Emerging Issues in HIV and Pregnancy

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Perinatal Transmission in the ART Era – What’s New?

- Antepartum ARV drug choice
- Timing of ART initiation in pregnancy
- Use of intrapartum intravenous zidovudine
- Acute HIV in pregnancy
- Pregnancy in perinatally-infected women
- Controversies on breastfeeding in the United States
ART in Pregnancy and Perinatal Transmission

- Life-long ART is recommended for all individuals with HIV infection regardless of CD4 cell count, including pregnant women.

- 3 components to perinatal prevention:
  - Lowering maternal viral load with ART:
    - However ARV drugs reduce transmission even with low viral load and even when antenatal drugs not given
  - Pre-exposure prophylaxis of infant (through transplacental drug passage mother to infant)
  - Post-exposure prophylaxis of infant (through continued ARV after birth)
Importance of the Infant Pre- and Post-Exposure Prophylaxis Component of PACTG 076 Regimen


Data on 939 HIV-exposed infants born 1995-1997 in New York State

Even When No Maternal AP AZT Given, Infant AZT Started Within 24 Hours Reduces Transmission
ARV Drug Choice in Pregnancy

- In general, ART guidelines during pregnancy are similar to non-pregnant with some modifications, primarily based on limited experience (PK/dosing and fetal safety) with new drugs during pregnancy.
- Goal of ART in pregnancy is full viral suppression, as in non-pregnant individuals.
- Risk/benefit for drug choice differs for ART-naive women first starting drugs during pregnancy compared to ART-experienced women who may require drugs with less data for their own health due to resistance, or other factors.
- Thus, considerations for ARV drug choices differ for naive vs experienced women.
ARV Drug Choice in Pregnancy

- Pharmacokinetics (PK) of NRTI and NNRTI similar in pregnant and non-pregnant women.

- PI PK are more variable, particularly in late pregnancy. With standard dosing, ATV/r, DRV/r, and LPV/r levels reduced in 2\textsuperscript{nd}-3\textsuperscript{rd} trimester.
  - Need for dose adjustment depends on specific PI, ART experience, concomitant meds, side effects.
  - Careful viral load monitoring recommended.
  - Once daily DRV/r or LPV/r not recommended in pregnancy.

- Limited data suggest RAL levels in 3\textsuperscript{rd} trimester very variable, but dose modification not needed.

- No data on newer drugs (ETV, DTG, EVG, COBI) yet.
ARV Drug Choice in Pregnancy

- Most older ARV drugs appear safe in pregnancy and for fetus, but dearth of data on newer drugs which form preferred regimens in non-pregnant persons.

- Antiretroviral Pregnancy Registry has not indicated increase birth defects for current NRTIs, PIs and most NNRTIs, but data insufficient for newer drugs such as etravirine, entry/integrase inhibitors.

- There has been controversy regarding use of EFV and TDF in pregnancy.
Efavirenz

- Initial concern from non-human primate studies and retrospective human case reports regarding potential rare CNS birth defects (neural tube defects) with 1st trimester EFV exposure.

- Led to black box warning about use of EFV in 1st trimester of pregnancy.

- Recent meta-analysis of 2,026 live-births with first trimester exposure to EFV found no evidence of increased risk overall birth defects or CNS defects; incidence neural tube defects was 0.05%, similar to general population.
Relative risk of birth defects with EFV vs non-EFV regimens in 1st trimester
Efavirenz

- Data sufficient to rule-out ≥3-fold risk of rare neural tube defects (NTD) with 1st trimester exposure (e.g., can rule out NTD incidence of >0.2% with 1st trimester exposure).

- Neural tube defect risk restricted to the first 5-6 weeks of pregnancy (before most pregnancies are recognized).

- Change in ARVs during pregnancy may be associated with lack of viral suppression and increased risk of perinatal transmission (Florida et al. HIV Clin Trials 2010;11:303-11).

- EFV now a preferred NNRTI in pregnancy; guidelines recommend that if initiating EFV in ARV-naïve women to start after 8 weeks gestation.

- Women on EFV-ART presenting for care in 1st trimester should have it continued, provided there is viral suppression.
Tenofovir Disoproxil Fumarate (TDF)

- Studies of high dose TDF (2-fold higher than human dosing) in non-human primates showed maternal toxicity with decreased fetal growth and reduction fetal bone porosity.

- Human studies demonstrate no effect on intrauterine growth but conflicting data on growth at 6-12 months.

- One study suggested decreased neonatal bone mineral density with 1\textsuperscript{st} trimester TDF exposure, but duration and clinical significance of finding requires further evaluation.

- Given potency of TDF, activity against HBV, less toxicity than AZT, and ability for once daily dosing, benefits of TDF outweigh risk for use in ART-naïve women, and is a preferred NtRTI in guidelines.
PROMISE 1084s: Impact of Maternal TDF on Infant Bone Mineral Content (BMC)
Siberry GK et al. CROI 2016 Boston Abs 36

- PROMISE: African PMTCT trial comparing AZT/sdNVP+tail to TDF/FTC/LPV/r vs AZT/3TC/LPV/r in women with CD4 >350.
- Neonatal DXA substudy in infants from all arms.

No significant difference in newborn mean LS BMC between study arms

Mean WB-BMC lower in triple than AZT arm but not between AZT triple vs TDF triple
Antenatal ARV Regimens Recommended for **ARV-Naïve** HIV-Infected Pregnant Women

Combination regimen – Dual NRTI *plus* PI or NNRTI or Integrase inhibitor

<table>
<thead>
<tr>
<th>ARVs in Pregnancy Recommendation</th>
<th>NRTI/NtRTI*</th>
<th>PI</th>
<th>NNRTI</th>
<th>Entry/Integrase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred</td>
<td>TDF/3TC or FTC, ABC/3TC, AZT/3TC</td>
<td>ATV/r, DRV/r</td>
<td>EFV after 8 weeks gestation</td>
<td>RAL</td>
</tr>
<tr>
<td>Alternative</td>
<td>TAF</td>
<td>LPV/r</td>
<td>RPV</td>
<td></td>
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<tr>
<td>Insufficient Data</td>
<td>TAF</td>
<td>F-APV</td>
<td>DTG, EVG/COBI, MVC</td>
<td></td>
</tr>
<tr>
<td>Not Recommended</td>
<td>ddI, d4T</td>
<td>IDV, NFV, SQV</td>
<td>NVP, ETV, TPV</td>
<td>T20</td>
</tr>
</tbody>
</table>

*Recommend at least 1 NRTI with good placental transfer
Timing of ART Initiation in Pregnancy
Transmission Rates by HIV RNA Levels in HAART Era

4,738 HIV+ Pregnant Women on ART In UK/Ireland 2007-2011

Townsend CL et al. AIDS 2014;28:1049-57
For Maximal Efficacy: Early ART Initiation Needed
4,327 HIV+ Women Starting ART in Pregnancy, UK/Ireland 2000-2011

Townsend CL et al. AIDS 2014;28:1049-57

Duration Antenatal ART, Baseline RNA at ART Start, and MTCT

MTCT declined rapidly initially as duration of ART increased but varied by baseline viral load at time ART started
Early Sustained Viral Control Needed for Lowest MTCT: Risk Factors for MTCT in Women With Delivery RNA <500

*Tubiana R et al. CID 2010;50:585-96*

- ANRS Perinatal Cohort case/control study - mothers all with delivery RNA <500: Case: transmitted HIV (N=19) vs Control: non-transmitter (N=60) matched on maternity unit and birth date.
- Earlier viral suppression (RNA <500 at 30+-4 wks) only significant factor in multivariate analysis (P<0.001).

![Graph showing HIV RNA level (log10 copies/mL) vs weeks of gestational age for cases (transmitted) and controls (no transmission).](image)

- 16% on ART before conception for cases (transmitted)
- 47% on ART before conception for controls (no transmission)
Enhanced Efficacy with Early ART, Especially Preconception, with Viral Suppression


- French Perinatal Cohort: Overall MTCT 0.7% and was 0% (95% CI 0-0.1%) in 2,651 women starting ART before conception and RNA <50 at delivery.

**Delivery RNA and MTCT According to Time ART**

*threshold if assay LLD >50 c/mL
Pre-Conception ART and Prematurity
Nachega J et al Meta-Analysis for WHO 2015 Guidelines


<table>
<thead>
<tr>
<th>Study</th>
<th>Pre-conception ART Events</th>
<th>Post-conception ART Events</th>
<th>Risk Ratio</th>
<th>95% CI W(random)</th>
</tr>
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<tbody>
<tr>
<td>Thorne 2000</td>
<td>24</td>
<td>114</td>
<td>1.13</td>
<td>[0.77; 1.66]</td>
</tr>
<tr>
<td>Kowalska 2003</td>
<td>3</td>
<td>9</td>
<td>2.62</td>
<td>[0.89; 7.73]</td>
</tr>
<tr>
<td>Boer 2006</td>
<td>8</td>
<td>15</td>
<td>2.29</td>
<td>[1.08; 4.85]</td>
</tr>
<tr>
<td>Martin 2007</td>
<td>7</td>
<td>23</td>
<td>0.56</td>
<td>[0.25; 1.25]</td>
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<tr>
<td>Areechokchai 2009</td>
<td>8</td>
<td>19</td>
<td>2.17</td>
<td>[1.02; 4.61]</td>
</tr>
<tr>
<td>Machado 2009</td>
<td>21</td>
<td>38</td>
<td>1.77</td>
<td>[1.08; 2.89]</td>
</tr>
<tr>
<td>Chen 2012</td>
<td>543</td>
<td>710</td>
<td>1.74</td>
<td>[1.57; 1.92]</td>
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<tr>
<td>Sibidue 2012</td>
<td>619</td>
<td>830</td>
<td>1.42</td>
<td>[1.29; 1.56]</td>
</tr>
<tr>
<td>Aniji 2013</td>
<td>16</td>
<td>41</td>
<td>0.87</td>
<td>[0.52; 1.45]</td>
</tr>
<tr>
<td>Dale 2013</td>
<td>4</td>
<td>1</td>
<td>4.96</td>
<td>[0.57; 43.51]</td>
</tr>
<tr>
<td>Darak 2013</td>
<td>45</td>
<td>40</td>
<td>1.90</td>
<td>[1.29; 2.79]</td>
</tr>
<tr>
<td>Li 2015</td>
<td>222</td>
<td>132</td>
<td>1.48</td>
<td>[1.24; 1.77]</td>
</tr>
</tbody>
</table>

Random effects model: 7244 | 14626
Risk Ratio: 1.50 [1.30; 1.74] 100%

Heterogeneity: I-squared=35.8%, tau-squared=0.0335, p=0.004
Timing of ART Initiation

- Early and sustained control of viral replication is critical for maximal reduction transmission.
- HIV+ women considering pregnancy should ideally be on fully suppressive ART prior to pregnancy.
- For pregnant women not already on ART, data favor initiating ART sufficiently early – including 1st trimester – to suppress replication by 3rd trimester.
- Initiation in 1st trimester particularly important in women with high baseline viral load.
- There are some potential risks with very early/pre-conception ART in terms of possible preterm delivery, but in high resource setting like US, benefits in lower transmission likely outweigh risk.
Intrapartum AZT
Intrapartum (IP) ART Management

- The availability of safe and suppressive ART regimens for pregnant women have changed IP management.

- PACTG 076 evaluated a 3-part preventive regimen targeting different times of transmission:
  - Antepartum AZT: target in utero transmission
  - Intrapartum intravenous AZT: target IP transmission
  - Infant AZT: post-exposure prophylaxis IP exposure

- AZT given intravenously IP because achieves rapid and sustained AZT drug levels in infant.

- Combination ART now recommended for all HIV+ pregnant women, continued during labor and delivery.

- Is there an additional benefit of IV AZT with ART?
Changing Risk Factors for Perinatal Transmission in ART Era


- 707 HIV+ women on ART delivering U. Miami 1996-2008
- When control for viral load and ART, traditional “risk factors” drop out.
- No longer associated with risk of transmission in women on ART:
  - Not receiving intrapartum AZT
  - Duration membrane rupture
  - Premature delivery
  - Low birth weight

Logistic regression model to identify predictors of perinatal transmission

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>P-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No intrapartum AZT</td>
<td>4.02</td>
<td>.201</td>
<td>0.48-33.78</td>
</tr>
<tr>
<td>Lowest CD4 count in pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;200</td>
<td>0.02</td>
<td>1.000</td>
<td>0.000</td>
</tr>
<tr>
<td>200-499</td>
<td>0.25</td>
<td>.333</td>
<td>0.05-2.14</td>
</tr>
<tr>
<td>≥500</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delivery viral load</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1000</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000-9999</td>
<td>11.94</td>
<td>.059</td>
<td>0.91-156.61</td>
</tr>
<tr>
<td>10,000-99,999</td>
<td>164.42</td>
<td>&lt;.001</td>
<td>10.96-2455.69</td>
</tr>
<tr>
<td>≤10 wks on ARV</td>
<td>1.34</td>
<td>.757</td>
<td>0.21-8.65</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>0.01</td>
<td>.999</td>
<td>0.000</td>
</tr>
<tr>
<td>Duration of membrane rupture, h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-8.9</td>
<td>2.57</td>
<td>.435</td>
<td>0.24-27.60</td>
</tr>
<tr>
<td>9-12.9</td>
<td>0.00</td>
<td>.997</td>
<td>0.000</td>
</tr>
<tr>
<td>≥13.0</td>
<td>7.20</td>
<td>.067</td>
<td>0.87-59.32</td>
</tr>
<tr>
<td>CS in labor</td>
<td>0.31</td>
<td>.275</td>
<td>0.04-2.56</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>0.57</td>
<td>.589</td>
<td>0.07-4.43</td>
</tr>
<tr>
<td>Low birthweight</td>
<td>1.86</td>
<td>.595</td>
<td>0.19-18.45</td>
</tr>
<tr>
<td>ARV in pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AZT only</td>
<td>0.57</td>
<td>.673</td>
<td>0.04-7.70</td>
</tr>
<tr>
<td>No treatment</td>
<td>24.02</td>
<td>.036</td>
<td>1.23-468.72</td>
</tr>
</tbody>
</table>

ARV, antiretroviral; AZT, zidovudine; CS, cesarean section; OR, odds ratio.
Is Intrapartum AZT Still Required in the Combination ARV Era?


- 11,538 HIV+ women who delivered between 1997-2010;
  - 10,984 received IV AZT; 554 did not receive IV AZT

IV AZT did not affect efficacy if HIV RNA <1000 c/mL
Intrapartum Recommendations for HIV-Infected Pregnant Women

- Continue combination AP ARV regimen during labor and delivery.

- If on ART and HIV RNA <1,000 c/mL consistently in late pregnancy/near delivery and no adherence concerns, addition of IV AZT is not required.

- If HIV RNA >1,000 c/mL near delivery or unknown, IV AZT recommended in addition to ART regimen along with elective cesarean delivery.
Acute HIV in Pregnancy
Acute Infection in Pregnancy and Breastfeeding

- Conflicting data on whether pregnancy increases HIV acquisition – studies in Africa, rates are high (possibly due to endemic state of HIV in these countries).
- Acute infection represents a significant proportion of residual perinatal transmission in the United States.
- High rates of perinatal transmission with acute infection, likely related to the combination of:
  - high viral load associated with acute infection, and
  - diagnosis is easy to miss, resulting in lost opportunities for prevention.
- Repeat HIV testing in 3rd trimester should be considered for all pregnant women, and recommended for high risk (including facilities with prevalence >0.1%).
## Incidence of HIV during Pregnancy/Postpartum: Meta-analysis 19 Studies (All in Africa)


### Incidence per 100 person-years (95% CI)

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>PY</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kieffer [56]</td>
<td>2011</td>
<td>Swaziland</td>
<td>346</td>
<td>16.8 (12.7, 21.7)</td>
</tr>
<tr>
<td>Taha [45]</td>
<td>1998</td>
<td>Malawi</td>
<td>338</td>
<td>8.0 (5.0, 11.0)</td>
</tr>
<tr>
<td>Mugo [38]</td>
<td>2011</td>
<td>Africa (multiple)</td>
<td>231</td>
<td>7.4 (4.3, 11.8)</td>
</tr>
<tr>
<td>Kinuthia [64]</td>
<td>2010</td>
<td>Kenya</td>
<td>779</td>
<td>6.8 (5.1, 8.8)</td>
</tr>
<tr>
<td>De Schacht [61]</td>
<td>2011</td>
<td>Mozambique</td>
<td>226</td>
<td>6.2 (3.4, 10.1)</td>
</tr>
<tr>
<td>Munjoma [58]</td>
<td>2010</td>
<td>Zimbabwe</td>
<td>298</td>
<td>5.7 (3.3, 8.1)</td>
</tr>
<tr>
<td>Mbizvo [57]</td>
<td>2001</td>
<td>Zimbabwe</td>
<td>370</td>
<td>4.3 (2.5, 7.0)</td>
</tr>
<tr>
<td>Keating [43]</td>
<td>2012</td>
<td>Malawi</td>
<td>275</td>
<td>4.0 (2.2, 7.2)</td>
</tr>
<tr>
<td>Wawer [66]</td>
<td>1999</td>
<td>Uganda</td>
<td>534</td>
<td>3.2 (1.9, 5.1)</td>
</tr>
<tr>
<td>Gray [6]</td>
<td>2005</td>
<td>Uganda</td>
<td>997</td>
<td>2.3 (1.5, 3.5)</td>
</tr>
<tr>
<td>Braunstein [63]</td>
<td>2011</td>
<td>Rwanda</td>
<td>250</td>
<td>2.0 (1.3, 3.8)</td>
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<tr>
<td>Imade [68]</td>
<td>2012</td>
<td>Nigeria</td>
<td>235</td>
<td>1.7 (1.0, 4.4)</td>
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<tr>
<td>Morrison [42]</td>
<td>2007</td>
<td>Zimbabwe</td>
<td>793</td>
<td>1.6 (0.9, 2.8)</td>
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<tr>
<td>Tabu [4]</td>
<td>2013</td>
<td>Uganda</td>
<td>312</td>
<td>1.6 (0.8, 2.4)</td>
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<tr>
<td>Traore [69]</td>
<td>2012</td>
<td>Burkina Faso</td>
<td>125</td>
<td>4.7 (3.3, 6.1)</td>
</tr>
</tbody>
</table>

*Subtotal (I²-squared = 90.4%, p < 0.001)*

### Postpartum

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>PY</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leroy [65]</td>
<td>1994</td>
<td>Rwanda</td>
<td>204</td>
<td>5.9 (3.0, 10.3)</td>
</tr>
<tr>
<td>Mbizvo [57]</td>
<td>2001</td>
<td>Zimbabwe</td>
<td>723</td>
<td>4.7 (3.2, 6.5)</td>
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<tr>
<td>Humphrey [46]</td>
<td>2006</td>
<td>Zimbabwe</td>
<td>7753</td>
<td>3.5 (3.1, 3.9)</td>
</tr>
<tr>
<td>Braunstein [63]</td>
<td>2011</td>
<td>Rwanda</td>
<td>375</td>
<td>3.2 (1.4, 5.1)</td>
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<tr>
<td>Morrison [42]</td>
<td>2007</td>
<td>Zimbabwe</td>
<td>1211</td>
<td>2.7 (1.9, 3.8)</td>
</tr>
<tr>
<td>Wawer [66]</td>
<td>1999</td>
<td>Uganda</td>
<td>746</td>
<td>1.5 (0.8, 2.8)</td>
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<tr>
<td>Gray [6]</td>
<td>2005</td>
<td>Uganda</td>
<td>3043</td>
<td>2.9 (1.8, 4.0)</td>
</tr>
</tbody>
</table>

*Subtotal (I²-squared = 90.8%, p < 0.001)*

### Pregnancy and Postpartum

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>PY</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moodley [5]</td>
<td>2011</td>
<td>South Africa</td>
<td>1946</td>
<td>2.5 (1.8, 3.2)</td>
</tr>
</tbody>
</table>

*Subtotal*  

### Overall

<table>
<thead>
<tr>
<th>Incidence</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>3.8 (2.0, 4.6)</td>
</tr>
<tr>
<td>Postpartum</td>
<td>2.9 (1.8, 4.0)</td>
</tr>
<tr>
<td>Pregnancy and Postpartum</td>
<td>2.5 (1.8, 3.2)</td>
</tr>
<tr>
<td>Overall</td>
<td>3.8 (2.0, 4.6)</td>
</tr>
</tbody>
</table>
5 studies compared risk perinatal transmission among women with incident versus chronic HIV infection.

9-15-fold ↑ in US women with acute infection as ART lowers transmission with chronic infection.

**Perinatal Transmission in Mothers with Incident vs Chronic HIV during Pregnancy/Postpartum: Meta-analysis**

*Drake AL et al. PLoSMed 2014;11:e1001608*

- **Author**
  - Singh [18] 2012 US 10308
  - Humphrey* [21] 2010 Zimbabwe 3204

- **Odds Ratio (95% CI)**
  - Birkhead*: 15.1 (6.9, 33.1)
  - Singh: 9.1 (4.9, 16.0)
  - Humphrey*: 2.9 (2.2, 3.9)
  - Moodley: 2.3 (1.2, 4.4)
  - Roongpisuthipong: 0.5 (0.1, 2.2)

- **Overall (I-squared = 82.2%, p < 0.001)** 2.8 (0.9, 4.7)
Data from 15 areas conducting Enhanced Perinatal Surveillance between 2005-2010 were examined.

Included 10,308 HIV+ pregnant women who delivered live infants during that period:
- 1.2% (124) were identified as seroconverting during pregnancy.

Perinatal transmission rate was 8-fold higher among women who seroconverted during pregnancy:
- Acute infection (seroconverted during pregnancy): transmission 12.9%
- Chronic infection (infected prior to pregnancy): transmission 1.6% ($p<0.0001$).
### Acute HIV in Pregnancy – New York State


- New York State: 3,396 HIV-exposed infants born 2002-6
- MTCT 65 infants born to 63 mothers (2.1%)
- Acquisition of HIV during pregnancy significant risk factor: 22% infected with acute infection vs 1.8% with chronic

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute HIV in pregnancy</td>
<td>15.19 (4.0-56.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Late/no prenatal care</td>
<td>2.37 (1.1-4.9)</td>
<td>0.023</td>
</tr>
<tr>
<td>Maternal HIV diagnosis at delivery or PP</td>
<td>3.24 (1.2-8.2)</td>
<td>0.018</td>
</tr>
<tr>
<td>Illicit drug use during pregnancy</td>
<td>2.66 (1.3-5.3)</td>
<td>0.005</td>
</tr>
<tr>
<td>BW &lt;2500 gm</td>
<td>2.46 (1.3-4.7)</td>
<td>0.007</td>
</tr>
</tbody>
</table>
Management of Acute Infection in Pregnancy or Breastfeeding

- If suspect acute infection, obtain plasma HIV RNA test with HIV antibody test (4th generation test preferred).
- Although positive RNA test should be confirmed, do not wait to initiate ART if RNA +.
- While resistance test should be obtained, initiation of ART should not be delayed; consider initiating PI-based ART (NNRTI transmitted resistance more likely).
- If pregnant, cesarean section (and IV AZT) likely needed due to insufficient time to achieve suppression.
- If breastfeeding, interrupt breastfeeding (can express and store milk awaiting confirmation); consult pediatric HIV specialist re: infant ARV management.
Pregnancy in Perinatally-Infected Girls

Jim Oleske, UMDNJ Newark
Long-term survivors, 2003
Growing Population in Need of Contraception Perinatally-Infected Young Women

- With availability potent ART, morbidity/mortality have decreased for perinatally-infected children.
- ↑ number girls with perinatal infection reaching childbearing age and becoming pregnant.
- Most pregnancies unplanned; repeat pregnancy not uncommon.
- Some studies show higher rates adverse pregnancy outcomes than behaviorally-infected pregnant women.
- However, since most treated, MTCT uncommon (3 infections/176 live births, 1.7%).
HIV, Pregnancy and Maternal Health: Perinatally-Infected vs Behaviorally-Infected Women


- Bronx, NY: 37 pregnancies/30 perinatally-infected women vs 45/39 age-matched behaviorally-infected women
- Perinatal women more likely earlier GA and lower BW.
- CD4 lower, RNA higher perinatal women; 4 deaths perinatal group vs 0 death in behavioral group.

**CD4 count lower in perinatal women**

**RNA higher in perinatal women**
Management of Pregnant Women with Perinatal HIV Infection

- General principles of antepartum care and ART do not differ with perinatal vs horizontal infection; however, are more likely to be young/adolescent.
- ART adherence key challenge for women with long-standing HIV infection – and adolescents.
- May be at risk of drug resistance due to extensive ART exposure prior to pregnancy; choice ART based on resistance testing, prior ART history. Non-preferred drugs in pregnancy may be needed to achieve optimal viral suppression.
- Careful monitoring for adverse pregnancy outcome due to combination of risk factors: HIV infection, perinatal infection, ART, adolescence.
Breastfeeding and HIV in the US
Recommendations on Breastfeeding and HIV in the United States

- Avoidance of breastfeeding is strongly recommended for HIV+ women in the United States because:
  - maternal ART reduces but doesn’t eliminate postnatal transmission
  - safe and affordable replacement feeding available
  - formula feeding is not associated with excess infant morbidity/mortality
  - potential infant toxicity from ARV in breast milk (variable penetration depending on drug)
  - potential for multi-drug resistant virus should infant become infected
Breastfeeding and HIV in the United States

- However, women may face social, familial, and personal pressures to consider breastfeeding despite recommendations.

- Without effective education and support, HIV+ women may breastfeed or use mixed feeding in resolving infant feeding pressures or conflicts, and increase risk transmission to infant.

- A 31-year-old HIV+ Nigerian woman just arrived in the United States, 34 weeks pregnant and on ART with an undetectable viral load. She plans to return to Nigeria when the baby is 6 weeks old. Because formula feeding was not a feasible or safe option when she returned home, she wanted to breastfeed her baby. She has only disclosed her HIV diagnosis to her husband; she has not disclosed to other family members or her community. There is a close Nigerian community in the area, and the patient explains that people suspect that a woman has HIV infection if she does not breastfeed.
Breastfeeding and HIV-Infected Women in the US: Harm-Reduction Counseling Strategies


- Important to discuss infant feeding choice with patient in antepartum period to:
  - allow addressing possible barriers to formula-feeding before delivery,
  - allow women to understand risk of HIV transmission even if she is on suppressive ART,
  - offer safe alternatives to breastfeeding, and
  - for women who choose to breastfeed
    - provide a harm-reduction approach to minimize transmission risk, including healthcare plan to achieve specific targets, such as an undetectable HIV viral load.
## Potential Risks and Benefits of Different Feeding Options for HIV-Exposed Infants in the US


<table>
<thead>
<tr>
<th>Feeding Option</th>
<th>Risk of HIV Transmission</th>
<th>Cultural Acceptability</th>
<th>Feasibility</th>
<th>Affordability</th>
<th>Sustainability</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula feeding</td>
<td>None</td>
<td>+/-</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Milk bank</td>
<td>None&lt;sup&gt;a&lt;/sup&gt;</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+++</td>
</tr>
<tr>
<td>Exclusive breastfeeding while on maternal ARVs</td>
<td>1.1% (Mma Bana)</td>
<td>Unknown in the US; +++ outside of US</td>
<td>Unknown in the US; +++ outside of US</td>
<td>Unknown in the US; +++ outside of US</td>
<td>Unknown in the US; +++ outside of US</td>
<td>+</td>
</tr>
<tr>
<td>Exclusive breastfeeding and infant ARV prophylaxis</td>
<td>1.7% (BAN)</td>
<td>Unknown in the US; +++ outside of US</td>
<td>Unknown in the US; +++ outside of US</td>
<td>Unknown in the US; +++ outside of US</td>
<td>Unknown in the US; +++ outside of US</td>
<td>No US data</td>
</tr>
<tr>
<td>Flash-heat treatment</td>
<td>No efficacy data available</td>
<td>Unknown in the US, + outside of US</td>
<td>Unknown in the US, + outside of US</td>
<td>++</td>
<td>Unknown</td>
<td>++</td>
</tr>
<tr>
<td>Lactational surrogate (&quot;wet nurse&quot;)</td>
<td>None/minimal&lt;sup&gt;b&lt;/sup&gt;</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>++</td>
</tr>
</tbody>
</table>

Abbreviations: +/-, potential for both risks and benefits; ++, benefit; ++++, great benefit; ARV, antiretroviral; BAN, Breastfeeding, Antiretrovirals, and Nutrition study; HIV, human immunodeficiency virus.

<sup>a</sup> Assuming adequate HIV testing of milk donor.

<sup>b</sup> Assuming adequate HIV testing of and no risk for incident HIV in wet nurse.
If Woman Decides to Breastfeed Despite Counseling: Harm-Reduction Strategies


- Discuss timing and methods of weaning and option to switch to replacement feeding at any time.
- Discuss what is known/not known about ↓ transmission with maternal ART, ARV penetration into milk, and infant safety.
- Explain exclusive breastfeeding for 1st 6 months appears safer than mixed formula/breastfeeding; provide support.
- Ensure woman receiving/adhering to fully suppressive ART.
- Monitor maternal viral load monthly while breastfeeding.
- HIV PCR testing for infant monthly while breastfeeding and 1, 3, and 6 months after weaning.
- Educate about need for immediate care if signs of mastitis and need for prompt treatment to minimize HIV shedding in milk.
Some Resources

- **AIDSInfo.nih.gov**: current US guidelines for maternal ART and prevention perinatal transmission. August 2015

- **www.APRegistry.com**: registry of birth outcomes for women on ART – critical participate to enable monitoring for safety

- Perinatal HIV Hotline - 888-448-8765: 24-7 availability for expert consultation
Thanks For Your Attention!

It always seems impossible until it’s done.
- Nelson Mandela
HIV Management 2016
THE NEW YORK COURSE