All HIV-exposed Infants Should Receive Triple Drug Antiretroviral Prophylaxis

Against the motion

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Acknowledgements:
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Timing of Mother-to-child Transmission of HIV

When can PEP prevent HIV?

In utero 10%

Peri-natal 15%

Post-natal 10%

Pregnancy

Breastfeeding

Labor and Delivery

UK → Birth PCR
6wk PCR
12wk PCR

To support optimal care we need timely & efficient EID
Infants most at risk of HIV Infection – need Triple PEP!

- Detectable maternal HIV at delivery
- Late presenters
- Less than 14 days of maternal ART
- Poor maternal adherence to treatment
- Premature delivery
- PROM with detectable HIV
- Maternal diagnosis at or after delivery
- Sero-conversion during pregnancy / lactation
First - get mother on to effective ART!

When to start ART in Pregnancy – BHIVA 2012

All should start ART by 24 weeks

VL > 100,000 c/ml → ASAP

VL > 30,000 c/ml → At 14 weeks

VL < 30,000 c/ml → By 24 weeks

French Cohort median duration of treatment

Transmitters 9.5 weeks

Non- transmitters 16 weeks (p < 0.001)

UK & Ireland(NSHPC) gestation started treatment

Transmitters 30.1 weeks

Non- transmitters 25.9 weeks (p < 0.001)
Second - start Infant PEP ASAP

Cohort Study New York State
Monotherapy ZDV

Timing of ZDV dosing
Transmission Rate

\[ n = 939 \]

- ante-partum + intra-partum + post-partum: 6.1%
- intra-partum + post-partum: 10.0%
- post-partum (within 48hrs): 9.3%
- post-partum (72hrs or after): 18.4%
- No ZDV: 26.6%


What ever PEP you can give – give it as soon as you can!
**Third - pre-load the foetus in Utero!**

**Maternal PRE- PEP**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine</td>
<td>0.80</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>0.90 (2hrs min)</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>1.00</td>
</tr>
<tr>
<td>Kaletra</td>
<td>0.20 (+/- 0.13)</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>0.6-0.99</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>1.2 (0.09-2.25)</td>
</tr>
<tr>
<td>Maraviroc</td>
<td>0.3</td>
</tr>
<tr>
<td>Enfurvitide (T20)</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Cord Blood : Maternal Plasma ratio

[http://www.pannastudy.com/]
Maternal PRE-PEP – neonatal half-life?

ART transplacental transfer and T1/2 in neonate:

SD Nevirapine → 7 days
DD Tenofovir → 24-48 hours
Raltegravir → 24-48 hours (longer in prems)
Other NRTI’s → < 24 hours
PI’s → very poor transplacental Tx

*ART which crosses the placenta “preloads” the infant for delivery & the 1st week of life*

*Reduces the need for oral infant PEP*

*Very important for the neonate who cannot feed*
Efficacy of Triple PEP in neonates? RCT - High Risk Women

Neonatal PEP with 2- or 3-ART is superior to ZDV mono in infants born to women who had NO ARV before delivery (Brazil, SA, Argentina, USA) 

BHIVA - Infant PEP – tailored to HIV risk

Low Risk PEP – monotherapy (Zidovudine)
maternal VL <50 HIV at 36 weeks

High Risk PEP – triple therapy (ZDV + 3TC + NVP)
Infants <72 hours old, maternal VL > 50
All circumstances where VL at 36 weeks / delivery is not <50

Neonatal PEP start < 4 hours after birth
Neonatal PEP continue for 4 weeks

PCP prophylaxis - co-trimoxazole, from 4 weeks only if:
- HIV infected or,
- mother’s VL at 36 weeks / delivery >1000 or unknown
HIV MTCT in antenatally diagnosed women, UK & Ireland 2000-2011

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

Efficacy of triple PEP in neonates?
UK cohort – Triple PEP only for High Risk

Use of neonatal PEP UK & Ireland, 2001-2008 (n = 8205)
99% infants received PEP (86% single; 3% dual; 11% triple)

Use of triple increased over time
2001-2004 2005-2008
Untreated women 43% (41/95) 71% (45/63)
Women viraemic despite ART 13% (114/883) 32% (344/1088)

Factors associated with receipt of Triple PEP (MVA)→
later time period, shorter duration / no ART, maternal VL > 50, low CD4, preterm delivery, unplanned delivery (emergency C/S or vaginal)
**Low rates of mother-to-child transmission of HIV: UK & Ireland 2000-2006**

Townsend *et al.* AIDS 2008; 22:973-81

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of transmissions</th>
<th>MTCT rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>61/5151</td>
<td>1.2% (CI 0.9-1.5%)</td>
</tr>
<tr>
<td>2000-2002</td>
<td>23/1456</td>
<td>1.6%</td>
</tr>
<tr>
<td>2003-2006</td>
<td>38/3695</td>
<td>1.0%</td>
</tr>
<tr>
<td>At least 14 days HAART</td>
<td>40/4864</td>
<td>0.8%</td>
</tr>
<tr>
<td>ZDV monotherapy + PLCS</td>
<td>0/464</td>
<td>0.0%</td>
</tr>
<tr>
<td>HAART + PLCS</td>
<td>16/2286</td>
<td>0.7%</td>
</tr>
<tr>
<td>HAART + SVD</td>
<td>4/559</td>
<td>0.7%</td>
</tr>
<tr>
<td><strong>VL&lt;50 copies/ml</strong></td>
<td><strong>3/2117</strong> (<em>2 with evidence of in utero transmission)</em>*</td>
<td><strong>0.1%</strong></td>
</tr>
</tbody>
</table>

ZDV: zidovudine  
PLCS: planned lower caesarean section  
SVD: spontaneous vaginal delivery  
VL: HIV viral load

National Study of HIV in Pregnancy and Childhood
no maternal viraemia in pregnancy

The “Swiss Statement” for neonates?

Mother fully suppressed on ART
ART with good transplacental transmission to infant
ART with good duration of plasma levels in the infant

→ Do we need to give these infants any PEP at all?
NO PEP for the low risk infant?

Mother with VL $< 50$ pre-conception

Mother with VL $< 50$ from 28 weeks

Mother with VL $< 50$ from 36 weeks

SHOW of HANDS
Can we shorten the duration of infant PEP?

**Historic ZDV Monotherapy - Randomised Controlled trials**

<table>
<thead>
<tr>
<th>weeks of gestation</th>
<th>Delivery</th>
<th>Rx</th>
<th>PL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACTG 076</td>
<td>14-34</td>
<td>6w</td>
<td>8%</td>
</tr>
<tr>
<td>SC Thai</td>
<td>36</td>
<td></td>
<td>9%</td>
</tr>
</tbody>
</table>

When ZDV started at 28 weeks – 3 days or 6 weeks PEP same Tx rate

<table>
<thead>
<tr>
<th>Thai PHPT</th>
<th></th>
<th>Rx</th>
<th>CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>LL</td>
<td>28</td>
<td>6w</td>
<td>6.5%</td>
</tr>
<tr>
<td>LS</td>
<td>28</td>
<td>3days</td>
<td>4.7%</td>
</tr>
<tr>
<td>SS</td>
<td>35</td>
<td>3days</td>
<td>10.5%</td>
</tr>
<tr>
<td>SL</td>
<td>35</td>
<td>6w</td>
<td>8.6%</td>
</tr>
</tbody>
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**NEJM 2000 Oct 5;343(14):982-91**
Bearing in mind PHPT – 3 days v 6 weeks

Mother with VL < 50 pre-conception
→ 1 week mono PEP

Mother with VL < 50 from 36 weeks
→ 4 weeks mono PEP

Mother with VL > 50 at 36 weeks
→ 4 weeks triple PEP

Could there ever be a randomised controlled trial?
Target Prevention for HIV Transmission – Save triple PEP for high risk infants

<table>
<thead>
<tr>
<th>Scenarios</th>
<th>Post Exposure Prophylaxis - Non Breast feeding infant</th>
<th>Post Exposure Prophylaxis - Breast Feeding infant – mother on ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>No maternal Rx – very high risk</td>
<td>Triple 4 weeks</td>
<td>Triple how long?</td>
</tr>
<tr>
<td>VL &gt; 50 (VL at 36 wks) – higher risk</td>
<td>Triple 4 weeks</td>
<td>Triple how long?</td>
</tr>
<tr>
<td>VL &lt; 50 (VL at 36 wks) – low risk</td>
<td>Mono 4 weeks</td>
<td>Mono 4-6 weeks</td>
</tr>
<tr>
<td>VL &lt; 50 since conception – lowest risk</td>
<td>None ???</td>
<td>None ???</td>
</tr>
</tbody>
</table>

Reduce toxicity - Reduce drug errors - Reduce cost - Do not give unnecessary Triple PEP to low risk infants