COMPREHENSIVE WOMEN'S CARE: AN ESSENTIAL COMPONENT FOR THE PREVENTION OF PERINATAL TRANSMISSION

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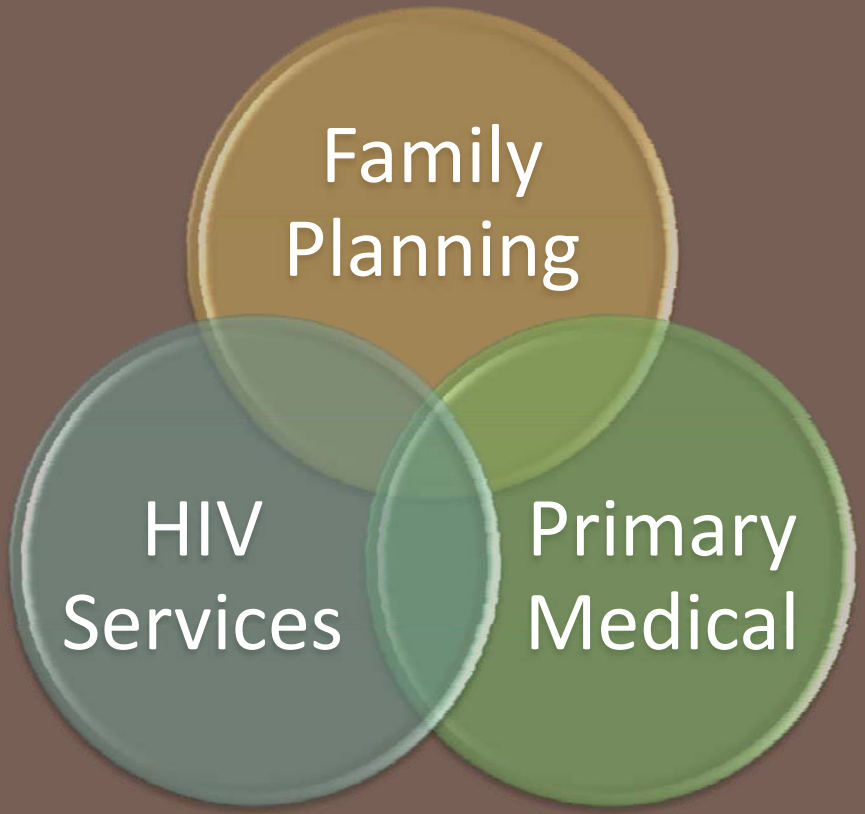
Components of Comprehensive Care for Women with HIV

- Primary care
- HIV care
- Comprehensive reproductive health
- Universal Testing
- Secondary Transmission Prevention
- Pregnancy Care
- Outreach to “hard to reach” persons

INTEGRATION OF SERVICES:
AN EFFECTIVE MEANS FOR THE PREVENTION OF PERINATAL TRANSMISSION

Integration of Services



Ryan White Providers' Roles

- Maximize women's health
  - HIV care/primary care/GYN/OB care co-located
    - One-stop shop (case management, psychosocial services, substance abuse services, adherence counseling, peer support etc.)
- Comprehensive reproductive health
  - Family Planning: offer contraception/STD treatment/pregnancy testing/partner treatment on site
  - Prevent unintended pregnancy
  - Safe conception
  - Preconception counseling
- Universal Testing
  - Opt-out HIV testing for pregnant women - repeated 3rd trimester
  - Testing in L&D
  - Partner testing

Ryan White Providers' Roles

- Pregnancy
  - Test all pregnant women
  - Link pregnant women into care early in pregnancy
    - Early initiation of prenatal care improves outcomes
  - Outreach to "hard to reach" persons
  - Provide ART for woman's health and to prevent perinatal transmission
  - HIV specific childbirth classes
  - Secondary prevention counseling during pregnancy
  - Educate early of reasons to avoid breastfeeding
  - Include partners
  - Ensure L&D testing
  - Linkage with HIV pediatric program
    - AZT dispensed prior to discharge
    - ART for exposed infants as post-exposure prophylaxis
  - Birth control PP

Model of Care in an HIV Clinic

- Integrate on-site Title X family planning services.
  - Linkage with FP clinic if unable to provide FP services
- Become a Center of Excellence for HIV+ Women.
- Integrate on-site GYN and colposcopy services.
- Co-manage pregnant women with OB/GYN.
  - HIV specific childbirth classes
- O% Perinatal Transmission Campaign.
- Secondary prevention programs
- Link with pediatric HIV program for infant f/u

TRANSMISSION

HIV Transmission Depends on…

Cohen and Galvin, Nat Micro Rev 2004
Cohen et al JIAS online Oct 2008

Infectious → **Susceptible**

Inoculum (concentration)

Phenotypic factors

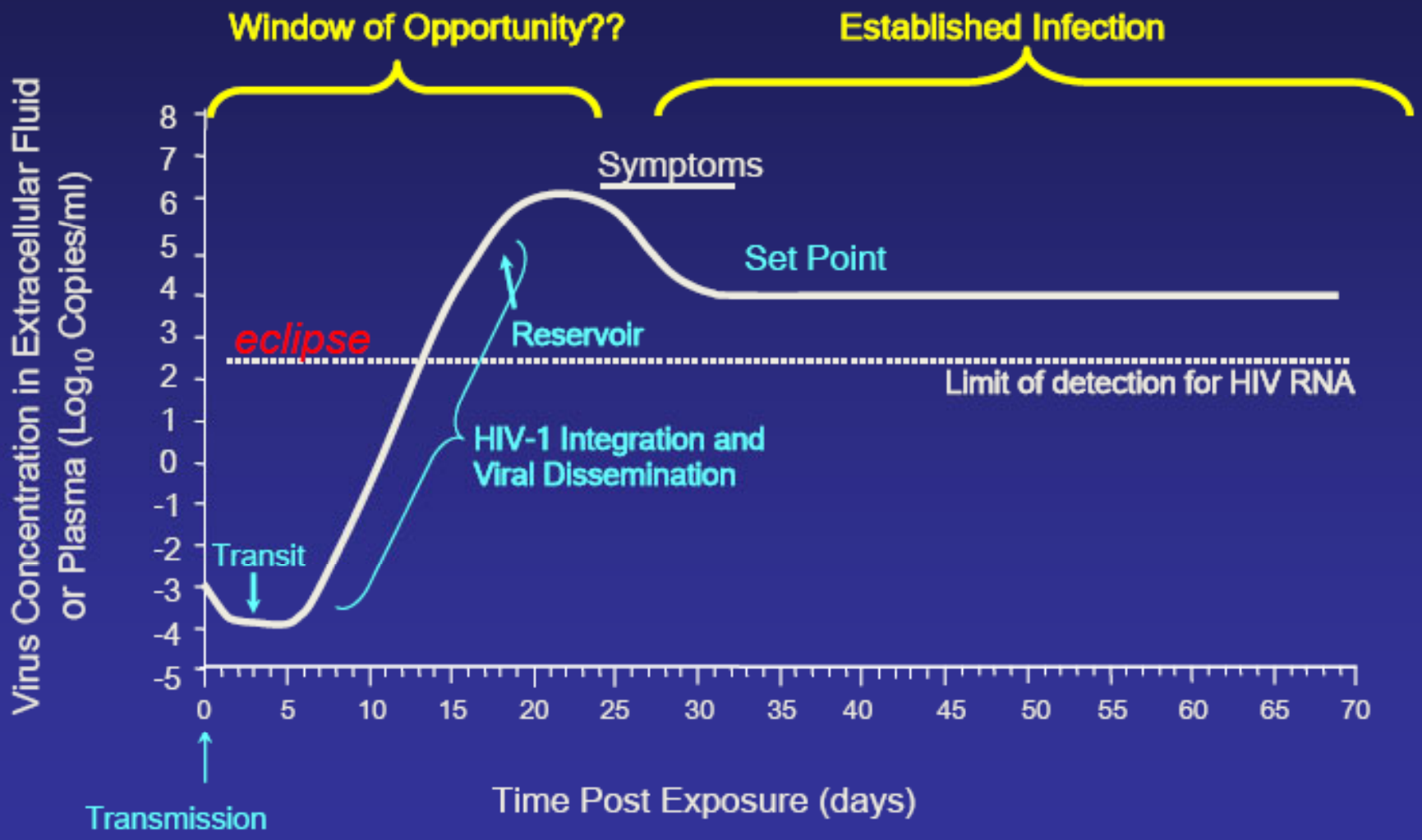
Hereditary resistance

Innate resistance

Acquired resistance

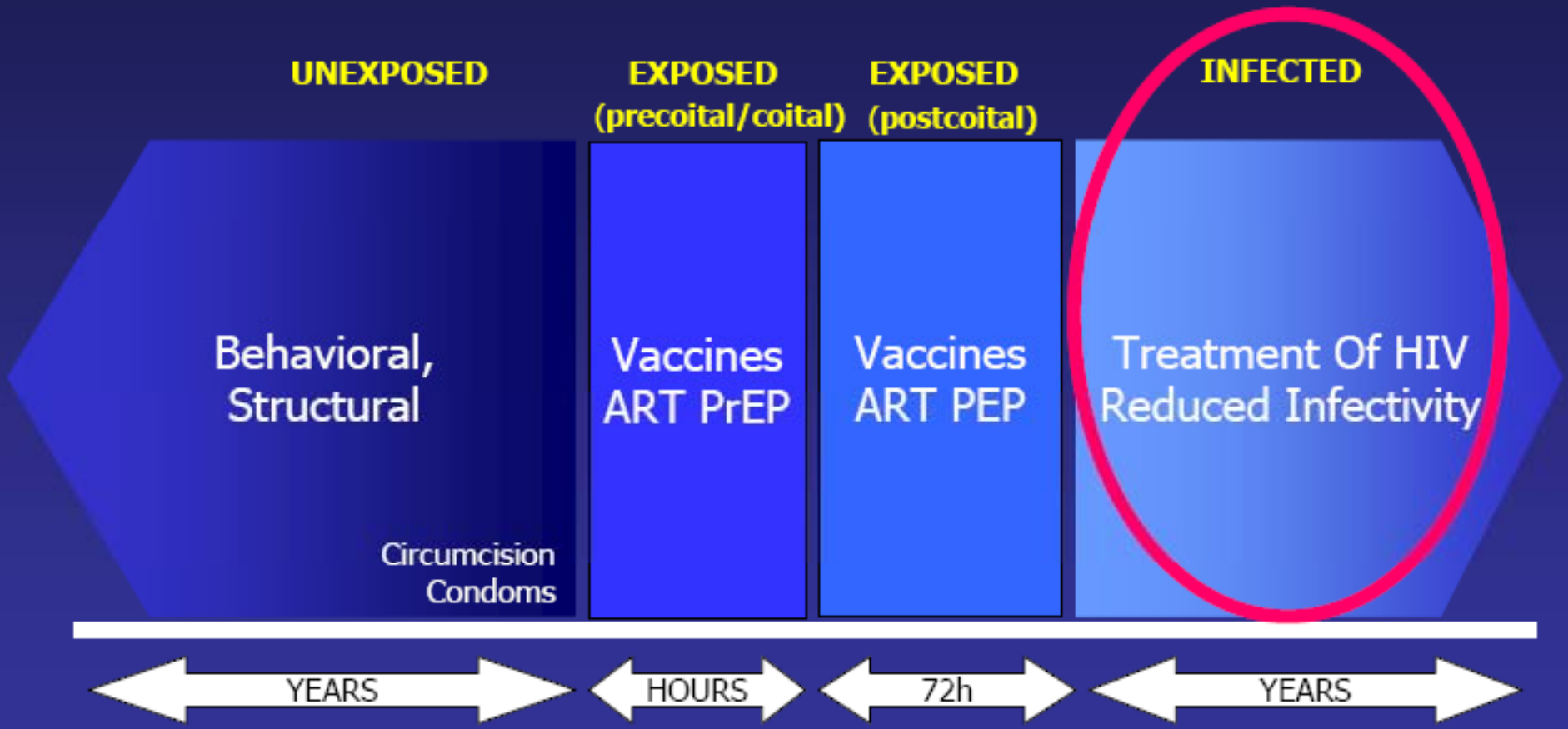
The HIV-1 Transmission Event

Adopted from Johnston and Fauci, NEJM,2007



Four Prevention Opportunities

Cohen et al, JCI, 2008
Cohen IAS 2008



VL and transmission

- HIV risk of transmission linked to plasma HIV

  Lingappa et al AIDS Vaccine 2009

- Higher genital HIV levels associated with linked transmission

  Baeten et al., IAS 2009

- "Test and Treat" – will starting ART with diagnosis decrease incidence of HIV
- Acute seroconversion syndrome

Male Circumcision (MC)

- Adult MC reduces significantly their risk of acquiring HIV heterosexually. Circumcised men are 40 - 60% less likely to acquire HIV from an infected female partner.

- Circumcision was associated with a 38% lower risk of HIV transmission to female partners

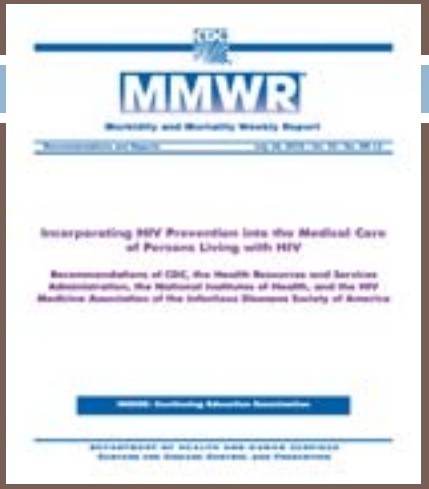
  Baeten et al AIDS 2010

- African countries with high MC have at least 3x lower HIV prevalence

Pregnancy and Female-to-male Transmission

- Recent study demonstrated an increase in female-to-male HIV risk is associated with pregnancy
  - Adjusted HR (95%Cl) =1. 6 (0.9-2.9) p=0.12
- May be due to increased HIV genital shedding in pregnancy

Incorporating HIV prevention into medical care



Medical providers may reduce risk of transmission when they:

- screen for risk behaviors
- identify and treat other STDs
- communicate prevention messages
- discuss sexual and drug-use behavior
- positively reinforce changes to safer behavior
- refer patients for services (substance abuse treatment)
- facilitate partner notification, counseling, and testing

(CDC. MMWR. 2003 July 18)

FAMILY PLANNING:

A CRITICAL COMPONENT IN THE PREVENTION OF HIV TRANSMISSION

Linkages prevent HIV transmission

- HIV integration in FP / FP integrated into HIV:
  - promotes testing
  - Decreases stigma
  - Allows prevention messages
  - Links newly diagnosed persons to get immediate medical care
    - “hard to reach” individuals
    - decreases M&M
  - Decreases transmission

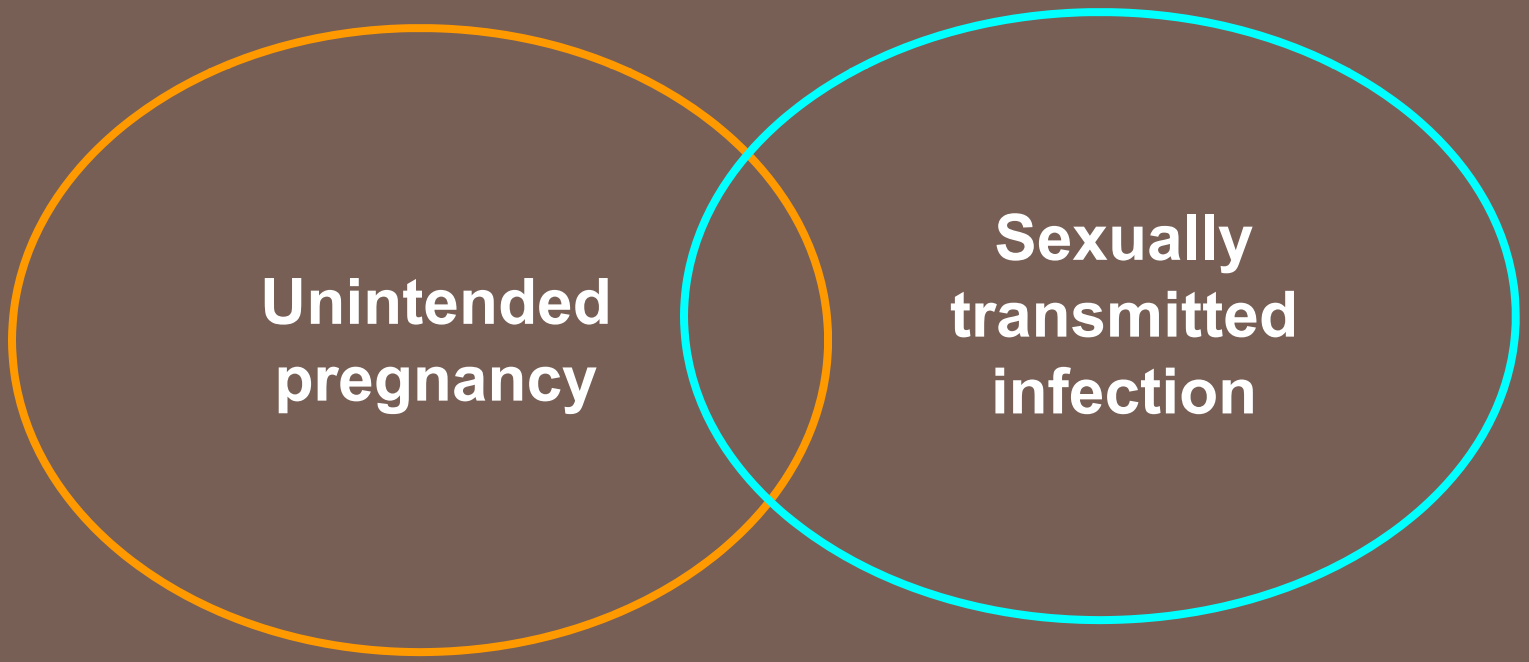
HIV services integrated into FP clinics

- Prevention in FP clinics (primary prevention)
- Rapid testing for all FP patients and their partners
- Linkages with HIV services for HIV-infected FP patients
- On-site or referrals for case management, peer educators, and psychological services
- Ask about pregnancy intentions: ***every woman, every visit***

FP Services integrated into HIV Care

- Prevention in HIV clinics (secondary prevention)
- Ask about pregnancy intentions: ***every woman, every visit***
  - Include partners
- Prevent new transmissions to infants and partners:
  - partner testing
  - treatment of STDs
  - contraceptive availability
  - planned pregnancy/ prevent unintended pregnancy
  - provision of barrier techniques

Dual Protection



Impact of HC on HIV

- Hormonal contraception (HC) does not increase HIV acquisition
- HC does not increase infectivity
- HC does not affect HIV progression
- HC may decrease estrogen efficacy
- HC may interact with HIV medications

Safety of contraceptives with HIV

- Women with HIV/AIDS can use medroxyprogesterone acetate without restriction. May consider Implanon
- IUD: not associated with increased risk of HIV acquisition, with increased transmission of HIV, with infectious complications, with progression of HIV ds Baeten, 2007
- Emergency Contraception to all HIV infected women and their partners of childbearing potential.
- No added protective benefit of diaphragm and lubricant

Padian 2007

WHO, 2009; U.S. Medical Eligibility Criteria for Contraceptive Use, 2010 MMWR 2010

Conclusions

- Condoms - male or female- used with all forms of contraception
- All forms of contraception are safe and effective and should be offered and available to HIV infected persons
- HIV infected persons should have the same access to reproductive options as uninfected women

PRECONCEPTION CARE:
A NECESSARY COMPONENT IN THE PREVENTION OF HIV TRANSMISSION

Pregnancy Intentions

- Most women with HIV are child-bearing age
- With widespread use of ART women can enjoy improved health status and life expectancy
- 29% HIV + men and women desired children in future Chen 2001
- The rate of tubal regret was higher than in the general population (13%) Stanwood 2007
- Predictors of wanting future children were not being on HIV meds, younger age, being with a partner <2 yrs and having higher CD4 count Stanwood 2007

Harm Reduction approach

- Managed Conception
- Informed Natural Conception
  - Delay conception attempts until HIV positive partner is on ART with an undetectable VL
  - Receive treatment for STIs
  - Limit unprotected sex to peak fertility

Serodiscordant Couple: HIV infected woman

- Low-cost self-insemination techniques
  - needle-less syringe
  - turkey baster
  - diaphragm to insert semen close to the cervix.
- Instruct ovulation prediction by using over-the-counter ovulation-prediction kits
- Delay conception attempts until infected partner is on ART VL suppressed
- Treat STIs
- Pre-exposure prophylaxis for uninfected partner

Mathews AIDS 2010; Barreiro *JAIDS*. 2006

Serodiscordant Couple: HIV infected male

- Sperm washing, column purification, and intra-cytoplasmic sperm injection.
- Sperm washing technique has shown significant success in pregnancy outcomes with zero HIV transmissions to the woman.

Sauer MV, Chang PL. *Am J Obstet Gynecol* 2002;186

Semprini et al *Curr Opin Obstet Gynecol* 2004;16

- Timing intercourse to coincide with ovulation decreases the number of unprotected sexual acts necessary to achieve pregnancy.

Mandelbrot et al Lancet 1997;349

"Assisted Reproductive Technologies should not be denied to HIV-infected couples solely on the basis of their positive serostatus"

Fertil Steril 2010 by American Society for Reproductive Medicine

1. HIV is a manageable chronic disease that affects persons of reproductive age, many of whom express a desire for biologic parenthood.
2. Current treatments for HIV can limit the risk of viral transmission to partner and can reduce the chance of newborn infection to ~2%.
3. In couples in which the man is HIV infected, the use of sperm preparation techniques coupled with either inseminations or IVF with ICSI has proven to be highly effective in avoiding seroconversion of uninfected women and offspring.
4. Fertility clinics, to the extent it is economically and technically feasible, should offer services to HIV-infected individuals and couples who are willing to use risk-reducing therapies.

Patient information for serodiscordant couples see:

"Thinking about Having a Baby? Preconception Counseling for HIV Discordant Couples"

hhtp://www.womenchildrenhiv.org/

PRE-EXPOSURE PROPHYLAXIS AND CONCEPTION :

The potential future option for reducing HIV transmission

Pre-Exposure Prophylaxis

- HIV negative partner takes ART to maintain blood and genital drug levels to prevent HIV acquisition
  - Long half life
  - Low incidence of SE
  - Excellent genital tract penetration
  - Oral or topical
- Five efficacy trials of TDF and FTC/TDF underway
- Female controlled protective option
- For male uninfected partner PrEP plus male circumcision

On-going PrEP Trials

Ongoing ARV-based Prevention (Oral PrEP and Topical Microbicide) Trials (December 2009) AVAC

Study; Study phase	Location	Sponsor; Funder	Population (*mode of exposure*)	Intervention arm(s)	Status/ Expected completion
US Extended Safety Trial (CDC 4323) Phase II, safety	United States	CDC	400 gay men and other men who have sex with men (*penile/rectal*)	Daily oral TDF	Fully enrolled / 2009 *Final data analysis Q1/10*
Bangkok Tenofovir Study (CDC 4370) Phase II/III, safety and efficacy	Thailand	CDC	2,400 injecting drug users (*parenteral*)	Daily oral TDF	Enrolling / 2010
CAPRISA 004 Phase II, Safety and Effectiveness	South Africa	CAPRISA, FHI, CONRAD, USAID, LIFElab	1,200 heterosexual women (*vaginal*)	Coitally dependent topical tenofovir gel	Fully enrolled / 2010 *Final data analysis Q3/2010*
iPrEx Phase III, safety and efficacy	Brazil, Ecuador, Peru, South Africa, Thailand, US	NIH, BMGF	3,000 gay men and other men who have sex with men (*penile/rectal*)	Daily oral TDF/FTC	Fully enrolled / 2011
TDF2 (CDC 4940) *Phase II, safety and adherence*	Botswana	CDC	1,200 heterosexual men and women (*penile and vaginal*)	Daily oral TDF/FTC; *switched from TDF Q1 2007*	Fully enrolled / 2010
Partners PrEP Phase III, safety and efficacy	Kenya, Uganda	BMGF	3,900 serodiscordant heterosexual couples (*penile and vaginal*)	Daily oral TDF; daily oral TDF/FTC	Enrolling / 2012
FEM-PrEP Phase III, safety and effectiveness	Kenya, Malawi, South Africa, Tanzania, Zambia	FHI, USAID, BMGF	3,900 heterosexual women (*vaginal*)	Daily oral TDF/FTC	Enrolling / 2013
VOICE (MTN 003) Phase IIb, safety and effectiveness	South Africa, Uganda, Zambia, Zimbabwe	MTN, NIH	4,200 heterosexual women (*vaginal*)	Daily oral TDF; daily oral TDF/FTC; daily topical tenofovir gel	Enrolling / 2013
IAVI E001 & E002 Phase I/II, safety, acceptability, adherence	Kenya, Uganda	IAVI	150 serodiscordant couples and men and women (*vaginal and penile/ rectal*)	Daily oral TDF/FTC; intermittent oral TDF/FTC (twice weekly + coital dosing)	Fully enrolled / 2010
PrEP in YMSM (ATN 082) Phase II, safety, acceptability, feasibility	United States	ATN, NICHD	99 young men who have sex with men (YMSM) (*penile/rectal*)	Daily oral TDF/FTC	Enrolling / 2011

ATN – Adolescent Trial Network; BMGF – Bill & Melinda Gates Foundation; CAPRISA – Centre for the AIDS Programme of Research in South Africa; CDC – US Centers for Disease Control and Prevention; FHI – Family Health International; FTC – emtricitabine; IAVI – International AIDS Vaccine Initiative; MTN – Microbicide Trials Network; NICHD – National Institute of Child Health and Human Development; NIH – US National Institutes of Health; Q1-4 – quarters 1-4; TDF – tenofovir disoproxil fumarate; USAID – United States Agency for International Development

http://www.avac.org/ht/d/sp/a/GetImageAction/i/4474

Issues to guide future implementation

- Feasibility
- Acceptability
- Adherence
- Resistance
- Role of less expensive drugs
- Behavioral change

Considerations for PrEP: TDF & FTC/TDF

- Broad antiviral activity (HIV-1&2)
- acts early in life cycle of HIV (preintegration so it can block initial infection)
- rapidly active (intermittent use possible)
- Safe, tolerable, low pill burden

PrEP safety: teratogenicity

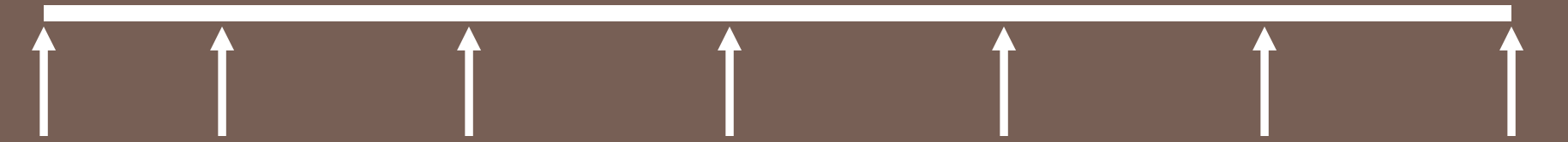
- Tenofovir
  - 1st trimester exposure: 18/756 = 2.4% (1.4%, 3.7%)
  - 2nd/3rd trimester: 8/461 = 1.7% (0.8%, 3.4%)
- Emtricitabine
  - 1st trimester exposure: 11/384 = 2.9% (1.4%, 5.1%)
  - 2nd/3rd trimester: 5/247 = 2.0% (0.7%, 4.7%)

  Pregnancy Registry Dec. 2009
- Birth defects in US population: 2.72/100 live births
  - CDC's birth defects surveillance system (MACDP), 1989-2003

Options for safe conception?

Low tech
Low cost
Lower effectiveness?

High tech
High cost
Higher effectiveness?



Timed coitus

HAART for HIV+

HAART + timed coitus

(HAART) + PrEP/(PEP) + timed coitus

Sperm washing + intravag or cervical insemination

Sperm washing + IUI

IVF-ICSI

Other options: Adoption, sperm donation

Pregnancy: prevention of perinatal and sexual transmission

Estimated* Number of Births to HIV-Infected Women in the US Has Increased >30% 2000 – 2006

Whitmore S et al. 16th CROI, Montreal, Canada Feb 2009 Abs 924

	Estimates		
	Low	Mid	High
Living with AIDS 2000	**N/A**	**49,238**	**N/A**
Living with HIV 2000	**80,293**	**N/A**	**86.080**
Estimated # births 2000	6,075		6,422
Living with AIDS 2006	**N/A**	**56,822**	**N/A**
Living with HIV 2006	**125,050**	**N/A**	**128,653**
Estimated # births 2006	8,650		8,900

*HIV estimate extrapolated from HIV-reporting states & back-calculation for # HIV-infected without AIDS, and pregnancy rate estimate from ASD study

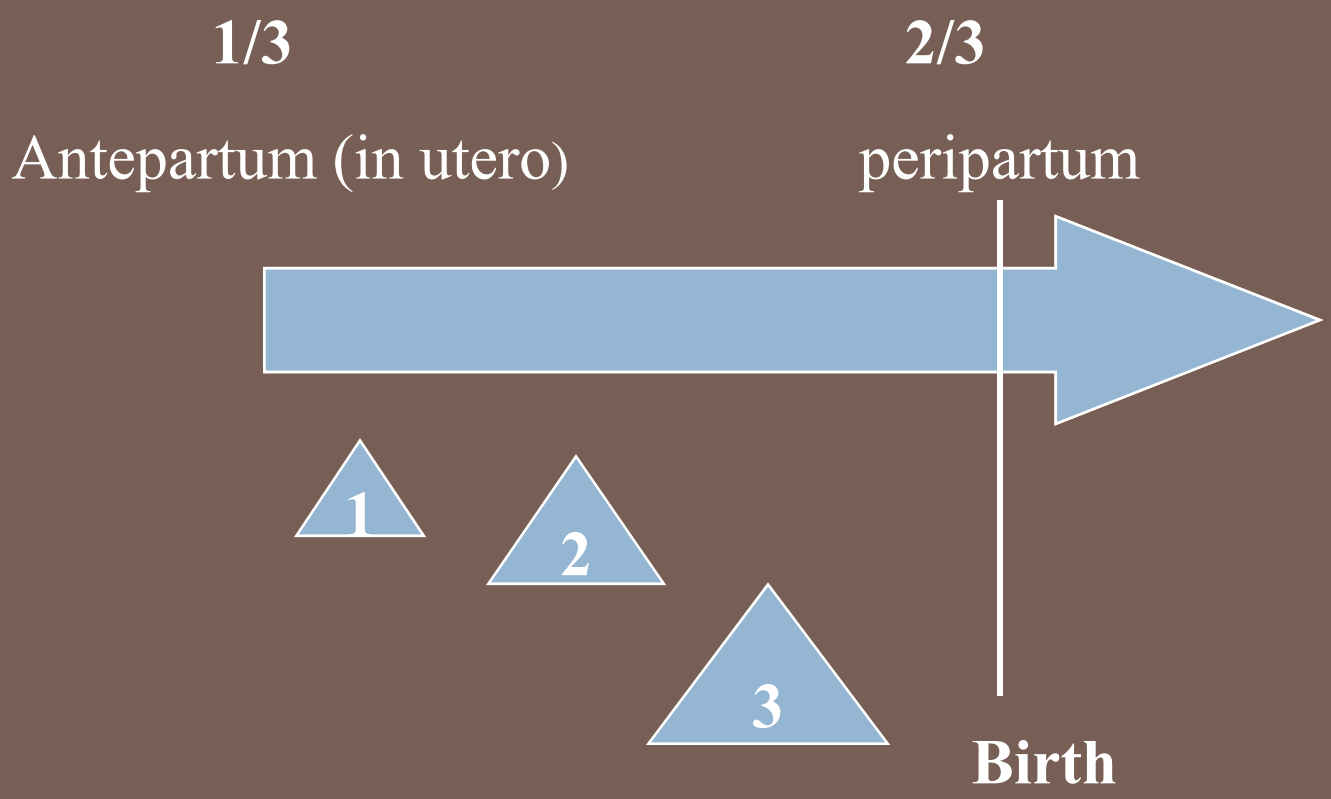
Peri Partum and Intra Partum

- Universal, opt-out HIV testing for pregnant women
  - Repeat testing in 3rd trimester
- Early initiation of prenatal care improves outcomes
- Outreach efforts to “hard to reach” persons
- Secondary prevention counseling during pregnancy
- ART for the woman’s health and to prevent perinatal infection
- HIV specific childbirth classes:
  - Educate early of reasons to avoid breastfeeding
  - ART for exposed infants as post-exposure prophylaxis
  - Birth control PP
- L&D testing
- Include partners

Post Partum

- Risk Reduction Counseling
- Birth Control
- Refer Mother and Baby to HIV specialist
- Ensure mother has liquid AZT prior to discharge
- No Breast Feeding
- Assess for PP depression

Timing of Transmission



Linkage to Care:
a critical component for the prevention of perinatal transmission

Gaps in services

- Huge efforts to identify persons unaware of their status
- The silent epidemic: “hard to reach” persons
  - Lost to care / sporadic engagement in care
- Identify gaps in services
- Innovative models of care
  - Home based care
  - Community outreach
  - Other ideas?