

Jean Anderson M.D.

Director, Johns Hopkins HIV Women's Health Program

Special Topics in Reproductive Health: Preconception Care in the Setting of HIV

Objective

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

Apply best practices in the provision of preconception counseling and care in the setting of HIV

Off-Label Disclosure

- This presentation will include discussion of the following non-FDA-approved use of:
 - Antiretroviral drugs for the purpose of pre-exposure prophylaxis of HIV

Case # 1:

- 36 yo P2012 HIV+ diagnosed 1990, followed Health Dept
 - Long hx of nonadherence and active drug use
 - Hx HSIL dating to 1998
- Jan 2002: presentation to JHH colpo clinic
 - CD4 182; HIV-RNA 13,000; Hx PCP-on Bactrim only
 - Pap HSIL, Bx/ECC HSIL: scheduled for cervical conization (CKC)- did not show
- Oct 2004: presentation to JH HIV WHP, recently resumed care
 - CD4 186, HIV-RNA 271 on Truvada, ATZ, RTV
 - 24 oz beer/da, clean 3 mo illicit drugs
 - CKC 12/04: HSIL, + margin

Case # 1: continued

- June 2005: follow-up
 - CD4 390, HIV-RNA-ND
 - No drugs x 11 mo, new housing, new partner (also HIV+)
 - Expresses interest in getting pregnant
 - Expresses ambivalence, “I want something to love”, recent loss of mother and sister
 - Unprotected sex-counseled on condom use
 - Pap/ECC: HSIL, atypical keratinized squamous cells
- Aug 2005: scheduled for CKC
 - Preop visit: + pregnancy test
 - Relapse of drug use

Mother to Child Transmission, 2000-2006, 5,930 Births to HIV+ Women, UK/Ireland

Townsend CL, et al. AIDS 2008;22:973-981

Prophylaxis	MTCT	Adjusted Odds Ratio (for mode delivery, sex, viral load)
Overall	1.2%	
ART >14 days	0.8%	
HAART with NNRTI	0.9%	1.31 (0.6-2.8) p=0.48
HAART with PI	1.1%	
HAART at conception	0.1%	0.18 (.02-1.3) p=0.09
HAART during pregnancy	1.3%	
HAART Elective CS	0.7%	p=0.15
HAART Planned vaginal	0.7%	
AZT Elective CS	0%	

Live births Among HIV+ Women Before and After HAART Availability

- **WIHS** (Sharma, et al. AJOG 2007;196:541e1-6)
 - Comparison of live birth rates 1994-1995 (pre-HAART era) and 2001-2002 (HAART era) in HIV+ and HIV- women 15-44 yrs
 - Women in HAART era younger, higher CD4 counts
 - In HAART era 150% increase in live birth rate among HIV+ women vs 5% increase among HIV- women
 - Live birth rate higher in all age categories with largest difference (306%) seen in women >35 Yrs
 - Among HIV+ women with more than high school education, live birth rate was approx ½ that of HIV- women in pre-HAART era but more than double HIV- rate in HAART era
 - Birth rate higher in HAART era within each category of CD4 count
 - Women with history of IDU were the only group in both HIV+ and HIV- women who experienced a decline in birth rates

Effective Contraceptive Methods are Underused in HIV Care Settings and Unwanted Pregnancy is Common

- WIHS: (1994-2005), n=2784; 26,832 visits (J Women's Health 2007, 16:857)
 - Barrier methods: 30.5-36.3% of visits
 - Tubal ligation: 21.-26.5%
 - Hormonal method: <10% of visits
 - No contraception: >30%
 - HIV+ less likely to use hormonal method
- Italy: 334 women on ART at time of conception—57.6% unplanned pregnancies (Florida M et al. *Antivir Ther* 2006;11:941-946)
- HIV+ pregnant US adolescents (n = 1090): HIV status known prior to pregnancy in 50%; 83.3% of pregnancies unplanned—43% of these resulted from lack of contraception (Koenig LJ et al. *Am J Obstet Gynecol.* 2007;197(3 suppl):S123-S131)

Goals of Preconception Care

- Prevention of unintended pregnancy
- Protection of maternal and fetal health during pregnancy
- Prevention of mother-to-child transmission of HIV
- Reduce risk of transmission to uninfected partner

When to Discuss Pregnancy (level of evidence C)

- Initial evaluation: assess childbearing plans/desires
- Early in course of care
 - desire for future pregnancy or uncertain
 - nonuse/inadequate use of contraception
- At intervals during routine care, especially:
 - interest in conceiving
 - nonuse/inadequate use of contraception
 - change in relationship
 - medications with potential reproductive toxicity
 - new developments in pregnancy and HIV
 - at risk for unintended pregnancy
 - enrollment in clinical trials
- Refer for preconception counseling and care!

Preconceptional Care for HIV-Infected Women

- Evaluation
 - Comprehensive HIV hx
 - Pregnancy hx
 - General medical/surgical hx
 - Medications
 - Family hx of heritable disease
 - Nutritional assessment
 - Social assessment (lifestyle, work, support, disclosure, domestic violence, substance abuse)
 - Advanced maternal age

Preconception Care

■ Interventions

- Contraception to reduce unintended pregnancy (level A)
- Counseling
- Treat anemia
- CD4 count/HIV-RNA (level A)
- Treat OIs, if present, or start prophylaxis, if indicated (level A)
- Initiate/modify ART, if indicated (level A)
 - Avoid efavirenz (EFV)
 - Ensure tolerability/lack of toxicity
 - Monitor improvement
- Address other medical/psychosocial issues (level A)

HIV and Fertility

- HIV appears to have an adverse effect on fertility in both symptomatic and asymptomatic women (16% to 55% decrease)¹⁻⁵
 - Chronic drug use (especially opiates)
 - Poor nutrition
 - Menstrual dysfunction/amenorrhea
 - STI history common
 - Sexual dysfunction common
 - 53% to 71% of HIV+ men
 - Depression, anxiety
 - Semen abnormalities more common in HIV+ men (lower volume, lower sperm concentration, lower motility) correlated with CD4⁶
 - Advanced disease: associated with viral load⁷

1. Desgrées du Lû A et al. *AIDS*. 1999;13:517-521. 2. Zaba B et al. *AIDS*. 1998;12(suppl 1):S41-S50.

3. Lee LM et al. *Am J Epidemiol*. 2000;151:1020-1028. 4. Glynn JR et al. *J Acquir Immune Defic Syndr*. 2000;25:345-352.

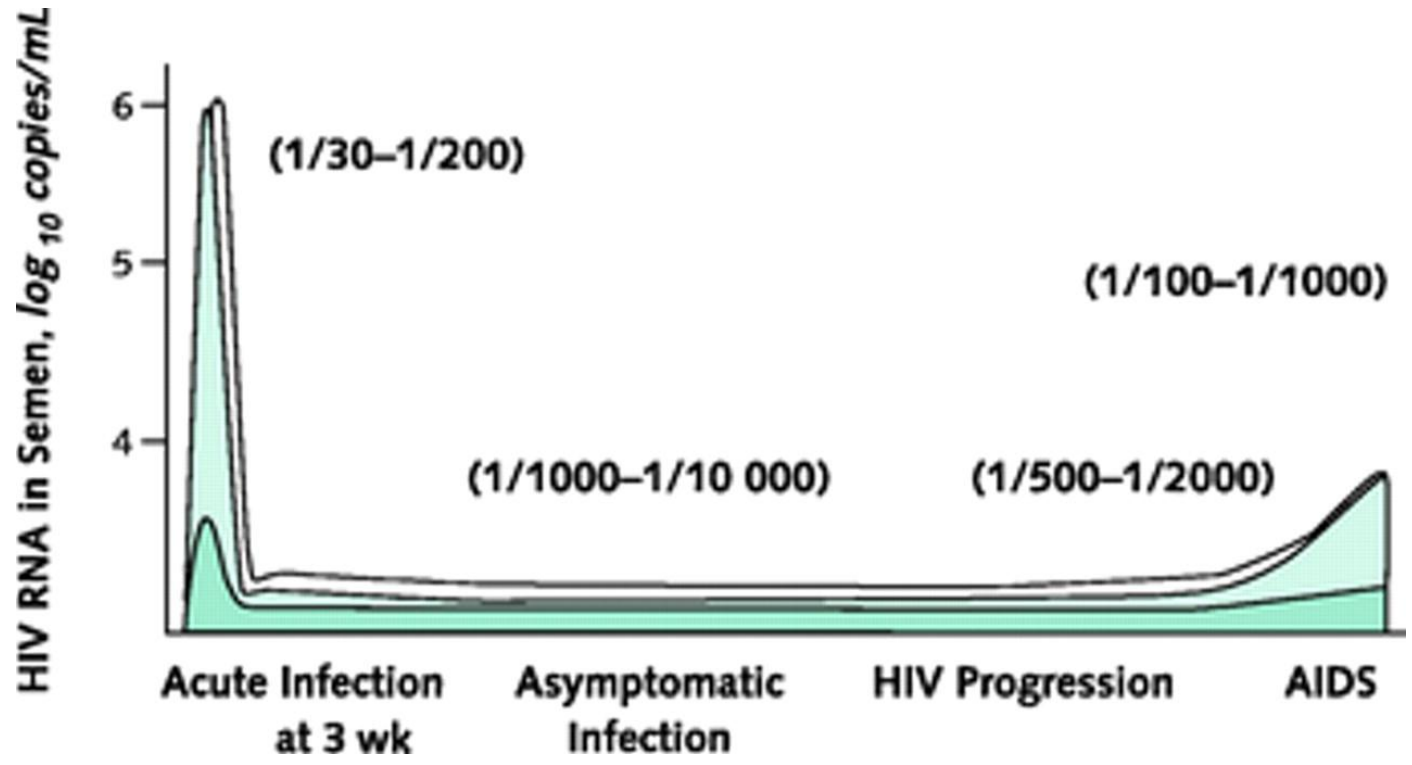
5. Gray RH et al. *Lancet*. 1998;351:98-103 6. Nicopoulos JD et al. *Hum Reprod*. 2004;19:2289-2297.

7. Gray RH et al. *Lancet*. 2005;366:1182-1188.

HIV Serodiscordant Couples (level of evidence C)

- HIV+ woman
 - Artificial insemination
- HIV+ man
 - Antiretroviral treatment
 - Semen analysis (hypogonadism frequent occurrence in HIV+ men with decreased serum testosterone; abnormal semen analyses)
 - Screen for genital tract infections
 - Timed intercourse (ovulation predictors)
 - Peri-exposure prophylaxis (PrEP)
 - Assisted Reproductive Technology
 - Semen washing
 - IVF/ICSI

Sexual Transmission of HIV



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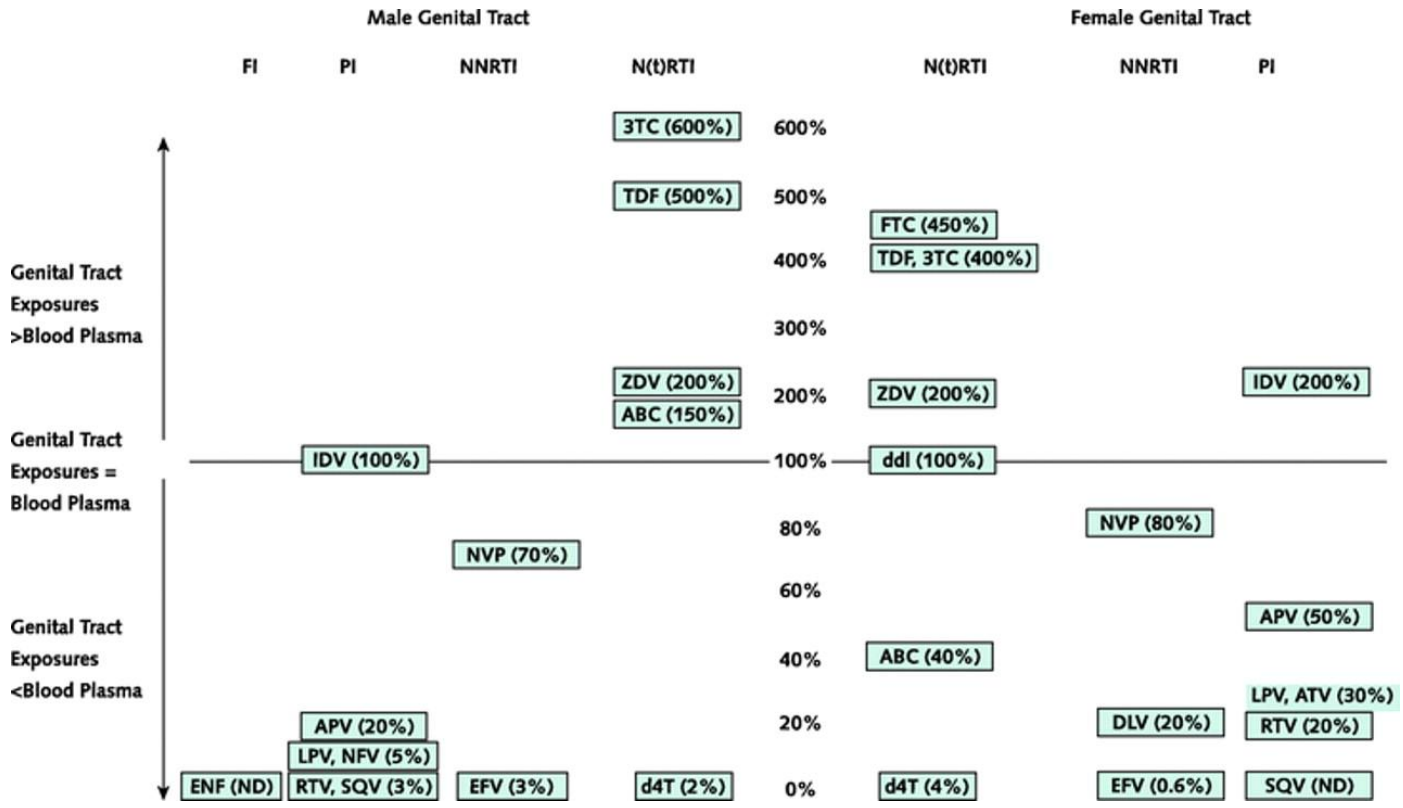
Sperm Washing in HIV+ Men

- Current techniques: detectable HIV 5% to 6%
 - Washed sample should be tested for HIV
- No reported cases of seroconversion in either female partner or child born in >3000 cycles of sperm washing combined with IUI, IVF or ICSI

Issues to Consider: PrEP

- Clinical
 - HIV-infected male partner:
 - Require that he be on ARVs?
 - What meds should he be on? Consider genital penetration of ARVs?
 - HIV-uninfected female partner:
 - What to prescribe? Timing of dosing? Intermittent vs. continuous?
 - Take into account male partner's resistance profile?
 - Who should prescribe?
 - How to monitor safety?
 - What is the schedule of follow up HIV testing?
- Implementation/Systems
 - How to implement services?
 - How to systematically track adverse events?
 - How to pay for services?

Antiretroviral Drug Concentrations in the Male and Female Genital Tract Relative to Blood Plasma Concentrations (ratio of genital to blood plasma concentrations)

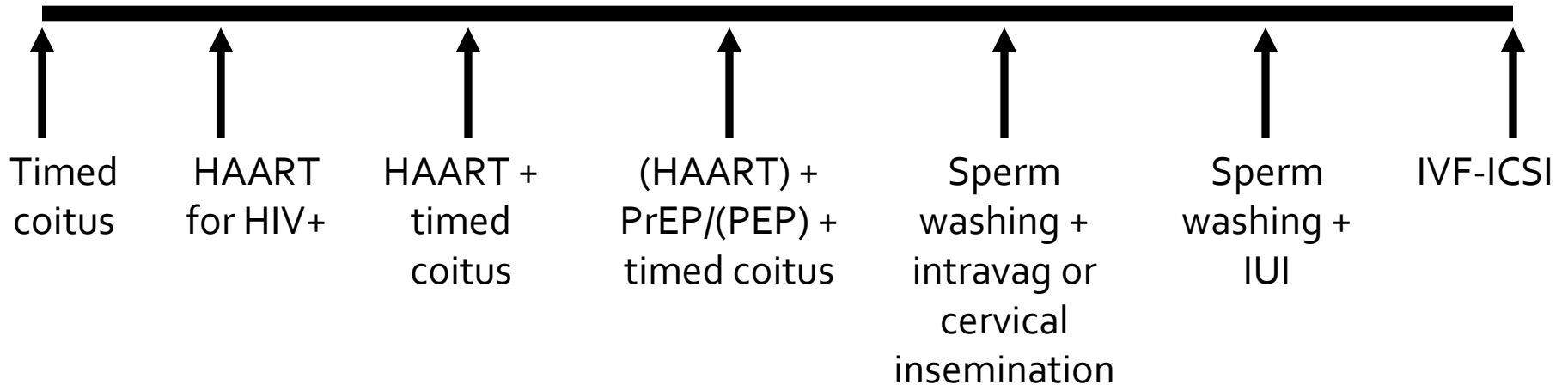


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Options for safe conception?

Low tech
Low cost
Lower effectiveness?

High tech
High cost
Higher effectiveness?



Other options: Adoption, sperm donation

Legal Rights of HIV+ Patients for Infertility Services

- HIV+ patients cannot be denied access to health services solely based on HIV status
- HIV antidiscrimination laws apply to healthcare providers in private clinics and in university settings
- Patients may be referred to providers with more expertise in providing infertility services
 - Referring provider must show they lack capability and referral is for medical benefit of the patients and their potential offspring

Preconception Care in HIV+ Women—Has the Time Come to Consider in LRS?

- High rates of unintended pregnancies among HIV+ women—likely higher than in the general population¹⁻³
- Low levels of contraceptive use
- High rates of serodiscordance in couples (>50% in Kenya/Botswana)
 - Transmission from an HIV+ spouse or partner accounts for a large proportion of new HIV infections
- Cultural/personal value placed on pregnancy
- Termination of pregnancy often illegal or unsafe

LRS = low-resource settings.

1. Homsy J et al. XVI International AIDS Conference; August 13-18, 2006; Toronto, ON, Canada. Abstract WePE0294.
2. Mohohlo M et al. 2006 HIV/AIDS Implementers Meeting of the President's Emergency Plan for AIDS Relief; June 12-15, 2006; Durban, South Africa. Abstract 113.
3. Wilcher R et al. *Sex Transm Infect.* 2008;84(suppl 2):ii54-ii60.

Unintended and Unwanted Pregnancies Among HIV+ Women

Table 2 Number of unintended and unwanted HIV-positive births per year in the absence of antiretroviral prophylaxis and cost savings associated with family planning relative to preventing mother-to-child transmission of HIV (PMTCT) services, by PEPFAR country

PEPFAR country*	Unintended births to all women ^{4 17 18} (%)	Unwanted births to all women ^{4 17 18} (%)	Annual no of births to HIV+ women ²³	No of unintended HIV+ births [†]	No of unwanted HIV+ births [†]	Cost savings of averting unintended HIV+ births [‡] (US\$)	Cost savings of averting unwanted HIV+ births [‡] (US\$)
Botswana	58.4	6.2	11370	1992	211	384839	40856
Mozambique	19.7	3.7	95482	5643	1060	1090169	204752
Namibia	33.7	23.3	9316	942	651	181956	125803
South Africa	52.8	17.3	222415	35231	11543	6806187	2230058
Zambia	40.3	18.9	73668	8906	4177	1720639	806950
Ethiopia	34.9	17.3	65585	6867	3404	1326587	657592
Kenya	44.5	19.6	77799	10386	4575	2006504	883763
Rwanda	39.8	12.5	14107	1684	529	325405	102200
Tanzania	23.5	5.2	99775	7034	1556	1358925	300698
Uganda	45.8	12.5	79950	10985	2998	2122217	579208
Côte d'Ivoire	28.7	4.9	30412	2618	447	505863	86367
Nigeria	14.5	5.0	187544	8158	2813	1576076	543474
Haiti	47.4	29.8	4946	703	442	135875	85423
Vietnam	22.9	11.9	3796	261	136	50381	26181

*Guyana is excluded due to lack of data.

[†]Calculated as: proportion of unintended (or unwanted) births × annual number of births to HIV-positive women × 30% vertical transmission rate in absence of prophylaxis.¹⁶

[‡]Calculated as: [number of unintended (or unwanted) births × \$857] − [number of unintended (or unwanted) births × \$663].²⁴

Case #1: Conclusion

- April 2006: delivered by Cesarean hysterectomy
 - Pathology: negative for invasive cancer
 - Baby girl with Down syndrome

Conclusion

- Prevention of unintended pregnancy should be a priority for HIV+ women and men (A)
- Preconception counseling and care should be offered routinely in the setting of HIV (C)
- Fertility concerns, including safe conception in serodiscordant couples, are likely to be an increasing issue