Paediatric Antiretroviral Therapy

Dr Leon J. Levin
Head - Paediatric HIV Programmes
Right to Care
Differences between Adults and Children

- Viral Loads
- CD4 counts
- Response to therapy
- Pharmacokinetics
- Lack of Trial Data
- Adherence issues
- Drug formulations
- Taste issues
- Immune reconstitution
Viral Load in Adults

Plasma HIV RNA levels in Adults

Viral load no. copies/mL (log)
Viral load in Infants

Plasma HIV RNA levels in Infants

Viral load no. of copies/mL (log)

Months/Years

1 2 years 2 2.5 3
PACTG 338
Proportion of Children with undetectable HIV RNA Levels categorized by Baseline HIV RNA

Ritonavir containing arms

<table>
<thead>
<tr>
<th>Baseline HIV RNA (cps/ml)</th>
<th>WEEK 24</th>
<th>WEEK 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>400-1000</td>
<td>9/13 (69%)</td>
<td>9/13 (69%)</td>
</tr>
<tr>
<td>1000-10 000</td>
<td>21/46 (46%)</td>
<td>20/46 (44%)</td>
</tr>
<tr>
<td>10 000 –100 000</td>
<td>36/89 (40%)</td>
<td>28/89 (32%)</td>
</tr>
<tr>
<td>100 000-1000 000</td>
<td>9/37 (24%)</td>
<td>7/37 (19%)</td>
</tr>
</tbody>
</table>

S. A. Nachman et al JAMA 2000;283:492-498
### Monitoring HIV Infection and Therapy - CD4 counts

**HIV Paediatric Classification System:** Immune categories based on Age specific CD4 lymphocyte count and %

<table>
<thead>
<tr>
<th>Immune category</th>
<th>&lt;12months</th>
<th>1-5yrs</th>
<th>6-12yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1: No suppression</td>
<td>No./µL</td>
<td>(%)</td>
<td>No./µL</td>
</tr>
<tr>
<td></td>
<td>&gt; 1,500</td>
<td>(&gt;25%)</td>
<td>&gt; 1,000</td>
</tr>
<tr>
<td>Category 2: Moderate suppression</td>
<td>750-1,499</td>
<td>(15%-24%)</td>
<td>500-999</td>
</tr>
<tr>
<td>Category 3: Severe suppression</td>
<td>&lt;750</td>
<td>(&lt;15%)</td>
<td>&lt;500</td>
</tr>
</tbody>
</table>

*CDC 1994 Revised Classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43 (no.RR12):1-10.*
CD4 counts in children

- < 5 years  CD4 %
- ≥ 5 years  CD4 absolute count
Efficacy of HAART

Adults
43 - 75% undetectable Viral Loads

Children
25 - 40% undetectable Viral Loads
Efficacy of HAART

Adults
43 - 75% undetectable Viral Loads

Children
25 - 40% undetectable Viral Loads
Differences between Adults and Children

- Viral Loads
- CD4 counts
- Response to therapy
- Pharmacokinetics and Lack of Trial Data
- Adherence issues
- Drug formulations
- Taste issues
- Immune reconstitution
Differences between Adults and Children

- Viral Loads
- CD4 counts
- Response to therapy
- Pharmacokinetics
- Adherence issues
- Taste issues
- Drug formulations and dosing
- Immune reconstitution
Adherence

• Simplicity of Regimen
  – Twice or once daily dosing
  – Reduced nos of pills- FDC
  – No food restrictions
  – Medication all taken together
  – Volumes of liquids easy to measure
  – Twice daily does not = 12 hourly
Adherence

* • Simplicity of Regimen
  - Twice or once daily dosing
  - Reduced nos of pills- FDC
  - No food restrictions
  - Medication all taken together
  - Volumes of liquids easy to measure
  - Twice daily does not = 12 hourly

• Choose a regimen that is forgiving of poor adherence

• Education
  - Don’t start HAART on first visit
  - Educate whoever is giving the medication

• Taste issues

• Monitoring adherence
  - Pharmacy Records
  - Bring Meds to each visit
  - Treatment chart
Drug Formulations

• Solutions vs Tablets/capsules
  – Try change to capsules/tablets as soon as possible
  – EFV capsules- disperse contents in jam etc
  – EFV tablets- film coated. Cannot be crushed
  – d4T solution- big volumes
  – d4T caps can be dispersed in water – stable for 24 hours at room temp
  – Aluvia (can’t be crushed)

• Palatability
  – Kaletra, Ritonavir

• Storage in Fridge
  – d4T solution
  – Kaletra solution should be kept in fridge until dispensed. Thereafter stable at room temp for 42 days

• Dosing in relation to meals
  – Empty stomach- ddI, EFV
Drug Dosing

- Increase Doses as child grows
- Body Surface Area (BSA) and weight
- Dosing Chart
- BSA formula

$$\text{BSA} (m^2) = \sqrt{\frac{\text{weight (kg)} \times \text{height (cm)}}{3600}}$$
# Antiretroviral Drug Dosing Chart for Children 2012

Compiled by the Child and Adolescent Committee of the SA HIV Clinicians Society in collaboration with the Department of Health

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Abacavir (ABC)</th>
<th>Lamivudine (3TC)</th>
<th>Efavirenz (EFV)</th>
<th>Lopinavir/ritonavir (LPV/rvt)</th>
<th>Ritonavir boosting (RTV)</th>
<th>Stavudine (d4T)</th>
<th>Didanosine (ddI)</th>
<th>Nevirapine (NVP)</th>
<th>Zidovudine (AZT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>2ml bd</td>
<td>2ml bd</td>
<td>*1ml bd</td>
<td>1ml bd</td>
<td>7.5ml bd open 15mg capsule into 5ml water: give 2.5ml</td>
<td>0.6ml bd</td>
<td>100mg od: (2x50mg tabs)</td>
<td>125mg od (1x100mg + 2x25mg tabs)</td>
<td>8ml bd</td>
</tr>
<tr>
<td>3-4.9</td>
<td>3ml bd</td>
<td>3ml bd</td>
<td>*1.5ml bd</td>
<td>1.5ml bd</td>
<td>10mg bd open 20mg capsule into 5ml water: give 2.5ml</td>
<td>1.5ml bd</td>
<td>100mg od: (1x100mg + 3x25mg tabs)</td>
<td>8ml bd</td>
<td>12ml bd</td>
</tr>
<tr>
<td>5-5.9</td>
<td>4ml bd</td>
<td>4ml bd</td>
<td>*2ml bd</td>
<td>2ml bd</td>
<td>20mg bd open 5mg capsule into 5ml water: give 2.5ml</td>
<td>2ml bd</td>
<td>150mg od (1x100mg + 3x25mg tabs)</td>
<td>10ml bd</td>
<td>12ml bd</td>
</tr>
<tr>
<td>6-6.9</td>
<td>6ml bd</td>
<td>6ml bd</td>
<td>*3ml bd</td>
<td>3ml bd</td>
<td>250mg bd open 10mg capsule into 5ml water: give 2.5ml</td>
<td>3ml bd</td>
<td>200mg od (2x100mg + 3x25mg tabs) + Oil</td>
<td>1 cap bd OR 12ml od</td>
<td>20ml bd</td>
</tr>
<tr>
<td>7-7.9</td>
<td>8ml bd</td>
<td>8ml bd</td>
<td>*4ml bd</td>
<td>4ml bd</td>
<td>300mg bd open 20mg capsule into 5ml water: give 2.5ml</td>
<td>4ml bd</td>
<td>250mg od (1x100mg + 3x25mg tabs + Oil)</td>
<td>1 cap bd OR 15ml od</td>
<td>30ml bd</td>
</tr>
<tr>
<td>8-8.9</td>
<td>10ml bd</td>
<td>10ml bd</td>
<td>*5ml bd</td>
<td>5ml bd</td>
<td>400mg bd open 30mg capsule into 5ml water: give 2.5ml</td>
<td>5ml bd</td>
<td>300mg od (2x150mg + 3x25mg tabs + Oil)</td>
<td>1 cap bd OR 20ml bd</td>
<td>40ml bd</td>
</tr>
<tr>
<td>9-9.9</td>
<td>12ml bd</td>
<td>12ml bd</td>
<td>*6ml bd</td>
<td>6ml bd</td>
<td>600mg bd open 60mg capsule into 5ml water: give 2.5ml</td>
<td>6ml bd</td>
<td>400mg od (2x150mg + 3x25mg tabs + Oil)</td>
<td>2 cap bd OR 30ml bd</td>
<td>&gt;40 ml</td>
</tr>
</tbody>
</table>

* Consult with a clinician experienced in paediatric ARV prescribing for neonates (<28 days of age) and infants weighing <3kg

**Note:**
- Avoid PLV/rvt solution in any full term infant <14 days of age and any premature infant <14 days after their due date of delivery (40 weeks post conception) or obtain expert advice.
- Children 25-34.9kg may also be dosed with LPV/rvt 200/50mg adult tabs: 2 tabs am, 1 tab pm

### Cotrimoxazole Dose
- 3-4.9 kg: 2.5ml od
- 5-9.9 kg: 5ml od
- 10-13.9 kg: 10ml or 1 cap od
- 14-29.9 kg: 2 caps od

### Multivitamin Dose
- 3-4.9 kg: 2.5ml od
- 5-9.9 kg: 2.5ml od
- 10-13.9 kg: 5ml od
- 14-29.9 kg: 5ml od
- >30 kg: 10ml or 1 cap od
<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th><strong>Abacavir</strong> (ABC)</th>
<th><strong>Lamivudine</strong> (3TC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-10.9</td>
<td>Choose only one option:</td>
<td>Choose only one option:</td>
</tr>
<tr>
<td>11-13.9</td>
<td>6ml bd</td>
<td>12ml od</td>
</tr>
<tr>
<td>14-16.9</td>
<td>8ml bd</td>
<td>1 tab od OR 1.5ml od</td>
</tr>
<tr>
<td>17-19.9</td>
<td>10ml bd</td>
<td>20ml od</td>
</tr>
<tr>
<td>20-24.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-29.9</td>
<td>1x300mg tab bd</td>
<td>2x300mg tabx od</td>
</tr>
<tr>
<td>30-34.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-39.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Abacavir 60mg tablets

- Abacavir 60mg scored tablets
- Dispersible in water
- 1 tablet = 3ml of Abacavir solution
- Now for
  - 20-22.9kg give one 300mg tablet Abacavir + 1 60mg Abacavir tablet
  - 23-24.9kg give one 300mg tablet Abacavir + 2 60mg Abacavir tablet
Kivexa®, Dumiva®

- Fixed dose Combination tablet 3TC & Abacavir
- 300mg 3TC/600mg Abacavir per tablet
- Dose: 1 tablet once a day
- Very large tablet
- Use from 25kg if child can swallow big tablets
# Antiretroviral Drug Dosing Chart for Children 2013

Compiled by the Child and Adolescent Committee of the SA HIV Clinicians Society in collaboration with the Department of Health

<table>
<thead>
<tr>
<th>Drug</th>
<th>Target Dose</th>
<th>Available Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>abacavir (ABC)</td>
<td>8mg/kg TWICE daily OR a 10kg 16mg/kg ONCE daily</td>
<td>Sol. 25mg/ml Tabs 60mg (dispensable), 300mg (not scored), ABC/ITC 600/300mg</td>
</tr>
<tr>
<td>lamivudine (3TC)</td>
<td>4mg/kg TWICE daily OR a 10kg 8mg/kg ONCE daily</td>
<td>Sol. 10mg/ml Tabs 30/50mg, ABC/ITC 600/300mg</td>
</tr>
<tr>
<td>efavirenz (EFV)</td>
<td>By weight band ONCE daily</td>
<td>Sol. 50/200mg Adults Tab 50/200mg, Paeds Tabs 100/25mg</td>
</tr>
<tr>
<td>lopinavir/ritonavir (LPV/rtv)</td>
<td>300/75mg/m2 dose LPV/rtv PR TWICE daily</td>
<td>Sol. 1mg/kg/dose LPV/rtv PR TWICE daily</td>
</tr>
<tr>
<td>ritonavir boosting (RTV)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Target Dose</th>
<th>Available Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>stavudine (d4T)</td>
<td>1mg/kg/dose LPV/rtv PR TWICE daily</td>
<td>Tabs 25/50/100mg (dispensable in 30mg Caps 200mg EC)</td>
</tr>
<tr>
<td>tenofovir (TDF)</td>
<td>180-240mg/m2 dose ONCE daily (after once daily lead-in x 2 weeks)</td>
<td>Sol. 10mg/ml Tabs 200mg (scored)</td>
</tr>
<tr>
<td>nevirapine (NVP)</td>
<td>180-240mg/m2 dose TWICE daily</td>
<td>Sol. 10mg/ml Caps 100mg (dispensable in 100mg Caps 150/150mg)</td>
</tr>
<tr>
<td>zidovudine (AZT)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Current available tablet formulations of abacavir (except 60mg), efavirenz, LPV/rtv and AZT must be swallowed whole and NOT chewed, divided or crushed

Consult with a clinician experienced in paediatric ARV prescribing for neonates (<28 days of age) and infants weighing <3kg

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>3.4-9</th>
<th>5.9-9</th>
<th>10.12.9</th>
<th>14.29.9</th>
<th>&gt;30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotrimoxazole Dose</td>
<td>2.5ml od</td>
<td>2.5ml od</td>
<td>5ml od</td>
<td>5ml od</td>
<td>5ml od</td>
</tr>
<tr>
<td>Multivitamin Dose</td>
<td>2.5ml od</td>
<td>2.5ml od</td>
<td>5ml od</td>
<td>5ml od</td>
<td>10ml or 1 tab od</td>
</tr>
</tbody>
</table>

* Avoid LPV/rtv solution in any full term infant <14 days of age and any premature infant <14 days after their due date of delivery (40 weeks post conception) or obtain expert advice.

# Footnotes

- od = once a day (usually at night)
- bd = twice a day
- Children 25-34.9kg may also be dosed with LPV/rtv 200/50mg adult tabs: 2 tabs am, 1 tab pm
# AIDS 2002 - Impact of HAART on Morbidity and Mortality

**USA 81 children 1994-2000**

<table>
<thead>
<tr>
<th>YEAR</th>
<th>1994</th>
<th>2000</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAART</td>
<td>0%</td>
<td>89%</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Mean CD4</td>
<td>22.2%</td>
<td>31.5%</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Mean VL</td>
<td>4.41 log_{10}</td>
<td>3.16 log_{10}</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>% needing hospital</td>
<td>39%</td>
<td>9%</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>No of Hospitalizations</td>
<td>16.4 /1000 person-months</td>
<td>2.06/1000 person-months</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Mortality</td>
<td>15%</td>
<td>0%</td>
<td>P&lt;0.01</td>
</tr>
</tbody>
</table>
Finer Details
Eligibility for Antiretroviral Therapy for SA DOH

Clinical Criteria

<table>
<thead>
<tr>
<th>Age</th>
<th>All children</th>
<th>CD4 count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 5 years</td>
<td>All children</td>
<td>Any CD4 count</td>
</tr>
<tr>
<td>&gt;5 years-15 years</td>
<td>WHO stage III, IV</td>
<td>CD4 &lt;500 cells/μl</td>
</tr>
</tbody>
</table>

Social criteria

At least one identifiable caregiver who is able to supervise child or administer medication

Disclosure to another adult living in the same house is encouraged so that there is someone else who can assist with the child’s ART

Treatment of mother/caregiver/other family members
ART Eligibility for children

Fast Track (i.e. start ART within 7 days of being eligible)

- Children less than 1 year of age
- WHO clinical Stage 4
- MDR or XDR-TB
- CD4 Count < 200 cells/ul or < 15%
CHOOSING a REGIMEN

NRTI Backbone (2 NRTIs) + Protease Inhibitor (PI) or NNRTI
NRTI Backbone

FIRST LINE

• Popular choices

• D4T + 3TC (high incidence of lipodystrophy)

• AZT + 3TC (high incidence of early S/E. Locks you into twice daily regimen)

• 3TC+ABC

• AVOID d4T + ddI
Abacavir +3TC Backbone

• Can’t use Tenofovir routinely in children because of osteopaenia and nephrotoxicity
• Very good long term data from PENTA 5
• Spares Thymidine analogue for next regimen
• Both drugs select for the same résistance pathway(M184V)
• Abacavir should only be used for 1st line (Without Genotyping)
• (> 3 TAMS + M184V confers high level resistance)
• Hypersensitivity linked to HLA B*5701
• HLA B*5701 rare in Black population
• HSR 5% in whites, 0.2% in Blacks
Abacavir Hypersensitivity Reaction

- Therefore
- If you stop Abacavir for a suspected Hypersensitivity reaction, you can **NEVER** give the patient Abacavir again
Abacavir Hypersensitivity reaction

Table 1. Grouping of HSR Signs and Symptoms

<table>
<thead>
<tr>
<th>Signs and Symptoms of Abacavir HSR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
</tr>
<tr>
<td>Group 2</td>
</tr>
<tr>
<td>Group 3 (Gastrointestinal)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Group 4 (Constitutional)</td>
</tr>
<tr>
<td>Group 5 (Respiratory)</td>
</tr>
</tbody>
</table>

A sign or symptom in two or more groups
Abacavir Hypersensitivity Reaction

May or may not be accompanied by rash
Systemic symptoms, may be severe
Multisystem disorder
Usually in first 6 weeks of treatment
Gets visibly worse with each dose
Have been fatalities with rechallenge
Abacavir Hypersensitivity Reaction

- Hypersensitivity linked to HLA B*5701
- Blood test available in South Africa but not frequently requested
- Why not?

- HSR 5% in whites, 0.2% in Blacks

(Clin Pharmacol Ther 2012;91:734–8)
## Choice of 3rd drug in a triple drug regimen

<table>
<thead>
<tr>
<th>NNRTIs</th>
<th>Protease Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Potent Drug</strong></td>
<td><strong>Potent Drug</strong></td>
</tr>
<tr>
<td><strong>Good long term safety</strong></td>
<td><strong>Long term safety concerns eg hypercholesterolaemia, CHD</strong></td>
</tr>
<tr>
<td><strong>Early adverse events, rash, hepatitis, CNS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Don’t need refrigeration</strong></td>
<td><strong>Kaletra Needs refrigeration up to point of dispensing (Aluvia not)</strong></td>
</tr>
<tr>
<td><strong>Rapid Development of resistance-Poor genetic Barrier to resistance</strong></td>
<td><strong>Slow development of resistance</strong></td>
</tr>
</tbody>
</table>
No of mutations needed to develop high level Resistance

- **NNRTIs** – 1 mutation

- **Protease Inhibitors** - up to 8 mutations

- i.e PI’s are more forgiving than NNRTIs
IMPAACT P1060

- 452 children ages 2 to 35 months from India, Malawi, South Africa, Tanzania, Uganda, Zambia and Zimbabwe.
- Cohort 1: 164 children SD NVP at birth
- Cohort 2: 287 children who did not receive SD-NVP
- Children in each cohort were randomly selected to receive AZT/3TC/NVP or AZT/3TC/LPV/r
IMPAACT P1060

Cohort 1 (SD-NVP)

• 2009, interim review showed that the LVP/r-based regimen was more effective than the NVP-based regimen in children previously exposed to SD-NVP.

Cohort 2 (No SD-NVP)

• study defined failure occurred in :
  – 40.1% of children taking the NVP-based regimen
  – only 18.6% of children taking the LPV/r-based regimen

NEJM. 14 Oct 2010
New Regimens for DOH and Private Sector in SA

<table>
<thead>
<tr>
<th></th>
<th>0-3 years</th>
<th>&gt;3 years and &gt;10 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1st Line</strong></td>
<td>Abacavir (ABC) Lamivudine (3TC) Lopinavir/ritonavir (LPV/r)</td>
<td>Abacavir (ABC) Lamivudine (3TC) Efavirenz</td>
</tr>
</tbody>
</table>

(Children should remain on this regimen even after they turn 3 years or are > 10kg)
What about patients currently on d4T regimens

- Change d4T to ABC if Viral Load is undetectable (<50 copies/ml)
- If Viral load >1000 copies/ml manage as treatment failure
- If Viral load between 50 – 1000 copies/ml – consult with expert for advice
What about patients on ddI regimens

- Change from ddI to ABC
- Don’t have to have an undetectable Viral Load
Failed First line NNRTI based regimen discuss with expert before changing

<table>
<thead>
<tr>
<th>Failed First line NNRTI Based regimen</th>
<th>Recommended Second line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC + 3TC + EFV (or NVP)</td>
<td>AZT + 3TC + LPV/r</td>
</tr>
<tr>
<td>d4T + 3TC + EFV (or NVP)</td>
<td>AZT + ABC + LPV/r</td>
</tr>
</tbody>
</table>
## Second Line Regimen

### Failed First line Protease Inhibitor (PI) based regimen

<table>
<thead>
<tr>
<th>Failed First line PI Based regimen</th>
<th>Recommended Second line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC + 3TC + LPV/r</td>
<td></td>
</tr>
<tr>
<td>D4T + 3TC + LPV/r</td>
<td>Consult with expert for advice</td>
</tr>
<tr>
<td>Unboosted PI based regimen</td>
<td></td>
</tr>
</tbody>
</table>
# Third line Regimens

| Failing any 2\textsuperscript{nd} line regimen | Refer for specialist opinion – Regimen based on genotype resistance testing, expert opinion and supervised care. Access to third line ART will be managed centrally by the National Dept of Health. |
3rd Line Committee

- Khadija Jamaloodien
- JamalK@health.gov.za
- 3rd line committee will only authorize 3rd line drugs where there is PI resistance, as per Earnest study
Transition from paediatric ART regimens to adolescent/adult regimens

- Adolescents with an undetectable VL (< 50 copies/ml) and no side-effects on ABC + 3TC + EFV, can remain on the same regimen until the patient becomes eligible for the TDF + FTC + EFV (FDC) at 15 years old and weighing > 40kg.

- When an adolescent with an undetectable viral load (within the last 8 weeks) reaches 15 years and 40kg, a Creatinine Clearance (Cr Cl) and urine dipstix should be performed.

- If the Cr Cl is >80 and No proteinuria on urine dipstix, then the patient can be switched to the FDC (TDF + FTC + EFV).
TB Treatment and HAART

Potential Problems

• Increased Pill Burden
• Overlapping toxicities
• Immune Reconstitution Inflammatory Syndrome (IRIS)
• CYP3A4 induction by rifampicin
TB Treatment and HAART

OPTIONS

1) Delay ART for 2-4 weeks of TB treatment to prevent immune reconstitution disease.

2) Standard TB treatment together with ARV's compatible with rifampicin. 
   2 NRTI’s + :
   - EFV (children > 3yrs). 
   - Kaletra + additional ritonavir - Data scanty 
   - Double dose Kaletra - AVOID 
   - Full dose ritonavir – avoid if possible

3) Standard TB treatment with a triple NRTI regimen, e.g. ZDV/3TC/ABC. (less effective than other ART regimens

4) Use rifabutin instead of rifampicin (difficult to obtain and very expensive)
NB
If a child is on TB treatment and Kaletra/Alluvia they need to be boosted with Ritonavir
Side Effects

• The same side effects seen in adults occur in children.
  – Generally side effects are less common in children
  – Some are rare in children, e.g., Stavudine related peripheral neuropathy
  – Some are less common in children eg EFV CNS effects 14% vs > 50%
  – Some are more common, e.g. EFV-related rash
  – Some occur only in children, e.g. Tenofovir-related osteopaenia
LIPODYSTROPHY

3 Types of Lipodystrophy

Lipoatrophy - d4T, AZT

Visceral fat accumulation – All ARVs

Lipomastia - Efavirenz
Lipodystrophy
Lipodystrophy
Lipodystrophy
Lipodystrophy

THEREFORE SWITCH ALL PATIENTS FROM d4T to ABACAVIR NOW!

Also for lactic acidosis, peripheral neuropathy
Monitoring ART

• Toxicity Monitoring
  – Is it safe?

• Efficacy Monitoring
  – Is it working?
## Monitoring

<table>
<thead>
<tr>
<th>At initial Diagnosis of HIV</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verify HIV status</td>
<td>Ensure that national testing algorithm has been followed</td>
</tr>
<tr>
<td>Document weight, height, head circumference (&lt;2yrs) and development</td>
<td>To monitor growth and development + identify eligibility for ART</td>
</tr>
<tr>
<td>Screen for TB symptoms</td>
<td>To identify TB/HIV co-infected</td>
</tr>
<tr>
<td>WHO Clinical Staging</td>
<td>To determine if patient is eligible for ART</td>
</tr>
<tr>
<td>Do the CD4 count</td>
<td>Children &lt; 5 years – Baseline, DO NOT wait for CD4 count to start ART</td>
</tr>
<tr>
<td></td>
<td>Children ≥ 5 years - To determine eligibility for ART and start cotrimoxazole prophylaxis as per national guideline</td>
</tr>
<tr>
<td>Hb or FBC if available</td>
<td>To detect anaemia or neutropenia</td>
</tr>
</tbody>
</table>
## Monitoring

<table>
<thead>
<tr>
<th>At Routine Follow-Up Visits (non-eligible patients)</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Document weight, height, head circumference (&lt;2 years) and development</td>
<td>To monitor growth and development and to see if patient has become eligible for ART</td>
</tr>
<tr>
<td>Check that a CD4 count has been done in the last 6 months</td>
<td>To determine if patient has become eligible for ART</td>
</tr>
<tr>
<td>WHO Clinical Staging</td>
<td>To determine if patient has become eligible for ART</td>
</tr>
<tr>
<td>Screen for TB symptoms</td>
<td>To identify TB/HIV co-infection</td>
</tr>
</tbody>
</table>
## Monitoring

### At Initiation of ART (Baseline)

<table>
<thead>
<tr>
<th>Test</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb or FBC</td>
<td>If less than 8 g/dl start ART and refer for specialist opinion</td>
</tr>
<tr>
<td>CD4 count (if not performed in last 6 months)</td>
<td>Baseline assessment</td>
</tr>
<tr>
<td>Cholesterol + Triglyceride if on PI based regimen</td>
<td>Baseline assessment</td>
</tr>
<tr>
<td>Creatinine + urine dipstix if on TDF regimen</td>
<td>If abnormal refer for specialist opinion</td>
</tr>
<tr>
<td>ALT (if Jaundice or on TB treatment)</td>
<td>To assess for liver dysfunction</td>
</tr>
<tr>
<td>On ART</td>
<td>Purpose</td>
</tr>
<tr>
<td>-----------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Height, weight, head circumference (&lt;2yrs) and development</td>
<td>To monitor growth and development stages</td>
</tr>
<tr>
<td>Clinical assessment</td>
<td>To monitor response to ART &amp; exclude A/Es</td>
</tr>
<tr>
<td>CD4 at 1 year into ART, and then every 12 months</td>
<td>To monitor response to ART, stop cotrim prophylaxis as per national guideline</td>
</tr>
<tr>
<td>VL at month 6, 1 year into ART, then every 12 monthly</td>
<td>To monitor viral suppression response to ART</td>
</tr>
<tr>
<td></td>
<td>To identify treatment failure and to identify problems with adherence</td>
</tr>
</tbody>
</table>
Confirmatory testing

ALL positive PCR tests must be confirmed with a 2nd PCR test

In the new South African guidelines, a second PCR is done as a confirmatory test

Therefore in the new Guidelines paediatric patients will no longer have a baseline Viral Load
ART in Special Populations

Neonates

Adolescents
Neonates

• Get expert advice in Every case

Issues

• LPV/r cant be used until the baby is 14 days old (or 14 days after expected date of birth in prems)
• Abacavir not registered < 3 months
• No therapeutic dose of NVP in neonates
• NVP less effective in under 3 years
• Invariably will be NNRTI resistance due to PMTCT
HAART and Adolescence

- Adherence
- Disclosing Diagnosis
- Adolescent Groups
Email based case discussions
Approximately 1 case per month
Overseas opinions obtained once case fully discussed
Fill in circulating forms
Practical Resources

• SA HIV Clinicians Society
  – http://www.sahivsoc.org/
  – sahivsoc@gomail.co.za

• Right to Care Paediatric ARV Helpline
  – 0823526642

• Dr Leon Levin  leon.levin@righttocare.org

• SA HIV Clinicians Paeds Guidelines

• American Guidelines www.aidsinfo.nih.gov

• PENTA (European)
  Guidelines   www.ctu.mrc.ac.uk/PENTA

• WHO Guidelines  www.who.int
0713723550

Right to Care
Psychosocial Helpline

For social workers, counsellors and other healthcare workers needing advice on adolescent and paediatric psychosocial issues.
Call during office hours.
“Please call me” may be sent

Email: pshelp@righttocare.org

Right to Care
Paediatric ARV Helpline

For clinicians needing expert advice on all paediatric ART concerns
Call during office hours.
“Please call me” may be sent

Email: paedshelp@righttocare.org

0823526642
THANK YOU!