South to South
Tuberculosis in HIV infected Children
Epidemiology of TB and HIV

TB Prevalence rate

100 – 299/100 000

>300/100 000

HIV prevalence (%) in adults in Africa, 2005

10.0%–<20.0%
5.0%–<10.0%
1.0%–<5.0%
<1.0%
Epidemiological and pathogenesis considerations of pediatric tuberculosis

- Spread through droplet infection
- Adult act as the maintenance host
- Children are the spill over host
- Infection depends on
  - Exposure
  - Vulnerability
- The majority of disease is pauci-bacilary and pulmonary in nature
- HIV and poverty are important drivers of the tuberculosis epidemic
- TB may accelerate HIV progression
Epidemiological and pathogenesis considerations of pediatric tuberculosis cont.

- Infection may lead to
  - Latent infection
    - Can be treated with if identified
  - Disease
    - The risk to develop disease is influenced by the age, immune function of the child and the time since infection
- Pathology is diverse and includes intra and extra thoracic disease
The risk of developing disease is related to age.
Time after infection as a determinant of symptom profile

- Phase of disease
- I  Hypersensitivity
- II  Miliary TB and TB Meningitis
- III  Lymph node disease / Pleural effusion
- IV  Adult-type disease
Know The Scenario: Time-related Risk for Disease Phase and Symptom Profile

Phase of disease
I  Hypersensitivity
II  Miliary TB and TB Meningitis
III Lymph node disease / Pleural effusion
IV  Adult-type disease

Timeline

Infection Months Years
0       1        2        3        4        6        8        10 12         2         3

Courtesy of Prof BJ Marais
Considerations for HIV infected children

- Dual pandemic in sub-Saharan Africa
- Important cause of acute and chronic pneumonia in HIV infected children
- Immune decline leads to reactivation of latent disease
- High TB burden leads to re-infection
- Important cause of mortality
- Zar et al reported rates of 23.4/100 children/year in Cape Townian children not receiving INH preventative therapy
Age Related Clinical Presentation in Immune Compromised Children

- HIV-infected children reflect disease profile similar to that seen in young children, irrespective of age.
- Most common manifestations are hilar adenopathy, miliary disease, and complicated Ghon focus
## Risk of Developing TB Following Primary TB Infection

<table>
<thead>
<tr>
<th>HIV-uninfected</th>
<th>HIV-infected</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children</strong></td>
<td><strong>Children</strong></td>
</tr>
<tr>
<td>Within 1yr of infection</td>
<td>Not restricted to first yr</td>
</tr>
<tr>
<td>&lt;2yrs</td>
<td>All ages</td>
</tr>
<tr>
<td>20-40%</td>
<td>high-risk</td>
</tr>
<tr>
<td>&gt;2yrs</td>
<td></td>
</tr>
<tr>
<td>5-10%</td>
<td></td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td><strong>Adults</strong></td>
</tr>
<tr>
<td>Lifetime risk</td>
<td>Annual risk</td>
</tr>
<tr>
<td>5-10%</td>
<td>5-10%</td>
</tr>
</tbody>
</table>
Preventing TB – BCG Vaccination

• General observations
  • Does not prevent pulmonary tuberculosis
  • Shown to prevent miliary tuberculosis and TB meningitis in HIV negative children

• In HIV infected children
  • Has never been shown to prevent any form of TB in HIV infected children
  • Current recommendations are to vaccinated all children at birth. At this stage infection status is not known
  • Symptomatic unvaccinated children should not be vaccinated
Preventing TB – BCG Vaccination cont.

- Vaccine Adverse events include
  - Local disease
  - Regional disease
  - Distant disease
  - IRIS
  - All adverse events should be reported to the EPI-surveillance programs.
  - Expert should be consulted regarding appropriate management of distant disease as well as complicated regional disease and IRIS
  - Local disease requires no treatment
Preventing TB – Chemoprophylaxis for children with a contact or with positive TST and no TB

• Preventative therapy for children with a TB contact
• The national program allows for chemoprophylaxis to be used in all children < 5 years with a sputum smear positive household contact.
• This should be extended to include all HIV infected children at any age as well as smear negative culture positive household contacts
• Prevention for HIV infected children found to be TST positive but assessed not to have TB
• All TST positive children thought not to have disease should receive prevention
Which drugs should be used

- INH for 6 months
- INH and Rifampicin for 3 months can be used according to the TB program, however using this in children on HAART or about to initiate therapy is not recommended due to the drug interactions between rifampicin and antiretroviral drugs
Routine Preventative therapy INH preventive therapy

Routine Preventative therapy (IPT)
• INH preventive therapy has been shown to prevent TB in HIV infected adults and this is part of the WHO recommendation for management of HIV infected adults
• South African data from Zar et al suggest that this intervention could:
  • Reduce the incidence of TB by 70%
  • Reduce all cause mortality by 50%
• Currently there is no recommendations regarding routine IPT to all HIV infected children although is thought to be beneficial
Routine Preventative therapy INH
preventive therapy

Unresolved issues are:
• What is the role of IPT for children on HAART
• Would routine IPT increase primary INH resistance in the community
• What is the treatment strategy that should be used for children developing TB whilst in IPT
• What are the programmatic implications
Preventing TB – HAART

- Timely initiation of HAART
- Adult data suggests that HAART will reduce TB in HIV infected individuals but that the risk is still more than that of the community.
- The same has not been proven for children, but is likely to be true
Features of TB in HIV infected children

• Primary TB infection progresses more rapidly to active disease

Presentation:
• More likely to be atypical
• Greater number of extrapulmonary manifestations
• Increased risk of relapse and treatment failure
• Multi-drug resistance is thought to be more common
History

- Overlapping in co-infected children
- High index of suspicion
- No scoring system successful in co-infected children
• Contact history important and be sought at every clinical contact, remember that:
  • HIV infected adults often smear negative
  • cough, weight loss, fever >3 week are indicators if TB in HIV infected adults
  • Remember to ask about the regimen as well as treatment adherence in the contact
• Asking for new symptoms or exacerbation of old
Clinical assessment

• General assessment
  • Febrile
  • Asses the road to health card or percentile chart for lack of appropriate weigh gain / weight loss

• Pulmonary
  • Dullness on percussion- generally unilateral
  • Chest pain and/or large airway obstruction
Clinical assessment cont.

- Extra-Pulmonary
  - New organomegaly
  - New Abdominal distention
  - New Enlarged, non-tender lymph nodes (> 1.5x1.5 cm)
  - Symptomatic meningitis including headaches, CNS symptoms and/or fever
  - Swelling and/or growth of bone or joint including spine
Using the tuberculin skin test

• Positive test - infection, not necessarily active disease
• Non-reactive test does not exclude infection or disease
  • Anergy- 10% normal children
• Interpretation complicated by exposure to
  • environmental mycobacteria
  • BCG
  • HIV
Using the tuberculin skin test cont.

- Interpretation adjust for HIV status
  - Considered positive if $\geq 5$mm
  - This is based on assumption and no/little data
- Interestingly Zar et al found reduced mortality in skin test positive children
  - This is probably a reflection of immune status
Using culture

- Culture remains the gold standard
  - Should attempt to culture all children investigated for TB
  - No need to wait for result before starting treatment in probable TB cases
  - Gastric washing can be performed in the community
  - Sputum can be obtained from older children
  - Induced sputum currently under investigation
  - If possible also obtain speciation and resistance testing

- Problems with culture
  - Takes time to get result
  - Negative cultures do not exclude TB
Using immunological diagnosis

- All the immune diagnostic methods currently available require further validation for children and specifically for HIV infected children
- These tests are costly and not accessible to all
Intra-Thoracic Spectrum of TB in Children

- Ghon focus
- Lymph node disease
- Disseminated (miliary) disease
- Pleural/pericardial disease
  - Pleural tap
- Adult-type disease
Remember

• Jeena et al found that in HIV infection TB may present with acute pneumonia in up to 43% of cases
• Abnormalities on CXR is common in HIV infected children with/without TB
• Cavitations may be more common in HIV infected children
• Bi-lateral or disseminated findings are common
• Hilar and mediastinal adenopathy may be part of TB or HIV associated lung disease
Ghon focus
Complicated Ghon focus
Node disease
Lymph node disease - Lateral
Lymph node complications

- Obstruction
- Ball valve
- Herniation into the lumen with bronchial spread
Complicated lymph node disease

Expansible pneumonia with cavity

Narrow bronchus
Expansible TB pneumonia
Pleural effusion
Disseminated (miliary) disease
Adult-type disease
Extra Thoracic disease

- TB adenitis
- TB Meningitis
- Abdominal Tuberculosis

Other (Rare)
- ENT: Tonsils, Ear
- Osteo-articular TB
  - TB of vertebra (gibbus)
  - TB involving other bones
  - TB of the joint (non-reactive)
- Skin
TB Cervical Lymphadenitis

- **Diagnosis**
  - persistent mass >2x2cm
  - no visible local cause
  - no response to antibiotics
  - Fine needle aspiration helpful diagnostic tool
TB Meningitis (TBM)

- Most severe disease manifestation
- Diagnosis
  - Clinical: poor growth often precede clinical symptoms in HIV negative children
  - LP - glucose low / protein high/ lymphocyte predominance
  - CT-Scan – changes my be less prominent in HIV negative children
  - Air encephalogram
- Clinical staging: Stage I,II,II
TB Abdomen

- M.tuberculosis or M.bovis
- Through dissemination or swallowing
- Peyer patches and the appendix common sites of involvement.
- Shallow ulcers that may cause pain, diarrhea or constipation.
- Mesenteric adenitis is common, resulting in lymph flow obstruction with ascites
- Wasting due to malabsorption, and abdominal distention are common findings
- Important to differentiate from MAC and malignancy particularly in children with low CD4
TB Abdomen cont.

- **Ascites fluid**
  - Exudate

- **Imaging**
  - Ultra sound and CT scan are helpful imaging techniques to visualize glands

- **Biopsy**
  - Try to obtain where possible
WHO- Diagnostic Criteria

• The same for HIV infected and un infected children

• Probable TB
  • Known contact with TB case and/or +TST
  • AND Suspicious symptoms and suggestive CXR
  • OR Extra-thoracic TB manifestations

• Confirmed TB
  • Bacteriologic confirmation
    • Sputum smear
    • Sputum or gastric aspirate culture
    • Confirmation from other specimen
Bacteriological confirmation

• Sputum / Gastric washing
• Gastric washings or induced sputum should be used in younger children
• Children > 5y can often produce a sputum specimen (with/without help)
• Children >10y frequently have sputum smear-positive adult-type disease
• Cytology / Histology
• Fine needle aspiration (FNA)
  • Easy to perform and very helpful in case of accessible mass/gland
• Other biopsy material as indicated
Summary

• Diagnosis can be problematic
• A constellation of signs symptoms and special investigations should be used to optimize accuracy
• Carefully document findings over time
• Try to get cultures – A confirmation is helpful in context of possible poor treatment responses and diagnostic certainty
Treatment

• General comment
• There is ongoing discussion regarding the duration of treatment in HIV infected children.
• Currently there is no recommendation to increase the duration of therapy
  • Increasing the duration from 6-9 months is practiced by experienced clinicians for specific cases of pulmonary TB.
  • Giving 9 months of B therapy in TB meningitis is the common practice
Pulmonary tuberculosis
- 2/12 - Intensive phase (Isoniazid, Rifampicin, PZA)
- 4/12 - Continuation phase (Isoniazid, Rifampicin)
- In the case of very complicated nodal disease prednisone 2 mg/kg/day for 3 weeks is added

TB meningitis
- 4 drugs (at double the normal dose) – ethionamide is the preferred agent
- Prednisone 4 mg/kg/day is added for 4 weeks then tapered

Extra-pulmonary Tuberculosis not TB meningitis
- 4 Drugs at the normal dose - ethambutol is the preferred agent
Drug Resistance

- Emerging problem – severe consequences
- Children usually become infected from adults
- Majority of drug resistance is due to transmitted drug resistant disease
- In Cape Town
  - 10% of child cultures INH resistant
  - 5% are MDR (INH and Rif resistant)
- History: Look for a history of treatment failure/ re-treatment or non-adherence in the contact
- MAJOR implications for preventive chemotherapy and Rx regimens
- When in doubt contact an expert
Measuring responses to treatment

- Follow-up is an important
- Look for clinical improvement with reduction in symptoms and improvement of the signs
- Weigh the child and plot on percentile charts
- Make sure the child is adherent
- Provide nutritional support and CD4 determination where needed
• What are the reasons for a poor response to TB treatment or repeated episodes of TB?
Possibilities

- Wrong diagnosis
  - Not Mycobacterium infection
  - Not Mycobacterium Tuberculosis
- Drug resistance
- Insufficient duration of treatment
- Requires HAART
- Non adherence to therapy
- Re-infection
Possibilities cont.

- Malabsorption of drugs
  - Concern has been expressed about potential malabsorption of both TB and/or ARV drugs
  - Concern about relatively low dosages of INH and RMP guidelines (4-6 mg/kg and 8-12 mg/kg/day, respectively)
  - Data shows similar INH serum concentrations in HIV+/- children
  - RIF – concentrations lower in some HIV-infected adults
  - When prescribing FDC TB Rx it is better to err on the higher range of the allowed TB dosages
Immune reconstitution inflammatory syndrome (IRIS)

- Paradoxical deterioration in clinical condition after initiation of HAART
- With in 3 months after initiation of HAART (does not signify failure)
- Accompanied by drop in viral load and increase in CD4
- Good pre-initiation screening can reduce the risk
- TB very common in adult
- Less frequent in children
When to Start HAART in a Child with TB?

• This is a difficult question
• With newly diagnosed TB the treatment of the TB should be the priority however undue delay in severely ill patient will compromise these patients and could negatively impact TB outcome as well
• Treating clinicians should consider the clinical as well as immunological status of the child
• Follow-up and evaluation of response to TB treatment is essential
• In children with MDR-TB HAART should always be considered regardless of clinical and immunological status
When to Start HAART in a Child with TB?

Options are

- Wait for TB treatment to finish
- Start HAART soon (2 weeks) after starting TB treatment
- Delay for 2 months before initiating HAART
## WHO Recommendation on the timing of HAART in patients on TB treatment

<table>
<thead>
<tr>
<th>Stage</th>
<th>When to initiate HAART if on TB therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Start HAART 2-8 weeks later</td>
</tr>
<tr>
<td>3</td>
<td>Severe advanced suppression</td>
</tr>
<tr>
<td></td>
<td>Start HAART 2-8 weeks later</td>
</tr>
<tr>
<td></td>
<td>Mild or moderate suppression</td>
</tr>
<tr>
<td></td>
<td>Evaluate the possibility of delaying HAART till after completion of TB treatment. If poor response to TB treatment HAART should be started</td>
</tr>
</tbody>
</table>
What are the issues with co treatment?

• Overlapping toxicity profile - rash, hepatitis etc.
• Drug interactions
• Increased drug burden – adherence
## Overlapping Toxicities

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Anti-TB Drugs</th>
<th>Anti retroviral</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>PZA, RMP, INH</td>
<td>NVP, EFV,ABC</td>
<td>Clinical monitoring and pre treatment guidance</td>
</tr>
<tr>
<td>Nausea &amp; Vomiting</td>
<td>ETH, EMB, PZA, RMP, INH</td>
<td>AZT, RTV, Kaletra</td>
<td>Address</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>PZA, RMP, INH, ETH</td>
<td>NVP, all PIs, EFV</td>
<td>Regular monitoring of ALT</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>INH, RMP</td>
<td>AZT</td>
<td>Monitor clinical and FBC</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>INH</td>
<td>D4T / DDI</td>
<td>Add B6 to management in all children</td>
</tr>
</tbody>
</table>
Adverse drug reactions in patients on co-treatment for TB and HIV

- These reactions are common in adults
- Little pediatric data
- Most experienced providers feel that there few cases where stop or drug switch is needed
- Extremely careful follow-up is needed
Drug interaction

- Low plasma levels of anti retroviral drugs leads to resistant virus with failure as a consequence

- P-glycoprotein interactions
  - Rifampicin increases P-gp expression
    - Decreases PI absorption
    - Decreases tissue penetration (Very important for the sanctuary CSF & testis)
    - Increases PI elimination
Drug interaction cont.

- The cytochrome p-450 family of system (many sub enzymes)
  - Inducers
    - Rifampicin – this is a potent inducer of all the sub enzyme classes
    - Nevirapine
    - Efavirenz
    - Ritonavir
  - Inhibitors
    - Protease inhibitors
    - Efavirenz
The result of the interactions and strategies to overcome the problem: Protease inhibitors

• Result
  • Ritonovir: Reduction in serum concentration 35% - Levels acceptable
  • Other : Reduction in serum concentrations of 75-95% - levels unacceptable

• Overcoming the drug interactions
  • Ritonovir – current guideline but little data to support
  • Ritonavir boosted Kaletra- Adult data and some peadiatric data
  • Double dose Kaletra – Adult data
The result of the interactions and strategies to overcome the problem

- Result: Non Nucleoside Reverse Transcriptase Inhibitors:
  - Efavirenz reduced by 22%, - Levels acceptable
  - Nevirapine reduced by 37-58% - Levels unacceptable

- Overcoming the drug interactions
  - Efavirenz:
    - Adult guidelines suggest dose increase despite data that suggest that it is not required
    - Little pediatric data, current guideline does not require this, but there is concern that the dose of efavirenz may by to low in all children regardless of rifampycin exposure
  - Nevirapine
    - Some adult data suggests that an increase of the dose may overcome this problem
    - No pediatric data available and co treatment is currently not recommended
The result of the interactions and strategies to overcome the problem

- Result: Nucleoside Reverse Transcriptase Inhibitors
  - Very little interaction with anti TB treatment
- Overcoming the problem
  - No adaptation of dose or drug needed
  - Regimens based on the use of abacavir with 2 further NRTI (ABC usually the 3rd drug) seems an attractive option in patients on rifampicin and are currently recommended by the WHO, however they are associated with earlier failure and are not generally recommended.
Which Drugs to Use?

- The TB regimen should not alter
- Although alternative rifamycins (ie rifabutin) have fewer interactions they are too expensive and are not part of the current available FDC
- Choose a HAART regimen that incorporates drugs that are freely available in your country
  - consider country and/or WHO guidelines
  - Bear in mind previous and current drugs received
HAART regimen for children on TB treatment that require initiation

<3 years < 10 kg:

• 2 NRTI + Ritonavir boosted Kaletra Or Abacavir
• Calculating the dose of ritonovir to boost
  • Take the dose of Kaletra in ML
  • Multiply by 0.75
  • The answer = the dose in ML of ritonovir required to boost

• 2 NRTI + Double dose Kaletra
• Pros: Easy to use
• Cons:
  • Still under investigation,
  • If using this strategy do therapeutic drug monitoring where available
HAART regimen for children on TB treatment that require initiation cont.

>3 years > 10 kg
  - 2NRTI + efavirenz
HAART regimen for children on HAART that require TB treatment

- Adjust the HAART according to guideline
- Children on nevirapine based regimens that can not switch to efavirens due to age or weight remains a problem. Contact an expert to discuss these cases
Drug adherence in co-treated children

- Care givers require additional support
- Make sure that there is good communication with TB clinic
- Ask to see the TB treatment card at each visit
Can therapeutic drug monitoring assist us

- May be helpful where:
  - Clinical response not as predicted
  - Drug interaction
  - Issues with absorption and administration

- Problems:
  - Optimum level not defined for all drugs
  - High intra patient variability
  - QA / QC in Laboratory very important
MAC

- Comprises two closely related organisms, M. avium and Mycobacterium intracellulare.
- Acquired through inhalation or ingestion
- Less common in children than adults
  - seen rarely in patients with greater than 100 CD4+ cells/mm³
  - Suspect in severe suppression and advanced disease
  - Treatment varies from MTB treatment since these organisms are resistant to INH and partially resistant to RIF

- Three major disease syndromes
  - pulmonary disease
  - cervical lymphadenitis
  - disseminated disease
Disseminated MAC disease

- In AIDS 80% to 90% of infections are acquired by ingestion
- any organ can be seeded secondarily -most common sites are liver, spleen, and bone marrow
- predominant symptoms of fever, night sweats, and cachexia
- severe anemia common feature
- 5% marked elevation of serum alkaline phosphatase
- hepatosplenomegaly
Principles of Treatment

• Treatment of MAC is a challenge.
• Paucity of drugs that are highly active against MAC
• Drug Combinations are essential
• Minimum requirement
  • Clarithromycin
  • Ethambutol
  • Rifabutin (adapt antiretroviral doses, rifampin also effective)
• Treat at least 12 month and Cd4>100 cells
• Prevention if feasible
M Bovis BCG – General comment

- Part of MTB complex
  - Most laboratories will not do routine species differentiation once MTB – complex is found
- Drug resistance profile of M Bovis BCG
  - Partial resistance to INH and RIF
  - Full resistance to PZA
- Vaccine adverse reaction +/- 3% normal children
Proposed Classification if BCG disease spectrum

- Local
  - Injection abses >10mm x 10mm
  - Severe scar ulceration
- Regional
  - Ipsilateral adenitis >15x15mm
  - Other regional adinitis
- Distant
  - Culture from 1 additional site
- Disseminated
  - Culture from 2 separate additional sites
- IRIS – In HIV infected children
- Dual disease
- Other
BCG in HIV infected children

- Distant and disseminated disease
- Risk of distant disease estimated at 110-417/100 000
- Distant disease can present without local or regional signs
- Suspect in cases of
  - Young children <12 months
  - Severe suppression
  - Not responding to conventional TB treatment and HAART
- Treat aggressively
BCG in HIV infected children cont.

- IRIS
- Risk not totally established
- Common in young children with severe immune suppressions
- Very painful regional adenitis
- Suspect if ipsilateral adenitis 10 days to 6 weeks post initiation on HAART
- No other clinical deterioration or weight loss
- Management still controversial and study required
Suspected or confirmed BCG disease

Suspected BCG disease: All children <2 years with right-sided local or regional lesions that may indicate BCG disease (see revised BCG disease classification, figure 1). In immune compromised children, a high index of suspicion for primary systemic BCG disease should be maintained, even in the absence of local or regional BCG disease. Systemic symptoms may include fever of unknown origin.

Confirmed BCG disease: BCG confirmation: M. bovis BCG confirmed by molecular or culture and biochemical methods.

HIV-uninfected children

A. Local or regional disease
- Observe
- Consider therapeutic aspiration or excision biopsy in the following: fluctuant node or abscess, persistent, rapidly enlarging node or fistula formation, or in the presence of a large injection site abscess
- Report as vaccine-related adverse event to EPI

B. Suspected or confirmed distant or disseminated disease
Treat medically:
- Isoniazid 15-20mg/kg/day
- Rifampicin 20mg/kg/day
- Pyrazinamide 20-25mg/kg/day (2 months, or until tuberculosis excluded)
- Ethambutol 20-25mg/kg/day
- Ofloxacin 15mg/kg/day or Ciprofloxacin 30mg/kg/day
- Refer to infectious diseases and immunology service; screen immune function
- Monitor for drug toxicity
- Report as vaccine-related adverse event to EPI

HIV-infected or immunocompromised children

A. Local or regional disease
- Treat medically:
  - Isoniazid 15-20mg/kg/day
  - Rifampicin 20mg/kg/day
  - Pyrazinamide 20-25mg/kg/day (2 months, or until tuberculosis excluded)
  - Ethambutol 20-25mg/kg/day
  - Ofloxacin 15mg/kg/day or Ciprofloxacin 30mg/kg/day
- Consider therapeutic aspiration if node fluctuant
- 2-4 weekly follow-up; if no improvement, or deterioration of adenitis after 6 weeks antituberculosis therapy, consider excision biopsy
- If on HAART, ensure HAART is antituberculosis-drug compatible
- Refer to infectious disease service
- Monitor for drug toxicity
- Report as vaccine-related adverse event to EPI

B. Suspected or confirmed distant or disseminated disease
- Treat medically as above
- Consider expedited initiation of HAART
- Monitor for drug toxicity
- Report as vaccine-related adverse event to EPI

C. Local or regional disease not conforming to EPI criteria, regional BCG IRIS with no suspected dissemination
- Observe, follow regularly for progression
- Report as vaccine-related adverse event if progression to EPI case definition

Figure 3. Preliminary guidelines for the management of bacille Calmette-Guérin (BCG) disease in children. EPI, Expanded Programme on Immunization; IRIS, immune reconstitution inflammatory syndrome; M. bovis, Mycobacterium bovis.
In summary

- HIV infected children have high risk of developing tuberculosis
- Tuberculosis is a significant cause for mortality in children with HIV that are not on HAART
- It may be difficult to diagnose due to overlapping symptoms and complicated CXR pictures
- Clinical progression of TB may be faster in HIV infected children
- Co-treatment is common but requires special attentions to:
  - Timing of HAART initiation
  - Choice of antiretroviral