



# 'So you want to have a baby...?'

Pre-conception counselling for the HIV affected couple

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# Meet Miss LM...

- A 30 yr old lady
  - HIV positive, well, on ART for the past 5 years
  - Latest bloods: CD4 - 540, viral load – undetectable
  - 2 children aged 8 and 10 years
  - No children with her current partner of 4 years
  - Her partner is HIV negative
- 
- She wants to have a baby...



Should HIV affected couples  
have children?





## National statistics (2009)

- Majority of people living with HIV in South Africa are in the reproductive age group
- More than half (3.3 million) are women
- Adult HIV sero-prevalence of 17.8%
- Antenatal HIV sero-prevalence of 29.4%
- 1 million births in South Africa annually

# MTCT: The four-pronged strategy

Prevention  
of HIV in  
Women,  
(Especially  
Young  
Women)

Phase 1

Prevention of  
Unintended  
Pregnancies  
in  
HIV-Infected  
Women

Phase 2

Prevention of  
Transmission  
from an  
HIV-Infected  
Woman  
to Her Infant

Phase 3

Support for  
HIV-Infected  
Mother and  
Family

Phase 4

# Should HIV affected couples have children?

- Reproduction is a basic human right
- Having children is part of many women's life plan
- In many parts of Southern Africa, being without a child attracts stigma



# HIV affected couples want children

- Literature suggests both men and women living with HIV desire children:
  - Survey of 1421 HIV-infected adults: 29% **desired children** sometime in their lives
  - Retrospective study, HIV-infected subjects cited raising children as a way to **'give purpose to life'**
- HIV infected women reported pregnancy and childbirth as a way to **'regain sense of womanhood and sexuality'**
- Many health workers focus on women, yet many HIV infected **males want children**

Chen et al, FP perspectives, 2001

Van de Vanter Repro Behaviour, 1998

Wesley Y Health Care Women International, 2001

Dyer SJ. J Psychosom Obstet Gynaecol, 2007



# HIV infected women are trying to get pregnant

- A survey conducted in the US, reported that 80% of HIV affected couples who had previously conceived had engaged in unprotected intercourse to achieve pregnancy
- ART initiation is associated with an increase in fertility intention
- HIV infected individuals on ART have improved life expectancy

Klein J, et al Obstet Gynecol 2003

Taulo F, et al AIDS Behav, 2009

Maier M, et al Aids Behav, 2009

Schwartz S, et al AIDS Behav, 2011

# Poor uptake of contraception

- High rates of unintended pregnancies in women in sSA!

- 84% among PMTCT clients in South Africa
- 51% among women in Cote d'Ivoire
- 99% among women in an ART program in Uganda
- 62% among women on ART in South Africa

Roch, et al JAMA 2006

Desgrées-du-Loû, et al Int J STD AIDS 2002

Smart T, Aidsmap 2006

Schwartz S, et al AIDS Behav 2011



Whether or not a couple  
desires a child-we need to  
address their fertility...





# Are Health Care Workers addressing these issues?

- US survey around reproductive concerns
- 69 HIV-Infected women
- <50% thought their physician had adequately counseled them about contraception and fertility choice
- Nurses and counsellors do better
- South African survey (2009) amongst HIV discordant couples
- 43% of the HIV positive participants reported having experienced some form of discrimination from their health-care professional

Duggan J Assoc Nurses AIDS Care 1999

HSRC's social aspects of HIV / AIDS and Health website, 2009



# Are Health Care Workers addressing these issues?

- 850 HIV-infected South African women on ART
  - 94% HCW had spoken about condoms
  - 48% spoke about hormonal contraception
  - 41% of HCW had spoken to women about fertility intentions
  - Hormonal contraception method use was higher in women whose HIV providers had initiated discussions over methods with them (37% vs 21%)

# Back to Miss LM...

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  - Latest bloods: CD4 - 540, viral load – undetectable
  - 2 children aged 8 and 10 years
  - No children with her current partner of 4 years
  - Her partner is HIV negative
- 
- She wants to have a baby...



# What concerns do we need to address?

1. Horizontal transmission (risk of HIV transmission to partner)
2. Vertical transmission (risk of HIV transmission to baby)
3. Sub-fertility related to HIV infection
4. Obstetric outcomes (including potential adverse effects of ARV's)
5. Possible reduced life expectancy of parents





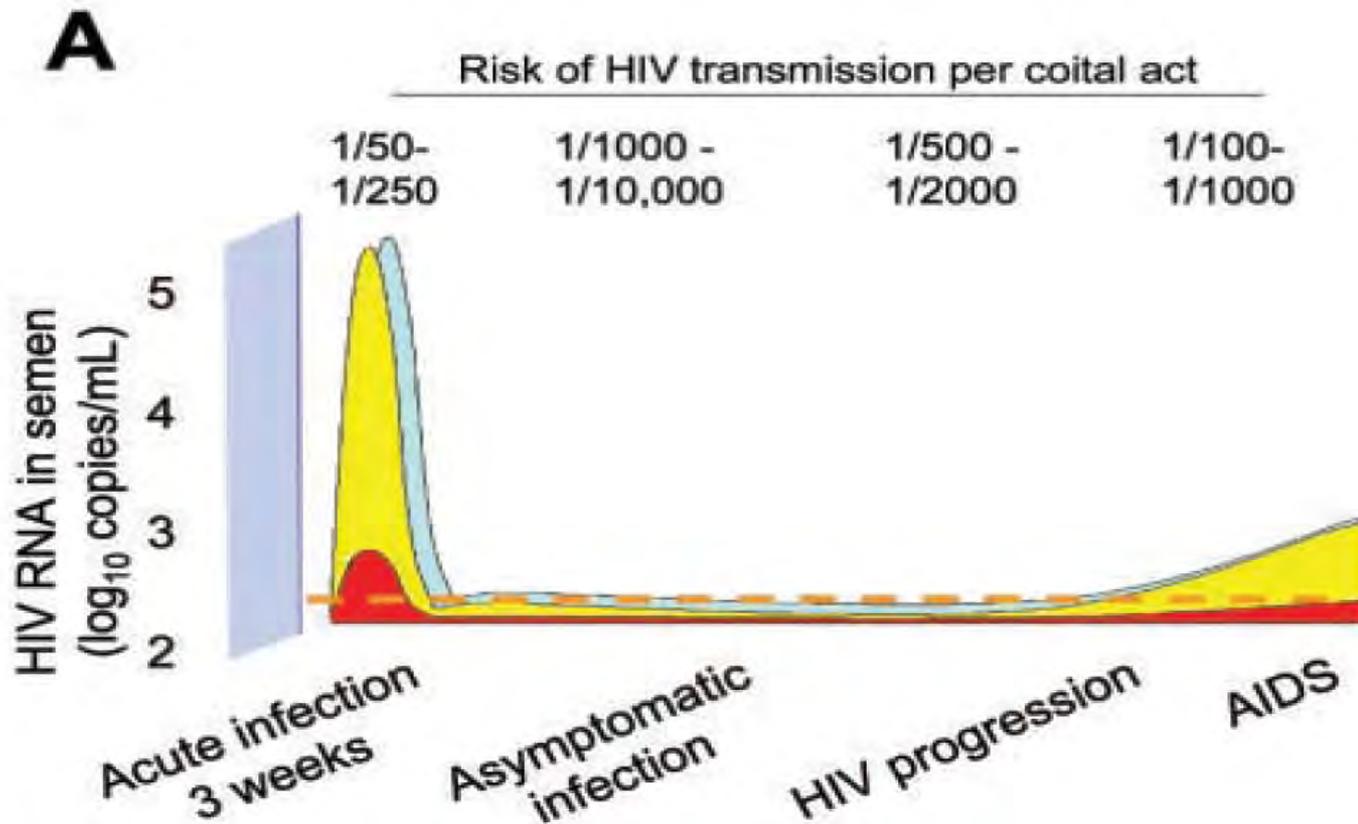
# 1. Horizontal transmission

- Heterosexual transmission is the major method of HIV infection among adults
- Sero-discordancy is important for transmission
- Among HIV affected couples, 2/3 are discordant
- In 30-50% of cases, the index case is a woman
- For the HIV negative partner, there is a 10% annual risk of infection

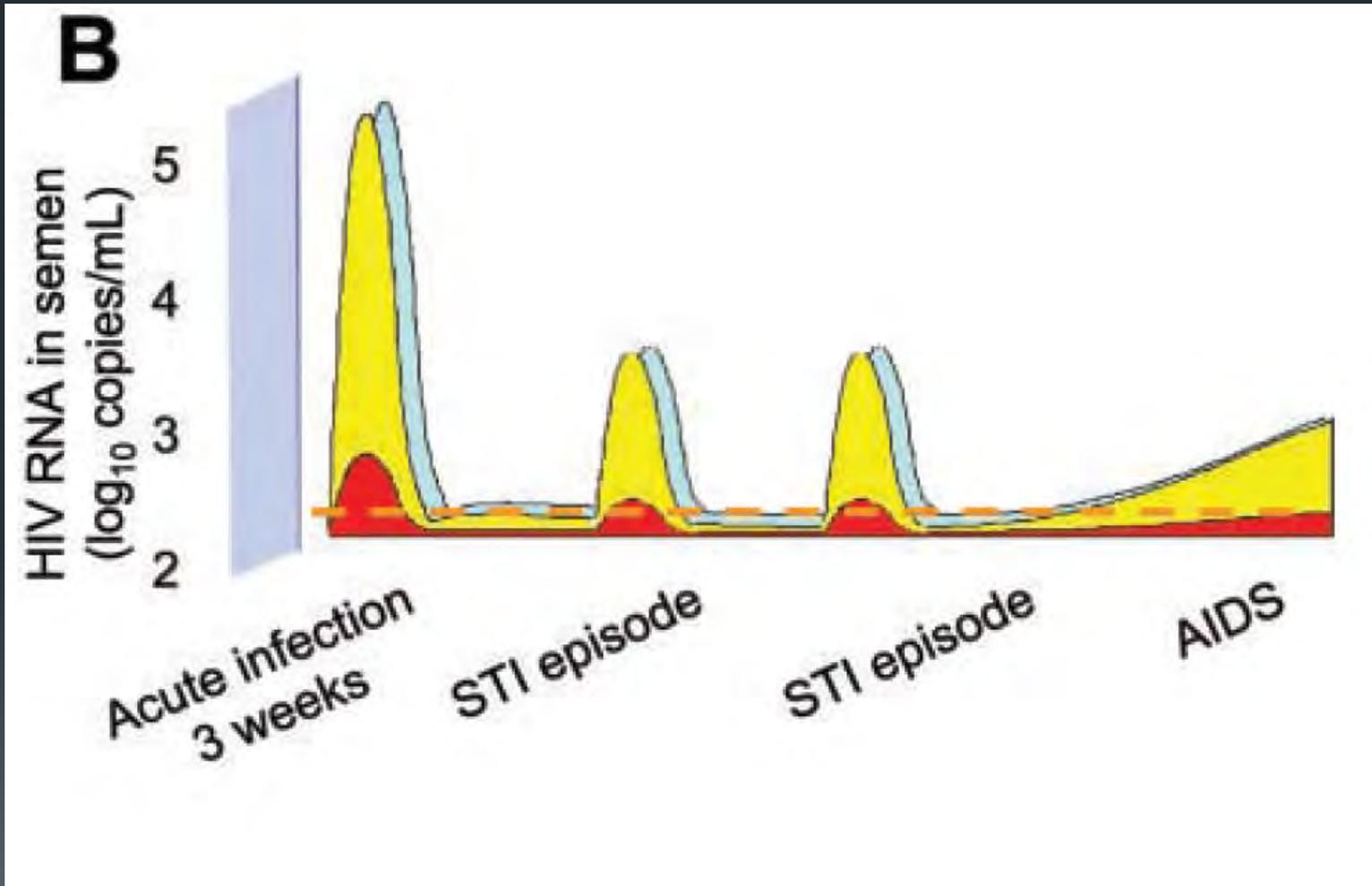


- Increased risk of transmission:
  - High viral load
  - Impaired mucosal integrity (STI's: esp HSV)
  - Increase length and frequency of exposure
  
- Decreased risk of transmission:
  - ART!
  - Circumcision

# Sexual transmission of HIV



# Acute HIV and STI episodes

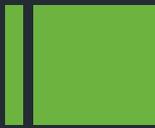




# HIV transmission to partner

- 415 HIV serodiscordant couples in Uganda:
  - 21.7% became infected over 30 months of follow-up
  - Transmission rates: 12 infections per 100 person years
- No transmission events occurred if infected partner had a plasma V/L <1500 copies/ml
- For every 10-fold increase in viral load, there was a >2-fold increased risk of transmission

Quinn et al. Viral load and heterosexual transmission of Human Immunodeficiency Virus type 1. Rakai Project Study Group. N Engl J Med 2000; 342: 921-927



# Partners in Prevention Study

- Trial examined HIV transmission risks in over 3000 heterosexual serodiscordant couples:
- Average risk per sexual exposure= 1: 1 000
- If V/L <1000 c/ml, risk per sex act was 1:3537
- If V/L <10 000 c/ml, risk per sex act was 1:1220
- If V/L <100 000 c/ml, risk per sex act was 1:434



# HPTN 052

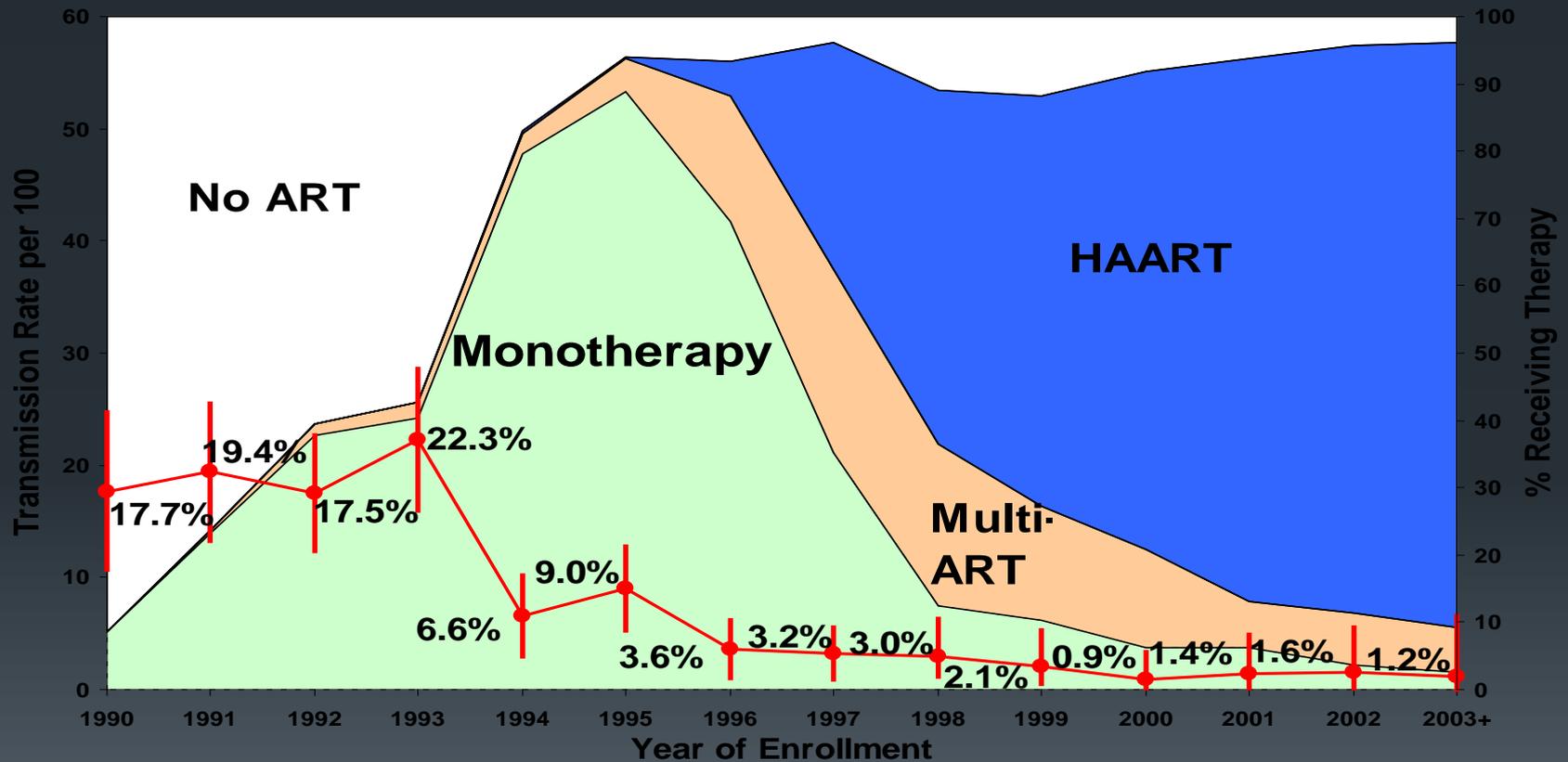
- Early ART treatment (ART initiated at CD4 count 350-500 cells/mm<sup>3</sup>)
- Serodiscordant couples
- 96% reduced risk of HIV transmission to an uninfected partner

# Circumcision

- Profound effect on the risk of HIV acquisition in heterosexual couples
- Several large randomised prospective studies performed in Africa have shown a 60% reduction in risk of HIV acquisition following circumcision



## 2. Vertical transmission



### 3. Fertility and HIV...

- HIV-infected women are 25 to 40% less fertile than their HIV-negative peers
- Causes of this reduced fertility are unclear
  - HIV itself?
    - Anovulatory cycles, amenorrhoea, link between HIV infection and ovarian failure
  - Other problems that HIV infected women are more prone to?
    - Stress, weakened immune systems, weight loss, presence of STI's?
- 19% of HIV infected women experienced pregnancy loss compared to 12% of HIV uninfected women
  - HAART reduces pregnancy loss in women with HIV

# ...fertility and HIV

- HIV infected men are more likely to produce insufficient testosterone levels and experience decreased libido
- 60% of HIV infected men experience erectile or ejaculatory dysfunction
  
- Fertility problems may be reversed by initiating HAART

# 4. Effects of HIV on pregnancy outcomes

- Increased risk of pregnancy complications
  - Increased maternal mortality
  - Opportunistic infections
  - Anaemia
  - Premature delivery
  - Low Birth Weight
  - Spontaneous abortion
  - Still birth
  - IUGR
  - Post surgical complications
  - Mental illness



- **Improved access to HAART has decreased AIDS mortality**

# Is Efavirenz Safe?

First Trimester Exposure Regimen	Defects/Live Births	Prevalence (95% CI)
Indinavir	6/285	2.1% (0.8%, 4.5%)
Lopinavir	16/738	2.2% (1.2%, 3.5%)
Atazanavirsulfate	12/502	2.4% (1.2%, 4.1%)
Stavudine	19/797	2.4% (1.4%, 3.7%)
Ritonavir	33/1401	2.4% (1.6%, 3.3%)
Tenofovir	26/1092	2.4% (1.6%, 3.5%)
<b>Nevirapine</b>	25/987	<b>2.5%</b> (1.6%, 3.7%)
Emtricitabine	17/641	2.7% (1.5%, 4.2%)
<b>Efavirenz</b>	17/623	<b>2.7%</b> (1.6%, 4.3%)
Abacavir	22/744	3.0% (1.9%, 4.5%)
Lamivudine	118/3864	3.1% (2.5%, 3.7%)
<b>Zidovudine</b>	118/3620	<b>3.3%</b> (2.7%, 3.9%)
Nelfinavir	46/1193	3.9% (2.8%, 5.1%)
Didanosine	19/406	4.7% (2.8%, 7.2%)

# Prevalence of Birth Defects

General US pop [1]	General South Africa pop [2]	1 <sup>st</sup> Trimester exposure to any ARV [3]	2 <sup>nd</sup> /3 <sup>rd</sup> trimester exposure to any ARV [3]	1 <sup>st</sup> trimester exposure to EFV [3]	2 <sup>nd</sup> /3 <sup>rd</sup> trimester exposure to EFV [3]	1 <sup>st</sup> trimester exposure to EFV [4] <i>Meta analysis</i>
<b>3%</b>	<b>5,3%</b>	<b>2.9%</b>	<b>2.7%</b>	<b>2,7%</b>	<b>2.9%</b>	<b>2.0%</b>
95% CI :		(2.5-3.4)	(0.88-1.32)	(1.6-4.3)	(0.3-10.0)	(0.82-3.18)
Numbers:		164/5555	205/7483	17/643	2/70	39/1437

Relative Risk 1<sup>st</sup> Trimester EFV to Non EFV ART was **0.85** (0.61-1.20) [4]

1. [CDC General Survey \(1989-2003\) Source- www.apregistry.com/forms/interim\\_report.pdf](http://www.apregistry.com/forms/interim_report.pdf)
2. <http://www.marchofdimes.com/downloads/BirthdefectsAppendix-B.pdf>
3. Antiretroviral pregnancy register 2011-- [www.apregistry.com/forms/interim\\_report.pdf](http://www.apregistry.com/forms/interim_report.pdf)
4. Ford et al. 2011 Safety of efavirenz in the first trimester of pregnancy: an updated systematic review and meta-analysis AIDS. DOI:10.1097/QAD.0b013e32834cdb71

# 5. Life expectancy with ART

- UK patients on HAART
- Life expectancy improved substantially between 1996 and 2008
- *'Patients who initiated HIV therapy when their CD4 cell count was in the region of 350 cells/mm<sup>3</sup> had an average life expectancy of approximately 75 years'*
- Uganda
- Patients on ART can expect an almost normal life expectancy
- *Survival of >25 years on ART*

# Fertility counselling for HIV infected couples



# Approach to fertility

1. Discuss recommended steps before conception
2. Optimise HIV therapy and other aspects of health
3. Couples based counselling
4. HIV testing of partner and treatment
5. Pre-conception workup
6. Advise of optimal conception strategies



# Alternative options

- Sperm donation
- Adoption
- Surrogacy
- Care of children in the community





# Pre-conception counselling

- Reasons for reproductive desire
- Basic understanding of transmission risks
- Basic understanding of conception
- Informed decision making
- Health of both partners important
  - HIV status known (CD4 and V/L)
  - Disclosure of HIV status



# Pre-conception counselling

- Reproductive options:
  - Risks
  - Risk reduction
  - Costs
  - Chances of success
- Balance the risk of natural conception with established risk-reduction methods
- Early identification of infertility
- Consequences of failure to prevent transmission to partner and child and importance of regular testing

# Non-medical assessment

- Gender violence
- Mental health
- Couple communication
- Parenting
- Inclusion of male partner is vital



# Male partner involvement:

- Kenya, 1999-2003
- 465 HIV+ pregnant women and infants followed up until 12 months postpartum
- After adjusting for maternal V/L and breast milk exposure, male partner attendance also associated with:
  - ~50% reduction in HIV transmission risk at 1yr postpartum
  - ~60% greater infant HIV-free survival, and
  - ~2.5 fold higher survival in HIV-uninfected children





# Pre-conception medical assessment

- Remember the basics: body weight, alcohol, smoking...
- STI's
  - Exclude STI's through syphilis serology and clinical assessment
- Clinically and immunologically should not have AIDS
  - Medical exam and CD4 cell count
- Those on ART should have an undetectable V/L
- Screen for infertility through history
- Resources available:
  - Hepatitis serology, CMV, rubella, HSV, toxoplasmosis, FBC, pap smear



# Medical management

- Optimise medical condition
- Treat any current infection
- Treat co-morbid illness
- Prevent infections as appropriate
- Determine ovulatory cycle
- Pregnancy: RH, haemoglobin
  
- Folate 5mg daily



# Strategies available:

- ART and viral load suppression in the positive partner (s)
- Male circumcision
- Timed, limited, peri-ovulatory, unprotected sex
- Intra-uterine insemination
- Intra-vaginal insemination (self insemination)
- Sperm washing
- PEP
- PrEP



# Determining the fertile period

- Fertile period=specific days relative to ovulation during which a woman is most likely to conceive
- Necessary to time peri-ovulatory intercourse
- Determined by using:
  - Length of menstrual cycle
  - Cervical mucous evaluation
  - Basal body temperature charts
  - Ovulation kits
  - Serial ovarian ultrasound

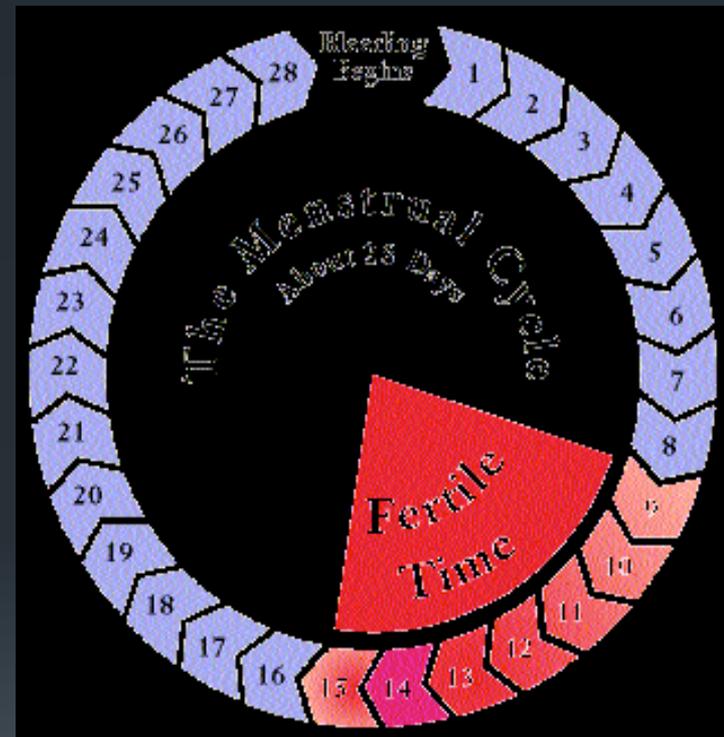
# Lifespan of sperm and egg

- Sperm
  - Survives 3 to 5 days or longer in a woman's cervix in the presence of fertile mucus
  - Sperm quality reduced with smoking and alcohol
- Egg
  - Survives 24 hours after ovulation



# Fertile dates

- Average normal duration of a woman's menstrual cycle is 28 days
- First day of menstrual period=day 1 of her menstrual cycle
- Ovulation is assumed to occur half way through her cycle
- Fertile period=5 days before predicted ovulation up until 1 to 2 days after ovulation



# Ovulation kits

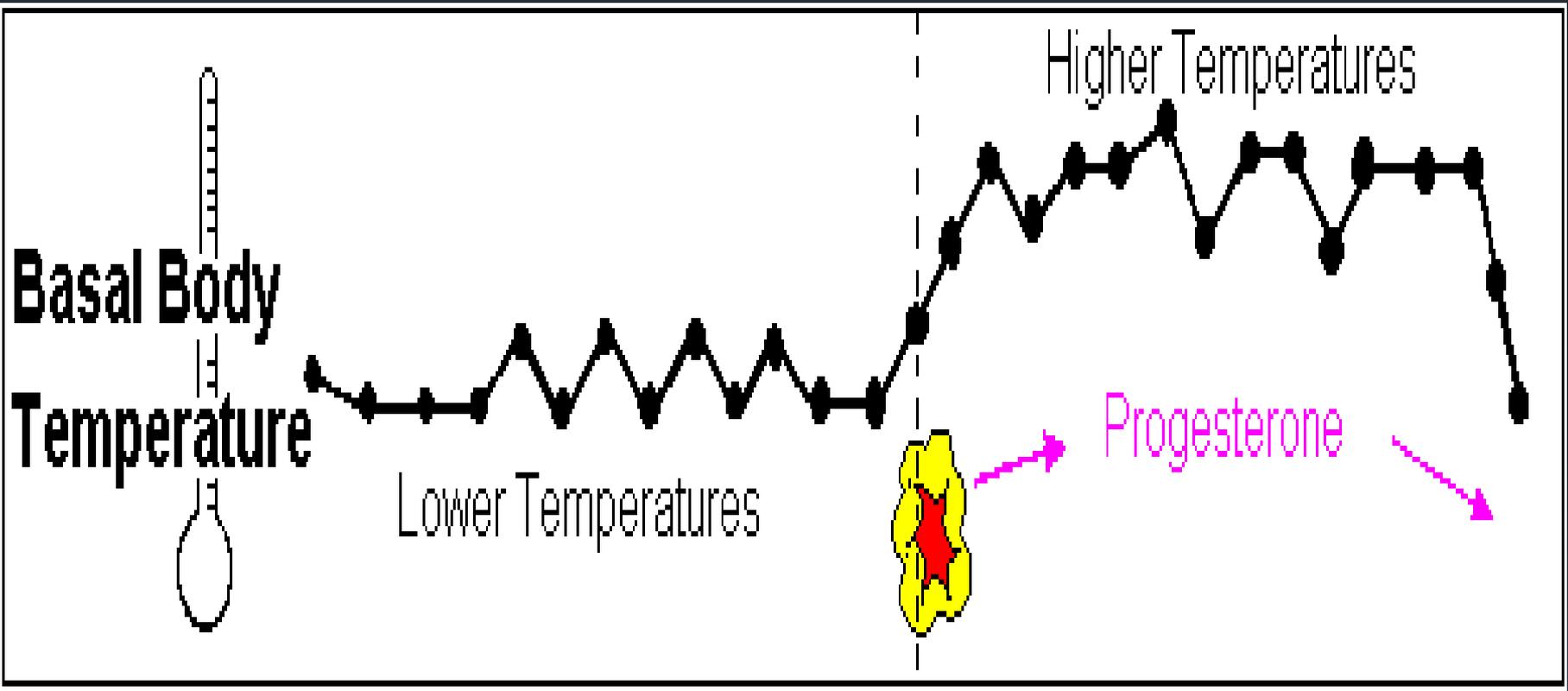
- Urine or saliva
- A number of OTC products are available that enable ovulation prediction
- Detect the surge of luteinising hormone (LH) that occurs immediately before ovulation





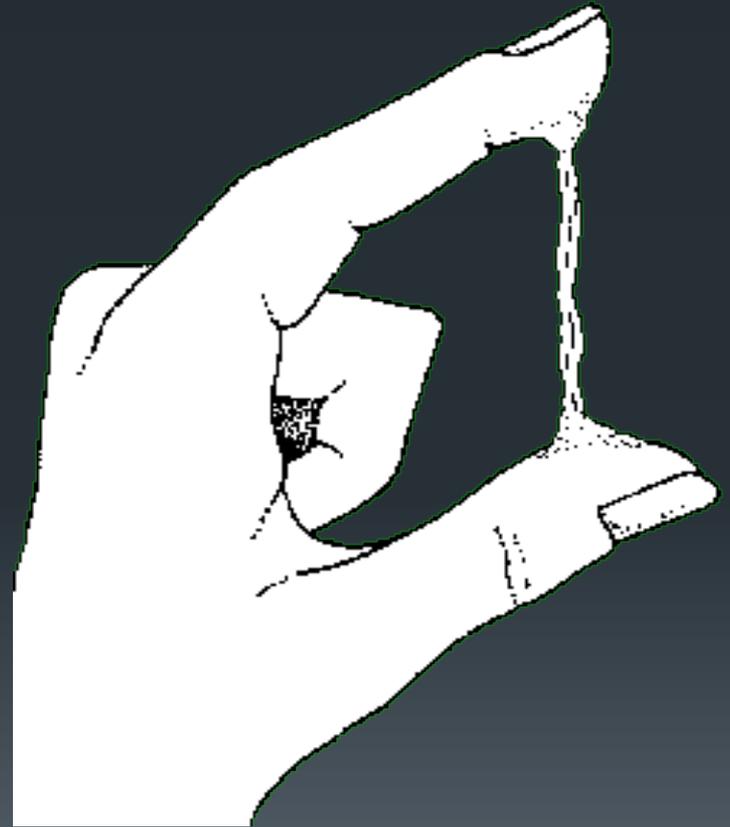
# Basal body temperature charting (BBT)

- A woman's body temperature increases by 0.25 to 0.5 °C during ovulation
- Charting BBT daily-pattern may assist in predicting ovulation
- Plot BBT at the same time every day
- Attempt conception after the first rise in BBT has been detected
- Chances of conceiving after the 3<sup>rd</sup> day of raised BBT are greatly reduced



# Cervical mucous monitoring

- Physiological changes occur around the time of ovulation
- Non-fertile days:
  - cervical mucous is thick and acidic
- Fertile days:
  - mucous becomes thin, profuse, transparent and 'stretchy'



# Natural conception and unprotected intercourse

- Risk to uninfected partner difficult to quantify-not zero
- Mathematical models cite a risk of 1: 100 000 per act of intercourse
- Viral shedding in semen has been reported to occur even in men fully suppressed on ART
- Retrospective study of 551 semen samples in HIV infected men
  - 15 cases of detectable HIV in semen in men with undetectable plasma viral load
- HIV has been identified in follicular fluid and endometrial samples from HIV-positive women even when plasma V/L was fully suppressed
- A need for caution when couples consider a natural conception approach

- 
- Barreiro outlined criteria for safer natural conception:
    - HIV positive partner on HAART for 6 months or longer
    - viral load undetectable on PCR (< 50 copies/ml)
    - perfect adherence to treatment and regular medical follow-up
    - mutually faithful relationship
    - no concomitant sexually transmitted infections
  - The responsibility of drug adherence rests with HIV positive partner
  - The decision of consenting to unprotected intercourse lay with the HIV negative partner
  - Limited to 6 months during ovulation period only
  - Condoms should be used at all other times
  - Only infections occurred in those who did not use condoms consistently

# Other experiences of natural conception...

- 3 clinics, Spain
- 62 HIV serodiscordant couples
  - If male HIV infected, V/L undetectable on HAART
  - If female HIV infected, V/L undetectable during pregnancy and at delivery, on HAART
- 76 pregnancies resulting in 68 children
- No cases of horizontal transmission
- 1 case of vertical transmission
- ***'serodiscordant couples attaining natural pregnancy are exposed to a negligible risk of sexual transmission of HIV when infected partner presents with complete viral suppression while receiving HAART'***

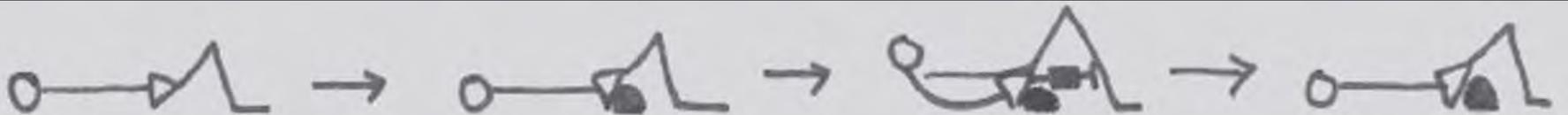
# Artificial insemination

- Semen introduced into the female reproductive tract other than by sexual intercourse
- Intra-uterine - specialist procedure
- Intra-vaginal - health care provider or patient herself
- Practiced during the time of ovulation (fertile period)



# Self insemination

- Semen needs to be provided in a clean receptacle
  - male ejaculation into a condom during intercourse
  - male ejaculation into a clean specimen jar provided for the purpose
  - Semen drawn up into a large syringe (10 - 20ml)
  - Syringe placed about 4 – 6 cm in woman's vagina in prone position and semen pushed out of the syringe
  - Can be done at home or in clinic
  - The semen (most men ejaculate 3 - 5 ml) should be inseminated as soon as possible. (plastic syringe or pipette)



# Sperm washing

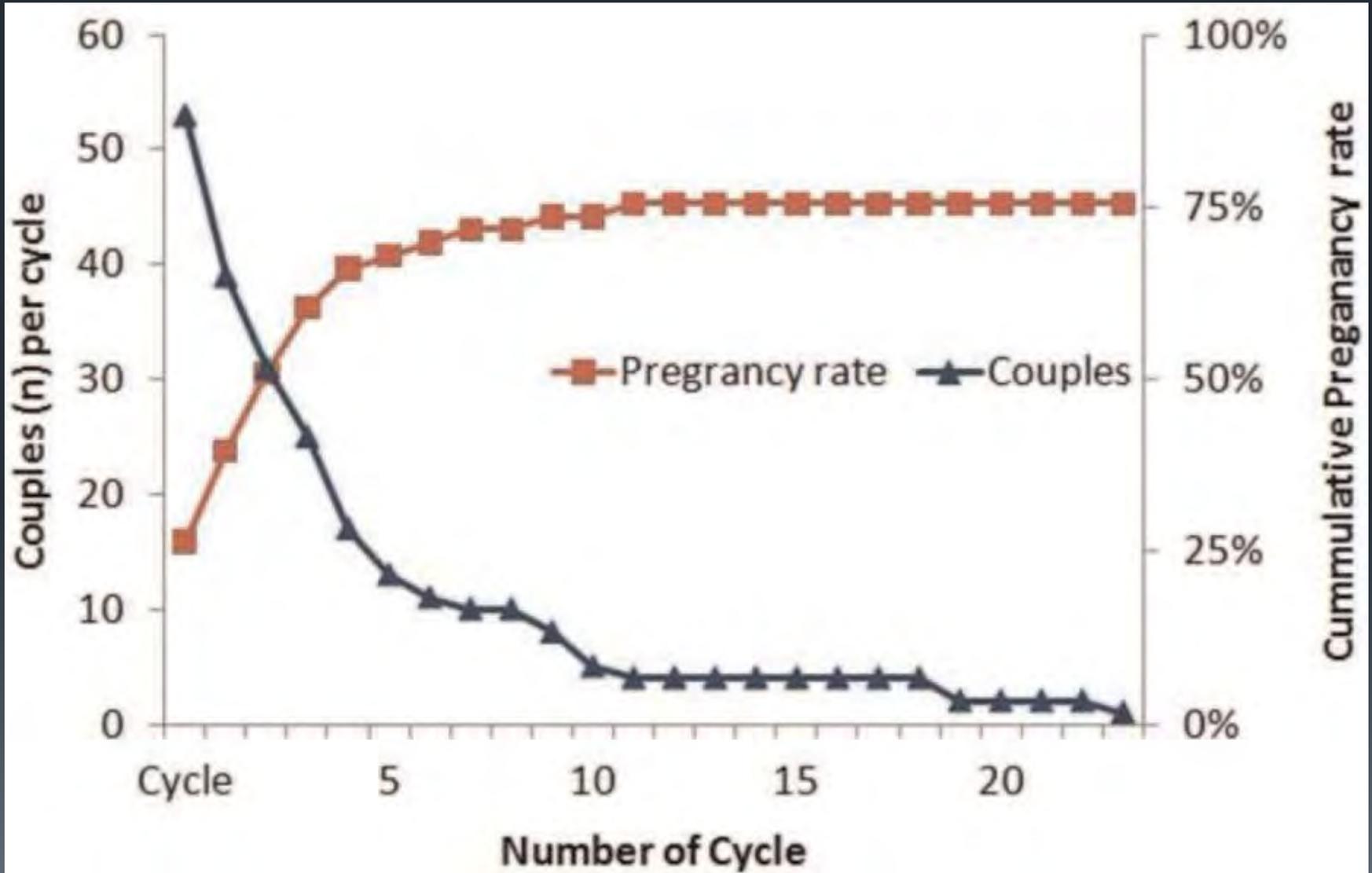
- Issues around sperm washing
  - Not feasible in resource constrained setting
  - HIV remains detectable in some samples
  - Success rates
    - 14.5% per cycle (*Semprini – 1998*)
    - 19% per cycle (*Servasi – 2007*)
    - Up to 78% with repeated cycles
    - Similar to non HIV rates
  - Semprini: 513 HIV negative women; 1600 inseminations; all women remained HIV negative
  - Servasi: 741 couples, all women remained HIV negative; overall pregnancy rate 70.3%
  - Bujan: 1036 couples; 3390 cycles; results of 967 women – all remained HIV negative



# PrEP and timed intercourse for conception (combined with HAART)

- Switzerland
- HIV infected males on ART with suppressed VL for at least 6/12.
- No evidence of genital tract infection nor concurrent sexual partners
- 53 couples attempted conception
- Did not exclude infertility
- Timed intercourse using LH urine surge test
- On morning of surge, woman had TDF 300mg and a 2<sup>nd</sup> dose 24hours later. That evening couple had intercourse
- Allowed 6 attempts before investigating for infertility

# Pregnancy rate/cycle



# Results

- After 6 months 75% success in conception
- Plateaued at 6 months
- Older age predictive of failure to conceive
- No HIV infections after 244 documented unprotected sexual exposures



# Pre exposure prophylaxis (PrEP) - microbicides

- CAPRISA 004 😊
  - Microbicide containing Tenofovir gel
  - July 2010
  - 39% effective in reducing HIV transmission
- FACTS study
  - To confirm results of CAPRISA 004
  - Results expected 2013

# Pre exposure prophylaxis (PrEP) – oral formulations

- iPrEx 😊
  - November 2010
  - Daily dosing of Truvada among high-risk MSM indicated a 44% reduction in the incidence of HIV
- FEM-PrEP ☹️
  - Oral Truvada once daily vs placebo among high-risk heterosexual, HIV-negative women to prevent HIV infection
  - April 2011
    - Study halted due to inability to determine effectiveness
    - Equal number of new infections in truvada and placebo arms
- 2 other studies looking at oral PrEP are still ongoing (VOICE and Partners PrEP)

No conclusive evidence that  
PrEP works...



# Different approaches to HIV infected couples

HIV Infected woman



HIV Infected man

HIV Uninfected woman



HIV Infected man

HIV Infected woman



HIV Uninfected man



# HIV + man / HIV + woman

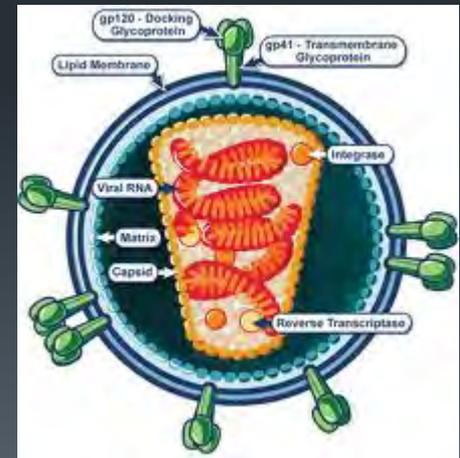
## Seroconcordant couples



- Woman:
  - Safe ART regimen or ART / PMTCT as soon as possible
  - No teratogenic drugs
  - Undetectable HIV viral load in blood
- Man:
  - ART until undetectable VL in blood
- Conception:
  - sperm collection
    - intra-uterine insemination;
    - Self-insemination
  - Peri-ovulatory unprotected sexual intercourse only in the face of demonstrated undetectable viral loads

# Concordant status

- HIV Superinfection risk poorly quantified
  - Can offer sperm washing if couple request maximum risk reduction
- Transmitted ARV resistance



# HIV + man / HIV - woman

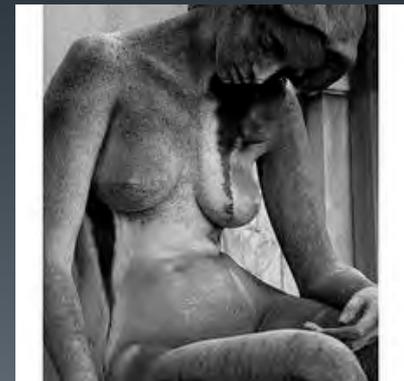
- Woman:
  - Repeated HIV testing before and during pregnancy
- Man:
  - Preconception ART
  - undetectable VL
  - Adherence support
- Conception:
  - sperm washing and intrauterine insemination
  - Unprotected sex during fertile period (ovulatory method)
  - PEP?
  - PrEP?

# HIV - man / HIV + woman

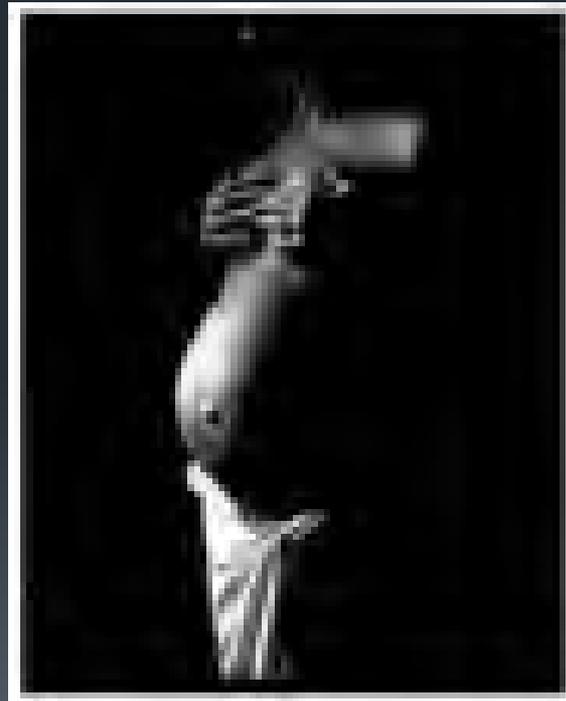
- Woman:
  - Safe ART regimen or PMTCT as soon as possible
  - No teratogenic drugs
  - Adherence support
  - Undetectable VL
- Man:
  - HIV testing
  - Circumcision
  - No need to be exposed
- Conception:
  - sperm collection
    - intra-uterine insemination
    - Self insemination at the time of ovulation
  - peri-ovulatory unprotected sexual intercourse

# Unsuccessful

- After attempting 6 ovulation cycles and the couple are unsuccessful in conceiving, consider reduced fertility and risk of continuing naturally may be more harmful than successful
- Counsel and if appropriate refer for further work-up
- Repeat HIV testing of exposed partner



# Successful



- Repeated HIV antibody testing for exposed partners
- If woman seroconverts during pregnancy, provide ART as soon as possible as seroconversion is associated with high rates of mother-to-child transmission



# Important to protect partner after conception

- Increased Risk of HIV-1 transmission in pregnancy:
- Prospective study among African serodiscordant couples
- HIV viral load in genital secretions during pregnancy is increased
- Increased risk of transmission of HIV from a pregnant woman to her sexual partner



We have to fix prevention!



2 new infections

For every person  
started on ART