Pediatrics in Myanmar

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M.B.,B.S M. Med.Sc
“Support needing populations through medical assistance and the transfer of knowledge to local medical practitioners.”

Our vision for the Medical Assistance & Medical Education (MAME) Programs
IHC (Mnadalay 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 patients /OPD day

• At least 3 Pediatricians and 3 Coordinators attend the OPD

• ART and OI Drugs dispensation is handled by pharmacists and nurses
Pediatrics ICU and Pediatrics OT
Total enrolled patients in MCH (2007 - June, 2014)
Total patients on regular follow up **MCH** (June, 2014)

- **Regular follow up with or with ART**
- **Regular follow up on ART**
Outcome of **MCH** (2007 -june,2014) Regardless of ART Status

- Total Patients  *(Total enrolled+ Transferred In)* = 1182
- Transfer Out = 189
- Death = 131
- Defaulted = 179
- Discharged = 13
- Active Follow up = 704
- Retention in Care = 75%
- % of Death among Total patient = ~10%
- % of Defaulter among Total patient = ~15%
  (among ART patient = 5.8%)
- Average Enrolment = 12/month
- Average ART initiation = 9/month
Age Distribution among patients attending IHC program of 550 bedded Children Hospital (June/2014)

Total no. of pt = 704

- 1-2 yr: 35 (5%)
- 2-5 yr: 80 (11.3%)
- 5-12 yr: 409 (57.7%)
- >12 yr: 180 (25%)

Series 1
2014 (January to December)

- New enrolled patient -145 children
- New ART initiation – 115 children
- Among 145 new patient 15 children were coinfected with TB at initial presentation and provide Anti –TB treatment first (10.3%)
Pediatrics HIV/AIDS Care and Management

- PMCT
- Antiretroviral therapy in children
- Management of OI
- HIV/ TB coinfection in children
- Challenges
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
What’s your zero?

Getting to Zero New Infection!!!
## 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 28wks + sdNVP +AZT/3TC 7days</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td>2010</td>
<td>Option A (AZT +infant NVP)</td>
<td>CD4 ≤350</td>
</tr>
<tr>
<td></td>
<td>Option B (triple ARVs)</td>
<td>CD4 ≤500</td>
</tr>
<tr>
<td></td>
<td>Option B or B + Moving to ART for all PW/BF</td>
<td></td>
</tr>
</tbody>
</table>

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

- **Mode of delivery**
  - NSVD (VL <1000cp/ml at the time of delivery) or ELSCS

- **Infant feeding mode**
  - Breast feeding or formula feeding
  - Avoid mixed feeding

- **Prophylaxis regimens for exposed infants**
  - All infants regardless of infant feeding mode – oral NVP for 6 weeks
Early Infant Diagnosis (EID)
HIVDNA PCR (DBS)
15/02/2012 to 31/03/2014
Total 127

- Detectable
- Undetectable

123

4
HIV diagnosis in <18 months with DNA PCR

- **HIV+ Pregnant woman**
  - HIV exposed infant (breastfed & non-breastfed)

1st HIV DNA PCR

- **Positive**
  - Repeat HIV DNA PCR to confirm
    - Repot HIV Positive

- **Negative**
  - Breastfed
    - 2nd PCR after 6-8 weeks of stopping breastfeeding
      - Repeat test & refer for follow up
        - Repot HIV Negative
  - Non-breastfed
    - 2nd PCR at 6 months to confirm
      - Repeat test & refer for follow up
      - Report HIV Negative
ART IN CHILDREN
3rd edition of guideline (2010)
## When to start

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

<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>
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<tr>
<td></td>
<td>Tipranavir</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Darunavir</td>
<td></td>
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</tr>
</tbody>
</table>
## What ART to start: age < 3 years

<table>
<thead>
<tr>
<th>Age group</th>
<th>Prior exposure to PMTCT ARV’s</th>
<th>2010 recommendations</th>
<th>2013 recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 months</td>
<td>Exposed</td>
<td>LPV/r + 2 NRTIs</td>
<td>LPV/r plus 2 NRTIs</td>
</tr>
<tr>
<td></td>
<td>Not Exposed</td>
<td></td>
<td>If LPV/r not available, NVP-based</td>
</tr>
<tr>
<td></td>
<td>Exposure unknown</td>
<td></td>
<td>Plus NRTI backbone:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• AZT or ABC + 3TC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• (d4T+3TC*)</td>
</tr>
<tr>
<td>12 to &lt;36 months</td>
<td>Regardless of exposure</td>
<td>NVP + 2 NRTIs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• AZT + 3TC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ABC + 3TC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• d4T + 3TC</td>
<td></td>
</tr>
</tbody>
</table>

• When HIV RNA monitoring is available, consider to substitute LPV/r with NNRTI after virological suppression is sustained (conditional, low quality)
Special circumstances may include situations where preferred or alternative regimens may not be available or suitable because of significant toxicities.

<table>
<thead>
<tr>
<th>Preferred regimens</th>
<th>ABC or AZT + 3TC + LPV/r³</th>
<th>ABC³ or AZT + 3TC + NVP³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternative regimens</td>
<td>d4T³ + 3TC + LPV/r</td>
<td>d4T³ + 3TC + NVP</td>
</tr>
<tr>
<td>Special circumstances</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## What to start in ≥ 3 years

<table>
<thead>
<tr>
<th>Age group</th>
<th>2010 recommendations</th>
<th>2013 recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-19 years</td>
<td>NVP or EFV plus 2 NRTIs in preferential order: AZT + 3TC ABC + 3TC d4T + 3TC TDF + FTC + EFV to be used as preferred regimen if HIV/HBV coinfection and &gt;12 years and &gt; 35 Kg</td>
<td>NNRTI</td>
</tr>
<tr>
<td>3-10 years</td>
<td>(Including &gt; 10 yrs who weighing &lt;35kg)</td>
<td>2NRTIs</td>
</tr>
<tr>
<td>10-19 years</td>
<td>(weighing ≥35 kg) (align with adults)</td>
<td>NNRTI</td>
</tr>
<tr>
<td>10-19 years</td>
<td>(weighing ≥35 kg) (align with adults)</td>
<td>2NRTIs</td>
</tr>
</tbody>
</table>
### Table 7.11 Summary of recommended first-line ART regimens for children and adolescents

<table>
<thead>
<tr>
<th></th>
<th>Children 3 years to less than 10 years and adolescents &lt;35 kg</th>
<th>Adolescents (10 to 19 years) ≥35 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred</strong></td>
<td>ABC&lt;sup&gt;a&lt;/sup&gt; + 3TC + EFV</td>
<td>TDF + 3TC (or FTC) + EFV&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Alternatives</strong></td>
<td>ABC + 3TC + NVP</td>
<td>AZT + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + EFV</td>
<td>AZT + 3TC + NVP</td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC (or FTC) + EFV</td>
<td>TDF + 3TC (or FTC) + NVP</td>
</tr>
<tr>
<td><strong>Special circumstances</strong></td>
<td>d4T&lt;sup&gt;b&lt;/sup&gt; + 3TC + EFV</td>
<td>ABC + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>d4T&lt;sup&gt;b&lt;/sup&gt; + 3TC + NVP</td>
<td>ABC + 3TC + NVP</td>
</tr>
</tbody>
</table>
Laboratory monitoring before and after initiating ART
Before initiation of ART

- Baseline investigation
- Hemogram
- LFT
- Creatinine
- RBS
- HBs Ag
- Anti-HCV
- CD4 count
- TB screening
After initiation of ART

- Hemogram, LFT, Creatinine
- CD4 3-6 monthly
- Viral Load only in cases of immunological failure
We Need Virological Monitoring

- VIROLOGICAL FAILURE
- IMMUNOLOGICAL FAILURE
- CLINICAL FAILURE
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><strong>LPV/r-based first-line regimen</strong></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><strong>NNRTI-based first-line regimen</strong></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 (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; TDF + 3TC (or FTC) + LPV/r&lt;sup&gt;b&lt;/sup&gt;</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>Yes</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>
1st Treatment @ 2nd line Treatment

- 1st Line: 498 (92%)
- 2nd Line: 43 (8%)
Patient Chart According to Regimen

MCH, OPD / Period – June/2014

- AZT+3TC+EFV: 26.5%
- AZT+3TC+NVP: 13.7%
- D4T+3TC+EFV: 12.6%
- D4T+3TC+NVP: 8.0%
- ABC+3TC+LPV/r: 0.9%
- TDF+3TC+EFV: 0.9%
- D4T+3TC+ABC: 0.4%
- AZT+3TC+LPV/r: 0.2%
- ABC+3TC+EFV: 0.2%
- ABC+3TC+NVP: 0.1%

Patient & Chart & According & to & Regimen & MCH, OPD & / Period – June/2014
Challenges in ART regime

**d4T be phased out**

- Still used D4T is because of the problem of Anemia (late stage, severe OI, Malnutrition, malaria)
- the duration of therapy with this drug should be limited to the shortest time possible.
- ABC
- Not provide HLA B5701 screening before initiation
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 LPV/r, ATV, and TPV
OI and Management

CPT – Cotrimoxazole prophylaxis therapy

- For PCP and toxoplasmosis infection and bacteria infection and malaria
- Give to all HIV exposed babies starting at 4-6 weeks after birth
  - <1 year
  - 1-5 year WHO stage 2,3,4
  - >5 year WHO stage 3,4 or CD4<350 cells /mm3
Challenges in Investigation and management of OI

- Limitation in diagnosis of OI
- Management of OI – limitation in available drugs for OI management
Challenges in Investigation and management of OI

Lab diagnosis of tuberculosis and M. avian complex disease in HIV positive patients

Tuberculosis

- Sputum or gastric lavage for AFB
- Culture
- Gene expert
- CXR- atypical
Challenges in Investigation and management of OI

- **MAC**

**Microscopy** – The presumptive diagnosis of MAC infection can be made quickly by demonstration of AFB in smears from tissue e.g. skin, bone marrow, lymph node, liver biopsy or buffy coat of blood in patients suggestive of MAC infection. Definite diagnosis still requires culture confirmation.

**Culture** – Isolation of MAC from blood or bone marrow cultures takes 2-6 weeks.
CMV retinitis
CMV retinitis is the most common opportunistic ocular infection in patients with AIDS
Progressive if left untreated
Potentially blinding disease
Asymptomatic – light flashing, floater, visual field loss
** limitation in treatment, out of reach of treatment for CMV retinitis**
** can save the life, but unfortunately cannot save the vision and more burden with preexisting HIV**
HIV and TB

- Acute respiratory symptoms - differential diagnosis of acute bacteria pneumonia, PCP and evaluate for coinfection with TB
- Chronic respiratory symptoms - Bronchiectasis and lung abscess
- Miliary TB
- TB meningitis
- TB effusion
- TB abdomen
- Spine involvement
- TB treatment regime for children with HIV
- Suspected or confirmed pulmonary TB and peripheral lymphadenopathy - 2 HRZE/4HR
- Suspected or confirmed TB meningitis or osteoarticular - 2 HRZE/10HR
Challenges in TB @ HIV

- TB is one of the most common opportunistic infections affecting children with HIV.
- Drug Interactions between anti-TB and ARV rifampicin and LPV/r or NVP

**co-treatment in children under three years is challenging**
Challenges in TB @ HIV

- Triple NRTI (AZT + 3TC + ABC)
- Substitute NVP for LPV/r, ensuring that dose is 200 mg/m2
- Continue LPV/r; consider adding RTV to achieve the full therapeutic dosed 1:1
IPT – Isoniazid Prophylactic Therapy

Children living with HIV who are more than 12 months of age who do not have poor weight gain, fever or current cough and have no contact with a TB case are unlikely to have active TB and should receive six months of IPT (10 mg/kg/day).
IPT – Isoniazid Prophylactic Therapy

In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive six months of IPT if the evaluation shows no TB disease.
Figure 2: Algorithm for TB screening in children more than one year of age and living with an HIV-infected person.

Children >12 months and living with HIV:

- Screen for TB with any one of the following symptoms:
  - Poor weight gain
  - Fever
  - Current cough
  - Contact history with a TB case

- HIV

Access for contraindications to IPT:

- Yes
- No

Tuberculosis

Investigation for TB and other diseases:

- TB
- Not TB
- Other diagnosis

Tuberculosis:

- Treat for TB
- Follow-up and consider IPT
- Other appropriate treatment and consider IPT

Screen for TB regularly at each encounter with a health worker or visit to a health facility.

1. All children and infants less than one year of age should be provided with IPT if they have a history of household contact with a TB case.
2. Poor weight gain is defined as reported weight loss or confirmed weight loss (>5%) since the last visit or growth curve flattening or very low weight (weight for age < -2z score) or underweight (weight for age < -3z score).
3. Contraindications include active acute or chronic hepatitis, symptoms of peripheral neuropathy, prior IPT and prior TB treatment.
case

- 9 months old boy was admitted for fever with severe respiratory distress
- History of hospitalization for 2 times at district hospital for similar problems
- Born by NSVD at home and give Breast feeding up to now
- Her mother is 25 years and it is her 2nd marriage
- 1st husband die due to ? HIV and 2 years later she got married again
- She never done VCCT & HIV testing
Case

- She has a problem of chronic cough with sputum production and L.O.A and L.O.W 2 months after delivery but took no treatment
- On examination
- GC- 1ll , weight < 3rd centile
- Oral thrush +
- fast breathing + CI+ periphery cyanosis+
- Anemic
- Lungs- VBS with course cerpitations
- Huge hepatosplenomegaly and generalised lymphadenopathy
Case

- Very severe Pneumonia with PEM? Bacteria? PCP? TB pneumonia

**Investigations**
- HIV ab test – mother + baby +
- CP--- Anemia
- CXR --- TB infection ,PCP
- T test negative
- ESR- 90
Case

- Blood culture- *Klebsiella pneumoniae*
- Contact tracing mother– Sputum for AFB ++
- CXR (mother) – TB
- CD 4 <15 %
- Viral load (baby)- 867,000 cp/ml
Case

- **Treatments**
- I /V Antibiotics
- Anti –TB -2HRZE/4HR
- Oral high dose cotrimoxazole 4 times/day
- Oral prednisolone
- Blood transfusion
- Nutritional support
- Nystatin for oral candidiasis
- ART – ABC/D4T/3TC ( 3 weeks after anti-TB)
Psychosocial Support
Care for Positive Children
Promotion of Adherence
Next Challenging Issues For The Grown-Up HIV-Infected Children

- Transitional care
- Adolescent problems
- Lifelong adherence
- Peer acceptance
- Future education and career
- Making own family
THANK YOU VERY MUCH
Thank you

For further information please contact:

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