♂)
- Currently married or with heterosexual partner
- Desire future fertility

51% of HIV+ women in SDC
46% of HIV+ men in SDC

Preconception management

- Antiretroviral therapy
  - If not on ARVs, start prior to attempting conception, esp if HIV- partner
  - If on EFV → switch to other Rx
- OI prophylaxis
  - TMP-SMX and NTD risk
  - 4-10mg folate vs. defer conception until CD4>200 x 3 mos
  - Azithro for MAC prophylaxis
  - Folate or prenatal vitamins
  - Screen/treat her and partner for STIs
  - Vaccinate prn
  - Weight loss, exercise
  - Tobacco, drug use
Safer conception

What method of safer conception would you recommend for HIV+ woman/HIV- man couple?

1. Timed coitus (aka sex during ovulation)
2. Sperm washing
3. Poke holes at the tip of a condom
4. Home vaginal insemination
5. PrEP to HIV- male partner

Heterosexual HIV Transmission

- Partners in Prevention Study (ACV vs plac.)
- 3297 couples with 86 linked transmissions
- Unadjusted risk per-unprotected act
  - Male-to-female 0.0019
  - Female-to-male 0.0010
- Each log ↑ viral load: 2.9-fold ↑ risk per-act
- Condom use: 78% ↓ risk per-act

Hughes et al, JID 2013

Timed, Unprotected Intercourse

- Timing unprotected sex with ovulation
- Barriero et al
  - 62 HIV serodiscordant couples, 22 H+F/H-M
  - Female receiving suppressive ART
  - No cases of sexual HIV transmission

Vaginal Insemination

1. Ovulation detection
2. Semen collected into condom or clean cup
3. Semen aspirated into needleless syringe
4. Vaginal insemination by her or partner

Ovulation predictor kits

These replace the old basal body temperature charts

Vaginal Insemination by Female

Vaginal Insemination by Male Partner
Julia calls your office to say her home pregnancy test was positive...

Perinatal HIV 101 (2 slides!)
- Consult Perinatal HIV Hotline early and often
- Perinatal HIV transmission < 0.5% if undetectable VL at delivery
- When?
  - Start ARVs as soon as woman able to tolerate
- What?
  - *Preferred* AZT, 3TC + NVP (<250), LPV/r or ATV/r
  - *Alternative* ABC, TDF, FTC; DRV, SQV
  - Avoid EFV in preconception/very early 1st trimester, ok to continue if presents to you pregnant
  - Late presentation; consider RAL
- Prescribe what they will take

Perinatal HIV 101 continued...
- Baseline genotype, frequent viral load (monthly)
- ARV dosing:
  - ↑ dose in 2nd/3rd trimester (LPV 600/150 BID; ATV 400/100 once daily)
  - DRV BID dosing (vs. QD for adherence)
- OI prophylaxis pm:
  - TMP-SMX (4-10mg folate in 1st tri); Azithro
  - Healthcare maintenance: tobacco, drug use, nutrition/exercise, immunizations, PARTNER testing/linkage to care, contraception planning
- Trial of labor if viral load < 1000 copies/mL

Case#2:
Conception for HIV- female/HIV+ male
- "Paul" is a 38 yo HIV+ man recently transferred care to your practice. His wife "Caitlin" is 37 yo and HIV-negative.
- His CD4 nadir 620, viral load 8300
- No history of hospitalizations, OIs
- ARV-naïve
- He explains he and Caitlin want to have a baby.
- "How can we have a baby safely?"
Men’s sexual and reproductive health


- Guidance on developing or enhance clinical services for male clients
- Defines scope of male sexual and reproductive health services
- Set standards for content and design of services

Video:
- HIV+ Men: Having a Healthy Sex Life and Healthy Family
- Clinical algorithms: integrating reproductive health into primary HIV care
- Educational brochures: safer conception, contraception
- http://hiv.ucsf.edu/care/perinatal.html

“How can we have a baby safely?”

1. Sperm washing with in-vitro fertilization or in-utero insemination
2. He begins ARVs & they try to conceive after he achieves viral suppression.
3. Ovulation predictor kit and she takes TDF/FTC as PrEP/PEP
4. Sperm bank
5. Adoption
6. None of the above
7. All of the above

Options for safe conception?

1. PEP/PEP for HIV
2. ARV for HIV+
3. Sperm washing + IUI
4. Sperm washing + IVF-ICSI

COST=yes
EFFECTIVENESS=??

Adoption, sperm donation, not having children
Options for safe conception?

COST = yes

EFFECTIVENESS = ??

PreP/PEP for HIV-

ARV for HIV+

Sperm washing + IUI

Sperm washing + IVF-ICSI

Adoption, sperm donation, not having children

Semen and HIV

Components

HIV present?

Spermatozoa NO

Seminal fluid possible

Non-sperm cells (wbc) possible

○ Spermatozoa

○ No CD4, CCR5 and CXCR4 receptors

○ Electron microscopy suggesting HIV viral particles in sperm not replicated

Semen and HIV

○ Components

○ Components

What is done with washed sperm?

○ Intrauterine Insemination (IUI)

○ Europe/Israel (CREATHe), South America

○ Increasing # of US sites

○ In-vitro fertilization (IVF)

Results of Assisted Reproduction

○ Single case of seroconversion with sperm washing/IUI (1990)

○ No density gradient, no semen VL prior to IUI

○ CDC recommends against insemination with semen

<table>
<thead>
<tr>
<th></th>
<th>Pregnancy/ cycle</th>
<th>Cumulative pregnancy</th>
<th>Sptn. Abortion</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUI</td>
<td>3900 cycles</td>
<td>18%</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>1184 couples</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11 studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVF/ ICSI</td>
<td>738 cycles</td>
<td>38.1%</td>
<td>52.9%</td>
</tr>
<tr>
<td></td>
<td>579 couples</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No seroconversions at birth, 3 months, 6 months</td>
<td></td>
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</tbody>
</table>

- **Observational cohort**
  - HIV+ men on ARVs; HIV-RNA <50 copies/ml x >3 mos
  - HIV-RNA in semen undetectable at baseline
  - Ovulation predictor kit
  - TDF 36 hrs and 12 hours before sex
- **Outcomes:**
  - March 2004-March 2007
  - 53 H-F/H+M couples, 46 opted for PrEP
  - Pregnancy rate per # attempts
    - 1 attempt – 26%
    - 5 attempts – 66%
    - 12 attempts – 75%
  - No seroconversions or adverse events

*Vernazza et al AIDS 2011*
### Antiretrovirals = Enough?

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Transmission</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barriero, 2006 Cohort</td>
<td>Cohort</td>
<td>62 SDC</td>
<td>0 (HAART and VL &lt;400)</td>
</tr>
<tr>
<td>Attia, 2009 Meta-analysis</td>
<td>Meta-analysis</td>
<td>11 cohorts 5021 SDC</td>
<td>0 (HAART and VL &lt;400)</td>
</tr>
<tr>
<td>Donnell Partners in Prevention, 2010 RCT</td>
<td>RCT ACV vs. placebo</td>
<td>3381 SDC 349 initiated ARVs</td>
<td>1 case/273 P-Y w/in 18 days of ARV initiation (vs. 102/4558 P-Y)</td>
</tr>
<tr>
<td>HPTN 052, 2011 RCT immediate vs. delayed ARV (CD4 350-500)</td>
<td>RCT</td>
<td>1763 SDC</td>
<td>Delayed: 3.1% Immediate: 0.1%</td>
</tr>
</tbody>
</table>


### The future is now.

Numerous methods to decrease HIV transmission while trying to conceive.

- Logistical, financial barriers
- Mindset that CD4 count should guide ART initiation

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### Swiss Federal Commission for HIV/AIDS

“HIV-positive people with no other STIs and on effective antiretroviral therapy do not transmit HIV sexually”

- Antiretroviral therapy is taken consistently.
- Viral load has been undetectable for at least six months.

January 2008
Case #3

- "Jane" is a 32 yo G4P1T3 coming for her routine HIV appointment.
- On TDF/FTC/DRV/r
- Sexually active with 1 male partner
- Irregular menses but no other complaints

She’s not pregnant.

- Right?
- Ask about last menstrual period (LMP)
- Low threshold for pregnancy test
- Determine fertility desires...

Case #3 continued...

- She is sexually active with HIV-negative male partner of 4 months.
- Uses condoms “always”
- Doesn’t want to get pregnant

Unintended pregnancy

<table>
<thead>
<tr>
<th>US general population</th>
<th>49% pregnancies unintended</th>
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</thead>
<tbody>
<tr>
<td>US, WIHS 232 adults</td>
<td>77% pregnancies while using contraception (vs. 60% HIV-)</td>
</tr>
<tr>
<td>US 1090 adolescents</td>
<td>83.3% unplanned 49-52% HIV status known</td>
</tr>
<tr>
<td>Italy 334 on ARV</td>
<td>57.6% unplanned</td>
</tr>
</tbody>
</table>

Finer/Henshaw Perspec Sex Repro Health 2006; Massad AIDS 2004; Koenig AJOG 2007; Florida Antivir Ther 2006
What method of contraception would you recommend?

1. Condoms (duh!)
2. Combined oral contraceptive pill (OCP)
3. Vaginal ring
4. Depo-provera (DMPA)
5. Intrauterine device (IUD)
6. Whatever she will use

Condoms
- The one method that protects against STDs and provides (some) contraception
- How do your clients feel about using male condoms? Female condoms?

Contraceptive Failure (1st year)

Counseling: Frequency of Intervention
- Permanent: sterilization
- Every 10 years: Copper T IUD
- Every 5 years: Mirena IUD
- Every 3 years: Implanon
- Every 3 Months: DMPA
- Monthly: vaginal ring
- Weekly: patch
- Daily: pill, natural family planning (NFP)
- Episodic: barrier methods, NFP

Increasing efficacy
**OCP-ARV Interactions**

<table>
<thead>
<tr>
<th>NO CHANGE</th>
<th>↓ HORMONE LEVELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF (FEM-PrEP?)</td>
<td>EFV</td>
</tr>
<tr>
<td>RAL</td>
<td>LPV/r</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
</tr>
<tr>
<td></td>
<td>APV</td>
</tr>
<tr>
<td>↑ HORMONE LEVELS</td>
<td></td>
</tr>
<tr>
<td>ETR</td>
<td>DRV/r</td>
</tr>
<tr>
<td>ATV</td>
<td>NFV</td>
</tr>
<tr>
<td>IDV</td>
<td>RTV</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
</tr>
</tbody>
</table>


**Other non-oral hormonal contraception**

- Patch (Ortho Evra)
  - Higher hormonal dose vs. OCPs
  - Higher failure among obese women
- Vaginal ring (Nuva Ring)
  - Lower hormonal dose vs. OCPs
- Transdermal implant (Implanon)
  - Reported failures among women on EFV

Conference on Retroviruses and Opportunistic Infections (March 2012), Seattle.

**Depo-Provera (DMPA) and ARVs = OK!**

- No change DMPA levels:
  - OEFV or NVP
  - ONFV
  - Other PIs?
- No change CD4 or viral load with DMPA


**Hormonal Contraception & HIV Progression**

- Observational: no difference in VL, CD4 or AIDS if DMPA vs. OCPs
- RCT: ARV-naive postpartum women
  - DMPA vs. OCP vs. IUD
  - Progression (CD4<200/death)
  - DMPA (AHR 1.6), OCP (AHR 1.7) vs. IUD
- Unanswered question:
  - Progression in setting of hormonal contraception and ARVs?

Hormonal Contraception: ↑ HIV Transmission/Acquisition?
- Partners in Prevention Study (RCT of acyclovir)
- 3790 serodiscordant couples, 2 yr f/u, no ARVs
- Uganda, Kenya, Rwanda, Tanzania, Botswana, South Africa, Zambia
- HIV acquisition among women (n=1314 HIV+ men)
  - Depo: AHR 2.05 (1.04-4.04)
  - OCP: AHR 1.8 (0.55-5.82)
- HIV transmission to men (n=2476 HIV+ women)
  - Depo: AHR 1.95 (1.06-3.58)
  - OCP: AHR 2.09 (0.75-5.84)

IUDs are safe for HIV+ women
- No evidence of ↑ infectious complications
  - 156 HIV+, 493 HIV- (Kenya; Copper IUD)
- Overall complications @ 24 mos: HR 1.0 (0.6-1.6)
- No evidence of ↑ genital tract shedding of HIV
  - Copper IUD n=98 (Kenya): 4 mos s/p insertion; OR 0.6 (0.3-1.7)
  - LNG-IUS (Mirena) n=12: no difference pre vs. post-insertion
- WHO Medical Eligibility Criteria category 2
  - Benefits > theoretical or proven risk

Worldwide Use of IUD

Postpartum tubal ligation


Heffron Lancet ID 2011

Morrison BJOG 2001; Sinei Lancet 1998; Richardson AIDS 1999; Heikinheimo Human Reprod 2006
Laparoscopic tubal ligation

Essure

Vasectomy

Resources
- Perinatal ARV Guidelines
  - www.aidsinfo.nih.gov
- National Perinatal HIV Hotline/Clinicians’ Network
  - www.nccc.ucsf.edu
- FXB preconception resources
  - www.fxbcenter.org/resources.html
- ACOG
  - http://womenandhiv.org/
Take it home...
- Call the perinatal hotline... available 24/7
- Take a sexual history
- Ask your female and male patients about desire for childbearing
- Determine serostatus of partners
- Safer conception options = harm reduction
- Couples will try to conceive with or without your help... so, you may as well help

Take it home...
- If doesn’t want to get pregnant...
  - Consider Rx-Rx interactions with hormonal contraception
  - IUDs = safe and effective!
- If does want to get pregnant...
  - Avoid efavirenz (EFV) in preconception period
  - Give extra folate if on TMP-SMX
  - Vaccinate
- If pregnant... keep her healthy

“Do we have to fill our patients’ lives with years or those years with life?”
Augusto Enrico Semprini

Thank you
- YOU!
- Drs. Diane Havlir and Meg Newman
- UCSF CME staff
- Shannon Weber
- Judy Levison