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Diploma in management of HIV infection (France)
Consultant Pediatrician (Junior)
Myanmar ART Guideline

- In Myanmar
  - First HIV positive case reported: 1988
  - First AIDS case reported: 1991
  - ART Provision was started in 2005
  - ART provision for Pediatrics HIV was started since 2006 (Mandalay Children’s Hospital)
3rd edition of guideline (2010)
Current Treatment Guideline
LISTS OF PRESENTATION

• Pediatric HIV; Magnitude of problems
• Myanmar HIV Estimation
• Clinical Management of HIV in children
• PEDIATRIC HIV Program at Mandalay Children Hospital
Pediatric HIV: Magnitude of problem

- HIV/AIDS is a worldwide health problem in the present day with 36.9 million people infected globally.
- Among them, 3 million are <15 yrs of age (UNAIDS, 2015)
- Children <15 yrs who are newly infected with HIV in 2015 were 220,000 & the total figure of death in 2015 was 1.2 million.
- Over 90% of HIV seropositive patients live in developing world. In Pacific & Asia region, the total figure of adult & children living with HIV is 5 million that is >10% of world HIV population (UNAIDS, 2015)
# Myanmar Pediatric HIV Estimation (0-14 years)

<table>
<thead>
<tr>
<th>Spectrum</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV INFECTION</td>
<td>11230</td>
<td>11077</td>
<td>10844</td>
</tr>
<tr>
<td>ART NEED</td>
<td>6640</td>
<td>6895</td>
<td>7081</td>
</tr>
</tbody>
</table>
Paediatric ART provision
(Public sector Vs National figure)
Paediatric ART (Sep 2015)

Service delivery points
(88 sites/64 public sector)

Total (6,444)
PMTCT
Milestones (PMCT)

- Initiated as **Pilot project** in **2001** as community based approach.

- Expanding yearly and as of (2013):
  - community based in **(256) townships**
  - hospital based in **(38) hospitals**
  - Strategic shift and refocusing
  - **Now, mainly Township based**
# Evolution of WHO 2013 PMTCT ARV Recommendations

<table>
<thead>
<tr>
<th>Year</th>
<th>PMTCT</th>
<th>ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>4 weeks AZT; AZT+3TC, or SD NVP</td>
<td>No recommendation</td>
</tr>
<tr>
<td>2004</td>
<td>AZT from 28 wks + SD NVP</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td>2006</td>
<td>AZT from 28 wks + sdNVP +AZT/3TC 7days</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td>2010</td>
<td>Option A (AZT +infant NVP) <strong>Option B</strong> (triple ARVs)</td>
<td>CD4 ≤350</td>
</tr>
</tbody>
</table>

**Launch July 2013**

- **Option B or B + Moving to ART for all PW/BF**

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**Move towards: more effective ARV drugs, extending coverage throughout MTCT risk period, and ART for the mother’s health**
Challenges in PMCT

Counselling and Testing of HIV infection

- should be voluntary and adhere to the five C’s:
  Consent
  Confidentiality
  Counselling – couple counselling with support for mutual disclosure
  Correct test results – If HIV test is negative at 1st trimester, retest at 3rd trimester
  Connections to care, treatment and prevention services.

**increase uptake of HIV counseling and testing in all pregnant women in ANC settings and especially in rural area**
PMCT

- **Following Option B is norm in Myanmar**
  ARV prophylaxis for pregnant women who do not need treatment for their own health
- CD4 more then 500/cmm and WHO stage 1 or 2
- **When to start ARV prophylaxis:**
  - As early as 14 weeks of pregnancy
  - *Prophylaxis regimens for the mother: TDF+3TC (FTC) + EFV or alternate first line*
  - **Option B:** - continue ARV till 1 week after cessation of breast feeding
PMCT

- **Option B plus**: Do not stop ARV to mother.
- **Option B plus can be considered**
- Areas with high prevalence of HIV
- Remote areas, hard to reach areas
- Availability of ART center (as ART initiation will happen at ART centers)
- Depending on patients’ choice, consent, ability for regular follow up and adherence counseling.
Challenges in PMCT

**ART for PMCT**

- Pregnant mothers who are on ART already have their treatment continued after checking the VL which should be undetectable and if necessary the ART is changed.

- If the viral load is < 1000 copies/ml vaginal delivery can be allowed as the transmission rate of HIV to the infant becomes very low.

**Limitation in checking VL and lacking drug resistant testing**
Challenges in PMCT

Care and management of pregnant women

- regular follow up antenatal visits and pregnancy care,
- nutritional support and infant feeding counselling – Mainly breast feeding
- family planning counselling

** loss to follow up and home delivery and failure to get infant prophylaxis **
PMCT linkage with ART

Women who became pregnant while receiving ART (HAART)

HIV positive pregnant women identified by PMCT

Accessibility to CD4 testing & ART sites

Pregnant women Indication for HAART during pregnancy (depend on CD4 testing & ART criteria)

Pregnant women with no indication of HAART during pregnancy

Option A, B, B+

Pre ART registration

HIV exposed new born babies

Accessibility of PCR & ART site

Indication of ART

No indication for Paediatric ART

Pre ART registration

Paediatric ART
Early Infant Diagnosis (EID)
- Dried blood spots tests (DNA PCR) All HIV exposed infants have HIV Virological testing at 4-6 weeks of age or at the earliest opportunity

- National Health Laboratory

- 2009

- All PMCT hospital ART sites, PMCT sites (INGO)
Figure 2: Algorithm for early infant diagnosis

HIV-exposed infant or child <18 months

- Conduct diagnostic viral test
  - Viral test available
    - Positive: Infant/child likely infected
      - <24 months: Immediately start ART
        - And repeat viral test to confirm infection
    - Negative
      - Infant/child is uninfected

- Viral test not available
  - Ever breastfed or currently breastfeeding
    - Infant/child remains at risk for acquiring HIV infection until complete cessation of breastfeeding
  - Never breastfed
    - Infant/child is uninfected

- Infant/child develops signs or symptoms suggestive of HIV
  - Viral test no available
  - Conduct HIV antibody test at approximately 9 months of age
    - Viral test available
      - Positive: Infant/child is infected
        - <24 months: Start ART
          - And repeat viral test to confirm infection
      - Negative: HIV unlikely unless still breastfeeding
    - Viral test not available
      - Assume infected if sick
      - Assume uninfected if well

- Infant remains well and reaches 9 months of age
  - Viral test available
    - Positive: Repeat antibody test 6 weeks after cessation of breastfeeding and/or Repeat antibody test at 18 months of age to confirm viral test diagnosis
    - Negative: Repeat antibody test 6 weeks after cessation of breastfeeding and/or Repeat antibody test at 18 months of age to confirm viral test diagnosis

- Regular and periodic clinical monitoring
Early Infant Diagnosis
Achievement in Myanmar (2008 to Nov 2015)

DNA PCR testing No

EID Training were given _all States & Regions_ in 2014
Exposed infant vs EID status 
(Jan to Nov 2015)(Myanmar)

Exposed infant
2990

# of Testing infant 1131 (38%)

# of tested positive 82

Positive rate = 7%
Maintain the healthy and happy life style

GOAL of treatment of comprehensive HIV infection
ART IN CHILDREN
# When to start

<table>
<thead>
<tr>
<th>AGE GROUP</th>
<th>2010 RECOMMENDATIONS</th>
<th>2013 RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&lt;1 YEARS</strong></td>
<td>Treat ALL Strong recommendation, moderate-quality evidence</td>
<td>Treat ALL Strong recommendation, moderate-quality evidence</td>
</tr>
<tr>
<td><strong>1-2 YEARS</strong></td>
<td>Treat ALL Conditional recommendation, very-low-quality evidence</td>
<td>Treat ALL Conditional recommendation, very-low-quality evidence Priority: children &lt; 2 years or WHO stage 3-4 or CD4 count ≤ 750 cells/mm³ or &lt; 25%</td>
</tr>
<tr>
<td><strong>2-5 YEARS</strong></td>
<td>Initiate ART with CD4 count ≤ 750 cells/mm³ or &lt; 25%, irrespective of WHO clinical stage</td>
<td>CD4 ≤ 500 cells/mm³ Conditional recommendation, very-low-quality evidence CD4 ≤350 cells/mm³ as a priority (As in Adults) Strong recommendation, moderate-quality evidence</td>
</tr>
<tr>
<td><strong>≥5 YEARS</strong></td>
<td>Initiate ART with CD4 count ≤ 350 cells/mm³ (As in adults), irrespective of WHO clinical stage AND WHO clinical stage 3 or 4</td>
<td></td>
</tr>
</tbody>
</table>
### Classes of ARVs – clinical practice

<table>
<thead>
<tr>
<th>NRTI</th>
<th>PI</th>
<th>NNRTI</th>
<th>Fusion inhibitors</th>
<th>Entry inhibitors</th>
<th>INSTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine</td>
<td>Saquinavir</td>
<td>Nevirapine</td>
<td>Enfuvirtide</td>
<td>Maraviroc</td>
<td>Raltegravir</td>
</tr>
<tr>
<td>Didanosine</td>
<td>Ritonavir</td>
<td>Delavirdine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stavudine</td>
<td>Indinavir</td>
<td>Efavirenz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Nelfinavir</td>
<td>Etravirine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>Lopinavir/r</td>
<td>Rilpivirine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Atazanavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>Fosamprenavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Tipranavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Darunavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
WHAT ART REGIMEN TO START
### Table 5: Summary of first-line ART regimens for children younger than three years

<table>
<thead>
<tr>
<th>Preferred</th>
<th>(\text{ABC}^a) or (\text{AZT} + 3\text{TC} + \text{LPV/r}^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternative</td>
<td>(\text{ABC}^a) or (\text{AZT} + 3\text{TC} + \text{NVP})</td>
</tr>
<tr>
<td>Special circumstances</td>
<td>(\text{d}4\text{T}^c + 3\text{TC} + \text{LPV/r})</td>
</tr>
<tr>
<td></td>
<td>(\text{d}4\text{T}^c + 3\text{TC} + \text{NVP})</td>
</tr>
<tr>
<td></td>
<td>Children 3 to 10 years or Adolescents &lt;35 kg</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td><strong>Preferred</strong></td>
<td>ABC\textsuperscript{a} + 3TC + EFV</td>
</tr>
<tr>
<td><strong>Alternatives</strong></td>
<td>ABC + 3TC + NVP</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + NVP</td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC (or FTC) + EFV</td>
</tr>
<tr>
<td><strong>Special circumstances</strong></td>
<td>d4T\textsuperscript{b} + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>d4T\textsuperscript{b} + 3TC + NVP</td>
</tr>
</tbody>
</table>

\textsuperscript{a} If the child is weighing less than 25 kg, use ABC + 3TC + EFV. If the child is weighing more than 25 kg, use TDF + 3TC (or FTC) + EFV.

\textsuperscript{b} If the child is weighing less than 25 kg, use TDF + 3TC (or FTC) + NVP. If the child is weighing more than 25 kg, use ABC + 3TC + NVP.
IMPORTANT CLINICAL SIGNS OF ART FAILURE

- Lack of growth response to treatment
- Falling of the growth curve in children who show an initial growth response to therapy
- Loss of neuro-developmental milestones (regression)
- Recurrent oral thrush other OIs
## ART switching criteria

<table>
<thead>
<tr>
<th>Failure</th>
<th>Definition</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical failure</td>
<td>New or recurrent WHO stage 4 condition</td>
<td>Differentiate from IRIS; certain stage 3 conditions e.g., pulm TB, severe bacterial conditions may be due to treatment failure</td>
</tr>
<tr>
<td>Immunological failure</td>
<td>Fall of CD4 to baseline or below or 50% fall from on-treatment peak or persistent CD4 &lt; 100</td>
<td>Without concomitant infection to cause transient CD4 cell decrease</td>
</tr>
<tr>
<td>Virological failure</td>
<td>Plasma viral load &gt; 1000 copies/ml on two consecutive month viral load measurement with adherence support</td>
<td>Optimal VL threshold not determined</td>
</tr>
</tbody>
</table>
We Need Virological Monitoring

- VIROLOGICAL FAILURE
- IMMUNOLOGICAL FAILURE
- CLINICAL FAILURE
Fig. 7.1 Viral load testing strategies to detect or confirm treatment failure and switch ART regimen in adults, adolescents and children

Targeted viral load monitoring (suspected clinical or immunological failure)

Routine viral load monitoring (early detection of virological failure)

Test viral load

Viral load >1000 copies/ml

Evaluate for adherence concerns

Repeat viral load testing after 3–6 months

Viral load ≤1000 copies/ml

Maintain first-line therapy

Viral load >1000 copies/ml

Switch to second-line therapy
WHAT ART TO SWITCH TO
Second line ART regimen
# Table 7.21 Summary of recommended first- and second-line ART regimens for children (including adolescents)

<table>
<thead>
<tr>
<th>Children</th>
<th>First-line ART regimen</th>
<th>Second-line ART regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPV/r-based first-line regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger than 3 years</td>
<td>ABC + 3TC + LPV/r</td>
<td>No change(^a)</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + LPV/r</td>
<td></td>
</tr>
<tr>
<td>3 years and older</td>
<td>ABC + 3TC + LPV/r</td>
<td>AZT + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + LPV/r</td>
<td>ABC or TDF(^b) + 3TC + EFV</td>
</tr>
<tr>
<td>NNRTI-based first-line regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>ABC + 3TC + EFV (or NVP)</td>
<td>AZT + 3TC + LPV/r(^c)</td>
</tr>
<tr>
<td></td>
<td>TDF(^b) + 3TC (or FTC) + EFV (or NVP)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + EFV (or NVP)</td>
<td>ABC or TDF + 3TC(^c) (or FTC) + LPV/r(^c)</td>
</tr>
</tbody>
</table>

\(^a\) No change is recommended unless in the presence of advanced clinical disease progression or lack of adherence specifically because of poor palatability of LPV/r. In this case, switching to a second-line NVP-based regimen should be considered. Based on the recent approval of the use of EFV in children less than 3 years, an EFV-based regimen could be considered as an alternative. However, more data are needed to inform how best to use EFV in this population.

\(^b\) TDF may only be given to children >2 years.

\(^c\) ATV/r can be used as an alternative to LPV/r in children older than 6 years.
### Table 7.17 Summary of preferred second-line ARV regimens for adults, adolescents, pregnant women and children

<table>
<thead>
<tr>
<th>Second-line ART</th>
<th>Preferred regimens</th>
<th>Alternative regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If a NNRTI-based first-line regimen was used</td>
<td>ABC + 3TC + LPV/r&lt;sup&gt;b&lt;/sup&gt;</td>
<td>ABC + 3TC + LPV/r&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC (or FTC) + LPV/r&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>If a PI-based first-line regimen was used</td>
<td>No change from first-line regimen in use&lt;sup&gt;c&lt;/sup&gt;</td>
<td>AZT (or ABC) + 3TC + NVP</td>
</tr>
<tr>
<td>&lt;3 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 years to less than 10 years</td>
<td>AZT (or ABC) + 3TC + EFV</td>
<td>ABC (or TDF) + 3TC + NVP</td>
</tr>
</tbody>
</table>
Third Line Drugs for children

- Etravirine
- Darunavir
- Raltegravir
- Maraviroc
- Elvitegravir
- Dolutegravir
Challenges in ART regime

d4T be phased out

- Still used D4T is because of the problem of Anemia (late stage, severe OI, Malnutrition, malaria)
- d4T also remains important in the situation in which toxicity to AZT
- the duration of therapy with this drug should be limited to the shortest time possible.
Challenges in ART regime

LPV/r

- The current LPV/r syrup formulation has cold chain requirements until the point of dispensing.
- The syrup is unpalatable, with the potential for suboptimal adherence.
- The risk of metabolic complications among children who initiate LPV/r early in life is unknown.
- LPV/r is costly and administering this with TB treatment is complex.
Challenges in ART regime

ABC

- HLA-B*5701 genetic testing should be performed before initiating abacavir-based therapy because of severe hypersensitivity reaction
- the cost of ABC may be a significant barrier especially when combined with LPV/r.
- Definitive data on the comparative efficacy of ABC and AZT are expected from ongoing studies
Challenges in ART regime

**TDF**

- Limited pediatric experience
- Potential for bone and renal toxicity; bone toxicity appears to be more frequent in younger children.
- Numerous drug-drug interactions with other ARV agents including ddI, LPV/r, ATV, and TPV
HIV care Clinic (Mandalay children Hospital)
IHC (Mandalay Children hospital)

- Started in August 2005, same place with adult OPD
- NAP and great partner UNION as PPP
- In 2012 - move to 300 bedded Children Hospital, separate with adult OPD
- Starting from March 2014 – moved to 550 bedded Children Hospital.
- OPD Day - Monday and Wednesday Evening
- Average 30 -40 patients /OPD day
- At least 3 Pediatricians and 3 Coordinators attend the OPD
- ART and OI Drugs dispensation is handled by pharmacists and nurses
Background data from August 2005 Up to Dec/2015

- Total enrolment = 1401
- Ever started on ART = 997
- Total Active follow-up = 719
- Active follow-up on ART = 610
Age distribution among Active Follow Up

- **0-2 yr**: [VALUE] (19.9%)
- **2-5 yr**: [VALUE] (11.1%)
- **5-12 yr**: [VALUE] (6.3%)
- **>12 yr**: [VALUE] (62.7%)

Total patient 71
- <2 year: 45
- 2-5 year: 80
- 5-12 year: 451
- >12 year: 143
Age distribution among active follow up

- <2 year
- 2-5 year
- 5-12 year
- >12 year
Active Follow Up in 2015
New Enroll vs. Newly ART Initiation

Average Enrollment = 12/mth
Average ART initiation = 11/mth
Outcome of the patients on ART up to December 2015

- Active follow up on ART = 610
- Transfer out to other IHC program = 228 (37.3%)
- Death = 93 (15.2%)
- Defaulters = 67 (11%)
- Discharge = 20 (3.3%)
- Stopped ART = 6 (0.9%)
Defaulter analysis

Since program started
- Defaulter (on ART) = 118
- Patients who retrieved back to program = 51
- Still defaulted = 67

During 2015
- Defaulter (on ART) = 25
- Patients who retrieved back to program = 8
- Still defaulted = 17
1st line vs. 2nd line ART

- 1st Line: 90.7%
- 2nd Line: 9%

- 553 total
- 57 total
ART Regimen Distribution
As of December, 2015

- AZT+3TC +EFV: 38.0%
- AZT+3TC +NVP: 12.1%
- AZT+3TC +LPV/r: 13.9%
- ABC+3TC +EFV: 1.0%
- ABC+3TC +NVP: 0.3%
- ABC+3TC +LPV/r: 0.2%
- TDF+3TC +EFV: 0.3%
Care for Positive Children
Promotion of Adherence
Transitioning to adults

- There are many concerns of adolescent’s issues
- Self esteems/self control
- High risk behavior, alcohol/drugs
- Sex/STD, HIV transmission
- Reproductive right and birth control
- Educations/Schooling

- Work, carrier ...... LIFE
Thank You