Making infant feeding safer – progress and challenges in feeding and infant prophylaxis

Dr Lee Fairlie

Priorities 2012
To Breastfeed or Not To Breastfeed? The Balancing Act

IATT October 2000 and 2006 recommendation:
HIV-positive women should exclusively breastfeed for the first 6 months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS) - in this instance all breastfeeding should be avoided.
WHO 2010

HIV and breastfeeding

“Together, breastfeeding and ARV interventions have the potential to significantly improve infants' chances of surviving while remaining HIV uninfected. WHO recommends that when HIV-infected mothers breastfeed, they should receive ARVs and follow WHO guidance for breastfeeding and complementary feeding”
Tshwane Declaration
August 2011

• Adopted WHO guidelines
• Exclusively breastfeed infants for 6 months with appropriate ARV cover for mothers and infants
• Formula feeding only on medical prescription
• Thereafter give appropriate complimentary foods
• HIV – mothers and HIV + mothers with HIV+ infants should breastfeed for up to 2 years and beyond
• HIV + mothers should breastfeed for 12 mo
### Infant prophylaxis

<table>
<thead>
<tr>
<th></th>
<th>Mother on triple therapy</th>
<th>Mother on PMTCT</th>
<th>Mother on no therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exclusive breastfeeding</strong></td>
<td>6 weeks NvP</td>
<td>NvP until 1 week POST weaning</td>
<td>NvP until 1 week POST weaning</td>
</tr>
<tr>
<td><strong>Replacement feeding</strong></td>
<td>6 weeks NvP</td>
<td>6 weeks NvP</td>
<td>6 weeks NvP</td>
</tr>
</tbody>
</table>

- In premature infants lower dose NVP, increased with age
- Use AZT if NVP toxicity develops
- Remember cotrimoxazole from 6 weeks
- Remember 6 week PCR, post breastfeeding PCR and 18 month HIV ELISA
SA data: Breastfeeding impact on HIV + mothers and their infants....

• Highlights the importance of supportive counseling during exclusive breastfeeding
• Exclusive breastfeeding rates were 92.1% at 3 months and 66.7% at 6 months
• Breastfeeding protective for maternal mental health and did not have any negative impact on maternal nutritional status
• Only 38.7% of women who chose to formula feed met AFASS criteria

Kindra et al. Matern Child Health 2012
Impact on infants....

- Significantly improved growth parameters in breastfeeding infants at 14 weeks, no longer significant at 6 or 9 months
- 69% lower incidence in diarrhea at 3 months in BF (p=0.006)
- Lower hospital admissions in BF (p=0.014)
- Improved milestone achievement until 6 m (p=0.047)

Kindra et al. Matern Child Health 2012
MASHI study: Increased mortality with abstinence from breastfeeding in a clinical trial in urban Botswana

Thior I, Lockman S, Smeaton LM et al. JAMA 2006; 296: 794-805
Increased mortality with abstinence from breastfeeding in a clinical trial in urban Botswana

Does “no benefit” = “no harm”? 

Thior I, Lockman S, Smeaton LM et al. JAMA 2006; 296: 794-805
“No benefit” means # deaths caused = # HIV prevented

% with outcome

Thior et al. Botswana
0-6 months
Breastfeed
0-6 months
Breastfeed
18m

ZEBS Zambia
6-24 months
Breastfeed 18m
Stop BF at 4 m

% with outcome

Breastfeed
Formula feed

Breastfeed 18m
Stop BF at 4 m

Uninfected child death
HIV infection

Uninfected child death
HIV infection

Breastfeed
Formula feed

Breastfeed 18m
Stop BF at 4 m

Uninfected child death
HIV infection

Breastfeed
Formula feed

Breastfeed 18m
Stop BF at 4 m

Uninfected child death
HIV infection
With ARVs, abstinence from breastfeeding or early weaning lead to worse outcomes.

# deaths > # HIV prevented

0-6 months
Thior et al. Botswana

6-24 months
ZEBS Zambia

% with outcome

Breastfeed
Formula feed
Breastfeed 18m
Stop BF at 4 m

Uninfected child death
HIV infection

Uninfected child death
HIV infection
PEPI-Malawi study....

Number of Events and Rates of Morbidity per 100 Person-Years (P-Y), PEPI-Malawi Study, Blantyre, Malawi, 2004–09

<table>
<thead>
<tr>
<th>Age interval</th>
<th>Number of infants by BF status</th>
<th>Total person-years</th>
<th>Any illness/hospital Admission since last visit</th>
<th>Malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td># Events Rate per 100 (95%CI)</td>
<td># Events Rate per 100 (95%CI)</td>
</tr>
<tr>
<td>6–9 mos</td>
<td>BF N = 549</td>
<td>126.6</td>
<td>65 51.3 (39.6–65.4)</td>
<td>26 20.5 (13.4–30.1)</td>
</tr>
<tr>
<td></td>
<td>NBF N = 1212</td>
<td>216.3</td>
<td>301 139.1 (123.9–155.8)</td>
<td>92 42.5 (34.3–52.2)</td>
</tr>
<tr>
<td>9–12 mos</td>
<td>BF N = 317</td>
<td>75.7</td>
<td>40 52.8 (37.8–71.0)</td>
<td>22 29.1 (18.2–44.0)</td>
</tr>
<tr>
<td></td>
<td>NBF N = 1316</td>
<td>322.8</td>
<td>291 90.2 (80.1–101.1)</td>
<td>122 37.8 (31.4–45.1)</td>
</tr>
<tr>
<td>12–15 mos</td>
<td>BF N = 212</td>
<td>49.6</td>
<td>15 30.2 (16.9–49.97)</td>
<td>10 20.2 (9.7–37.1)</td>
</tr>
<tr>
<td></td>
<td>NBF N = 1331</td>
<td>316.4</td>
<td>212 67.0 (58.3–76.7)</td>
<td>142 44.9 (37.8–52.9)</td>
</tr>
</tbody>
</table>

**NOTE.** Rates of morbidity calculated dividing number of events by total person-years × 100. BF, Breastfeeding; NBF, Not breastfeeding.

Cumulative mortality rates among HIV-exposed, uninfected infants 6–15 months of age, PEPI-Malawi Study, Blantyre, Malawi, 2004–2009. Extended Kaplan–Meier curves were used.
Early cessation of breast feeding is harmful to HIV-infected children

P = 0.01

Group A
Counseled to stop BF at 4 mo

Group B
Counseled to BF

Summary of studies 2010 WHO guidelines

<table>
<thead>
<tr>
<th>Study</th>
<th>Antiretroviral intervention</th>
<th>Infant regimen</th>
<th>MTCT risk (95% confidence interval)</th>
<th>Infant infection or death</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SIMBA, Rwanda [64]</strong></td>
<td>AZT + ddI from 36 weeks of gestation to 1 week postpartum</td>
<td>Daily NVP or daily 3TC * from birth up to 6 months</td>
<td>Overall: 6.9% at 1 mo (4.4—9.4) ** 7.7% at 6 mo (5.1—10.5)**</td>
<td>Not available</td>
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<tr>
<td>(Vyankandondera)</td>
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<tr>
<td><strong>MASHI, Botswana [65]</strong></td>
<td>AZT + sd-NVP from 36 weeks of gestation to 1 week postpartum</td>
<td>Daily AZT from birth up to 6 months</td>
<td>Overall: 4.6% at 1 mo ** 9.0% at 7 mo ** 9.5% at 18 mo **</td>
<td>6.1% at 1 mo** 12.9% at 7 mo** 15.1% at 18 mo**</td>
</tr>
<tr>
<td>(Thior)</td>
<td></td>
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<tr>
<td><strong>MITRA, Tanzania [61]</strong></td>
<td>AZT + 3TC from 36 weeks of gestation to 1 week postpartum</td>
<td>Daily 3TC from birth up to 6 months</td>
<td>Overall: 3.8% at 1.5 mo (2.0—5.6) 4.9% at 6 mo (2.7—7.1)</td>
<td>4.5% at 1.5 mo (2.4—6.5) 8.5% at 6 mo (5.7—11.4)</td>
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<tr>
<td>(Kilewo)</td>
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<tr>
<td><strong>PEPI, Malawi [59]</strong></td>
<td>sd-NVP at onset of labour</td>
<td>Daily NVP or NVP/ AZT from birth up to 14 weeks</td>
<td>Among infants who were HIV-uninfected at birth Infant NVP prophylaxis 5.9% at 9 mo (3.9—7.0) Infant NVP/AZT prophylaxis 6.4% at 9 mo (4.9—8.3)</td>
<td>10.6% at 9 mo 11.2% at 9 mo</td>
</tr>
<tr>
<td>(Kumwenda)</td>
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<tr>
<td><strong>SWEN, Ethiopia, Uganda, India [60]</strong></td>
<td>sd-NVP at onset of labour</td>
<td>Daily NVP from birth up to 6 weeks</td>
<td>Among infants who were HIV-uninfected at birth 2.5% at 1.5 mo ** 6.9% at 6 mo **</td>
<td>3.7% at 1.5 mo** 8.1% at 6 mo**</td>
</tr>
<tr>
<td>(SWEN Study Team)</td>
<td></td>
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<tr>
<td><strong>BAN, Malawi [62, 63]</strong></td>
<td>sd-NVP at onset of labour + AZT + 3TC during labour to 1 week postpartum</td>
<td>Daily NVP from birth up to 6 months</td>
<td>Among infants who were HIV-uninfected at age 2 weeks 1.7% at 6.5 mo **</td>
<td>Among infants who were alive and HIV-uninfected at age 2 weeks 2.6% at 6.5 mo**</td>
</tr>
<tr>
<td>(Chasela)</td>
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* Similar MTCT rates were observed in both groups.
** Confidence interval was not available.
BAN study

• Randomized: 3 arms
• High exclusive breastfeeding at 24 weeks (88-90%)
• At 48 weeks 71% reduction in transmission for infant NVP group and 49% for maternal HAART group
• 1/3 of infections between 29 and 48 weeks, post reported weaning
• Rapid weaning no longer recommended

HPTN 046

- Daily NVP up to 6 months/breastfeeding cessation
- 54% reduction in HIV infection in the NVP prophylaxis group at 6 months
- By 12 months no longer significant differences
- In women with high Cd4 count: infant infection 75% less in NVP group versus placebo

Figure 3
Kaplan-Meier analysis of cumulative rates of HIV-1 infection, by study group
## Pooled analysis

<table>
<thead>
<tr>
<th>Regimen</th>
<th>6 week NVP</th>
<th>14 week NVP</th>
<th>28 week NVP</th>
<th>NVP/AZT 14 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission rate (%)</td>
<td>5.8</td>
<td>3.7</td>
<td>1.8</td>
<td>4.8</td>
</tr>
</tbody>
</table>

Cox regression models adjusted for maternal CD4, infant birth weight: NVP reduces rate of HIV infection by 71% and reduces rate of HIV infection or death by 58% (p=0.001)

Longer duration of protection results in a lower risk of infection

Hudgens MG et al. *Clin Infec Dis.* 2012 Sep
Pasteurization of human milk

- Used variably in units in South Africa
- Can use maternal or donor milk
- Mother is able to do at home with a peanut butter jar and aluminium pot
- Flash heating: short period of time
- Pretoria pasteurisation: similar to Holder method with longer boil at lower temperature but no temperature monitor

Israel-Barnard et al. *JAIDS*. 2005
How safe and effective are these methods?

- PP and FH denature HIV but maintain most of nutritional and some of the antimicrobial properties of breastmilk
- FH more effectively eliminates RT activity
- No significant decreases in vitamin content
- Storage for up to 12 hours unrefrigerated, may be better to heat treat just before use
- Best time to use when complimentary foods introduced
- Necessary with good PMTCT? enhances

Israel-Barnard et al. JAIDS. 2005
WHAT’S HAPPENING IN THE FIELD?
2. Early vertical transmission in infants ≤ 2 months of age in SA:
“In the field” data with daily NVP implementation

Kenya:
• Prospective 12 month evaluation
• At 6.2 weeks transmission rates 1.8%
• At 10 months an additional 1.8 % transmission

Kinshasa, DRC:
• At a median of 7 weeks transmission rates 4% with extended NVP

Zambia:
• National data: 28 % of pregnant women eligible initiated HAART, 57% of exposed infants received prophylaxis, 50% adhered
• Overall HIV transmission 4%, option B 1.87%

Uganda:
• 6 week transmission rate of 2.5% with NVP

Diouf et al. IAS. 2012
Feinstein L et al. IAS. 2012
Tshikawa et al./IAS.2012
Namukwaya Z et al. IAS. 2012
CHALLENGES
PMTCT program implementation

SAPMTCTE 2011:
• High uptake of HIV testing and results
• 53% of HIV – women not offered a repeat test at 32 weeks
• 84% CD4 count
• 71% of women needing ART received it
• 85% of HIV exposed infants received NVP

• ART shortages (NVP)
• No “grey areas” in the guidelines
• High defaulter rate in women on HAART postpartum (54% in JHB cohort)

Woldesenbet S et al. IAS. Washington 2011
Black V et al. JAIDS. 2008
Infant feeding

- Lack of supportive counseling for those who choose to exclusively breastfeed
- Low exclusive breastfeeding rates (variety of reasons) → 18% at 6 weeks in SAPMTCTE study
- Mixed feeding
- Many women still choose to FF (how many meet AFASS criteria???)
BREASTFEEDING
It Rocks!
Testing of children....

**SAPMTCTE 2011:**

- Only **33 %** of infants intentionally brought to EPI clinic for HIV testing
- **99%** of caregivers offered EID accepted it
- Low (or poorly recorded) rates of post breast feeding cessation testing
- Low **18 month rapid/ELISA testing (10%)**
- Problems with phlebotomy for small children particularly at clinic level
Infant HAART

- HIV infected infants still initiate HAART late
- NVP resistance in high percentage of children exposed to SDNVP (62% at 6 months, fades with time)
- Higher rates in extended NVP: 92% in children infected < 6 weeks in the SWEN study
- Balanced by lower HIV transmission
- KIBS study: 25% of infants exposed to lamivudine, zidovudine and NVP/Nelfinavir developed K65R mutation

Hunt GM et al. 
Chikata S et al. IAS. 2012.
Conclusions

• Breast feeding safe and optimal in HIV exposed infants, BUT needs adherence to PMTCT guidelines
• Data from studies and the field supports this
• With potential B/B+ as new guidelines need improved maternal retention strategies
• Increased efforts in promoting exclusive breastfeeding in first 6 months required
• Infant testing and early referral into care needs to be a priority
Acknowledgements

• Dr Vivian Black
• Dr Nicola Wattrus
• Dr Louise Gilbert