Emerging evidence on prevention of mother-to-child transmission of HIV

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HIV Department, World Health Organization, Geneva

Satellite symposium
Scaling up comprehensive prevention of mother-to-child transmission programmes
International AIDS Conference
Mexico D.F., 3 August 2008
Content

- Progress made
- Key issues
- New data on use of antiretroviral drugs
- Doing better with what we have
- Keeping WHO guidelines up-to-date
Geographical distribution of HIV burden, 2007

- 67% of people living with HIV are in sub-Saharan Africa
- 50% of people living with HIV are women (60% in sub-Saharan Africa)
- 19 of 20 countries with highest PMTCT burden are in sub-Saharan Africa

Source: UNAIDS 2008
Prevention of HIV infection in infants and children
The four elements

- Primary prevention of HIV
- Prevention of unwanted pregnancies
- Prevention of transmission from HIV-infected women to their infants
- Appropriate treatment, care and support

Source: Strategic approaches to the prevention of HIV infection in infants. WHO 2002.
Provider-initiated HIV testing and counselling increases access for PMTCT

Percentage of pregnant women receiving an HIV test by region, 2004-2007 (low- and middle-income countries)

% Pregnant women with HIV who received ARV drugs to reduce mother-to-child transmission increased - 49% still received only single dose nevirapine

Percentage of pregnant women with HIV receiving ARVs for PMTCT in low- and middle-income countries, 2004-2007

Distribution of ARV regimens, 2007

- Unknown, 17%
- Single dose nevirapine, 49%
- Triple proph. ARV/ART, 8%
- Dual proph. ARV, 26%

WHO guidance on use of ARV drugs
Initiating ART is based on clinical and/or immunological assessment - only 12% of pregnant women were assessed for ART

<table>
<thead>
<tr>
<th>WHO Clinical Staging</th>
<th>CD4 testing not available</th>
<th>CD4 testing available</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Do not treat</td>
<td>Treat if CD4 cell count &lt; 200/mm³</td>
</tr>
<tr>
<td>2</td>
<td>Do not treat</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Treat</td>
<td>Treat if CD4 cell count &lt; 350/mm³</td>
</tr>
<tr>
<td>4</td>
<td>Treat</td>
<td>Treat irrespective of CD4 cell count</td>
</tr>
</tbody>
</table>

1 Women have lower CD4 cell counts during pregnancy compared to postpartum, partly due to pregnancy-related haemodilution. The impact of this on using CD4 350 threshold in pregnant women is not known.

Source: Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. WHO 2006
Recommended first-line ART regimens for eligible pregnant women

<table>
<thead>
<tr>
<th>Stage</th>
<th>Regimen</th>
</tr>
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<tbody>
<tr>
<td><strong>Mother</strong></td>
<td></td>
</tr>
<tr>
<td>Antepartum</td>
<td>AZT + 3TC + NVP twice daily</td>
</tr>
<tr>
<td>Intrapartum</td>
<td>AZT + 3TC + NVP twice daily</td>
</tr>
<tr>
<td>Postpartum</td>
<td>AZT + 3TC + NVP twice daily</td>
</tr>
<tr>
<td><strong>Infant</strong></td>
<td>AZT x 7 days*</td>
</tr>
</tbody>
</table>

* If the mother receives < 4 wks of ART during pregnancy, give 4 wks of infant AZT

Source: Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. WHO 2006
**Recommended ARV-prophylaxis for pregnant women not eligible for ART**

<table>
<thead>
<tr>
<th>Mother</th>
<th>Infant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antepartum</td>
<td>AZT</td>
</tr>
<tr>
<td>Intrapartum</td>
<td>Sd-NVP + AZT/3TC</td>
</tr>
<tr>
<td>Postpartum</td>
<td>AZT/3TC for 7 days</td>
</tr>
<tr>
<td>Infant</td>
<td>Sd-NVP + AZT for 7 days*</td>
</tr>
</tbody>
</table>

* If the mother receives < 4 wks of ART during pregnancy, give 4 wks of infant AZT

Source: Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. WHO 2006
Alternative and minimum ARV-prophylaxis for pregnant women not eligible for ART

<table>
<thead>
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<th>Minimum</th>
</tr>
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<tbody>
<tr>
<td><strong>Mother</strong></td>
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<tr>
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<td>Intrapartum</td>
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<td></td>
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<td></td>
<td>Sd-NVP + AZT/3TC</td>
</tr>
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<td>Intrapartum</td>
<td>Postpartum</td>
</tr>
<tr>
<td></td>
<td>AZT/3TC for 7 days#</td>
</tr>
<tr>
<td>Infant</td>
<td>Infant</td>
</tr>
<tr>
<td>Sd-NVP *+AZT for 7 days§</td>
<td>Sd-NVP *</td>
</tr>
</tbody>
</table>

* Administration of NVP less than 12 hours after birth = recommended; administration up to 72 hours after has been shown to be still moderately effective

# The AZT/3TC tail reduces the risk of the mother developing NVP resistance

§ If the mother receives < 4 wks of ART during pregnancy, give 4 wks of infant AZT

Source: Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. WHO 2006
HIV and infant feeding technical consultation
Geneva, October 25-27, 2006
CONSENSUS STATEMENT

• The most appropriate infant feeding option for an HIV-infected mother should continue to depend on her individual circumstances…………

• Exclusive breastfeeding is recommended for HIV-infected women for the first 6 months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS) for them and their infants before that time.

• When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected women is recommended.
Promoting HIV-free child survival requires avoiding HIV transmission and minimizing risk of other morbidity and mortality

Issues
- Operational and managerial
- Health systems
- Socioeconomic
- Technical
Interventions to prevent mother-infant HIV transmission, by timing

Maternal

- ARVs to the mother as treatment or for prophylaxis

- ARVs to mother as treatment or prophylaxis

Infant

Ongoing studies are evaluating:
- Provision of triple combination ARV regimens regardless of CD4 count ante- and post-partum
- Extended infant ARV prophylaxis

- Exclusive BF for 6 months or Replacement feeding if AFAS
- ARVs as prophylaxis to newborn
Maternal ARV prophylaxis studies antepartum and postpartum (Triple ARVs/ART)

Between age 4-6 weeks and 6-7 months HIV transmission rates

4 observational studies showed reduced HIV breastfeeding transmission rates

<table>
<thead>
<tr>
<th>Study</th>
<th>% TR at 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>DREAM (CROI 2008)</td>
<td>0.6%</td>
</tr>
<tr>
<td>Mitra Plus (IAS 2007)</td>
<td>0.9%</td>
</tr>
<tr>
<td>Amata (IAS2007)</td>
<td>0.6%</td>
</tr>
<tr>
<td>KiBS (CROI 2008)</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

6 mos EBF

Courtesy: Lynne Mofenson

XVII International AIDS Conference, Mexico D.F., 3 August 2008
Comparing maternal antepartum and postpartum triple ARV/ART study data by CD4

<table>
<thead>
<tr>
<th>Study</th>
<th>CD4 range</th>
<th>Regimen</th>
<th>Timing</th>
<th>Tx Rate % (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KiBS*</td>
<td>≤ 250/mm³</td>
<td>Triple (Nelfinavir)</td>
<td>12 mths</td>
<td>6.7 (3.2-13.9)</td>
</tr>
<tr>
<td></td>
<td>&gt; 250/mm³</td>
<td>Triple (Nelfinavir)</td>
<td>12 mths</td>
<td>5.5 (3.6-8.4)</td>
</tr>
<tr>
<td>Kesho Bora§</td>
<td>≤ 200/mm³</td>
<td>Triple (LPV/r)</td>
<td>12 mths</td>
<td>7.6 (2.5-12.6)</td>
</tr>
<tr>
<td></td>
<td>&gt; 500/mm³</td>
<td>ZDV + sd-NVP</td>
<td>12 mths</td>
<td>5.8 (1.6-9.9)</td>
</tr>
<tr>
<td>Abidjan§</td>
<td>Median 189/mm³</td>
<td>Triple (NVP)</td>
<td>12 mths</td>
<td>3.3 (0.0-6.9)</td>
</tr>
<tr>
<td></td>
<td>Median 467/mm³</td>
<td>ZDV + sd-NVP</td>
<td>12 mths</td>
<td>7.5 (2.8-12.3)</td>
</tr>
</tbody>
</table>

* Postnatal at birth until 12 months
§ cumulative transmission rate
What are consequences for mothers' health?

- Antiretroviral treatment interruptions are associated with increased risk of opportunistic infections (OIs) and death.
  - Rates of OIs/death were higher in patients discontinuing treatment versus those on continued treatment for periods with CD4 $\geq 350$ cells/mm$^3$
  - Rates of OIs/death were similar in patients discontinuing treatment versus those on continued treatment for periods with CD4 $< 350$ cells/mm$^3$

  SMART, JID 2008; 197: 1145-55, SMART NEJM 2006; 355: 2283-96

- Interruptions of triple prophylactic ARV drugs in 220 pregnant women who stopped drugs 6-months postpartum with mean CD4+ $496$/mm$^3$ and 7850 HIV RNA copies/ml had similar clinical and immunological values 12 months after drug interruption.

  Palombi L 15th CROI, Boston, MA 2008, Abstract 668
Two randomized controlled infant ARV prophylaxis studies

Negative at birth and 6 mos (SWEN) and 9 mos. (PEPI) HIV TR

RR 0.80, p=0.16
AHR 0.56, p<0.001

Questions remain (1)

Maternal triple ARV regimens for prophylaxis

• Impact of stopping triple ARVs on HIV+ive women's health
• Optimal regimen
• Safety for the mother and the infant
• Transmitted HIV drug resistance to the infant
• Additional infections prevented in women with CD4 count > 500 mm$^3$ compared to dual ARV prophylaxis
• Optimum duration of ARV prophylaxis (until EBF discontinued or lifelong)
• Feasibility and cost
Questions remain (2)

Extended infant ARV prophylaxis

- Risk of adverse events due to exposure of HIV-negative infants to nevirapine
- Optimal duration of single dose nevirapine administration
- NVP resistance and impact on prophylaxis and future treatment options
- Feasibility
Doing better with what we have

- Ensure that national PMTCT guidelines are implemented
- Pay more attention to ensuring women who need treatment are identified and receive ART
- Promote wider availability of CD4 count and uninterrupted supply of ARV drugs
- Build capacity of antenatal clinic staff to conduct or refer for clinical /immunological assessment and provide combination ARVs
- Strengthen infant feeding support to mothers who are exclusive breastfeeding or formula feeding
Keeping WHO guidelines up-to-date

WHO systematically reviews available evidence and programme performance, and will convene expert consultation with researchers, implementers, and programme planners in late 2008

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Department of Reproductive Health and Research
World Health Organization
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Tin Tin Sint
Siobhan Crowley
Charlie Gilks
Kevin De Cock
Links

Web pages:

Guidelines on PMTCT and antiretroviral therapy:
http://www.who.int/hiv/pub/guidelines/pmtctguidelines3.pdf

HIV and infant feeding:
http://www.who.int/child-adolescent-health/NUTRITION/HIV_infant.htm