Key Paediatric Guideline Updates 2013

• No separate pre-ART literacy sessions
• **All** children under 5yo are eligible for ART
• <18mo ANY VL confirms infection
• d4T should be changed to ABC if the child is virologically suppressed
• Children exposed to NVP for 6wks or more who are older than 3yo should be started on 3TC/ABC/Kaletra
CHAIN OF SURVIVAL
EARLY ACCESS
EARLY CPR
EARLY DEFIBRILLATION
EARLY ADVANCED CARE
CHAIN OF SURVIVAL

EARLY ACCESS
EARLY CPR
EARLY DEFIBRILLATION
EARLY ADVANCED CARE

PCR
STAGING
HAART
When To Start?

- CHER Study

- Early Diagnosis
- Early Treatment
- Better Outcome
Does the child have confirmed HIV infection?

• Child < 18-mo
  – **Diagnosis** requires HIV DNA PCR test
  – **Confirmation** is with a VL of any amount (NEW)

• Child >18- mo
  – **Diagnosis** is with a rapid test
  – **Confirmation** is with a second different rapid test (or ELISA)
Which baseline labs are required?

- *VL* (<18-mo)
- CD4
- Hb or FBC if available
- Cr + urine dip if planning to use TDF
- ALT if jaundiced or on TB treatment

**NB:** do not delay HAART initiation for baseline lab results
Is the child eligible for HAART?

<5 years

- All HIV infected children
- Regardless of WHO staging and CD4 count

>5 years

- Stage III or IV
- CD4 count <350
Who qualifies for fast track initiation?

Fast track: start HAART within 7 days

- Infants < 1 year of age
- CD4 Count < 200 cells/ul or < 15%
- WHO stage 4
- MDR or XDR TB
What is the baseline assessment?

- Weight, height, head circumference (<2yo)
- Developmental screen
- Screen for TB disease and exposure
- WHO Clinical Staging
- Counsel in regard to HIV readiness – do this on the same day. **NB:** do not delay HAART for counselling, do them concurrently
What is the TB screen for children?

- **TB Exposure**
- **Cough** (2 weeks)
- **Fever** (2 weeks)
- **Night sweats** (drenching)
- **Weight** loss or poor weight gain
- **Malaise** and fatigue
Staging in Children

Staging helps to determine disease progression.
1. WHO Clinical Staging
   - Relies on history and physical exam
2. Immunologic
   - Relies primarily on CD4 ct
   - When CD4 ct is low the VL and OI risk is high

NB: In children less than 5-yo staging does not determine whether they qualify for HAART.
# WHO Clinical Staging

<table>
<thead>
<tr>
<th>STAGE 1</th>
<th>STAGE 2</th>
<th>STAGE 3</th>
<th>STAGE 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>Unexplained persistent enlarged liver and/or spleen</td>
<td>Moderate unexplained malnutrition (low weight) not responding to standard therapy</td>
<td>Unexplained SEVERE MALNUTRITION not responding to standard therapy</td>
</tr>
<tr>
<td>Persistent generalised lymphadenopathy</td>
<td>Unexplained persistent enlarged parotid</td>
<td>Oral thrush (outside neonatal period)</td>
<td>Oesophageal thrush</td>
</tr>
<tr>
<td></td>
<td>Angular cheilitis</td>
<td>Oral hairy leukoplakia</td>
<td>Herpes simplex ulceration for one month or more</td>
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<tr>
<td></td>
<td>Minor mucocutaneous conditions (e.g. chronic dermatitis, fungal nail infections or warts (molluscum contagiosum))</td>
<td>The following conditions if unexplained and if not responding to standard treatment</td>
<td>Severe multiple or recurrent bacterial infections, two or more episodes in a year (not including pneumonia)</td>
</tr>
<tr>
<td></td>
<td>Recurrent or chronic respiratory tract infections (sinusitis, ear infection, pharyngitis, tonsillitis)</td>
<td>- Diarrhoea for 14 days or more</td>
<td>Pneumocystis pneumonia (PCP)</td>
</tr>
<tr>
<td></td>
<td>Herpes zoster</td>
<td>- Fever for one month or more</td>
<td>Kaposi sarcoma</td>
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<tr>
<td></td>
<td>Recurrent oral ulcerations</td>
<td>- Anaemia (Hb &lt; 8 g/dL) for one month or more</td>
<td>Extrapulmonary TB</td>
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<tr>
<td></td>
<td></td>
<td>- Neutropenia (&lt; $500/mm^3$) for one month</td>
<td>Toxoplasma</td>
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<td>- Thrombocytopenia (platelets &lt; 50,000/mm$^3$) for one month or more</td>
<td>Cryptococcal meningitis</td>
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<tr>
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<td></td>
<td>Recurrent severe bacterial pneumonia</td>
<td>HIV encephalopathy</td>
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<td></td>
<td>Pulmonary TB</td>
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<tr>
<td></td>
<td></td>
<td>TB lymphadenopathy</td>
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<tr>
<td></td>
<td></td>
<td>Symptomatic LIP*</td>
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<tr>
<td></td>
<td></td>
<td>Acute necrotising ulcerative gingivitis/periodontitis</td>
<td></td>
</tr>
</tbody>
</table>
WHO Clinical Staging

**WHO Stage 2:** HIV associated papular pruritic eruption
**WHO Clinical Staging**

**WHO Stage 2:** Parotid enlargement – unexplained, persistent.
Often associated with LIP
Usually painless and bilateral
May resolve and recur
Z-score less than -2 is WHO Stage 3.
Z-score less than -3 is WHO Stage 4.
Must not be caused by poor/inadequate feeding and must not respond to standard care.
WHO Clinical Staging

**WHO Stage 2:** Extensive wart virus infection (HPV)
RX: HAART, tincture of time, Podophyllin, surgery, laser therapy, cryotherapy
WHO Clinical Staging

Hepatomegaly

WHO Stage 2
Enlarged liver and/or spleen without obvious cause.

Splenomegaly
WHO Clinical Staging
WHO Clinical Staging

WHO Stage 2: Herpes Zoster/shingles
- Reactivation of VZV
- Neuralgia
- Grouped vesicular lesions, ulcers
- Herpes keratitis (eye)
- Do not cross the midline
- RX Acyclovir within 72hrs preferable
WHO Clinical Staging

• **WHO Stage 4: PCJ (PCP)**
  – High morbidity and mortality, especially in infants
  – Largely prevented by Bactrim prophylaxis
  – Cyanosis, tachypnea, dyspnea, fever, chest indrawing
  – Auscultation often unremarkable as compared to clinical picture
  – CXR: bilateral perihilar diffuse infiltrates
  – RX: HD Bactrim +/- steroid
WHO Clinical Staging

WHO Stage IV: Kaposi Sarcoma

Courtesy of Carrie Kovarik, M.D.

Courtesy of Carrie Kovarik, M.D. and Jeremy Kampp, M.D.
WHO Clinical Staging

• Vascular neoplasm associated with HHV8
• Skin or oropharynx but may be disseminated and involve any organ
• Pink, purple, red, brown lesions
• Initially flat but may develop into patches, papules, plaques, nodules tumors
• Clinical diagnosis, may be confirmed by biopsy
• Can be associated with IRIS
WHO Clinical Staging

- **WHO Stage 4**: HIV Encephalopathy
- At least 2 of the following progressing over at least 2 months with no other cause:
  - Failure to attain or loss of milestones/intellectual ability
  - Progressive impaired brain growth
  - Acquired symmetric motor deficit accompanied by paresis, pathological reflexes, ataxia, gait disturbances
- **HAART and PT/OT help**
WHO Clinical Staging

**WHO Stage 3: “Symptomatic LIP”**

- CXR – bilateral, diffuse, reticulonodular infiltrates with mediastinal LAD
- Caused by lymphoid cell proliferation in lungs and organs
- Symptoms - cough, tachypnea, low O2 sats, exercise intolerance
- Treatment – antibiotics for infections, bronchodilators, oral steroids
- Difficult to differentiate from TB.
Stage 3: Oral Thrush

- Suggestive of HIV outside of 6-8 weeks of life
- Qualifies children less than 15yo for HAART initiation
- Associated with progression of HIV disease
- Median time of survival between diagnosis and death is 3.4 years with no intervention in children
- Treatment: HAART, topical and systemic antifungals is recommended
WHO Clinical Staging

- **Stage 3: Persistent Diarrhea** – >14 days
- 3+ loose stools/day
- Associated with an **11-fold** increased risk of death
- Qualifies children <15yo for HAART: ask about this during history, qualifies for HAART
What have we done so far?

- Make the diagnosis
- Start HAART early!
- Confirm the diagnosis
- Send BL labs and determine eligibility
- Perform BL assessment
- Stage clinically and immunologically
# What are the Paeds Regimens?

<table>
<thead>
<tr>
<th>First Line Regimen</th>
<th>Details</th>
</tr>
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<tbody>
<tr>
<td>All infants and children under 3 years (or &lt; 10kg)</td>
<td>ABC + 3TC + LPV/r</td>
</tr>
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<td>Children ≥ 3 years (and ≥ 10kg)</td>
<td>ABC + 3TC + EFV</td>
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</table>
| Currently on d4T-based regimen                                                     | Change d4T to ABC if Viral Load is undetectable.  
If Viral load >1000 copies/ml manage as treatment failure.  
If Viral load between 50 – 1000 copies/ml – consult with expert for advise |

∞ Children ≥ 3 years and exposed to NVP for 6 weeks or longer (PMTCT) should be initiated on ABC + 3TC + LPV/r
### First Line Regimen

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∞ Children ≥ 3 years and exposed to NVP for 6 weeks or longer (PMTCT) should be initiated on ABC + 3TC + LPV/r

- **Tastes horrible!!**
- **Monitor Chol/Trig annually**
- **NB: double dose when on TB Rx or add Ritonavir**
- **This regimen can be daily dosed**
# What are the Paeds Regimens?

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∞ Children ≥ 3 years and exposed to NVP for 6 weeks or longer (PMTCT) should be initiated on ABC + 3TC + LPV/r

NEVER change one drug in a failing regimen
Can be daily dosed (also ddl).

Double-dose if on TB rx or add Ritonavir.
What factors influence adherence?

- Adolescence
- Drug side-effects
- Drug palatability
- Chemist error
- Drug stock-outs
- Social issues
- Mental health
- Holiday travel
- Disclosure not done
- Vulnerable child
- High pill burden
- BD dosing
When should ARVs be changed?

Toxicity/Adverse Events
- Short-term side-effects
- Long-term side-effects

Drug interactions

Treatment failure
- Clinical
- Virological
- Immunological
## How do I monitor treatment response?

<table>
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<tr>
<th>On ART</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<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 and exclude adverse effects</td>
</tr>
<tr>
<td>CD4 at 1 year into ART, and then every 12 months</td>
<td>To monitor response to ART, stop cotrimoxazole prophylaxis as per national guideline</td>
</tr>
<tr>
<td>VL at month 6, 1 year into ART, then every 6 monthly in children &lt; 5 years / 12 monthly in children 5 years to 15 years</td>
<td>To monitor viral suppression response to ART To identify treatment failure and to identify problems with adherence</td>
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</tbody>
</table>
# How do I monitor treatment response?

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<th>Purpose</th>
</tr>
</thead>
<tbody>
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<td>Hb or FBC at month 1, 2, 3 and then annually if on AZT</td>
<td>To identify AZT-related anaemia</td>
</tr>
<tr>
<td>Cholesterol + Triglyceride at 1 year and then every 12 months if on PI based regimen</td>
<td>To monitor for PI-related metabolic side-effects</td>
</tr>
<tr>
<td>Clinical drug-related adverse events</td>
<td>To identify drug-related adverse events</td>
</tr>
<tr>
<td></td>
<td>If develops jaundice or rash on EFV or NVP do</td>
</tr>
<tr>
<td></td>
<td>Liver function test and refer to specialist</td>
</tr>
</tbody>
</table>
Common Side-Effects

- NRTIs: GIT, HA, lactic acidosis with hepatic steatosis and lipodystrophy (esp. d4T)
- AZT: anaemia and neutropenia
- ddI: pancreatitis
- d4T: lipodystrophy, PN, LA, hepatic steatosis
Lipodystrophy

- NB: Don’t only look at the face!
- Thin and muscular arms and legs with prominent muscles and veins
- Thin face and buttocks
- Enlarged abdomen
- Enlarged breast and buffalo hump may be seen after puberty
**Lipodystrophy**

- Most commonly caused by d4T, ddI and less commonly AZT and can cause life-long stigma and poor adherence
- Caregiver may notice changes
- Increases the risk of heart disease and diabetes in future
- Monitor glucose, chol, TG annually
- TREATMENT: Change most likely drug ASAP if VL is lower than detectable levels. For example, change d4T to ABC or TDF based on child’s age and weight. **Never change only one ARV if VL is >400!**
Common Side-Effects: Kaletra/Aluvia

- Kaletra
  - Tastes like battery acid
  - GIT – N/V/D, **hyperlipidemia**, increased risk for MI

- Aluvia
  - Many older children do not tolerate the 200/50 but do tolerate the 100/25
Common Side-Effects: ABC

- Usually 1\textsuperscript{st} 2-6 wks (90%)
- >>in Caucasians with HLA-B*5701
- Dx – 2+ symptoms:
  - Fever (78%)
  - Rash (66%) - +/- itching
  - GIT (46%)
  - Constitutional- (46%)
  - Respiratory (6%)
- Symptoms usually worsen after taking the medicine
- NEVER re-challenge with ABC after this reaction - may be fatal
Common Side-Effects: NNRTIs

• Rash: mild to life-threatening
• Low genetic barrier to resistance
• NVP- potentially fatal skin and liver hypersensitivity reaction
• EFV: dreams, decreased concentration and exacerbations of psyche disorders such as depression and psychosis - usually resolve and better if taken on empty stomach b/c decreases absorption of EFV.
What is this rash?
* Associated with NVP, Bactrim, EFV, Lop/rit in that order
* Minor skin rash associated with NNRTIs does not involve the eyes or mouth
* Can be fatal and progress to TEN if not diagnosed early
What is the care plan for children who do not qualify for HAART?

• Review 3 monthly
  – WHO Clinical Stage (largely from history)
  – Screen for TB, give IPT
  – Check weight, height, head circumference
  – Check CD4 6 monthly
What about Children on d4T?

- d4T is associated with many serious side-effects such as PN, LD, LA, hepatic steatosis
- Change from d4T to ABC or AZT or TDF in children who are virologically suppressed
- **DO NOT** change one drug in a patient with a VL > 400

Dr. Aaron Motsoaledi
Minister of Health 2009 – 2019
Champion in the fight against HIV in South Africa
TDF and FDC in Adolescents

TDF 300 mg daily
- ≥15 years-old
- > 35kg
- > Tanner stage 2
- eGFR is ≥80

FDC = TDF, FTC, EFV
- >40kg (EFV) + TDF rules
What about TB co-infection?

Key points to remember:

• If TB treatment started first then can start HAART in 2 weeks

• If on Kaletra/Aluvia then remember to double-dose this drug or add Ritonavir if available
What have we done so far?

- Reviewed paeds regimens
- dd-Kaletra & Aluvia or add Ritonavir if on TB rx
- DO NOT change one drug if the VL is >400
- Daily dose ARVs if possible
- Get eligible kids off d4T
- Monitoring labs
- Common ARV side-effects
- Wellness care for children
That's Ayoba!
Case SM

- 10 month old girl:
  - 3 admissions for chest infections
  - Milestones delayed-sat 8 months
  - Oral thrush, hepatosplenomegaly, generalized lymphadenopathy
  - Weight = 7.9kg  3\textsuperscript{rd} centile, height = 71cm 10\textsuperscript{th} centile
  - CD4 count = 166 (6%), VL = 295 000 copies/ml

What treatment would you institute?
SA Guidelines (1st line)

<3yrs
ABC+3TC+Kaletra

>3yrs
ABC+3TC+Efavirenz
1 month after starting ART
After 1 month of treatment an enlarged right axillary lymph node is noticed

What is the diagnosis?
What investigations should you do?
How would you manage this case?
Case KL

• 2008:

10 year old boy:
  – WHO Stage IV (cryptococcal sepsis);
  – CD4% = 1.64% (65), VL > 750 000
  – LIP + cor pulmonale, 6 months PTB Rx completed x 2 months.
  – Started on HAART (3TC, d4T, EFV)

2012: 14 years
  – Much healthier, happier child.
  – CD4% = 11.5% (404), VL < 25
  – “Skinny” arms and legs
  – Granny reported abdominal distension: Abdo sonar no
After 4 years of HAART
Case KL – cont...

• What is the diagnosis?
• Do you want to do any further investigations?
• How should he be managed further?
Case SM

• Presented to clinic in April 2008
• Mom recently demised of HIV related disease
• SM tested HIV+ at the clinic
• Started on TB treatment
• Clinically:
  - Underweight for age
  - Generalised LAD; HSM
  - WHO stage 3
• CD4 203 (16%) VL 15 000
• FBC/ALT normal
SM continued

• Did very well on ART (D4T/3TC/EFV)
• Good adherence
• Completed TB treatment
• Virally suppressed at 6 months
• Increasing CD4 and % (Cotrimoxazole stopped)
• Developed lipodystrophy in 2010 (gynaecomastia, peripheral wasting)
• Changed from D4T to ABC
• Well until 2013
In July 2013

- CD4 count 834 (25%) VL LDL
- Changed from EFV to NVP
- Presented 3 weeks later......
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR</td>
<td>1.65</td>
</tr>
<tr>
<td>PTT</td>
<td>12.9</td>
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<tr>
<td>ESR</td>
<td>4.9</td>
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<tr>
<td>CRP</td>
<td>8.9</td>
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<td>K</td>
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<td>Cl</td>
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<td>CO₂</td>
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<td>Urea</td>
<td>0.93</td>
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<td>Creat</td>
<td>1.28</td>
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<td>Mg</td>
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<td>Phos</td>
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<td>Total bili</td>
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<td>Dir bili</td>
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<td>Total prot</td>
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<td>Albumin</td>
<td>4.3</td>
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<td>ALP</td>
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<td>GGT</td>
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<td>ALT</td>
<td>80</td>
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<tr>
<td>AST</td>
<td>95</td>
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<table>
<thead>
<tr>
<th>Parameter</th>
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<tbody>
<tr>
<td>Glucose</td>
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<tr>
<td>HbA1c</td>
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<td>LDH</td>
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<td>Uric acid</td>
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</tbody>
</table>
Diagnosis?

- Necrotic targetoid papules/plaques
- Blistering neck
- Urethritis
- Conjunctivitis

- Stevens Johnson Syndrome
- ? Drug responsible
Management...

- ART stopped
- Admitted for supportive care
- IVI fluids
- Analgesia
- Prednisone
- Chloromex
- Bactroban

What should we do about his ART???
Thank you