Preconception counselling and perinatal management for women living with HIV

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Objectives

- Overview and Epidemiology
- Principles of Perinatal transmission of HIV
- Preventative measures
- Neonatal testing
- Case Study
- Preconception counselling
HIV Prevalence

2013

107,800 people living with HIV in the UK

60,000 acquired through heterosexual contact
Approx. 30,000 women 1.9:1000
(London 3.9:1000)

6,151 New diagnosis in 2013

2,186 heterosexually acquired
1,540 women

24% of people unaware of their infection
21% for women (Antenatal screening programme detection rate)

(Public Health England, 2015)
30 years of HIV

Pre-treatment
Uncertain future, poor prognosis
High rates of sexual abstinence / avoidance of pregnancy

Antiretroviral therapy
Improved health
Increased quality of life
Reduced mother to child transmission of HIV
Reduced Risk of Sexual Transmission

Increased Desire for Pregnancy
Greater Need for Preconception / Contraception / Sexual Health / Fertility Services
HIV in Pregnancy

2013

- 2.5 per 1,000 pregnancies were to HIV-positive women
- five in six diagnosed prior to pregnancy
- 98% women had some form of antiretroviral therapy in pregnancy
- High number of subsequent pregnancies
- C&W 25 - 30 pregnancies per year
Data Collection

National Study of HIV in Pregnancy and Childhood (NSHPC)

- Anonymised
- UK based observational surveillance
- Obstetric and paediatric HIV
- Coverage and case ascertainment (>95%)
- 20,223 pregnancies reported through RCOG since 1989

(P. Tookey, 2012)
National Study of HIV in Pregnancy and Childhood
MRC Centre of Epidemiology for Child Health
Perinatal Transmission Rates

HIV transmission rate in women with diagnosed HIV infection has fallen to 0.46% (2011)
(2000-2006 1.3%, 2007–2011 0.58%)

5-10 Perinatal transmissions per year in UK
MTCT rates in diagnosed women, UK & Ireland 2000-2011

~12,500 singleton births; significant decline in MTCT over time ($p<0.001$)

Perinatal Transmission of HIV
How and when Transmission Can Occur

In Utero (Transplacental) transmission
The Placenta allows for gases exchange and nutrient uptake from the mother and provides a selective maternal-fetal barrier against transmission of microbes (Bacterial, Viruses and rarely parasites). Insufficiency in this function may allow MTCT of infection.

Higher risk in cases with a high viral load >100,000 copies/ml as this is more likely to penetrate the maternal-fetal barrier.

Delivery
Following rupture of membranes babies are exposed to maternal blood and other secretions in the uterus and genital tract without the placental barrier.
Risk Determinants:
- Viral load - level of free virus in the mother's blood or vaginal secretions
- Presence of Genital infection at the time of delivery (Candida, Bacterial Vaginosis)
- Development of Chorio-amnionitis during labour

Breastfeeding
HIV can be found in the breast milk and transmitted to the neonate.
Risk Determinants:
- Viral load level of free virus in the breast milk
- Cracked nipples - Risk of ingestion of maternal blood
- Prematurity - Immature gut lining prone to inflammation
Perinatal Transmission Risk

Overall risk with no treatment up to 40%
Low in utero (Transplacental) transmission 1.5 - 2%
Delivery = highest risk
Breastfeeding 15%
Key Principle

Viral load drives Perinatal transmission of HIV

The higher the viral load, the higher the transmission risk
3 steps to PMTCT ...

2012 British HIV Association Pregnancy Guidelines
(Interim Review 2014)
1. Antiretroviral Therapy

Used in pregnancy since early 1990s

First Therapy - Zidovudine monotherapy
ACTG076 Trial (1994)

Given in pregnancy, at delivery and to the infant this reduced the risk of transmission by 2/3
Transmission Rates - 8% of women randomised to AZT
26% in placebo arm.

Connor EM et al., 1994
Combination Therapy (HAART)

1994 - Zidovudine monotherapy + caesarean section
Use gradually declined ~20% in 2002-3, <5% since 2006, ~2% in 2009/10

Late 90s - HAART Introduced recognised as mainstay to prevention rather than mode of delivery
vaginal deliveries supported for women with undetectable viral loads

Majority of women on HAART prior to conception
New starters are started earlier
Uptake of antiretroviral therapy and MTCT rate by year of birth for 3703 infants born to diagnosed women 1990-2004

Graph taken from CROI 2007 Poster: Mother-to-child transmission of HIV in the UK and Ireland: 1990-2004
When to start HAART for treatment naïve women?

Previous guidance 24 + weeks of pregnancy
To avoid early fetal exposure and possible teratogenicity

New Guidance - Start early! (BHIVA Pregnancy guidelines 2012)

- Teratogenicity risk is no higher than background risk 2-3%
- Longer use of HAART reduces risk of transmission

- Many women will conceive on HAART if already on it for their own health (CD4<350)
  If already on treatment they should remain so

- Treatment naïve women - aim for undetectable viral load by 24 weeks of pregnancy

Viral load
- <30,000 c/ml by 24 weeks
- >30,000 c/ml by 14 weeks
- >100,000 c/ml start immediately

ART & congenital abnormalities: Infants born in UK & Ireland 1990-2007

Risk factors for congenital abnormalities (unadjusted odds ratio & 95% CI)

- No difference in abnormality rates by class of ART exposure in 1st trimester
- Findings consistent with international APR, & other European studies

Year of delivery  
≥1999  2000-2007  None  2nd/3rd trimester  1st trimester  NRTI only  NNRTI  PI  NNRTI & PI

Type of ART exposure

Townsend et al. AIDS 2009; 25:519-524

National Study of HIV in NSHPC  
Pregnancy and Childhood
Mode of Delivery / Management in labour
Planning delivery in the **fully suppressed** mother

Vaginal delivery is recommended

*Mode of delivery does not affect the risk of transmission (If viral load <50 copies/ml)*

Caesarean section offers no measurable benefit in reducing risk, poses a higher risk of maternal morbidity (increased with no. of caesareans)

Manage as per obstetric guidelines in well patient
- Amniocentesis
- Amniotomy
- Vaginal Birth after caesarean
- Induction / Augmentation of labour,
- Forceps or Ventouse,
- FBS / FSE
- birthing unit and birthing pool
2. Infant Post Exposure Prophylaxis (PEP)

A liquid form of antiretroviral medication Zidovudine given orally BD for 28 days which further decreases the risk of infection.

Used since 1990s
No experience of side effects in infants
Sugary sweet taste which is well-tolerated
3. Avoidance of breastfeeding

Continued recommendation is that women should avoid breastfeeding

Breast milk may contain virus even if the blood is undetectable - compartmentalization effect

Risk of transmission from zero for those who do not breastfeed, to between 1-2% for those that do.

*Based on research from developing countries only

(BHIVA/CHIVA Position Statement, 2010)
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>(PP) Transmission Rate</th>
<th>Reference</th>
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<tbody>
<tr>
<td></td>
<td>15 months FU</td>
<td>Never BF 20%</td>
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<td></td>
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<td>Mixed feeding 35%</td>
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<tr>
<td>DREAM Mozambique</td>
<td>Observational study</td>
<td>Observed 2.8%</td>
<td>Marazzi et al, PIDJ, 2009; 28:483-7</td>
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<tr>
<td></td>
<td>HAART + 6/12 Excl BF</td>
<td>Expected 40%</td>
<td></td>
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<tr>
<td>Tanzania</td>
<td>Observational study</td>
<td>6/52 4.1%</td>
<td>Kilewo et al, JAIDS, 2009; 52: 406-16</td>
</tr>
<tr>
<td></td>
<td>HAART + 6/12 Excl BF</td>
<td>6/12 5.1%</td>
<td></td>
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<tr>
<td>Uganda</td>
<td>Observational study</td>
<td>No Transmissions</td>
<td>Homsy et al, JAIDS, 2010;53:28-35</td>
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<tr>
<td></td>
<td>HAART + 6/12 Excl BF</td>
<td>19% MR</td>
<td></td>
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<tr>
<td>Maternal Choice</td>
<td>Breast Fed</td>
<td>0.5%</td>
<td>Peltier et al, AIDS 2009,23:AIDS 2415-2413</td>
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<tr>
<td></td>
<td>Formula-Fed</td>
<td>0 %</td>
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<tr>
<td>Mma Bana Botswana</td>
<td>Trizivir</td>
<td>0.7%</td>
<td>Shapiro et al, NEJM, 2010;362:2282-2294</td>
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<tr>
<td>RCT</td>
<td>CBV/Kaletra</td>
<td>0 %</td>
<td></td>
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<tr>
<td></td>
<td>CBV/NVP</td>
<td>0 %</td>
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</tr>
<tr>
<td>BAN Malawi</td>
<td>CBV/NVP or Kaletra</td>
<td>3.0%</td>
<td>Chesale et al, NEJM, 2010;362:2271-2281</td>
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<tr>
<td></td>
<td>Infant NVP</td>
<td>1.8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nutritional supplements</td>
<td>6.4%</td>
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The Dilemma...

- Known benefits of breastmilk
- Bonding
- Family Pressures
- Societal pressures
- Risk of disclosure
- WHO policies

*Deemed safer than artificial feeding in resource-limited settings due to morbidity/mortality risks of formula feeding

HIV Therapy for Breastfeeding Mothers Can Virtually Eliminate Transmission to Babies

Poster presentation at the 21st International AIDS Conference (AIDS 2016) Durban, South Africa.

For HIV-infected mothers whose immune system is in good health, taking a three-drug antiretroviral regimen during breastfeeding essentially eliminates HIV transmission by breast milk to their infants, according to results from a large clinical trial conducted in sub-Saharan Africa and India.

References
J Currier et al. Randomized trial of stopping or continuing ART among post-partum women with Pre-ART CD4 >400 cells/mm3 (PROMISE 1077HS). Oral presentation at the 21st International AIDS Conference (AIDS 2016) Durban, South Africa.
Promise Study

• Started 2010
• Multicentre study SSA, India
• 2,500 Pairs
• 2 Arms
  o Mother treated throughout b/feeding period. Baby for 6 weeks
  o Mother stopped ARVs after one week Baby treated with daily Nevirapine throughout b/feeding period

Findings
Same transmission rates 0.3% at 6 months and 0.6% at 1 year

Summary
Both equally protective against HIV transmission
Longer duration of breastfeeding increased risk
Protective benefits of breastfeeding demonstrated in lower mortality rates
Considerations to neonatal ARV exposure, maternal adherence
Key Principles

1. **Viral suppression** - High viral replication drives transmission
   Antiretroviral therapy to reduce viral load to <40c/ml

2. **Neonatal Post Exposure Prophylaxis (PEP)** - Extra layer of protection
   Oral Zidovudine for 28 days

3. **Avoidance of breastfeeding** - HIV may remain in the breast milk even if undetectable
Neonatal Testing

• Viral load testing
  - At delivery - In-utero transmission
  - 6 weeks - Transmission at delivery
  - 12 weeks - Window period
  - 18 months antibody clearance
Does Antenatal screening offer an opportunity to disclose HIV status?

Barriers to disclosure

- Consider the wider picture
- Woman positive first
- “Bringing HIV into the family”
- Risk of Domestic Violence
- Fear of abandonment at a vulnerable time
- Financial Worries
- Further disclosure to other family members / communities
Planning a Pregnancy

"Keep my fingers crossed! Is that it?"
Case Study  - Louise

Routine Antenatal clinic for booking at 11/40 Mid 2011

History
26 yr old
White British
Para 1 - SVD 2005  Delivered at  Queen Charlottes Hospital
New Partner of 6 months  - Russell
Semi-planned pregnancy
No relevant medical history
Bloods sent for routine antenatal screening

Any thoughts…?
Several days later...

• Positive HIV antibody result - Virology suggest request a further sample to confirm

• Patient contacted and asked to come in and result given

• Serology repeated incl. Viral load / Lymphocyte / LFT / U&E’s....
Results are back;

- Viral Load - 568,793 copies/ml
- CD4 count - 354
- LFT’s & U&E’s Nad
- Asymptomatic of HIV

What does this tell you about her disease?
Further information reveals……..

Declined HIV testing in previous Pregnancy
Past infection pre- 2005?

Partner disclosed HIV status 1 month into relationship

Did not test, Continued UPSI

Likely to be a recent infection
History of sero-conversion illness at 7 weeks of pregnancy
Transmission risk >40%
Antenatal Management

• Counseled, discussed Top - declined
• Commenced HAART: Truvada, Atazanavir, Ritonavir + Raltegravir
• Viral Load Results
  
<table>
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<tr>
<th>Week</th>
<th>Viral Load</th>
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<tr>
<td>16</td>
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<tr>
<td>20</td>
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<td>32</td>
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<td>36</td>
<td>144</td>
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• Desperate for a SVD (Previous SVD)
• Mode of Delivery?
Outcome

- Sexual Health screen – Positive for Bacterial Vaginosis
- Decision for Elective LSCS - 39/40
- Artificial feeding
- 1st & 2nd 3rd PCR - Negative
- Mum remained on HAART for own health
HIV and Fertility

- Evidence of sub-fertility in HIV population
- Higher rate of pregnancy loss and lower pregnancy rate
- Assisted conception IUI/IVF lower success rates

Cause unknown
- The Virus itself?
- Higher risk of other STI’s which may cause Pelvic Inflammatory Disease
- Maternal age
- Large African cohort - poorer general health, lower detection of underlying gynaecological problems

Aims of preconception counselling for HIV positive patients

To provide couples with up-to-date and evidence based information enabling them to make informed choices about mode of conception depending on individual circumstances / preferences

To maximise the chance of achieving a pregnancy whilst supporting patients to conceive safely with minimal risk to negative partners - calculating fertile periods etc.

To optimise maternal health prior to pregnancy - Antiretroviral therapy for PMTCT, folic acid, Rubella/Hep B Immunisation. Lifestyle; diet, smoking, alcohol intake.

Early identification of sub-fertility and timely referral for investigation and fertility treatment where required
Serodiscordant Couples

Female HIV Positive - Self-insemination

• Introduces semen into the vagina without unprotected intercourse

• Similar success rate to normal conception approx. 10-15%

• Cycle diary / Ovulation kit

• Sexual health screening / folic acid / rubella status

• <35yrs, presumed normal fertility, 9-12 months - Refer for fertility screen

• >35yrs, Presumed normal fertility, 6 months - Refer for fertility screening

• Immediate referral if suspected subfertility / advanced maternal age
Serodiscordant Couples

Male HIV Positive - Sperm washing (IUI/IVF)

- Cost £2000-2500 per cycle
- 5% chance of detectable HIV after washing
- IUI 18% success rate per cycle *
- IVF 36% per cycle* (more expensive)
- Refer to fertility clinic for fertility screen
- Aim for undetectable viral load
- PCT Funding for fertility treatment’s vary. Strict criteria - <40, no children, normal BMI

(*Sauer, 2005)
HIV treatment as prevention of sexual transmission

Long debated whether HIV drugs used to treat HIV might have double benefit and cut transmission rates
Experts hypothesised - ARVs reduce viral levels so individuals are less infectious

The Swiss Statement
‘Effective ARV treatment could virtually stop heterosexual transmission’
(Swiss Federal Commission for HIV/AIDS 2008)

Sceptics contended this was unproven and denounced the consensus statement as ‘appalling, misleading and dangerous’

WHO responded with alarm and urged people to continue using condoms stating vaginal secretions/semen may still harbour HIV despite undetectable blood levels
HPTN052 Trial

Multi-centre RCT Conducted by HIV Prevention Trials Network
5 SSA Countries, Brazil, India, Thailand, USA

1763 Discordant couples
Not on ARVs
CD4 Count between 350 - 550 cells/mm³ (Immune damage but not AIDS)
Half randomly assigned to start ARVs immediately
Half delayed treatments until CD4 count <250

Results
96% risk reduction in treatment group
28 became infected (matched partner’s virus)
1 became infected from early treatment group
Early treatment group experienced 41% fewer serious health problems

Trial stopped early and delayed treatment group offered ARVs immediately

Conclusions
Nearly 100% efficacy
ARVs are not a vaccine and efforts to develop a vaccine should continue
Treatment costly and patients must take drugs for the rest of their lives
Has led to a re-examination of conception choices for stable HIV positive patients

(Cohen et al, 2011)
Timed Unprotected Sexual Intercourse

Negligible risk of sexual transmission - Not Zero

Advantages
• Higher chance of conception (75% of 46 couples in 1 year *)
• Pregnancy rates higher than IUI
• No financial implications - available to all

Considerations
• Both partners must agree
• Good adherence vital (proven viral suppression >6 months)
• Sexual health screens
• Fertility screen
• Sero-conversion in early pregnancy 40 - 60% risk of perinatal transmission

(Vernazza et al, 2007; *Vernazza, 2011)
NICE Guidance (2013)- Options for conceiving for couples where the man is HIV positive

Advise couples where the man is HIV positive that the risk of HIV transmission to the female partner is negligible through unprotected sexual intercourse when all of the following criteria are met:

• The man is compliant with highly active antiretroviral therapy (HAART)
• The man has had a plasma viral load of less than 50 copies/ml for more than 6 months
• There are no other infections present
• Unprotected intercourse is limited to the time of ovulation.

Advise couples that if all the criteria above are met, sperm washing may not further reduce the risk of infection and may reduce the likelihood of pregnancy.

For couples where the man is HIV positive and either he is not compliant with HAART or his plasma viral load is 50 copies/ml or greater, offer sperm washing.

Inform couples that sperm washing reduces, but does not eliminate, the risk of HIV transmission.

If couples who meet all the criteria above still perceive an unacceptable risk of HIV transmission after discussion with their HIV specialist, consider sperm washing.

Inform couples that **there is insufficient evidence to recommend** that HIV negative women use pre-exposure prophylaxis, when all the criteria above are met.

(2013) NICE guideline CG156
Summary

• Viral Load drives both sexual and Perinatal transmission of HIV

• HAART can reduce risk sexual transmission to negligible levels and mother to child transmission to <1%

• Women should be supported in their desire to plan for or limit pregnancies through effective family planning

• On-going support of sexual, social and emotional health is vital
Any Questions?
References

- Cohen M et al. Antiretroviral treatment to prevent the sexual transmission of HIV-1: results from the HPTN 052 multinational randomized controlled trial. Oral abstract MOAX0102. Webcast


- Prospective reports from the Antiretroviral Pregnancy Registry June 2007.

• Townsend et al AIDS 2008;22:973-81

• Warszawaski et al AIDS 2008;22:289-299