

FERTILITY IN COUPLES WITH HIV

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Forum

African Women and HIV
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Outline

- Fertility in general
- Clinical scenarios
- Vertical transmission
- Future research

Desire for parenthood in couples with HIV

- Spontaneous desire in stable relationships
- Better quality of life and increasing life expectancy
- Decreased vertical transmission rate to $< 2\%$

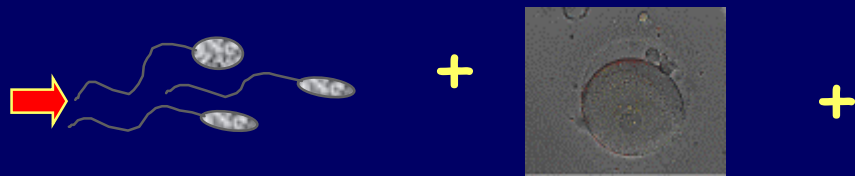


Planning vs happening

Fertility and what factors?

Infections!

Drugs



Normal Tube



Stress impacting on hormonal levels

Does HIV impact on any of this factors directly or indirectly?

Fertility is a definition which applies to couple!!!!

Estimated conception time

- 50% of fertile couples conceive in six months with at least two episodes of unprotected intercourse per week

- 90% of couples conceive in twelve months

Minimal number of episodes of sexual intercourse: 100 ...

... but in some couples each attempt at conception carries the risk of infection for the uninfected partner

Couples with HIV

- Man with HIV & uninfected woman
- Woman with HIV & uninfected man
- Both are with HIV
(different viral strain)
- Both are with HIV
(same viral strain)

FERTILITY IN COUPLES with HIV: what to expect

- At least 10% infertility as in general population
- Increased prevalence of infertility factors due to genital tract infections, tubal damage and male dyspermia.
- Standard diagnostic criteria for infertility do not always apply to these couples *
- *you are under the age of 35 and you and your partner have been trying to conceive for one year without success; or if you are over the age of 35 and have been unsuccessful after trying to conceive for six months, it is time to seek medical treatment for infertility.

Infertility factors in HIV-infected women when trying for a a baby (98)

• CHLAMYDIA	0
• MYCOPLASMA	9%
• UREAPLASMA	50%
• TUBAL DAMAGE	10%
• ANOVULATORY CYCLES	10%
• ENDOMETRIOSIS	5%

Semen Quality in HIV infected males

- HIV-induced immunodeficiency does not impair seminal quality until it reaches symptomatic stage of disease
- symptomatic immunodeficiency due to HIV infection can induce severe dyspermia in some males, but fertility can be maintained even with profound immune damage

Genital tract infections in HIV-infected males (n 865)

POSITIVE SEMEN BACTERIOLOGICAL CULTURE	10%
EVIDENCE OF PROSTATIC INFECTION BY Ultrasound	40%
CHLAMYDIA	3%
MYCOPLASMA	5%
UREAPLASMA	40%

Infertility factors in HIV discordant couples

<1.5mil/ml spermatozoa after washing	16.5%
Male genital tract infections	47%
Female genital tract infections	29%
Monolateral or bilateral tubal damage	12%
Abnormalities of the uterine cavity	7%
Endometriosis	1.5%
Hyperprolactinaemia	14%
Anovulatory cycles	10%

Request for reproductive counselling and care

- In couples where the man is infected we can expect the demand for ART to be to protect the uninfected woman and the offspring
- In couples where the woman is infected, irrespective from the infective status of the partner, the demand would be to overcome an infertility problem.

Desire for parenthood in couples with HIV

- Spontaneous desire in stable relationships
Change in their sexual behaviour
- Better quality of life and increasing life expectancy
- Decreased vertical transmission rate to < 2%
Available options

Use of condoms in HIV-discordant couples

(European Study Group of Heterosexual Transmission of HIV-NEJM,1994,331;341-346)

Use of condoms	N of couples	Rate (%)
Always	124	51
At least in 50%	61	25
Rarely or never	60	24
Total	245	100

The ideal approach to
reducing vertical
transmission is to
prevent HIV infection
among women

(MMWR Aug. 5, 1994: 43; RR-11)

Reproductive choices

Options for a seronegative woman with a partner infected with HIV

*Measure the
risk of infection*

NATURAL CONCEPTION IN HIV-NEGATIVE WOMEN WITH
HIV-INFECTED PARTNERS

L Mandelbrot
Lancet 1997

- ...104 consecutive pregnancies in 92 HIV-negative women with HIV-positive partners.
- Couples were advised to pinpoint ovulation in order to reduce possible exposure.
- Seroconversion was observed in two women at 7 months of pregnancy and in two others post partum.

PROGRAM OF ASSISTED CONCEPTION FOR HIV-DISCORDANT COUPLES

The central issue is whether it is possible to process HIV infected semen that allows conception without the risk of transmission to the woman

HIV-1 IN SEMEN

- HIV can be found in semen as cell-associated (proviral DNA) and cell-free virus (HIV RNA), respectively in seminal leukocytes and in seminal plasma
- Evidence for HIV-1 integration in spermatozoa is highly controversial
- Genital tract infections, stage of disease and the use of anti-retrovirals can influence the titres of HIV-1 in semen
- Titres are generally low (less than 550 infectious units/ml) but can be as high as 1.000.000 infectious units per ml
- The presence of HIV in semen is inconstant and titres can vary over time

*Measure the risk of
infection*

QUANTIFICATION OF HIV IN SEMEN: CORRELATION
WITH ANTIVIRAL TREATMENT AND IMMUNE STATUS
PL Vernazza
AIDS 1997

- "... the concentration of HIV in semen was inversely correlated with CD4 count and antiviral treatment ..."

*Measure the
risk of infection*

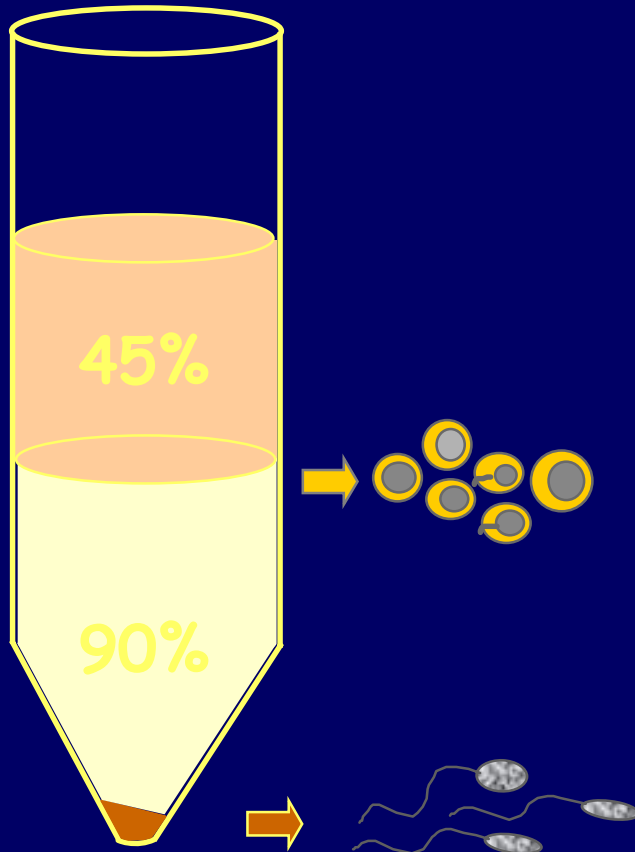
VIRAL BURDEN IN GENITAL SECRETIONS DETERMINES
MALE-TO-FEMALE TRANSMISSION OF HIV-1: A
PROBABILISTIC EMPIRIC MODEL

Chakraborty H
AIDS 2001

- Efficient transmission when burden is high:
- 100 000 copies HIV RNA/ml seminal plasma \approx 1 in 100 episodes
- Poor transmission when burden is low:
- 1000 copies HIV RNA/ml seminal plasma. \approx 1 in \cong 3000 episodes

ASSISTANCE: sperm washing HIV IN SEMEN

Percoll Gradient



HIV Infection

NSCs

yes

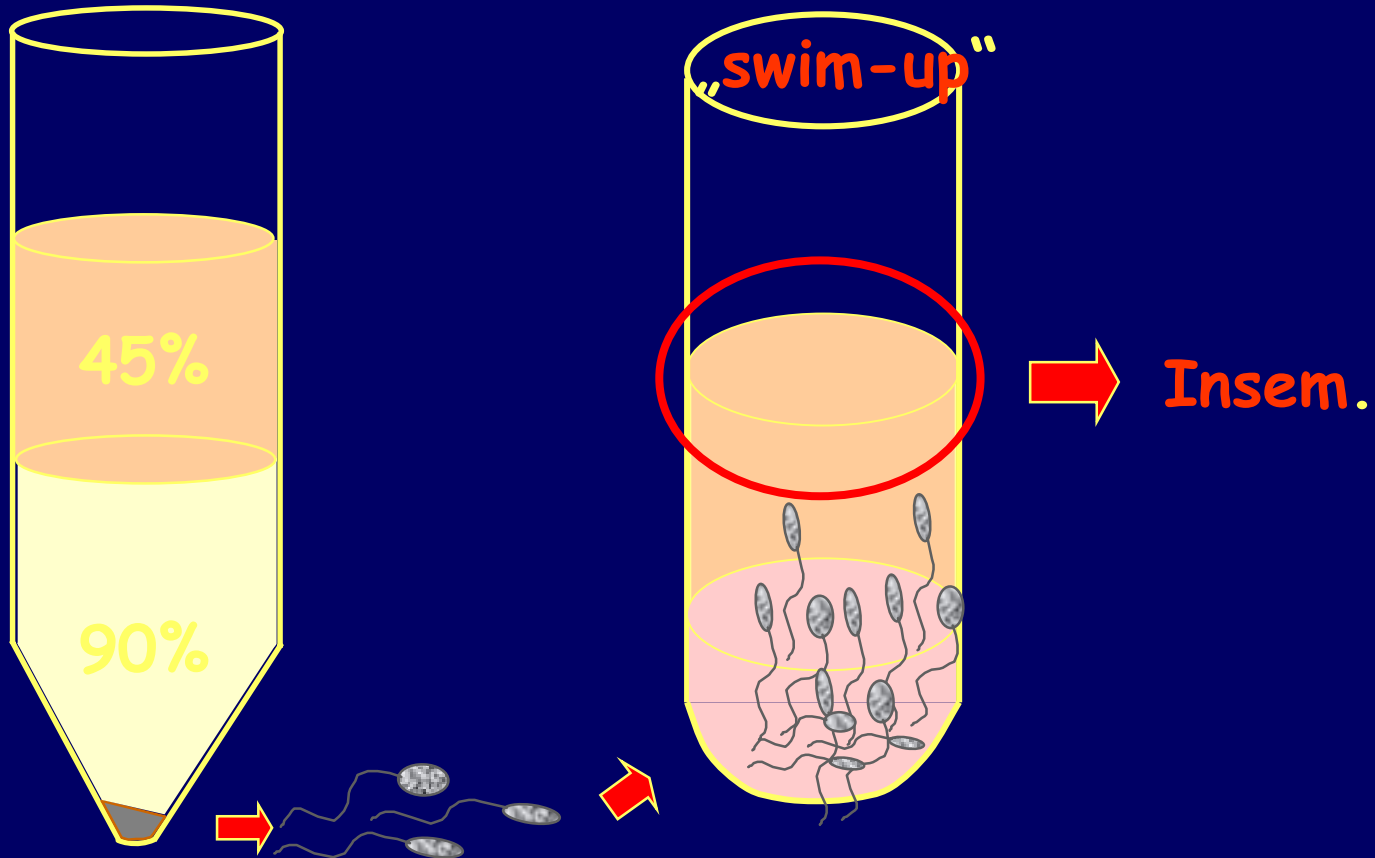
Motil spermatozoa

No

ASSISTANCE: sperm washing

SEMEN PREPARATION

Gradient



ASSISTANCE: sperm washing

All sperm samples are HIV RNA tested by nucleic acid sequence-based amplification (NSBA)

Insemination is performed only if the result is below the limit of detection (500 copies/ml)

By a combined technique of gradient centrifugation, washing and spontaneous sperm migration, this technique can reduce both the quantities of cells associated HIV, by removing seminal leukocytes, and of cell-free HIV

No existing method permits to definitively exclude the presence of HIV RNA in the final aliquot of spermatozoa to be used for the insemination.

A residual risk of HIV transfer to the HIV negative woman cannot still be excluded, but can be "under control".

REPRODUCTIVE COUNSELLING FOR HIV-DISCORDANT COUPLES

AE Semprini, S Fiore and G Pardi (Lancet 1997; 349: 1401-1402)

.. performed more than 1000 insemination attempts achieving 200 pregnancies, without a single case of female seroconversion or paediatric infection. Our results suggest that it is important to control for the main variable in sexual transmission: the presence of HIV in semen.

.... *We believe that every effort should be made to reduce the risk of sexual transmission of HIV in serodiscordant couples who want to have a child.*

Human immunodeficiency type 1-serodiscordant couples can bear healthy children after undergoing intrauterine insemination

S Marina, F Marina, R Alcolea, R Expòsito, Joan Huguet, Javer Nadal and A Verges. (Fertil Steril 70; 1,

July 1998)

Sixty three HIV-positive men provided 107 semen samples that underwent Percoll filtration and swim-up. The final fraction was tested for HIV RNA and DNA by PCR, before insemination of the seronegative partners

...HIV was detected in 6% of samples and insemination was cancelled.

Reproductive choices

Options for women infected with HIV and
their partners

Women should be helped to evaluate the medical aspects of having a child in relation to their chronic disease

The key point is to protect the fetus from vertical HIV infection.

PROTECTING PATIENTS FROM DISCRIMINATION THE AMERICANS WITH DISABILITIES ACT AND HIV INFECTION

GJ ANNAS FROM THE HEALTH LAW DEPARTMENT, BOSTON UNIVERISTY
SCHOOL OF PUBLIC HEALTH, BOSTON (NEJM 1998; 339: 17, 1255-59)

The Supreme Court concluded that an 8 percent risk of transmitting "a dread and fatal disease to one's child" is a substantial limitation on reproduction".

Of course, if vertical transmission were reduced to zero or nearly zero, HIV would then no longer substantially limit reproduction...

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Pre-conception counselling and reproductive assistance to HIV-infected women

- better care during pregnancy
- reduced risk of vertical transmission
- reduced risk of sexual transmission to the partner

Interventions to reduce vertical transmission of HIV-1

Approaches

Anti-retroviral therapy

Elective caesarean section

Avoidance of breastfeeding

It is now known that the risk of vertical transmission can be reduced to **less than 2%** with prophylactic monotherapy with Zidovudine, elective caesarean section delivery and no breastfeeding.

Crude MTCT rates

European Collaborative Study

No breastfeeding	16.1% (14.3-17.9)
No breastfeeding, elective CS	8.98% (6.40-12.2)
No breastfeeding, mono- or dual therapy	8.43% (5.74-11.8)
No breastfeeding, elective CS, mono or dual therapy	2.13% (0.98-4.00)
No breastfeeding, HAART	2.17% (0.71-5.00)
No breastfeeding, elective CS, HAART	1.12% (0.36-2.59)

PREGNANCY AND HIV

- No impact on progression of disease
- No pattern of congenital malformations
- No breast-feeding
- Open issues as viral load and mode of delivery
- Adverse gestational events (diabetes or HELLP) may due to ART use during gestation
- Rare surgical complications associated to caesarean section

Fertility care

- When the male is uninfected conception may be achieved through empirical artificial insemination, eliminating any risk of HIV transmission to the man.
- When the male is infected with a different strain : can we consider sperm washing to avoid dual infection??

Future research

No European policy on fertility care

No standardised procedures

Size of the problem in this selected population

Specific needs as interaction Fertility drugs and

ART

Any suggestion??

Thank you!!!!