Update of Pediatric ART Guidelines

1st National Conference on Pediatric AIDS Care
5 Feb. 2007

Dr. Sam Sophan
National Pediatric Hospital
Pediatric ART Guidelines

The First Edition of National Guidelines for the Use of Pediatric ARV was published in October 2004.
## Table of contents

- Introduction and Objectives of the Guidelines
- Establishing diagnosis of HIV infection
- When to start ART
- What to start ART: infants and children, TB
- ARV Drug Toxicity, Alternative 1st line regimen because of toxicity
- Treatment failure
- Choice of second line
- Clinical and Lab monitoring
- Adherence to ART
- TB Co-infection
- Strategies in the second-line regimens failure
Annex

- 1-WHO clinical staging of HIV for children
- 2-WHO classification of HIV-associated immunodeficiency in infants and children
- 3-Formulations and dosages of ARV drugs for infants and children
- 4-Serious acute and chronic toxicities caused by ARV drugs
- 5-Severity grading of selected clinical and laboratory toxicities in children
- 6-Abbreviations
Establishing diagnosis of HIV infection

- **Children aged 18 months and more:**
  - Antibody tests (National standard testing algorithms).

- **Children aged 18 months and more:**
  - Virological test:
    - at 6 weeks of age
    - A repeat test should be done at month 6 of age to confirm the initial positive test.
Anti-HIV Test+

<18 Months
- HIV virological test +
  - WHO III or CDC: C
  or
  - WHO I/II or CDC: AB
    With CD4<20%

If PCR not available
And Breastfeeding
was stopped for
6 months:
WHO III/ CDC:C
with CD4<20%

WHO stage III
or
CDC category C
irrespective
of CD4

≥18 Months
- WHO stage II
  or
  CDC category B
  with CD4<20%

WHO stage I
or
CDC category
N or A
with CD4<15%

ART Recommendation
When to Start for Children<18months

Virological test not available: Presumptive severe disease diagnosis:

- The infant is confirmed HIV antibody positive
- AND
  - Diagnosis of any AIDS-indicator condition(s) can be made;
- OR
  - The infant is symptomatic with 2 or more of the following:
    - Oral Thrush
    - Severe pneumonia
    - Severe sepsis
- Other factors that support the diagnosis of severe disease in an HIV seropositive infant include:
  - Recent HIV-related maternal death, or advanced HIV disease in the mother;
  - CD4 < 20%.
Summary of WHO recommendation for Starting ART

<table>
<thead>
<tr>
<th>WHO stage</th>
<th>≤11 mo</th>
<th>12-35 mo</th>
<th>36-59 mo</th>
<th>≥5ys</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or 2</td>
<td>&lt;25% (&lt;1500)</td>
<td>&lt;20% (&lt;750)</td>
<td>&lt;15% (&lt;350)</td>
<td>&lt;15% (200)</td>
</tr>
<tr>
<td>3</td>
<td>Treat All</td>
<td>Treat All, except TB, LIP, oral hairy leukoplakia or thrombocytopenia with CD4 above the threshold</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td>Treat All</td>
</tr>
</tbody>
</table>
### WHO classification of HIV-associated immunodeficiency in infants and children

<table>
<thead>
<tr>
<th>Classification of HIV-associated Immunodeficiency</th>
<th>≤11 months (%)</th>
<th>12–35 months (%)</th>
<th>36–59 months (%)</th>
<th>≥5 years (cells/mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not significant</td>
<td>&gt;35</td>
<td>&gt;30</td>
<td>&gt;25</td>
<td>&gt;500</td>
</tr>
<tr>
<td>Advanced</td>
<td>25–29</td>
<td>20–24</td>
<td>15–19</td>
<td>200–349</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;25</td>
<td>&lt;20</td>
<td>&lt;15</td>
<td>&lt;200 or &lt;15%</td>
</tr>
</tbody>
</table>

Source: Based on WHO global and regional consultations and data from references (45, 174).
WHO clinical staging of HIV for infants and children

Old:

- Stage 1: 2 events
- Stage 2: 5 events
- Stage 3: 5 events

NEW!

- Stage 1: 2 events
- Stage 2: 10 events
- Stage 3: 12 events
- Stage 4: 18 events
What to Start? First line

- **Children < 3 years:**
  - AZT/d4T + 3TC + NVP

- **Children ≥ 3 years:**
  - AZT/d4T + 3TC + NVP/EFV
What to Start?
Alternative First-line

Children exposed to SD NVP through PMTCT:

- AZT/d4T + 3TC + LPV/r

Or if cold chain requirements cannot be met:

- AZT/d4T + 3TC + NFV

- AZT/d4T + 3TC + ABC (if PIs is not feasible)
Choice of Second line

- **Preferred:** New 2NRTIs + bPI
  - ABC + ddI + LPV/r

- If ABC hypersensitivity or unavailable:
  - 3TC + ddI + LPV/r
  - 3TC + TDF + LPV/r (>10ys)
## Alternative Second-line Regimen

<table>
<thead>
<tr>
<th>1st line regimen at failure</th>
<th>Preferred 2nd line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT/d4T + 3TC + 1 NNRTI</td>
<td>ddI + 3TC + LPV/r</td>
</tr>
<tr>
<td>ABC + 3TC + 1 NNRTI</td>
<td>ddI + AZT + bPI</td>
</tr>
<tr>
<td>ABC + 3TC + AZT/d4T</td>
<td>ddI + NVP/EFV + bPI</td>
</tr>
</tbody>
</table>
### DHHS Guidelines 2005

**Virological Failure: Treatment Options**

Table 25. Treatment Options Following Virologic Failure on Initial Recommended Therapy Regimens

<table>
<thead>
<tr>
<th>Regimen Class</th>
<th>Initial Regimen</th>
<th>Recommended Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTI</td>
<td>2 NRTIs + NNRTI</td>
<td>- 2 NRTIs (based on resistance testing) + PI (with or without low-dose ritonavir) (AII)</td>
</tr>
<tr>
<td>PI</td>
<td>2 NRTIs + PI (with or without low-dose ritonavir)</td>
<td>- 2 NRTIs (based on resistance testing) + NNRTI (AII)</td>
</tr>
</tbody>
</table>
| 3-NRTI        | 3 nucleosides   | - 2 NRTIs (based on resistance testing) + NNRTI or PI (with or without low-dose ritonavir) (AIII)  
|               |                 | - NNRTI + PI (with or without low-dose ritonavir) (CIII)  
|               |                 | - Nucleoside(s) (based on resistance testing) + NNRTI + PI (with or without low-dose ritonavir) (CII) |

- **2 NRTIs (based on resistance testing) + PI (with or without low-dose ritonavir)**
Key Before Changing for
First-line NNRTI-Failure

Early detect virologic failure

VL one time per year?

Fix any correctable issues:
adherence, drug interaction

Choose 2 new active NRTIs + bPI
### ARV Drugs Pediatric Dosing Chart Based on Weight Bands

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Abacavir (ABC)</th>
<th>Lamivudine (3TC)</th>
<th>Stavudine</th>
<th>Zidovudine (AZT)</th>
<th>Didanosine (ddI)</th>
<th>Nevirapine (NVP)</th>
<th>Efavirenz (EFV)</th>
<th>Lopinavir/Ritonavir (LPV/r)</th>
<th>Nevirapine (NVP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (mg)</td>
<td>8mg/kg, BID</td>
<td>4mg/kg, BID</td>
<td>1mg/kg, BID</td>
<td>180-240mg/m²</td>
<td>90-120mg/m²</td>
<td>60mg/m²</td>
<td>15mg/kg, OD</td>
<td>150mg/m²</td>
<td>150mg/m²</td>
</tr>
<tr>
<td>6-8.8</td>
<td>2mi</td>
<td>3mi</td>
<td>6mi</td>
<td>1/2 Cap 15mg</td>
<td>7mi</td>
<td>4mi</td>
<td>2 Tabs 25mg</td>
<td>6mi</td>
<td>1mi</td>
</tr>
<tr>
<td>7-9.8</td>
<td>3mi</td>
<td>4mi</td>
<td>6mi</td>
<td>1/2 Cap 20mg</td>
<td>9mi</td>
<td>5mi</td>
<td>2 Tabs 25mg</td>
<td>5mi</td>
<td>1.5mi</td>
</tr>
<tr>
<td>10-11.8</td>
<td>4mi</td>
<td>5mi</td>
<td>6mi</td>
<td>1 Cap 100mg</td>
<td>8mi</td>
<td>6mi</td>
<td>2 Tabs 25mg</td>
<td>8mi</td>
<td>1 Cap 200mg</td>
</tr>
<tr>
<td>12-14.8</td>
<td>5mi</td>
<td>6mi</td>
<td>6mi</td>
<td>1 Cap 15mg</td>
<td>12mi</td>
<td>6mi</td>
<td>2 Tabs 25mg</td>
<td>12mi</td>
<td>1.5mi</td>
</tr>
<tr>
<td>15-16.8</td>
<td>6mi</td>
<td>7mi</td>
<td>6mi</td>
<td>1/2 Tab 30mg</td>
<td>14mi</td>
<td>7mi</td>
<td>2 Tabs 25mg</td>
<td>14mi</td>
<td>2mi</td>
</tr>
<tr>
<td>17-19.8</td>
<td>7mi</td>
<td>8mi</td>
<td>6mi</td>
<td>1/2 Tab 30mg</td>
<td>16mi</td>
<td>9mi</td>
<td>2 Tabs 25mg</td>
<td>16mi</td>
<td>2.5mi</td>
</tr>
<tr>
<td>20-24.8</td>
<td>9mi</td>
<td>1/2 Tab 30mg</td>
<td>6mi</td>
<td>1/2 Tab 30mg</td>
<td>18mi</td>
<td>10mi</td>
<td>2 Tabs 25mg</td>
<td>18mi</td>
<td>2.5mi</td>
</tr>
<tr>
<td>25-29.8</td>
<td>11mi</td>
<td>1/2 Tab 30mg</td>
<td>6mi</td>
<td>1/2 Tab 30mg</td>
<td>20mi</td>
<td>12mi</td>
<td>2 Tabs 25mg</td>
<td>20mi</td>
<td>2.5mi</td>
</tr>
<tr>
<td>30-44.8</td>
<td>13mi</td>
<td>1 Tab 30mg</td>
<td>6mi</td>
<td>1/2 Tab 30mg</td>
<td>22mi</td>
<td>14mi</td>
<td>2 Tabs 25mg</td>
<td>22mi</td>
<td>3.5mi</td>
</tr>
<tr>
<td>56-40</td>
<td>15mi</td>
<td>1 Cap 300mg</td>
<td>6mi</td>
<td>1/2 Tab 30mg</td>
<td>24mi</td>
<td>16mi</td>
<td>2 Tabs 25mg</td>
<td>24mi</td>
<td>4mi</td>
</tr>
</tbody>
</table>

Note: Induction dosing is OD for 2 weeks, then continue daily dosing.
Dosing Chart for FDC

Antiretroviral Drugs Pediatric Dosing Chart Based on Weight Bands
For Fixed-Dose Combinations

<table>
<thead>
<tr>
<th>Formulations</th>
<th>AZT300mg+3TC150mg</th>
<th>d4T30+3TC150</th>
<th>d4T40+3TC150</th>
<th>d4T30mg+3TC150mg+ NVP200mg</th>
<th>d4T40mg+3TC150mg+ NVP200mg</th>
<th>AZT300mg+3TC150mg+ ABC300mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT: 180-340mg/m²; BID</td>
<td>AZT: 1mg/kg</td>
<td>d4T: 1mg/kg</td>
<td>3TC: 4mg/kg; BID</td>
<td>3TC: 4mg/kg; BID</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight</th>
<th>10-11.9</th>
<th>12-14.9</th>
<th>15-16.9</th>
<th>17-19.9</th>
<th>20-24.9</th>
<th>25-29.9</th>
<th>30-34.9</th>
<th>35-40</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1 Tab</td>
</tr>
<tr>
<td>1 Tab AM +</td>
<td>1 Tab</td>
<td>1 Tab AM +</td>
<td>1 Tab</td>
<td>1 Tab AM +</td>
<td>1 Tab</td>
<td>1 Tab AM +</td>
<td>1 Tab</td>
<td>1 Tab</td>
</tr>
<tr>
<td>1/2 Tab PM</td>
<td></td>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1/2 Tab</td>
<td>1/2 Tab PM</td>
<td>1/2 Tab</td>
<td>1/2 Tab PM</td>
<td>1 Tab</td>
</tr>
<tr>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
</tr>
<tr>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
</tr>
<tr>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
</tr>
<tr>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
<td>1 Tab</td>
</tr>
</tbody>
</table>

Pediatric FDC by Clinton Foundation?
When the 2nd Edition of Pediatric ART Guidelines comes out?

- Early 2007?
- Before the Year of Pig?
Acknowledgment

Pediatric ART Working group

- Prof. Chhour Y Meng
- Dr. Ung Vibol
- Dr. Sam Sophan
- Dr. Olivier Marcy
- Dr. Seourng Sethaboth
- Dr. Sous Prem Prey
- Dr. David Pugatch