Paediatric TB

I want ZERO TB DEATHS

I want a WORLD FREE OF TB

Stop TB in my lifetime

WORLD TB DAY 24 MARCH 2012
“He was quiet when he died,” reported Thabo’s auntie. “He hardly made a sound. I would almost never have known if it hadn’t been for the flies, really.”
NDoH TB Mission Statement

To **prevent** TB and to ensure that those who do contract TB have easy access to **effective**, **efficient** and **high quality** diagnosis, **treatment** and **care** that reduces **suffering**.

Mandela was treated for TB in 1988.
Global TB Burden

Source: © WHO, 2010. All rights reserved.
Burden of Disease in South Africa

• Rate of TB cases:
  - Globally 139 cases/100,000
  - High burden countries 177 cases/100,000
  - Africa - 363 cases/100,000 population
  - South Africa – 940 cases/100,000 population
Factors that Influence the TB Pandemic in Africa

• South Africa has the highest TB incidence in the world, 5x the rate of high-burden countries. WHY?
  - Poverty and rapid urbanisation
  - Impact of the HIV pandemic
  - Poor health infrastructure
  - Poor programme management with inadequate case detection, diagnosis and cure
TB in South African Children

• 948 per 100 000 population
• 9th heaviest TB burden in the world
• South African TB prevalence:
  • 3% of children = annually infected with TB
  • Median age = 12 – 15 months
  • 8% of children presenting with acute lower respiratory tract infections have culture confirmed TB
  • 48% of 138 cases culture confirmed TB present as acute pneumonia (Jeena PM et al Int J Tuberculous Lung disease 2002)
TB in South African Children

- HIV / TB co-infection in 35 – 52% childhood TB cases
  - MUST perform HIV test on all children with TB
- 38% of HIV-infected children at CHB were on TB treatment at the time of starting ART! But very few cases proven
- Risk of TB disease 4 times higher in children with a CD4 < 15% (12.4%) compared to children with a CD4 > 15% (3.3%) in children older than 3 years (Elenga et al PIDJ 2005)
Transmission of TB is person-to-person via airborne droplet nuclei.

- Cough – 3000 droplet nuclei
- Sneeze – up to 1 million droplet nuclei
- Singing, Aerosol-producing investigations
- 10-200 droplets can cause TB infection
TB Transmission

- Droplet nuclei can stay airborne for up to 72 hours (like dark, damp rooms, sunlight kills them)
- The most infectious person has PTB and lung cavities – usually older than 12-years-old
- EPTB is generally not infectious unless they also have PTB
- Latent TB is not infectious because TB is not replicating or causing them to cough
Primary TB infection: usually asymptomatic.

- Occurs on 1st exposure
- Inhaled droplet nuclei lodge in the terminal alveoli
- Are phagocytosed by macrophages causing a local immune response - Ghon focus
- Bacilli/antigens drain to the hilum causing hilar LAD = primary complex
Primary TB Infection

- Eventually growth ceases and macrophages containing TB die and the primary complex is replaced by fibrous scar tissue (may have calcification)
- Will have a +TST within 4-6 weeks
What are the risks of developing active TB after primary TB infection?

- Normal immunity 10% or 1:10
  - Risk is highest in the first 2 years after infection and again late in life especially for children <5 and elderly

- Decreased immunity – 50-60% will progress to active TB disease

- So: IPT for all under 5yo and for all with immune impairment
TB screening should be done at every medical encounter for every patient.

- Maintain a high index of suspicion bearing in mind the high TB and HIV prevalence in RSA
- **TB exposure** is especially relevant in children (trace adults to prevent TB in children!!)
- TB is a paucibacillary disease in children – do not rely solely on sputum
Children with HIV have an increased risk of developing TB disease.

- Increased risk of TB exposure from parents with HIV/TB
- Increased risk of progressing from primary TB infection to TB disease
- Progression to TB disease occurs more rapidly
- Clinically more difficult to definitively diagnose TB due to confusing CXR and cross-over of HIV and OIs with signs/symptoms of TB (cough, FTT, LAD, LIP, abnl CXR)
- More likely to have a negative TST, AFB, and TB culture
Symptoms of TB

- **Cough** (2 weeks)
- **Fever** (2 weeks)
- **Night sweats** (drenching)
- **Weight** loss or poor weight gain
- **Malaise and fatigue**
- **Loss of appetite**
- **Shortness of breath**
- **Chest pain**
Signs of TB disease

- Painless LAD
- Hilar/mediastinal LAD
- HSM/abd pain on exam
- Acute angulation of the spine
- Scrofula
- CSOM
- HA- fits, vomiting, irritability
- Lung exam varies
- Others
Pott's disease

Destroyed vertebrae with Cold Abscess
TB Meningitis
Scrofula
Primary Disease of Cervical Lymph Nodes
How useful are TB investigations?

CXR – NOT a stand-alone TB test

- Generally non-specific
- Hilar LAD (lateral is useful)
- Widened mediastinum
- Compression of the airways
- Opacification
- Millet-sized lesions (1-2mm) = miliary TB
- Pleural effusions (usu >6yo)
- Cavitary lesion (~12yo)
- May be normal (esp. EPTB)
Hilar Adenopathy

Figure 7.5 – Hilar adenopathy. A. Unmarked image. B. Marked image to outline the presence of bulky, bilateral hilar adenopathy. Occasionally even large lymph nodes like this are dismissed as pulmonary arteries.
Hilar Adenopathy

*Figure 7.5 – Hilar adenopathy. A. Unmarked image. B. Marked image to outline the presence of bulky, bilateral hilar adenopathy. Occasionally even large lymph nodes like this are dismissed as pulmonary arteries.*
Hilar Adenopathy
Lateral Chest X-Ray

Labelled lateral CXR

Normal Lateral CXR
Normal and Abnormal Lateral CXR
Lateral View of Hilar Adenopathy
Miliary TB
Cavitary Pulmonary TB
TB AFB and Culture in Children

Egyptian beggar with likely spinal TB – 3rd century B.C.

TB Smear and Culture

• Paucibacillary disease in children (low organism load) so unlikely to have AFB/cx
  • Collection of a good sample is difficult (esp. <8yo)
  • Gastric aspirates are difficult to attain in clinic
  • Sputum induction not always available
  • FNA useful from lymph nodes – stain and cx
TB Lymphadenopathy (EPTB)

• Most common EPTB
• Usually cervical
• Present >14 days
• Usually non-tender
• No response to antibiotics
• FNA useful (especially for culture) but not required
• **Caution** to RX without firm diagnosis in setting HIV infection
• TST may be positive
How is TB Diagnosed in Children

- Exposure
- History/clinical presentation
- Exam (including weight)
- Labs/studies (+/-)
- Rx with abx and wait
- Clinical judgement
- ALWAYS test for HIV in children as in adults
**Documented TB exposure**
Close contact with an adult or adolescent with pulmonary TB or child with smear-positive TB

Close contact is defined as any household contact or contact outside the household that is of sufficient duration and proximity to pose a high risk of infection.

**Are there any current symptoms or signs suspicious of TB?**
Cough, wheeze, fever, lethargy, fatigue, weight loss, or visible mass in the neck

<table>
<thead>
<tr>
<th>No current symptoms or signs</th>
<th>Symptoms or signs present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigate for TB</td>
<td></td>
</tr>
</tbody>
</table>

**Not TB**
Follow up after 1-2 weeks
Child is well

<table>
<thead>
<tr>
<th>&lt;5yrs or HIV-infected</th>
<th>≥5yrs and HIV-uninfected</th>
<th>Persistent non-remitting symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH for 6/12</td>
<td>No preventive therapy</td>
<td>Refer to hospital</td>
</tr>
</tbody>
</table>

**TB diagnosed**
Treat for TB
Enter into TB register
Follow up after 1-2 weeks
Child is well

Observe for symptoms
Evaluate / refer if symptoms indicative of TB
TB Treatment Regimens for Children

• **Uncomplicated PTB that is smear-negative** and less severe forms of EPTB (LAD)
  - Treat with 3 drugs (HRZ) x 2 mo/2 drugs (HR) x 4 mo

• **Smear positive or cavitary TB** = high bacillary load
  - Treat with 4 drugs (HRZE) in intensive phase

• **Severe TB** – child very ill/malnourished, HIV with very low CD4 count, meningitis, bone, abdomen, miliary: treat with 4 drugs and intensive phase duration may need to be prolonged – consult guidelines/expert
Regimen 3A: Uncomplicated TB with a low bacillary load for children up to 8-years-old

<table>
<thead>
<tr>
<th>Body weight kg</th>
<th>Intensive Phase: 2 months</th>
<th>Continuation Phase: 4 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RH 60,60</td>
<td>PZA 500 mg</td>
</tr>
<tr>
<td>R: Rifampicin</td>
<td></td>
<td>PZA: Pyrazinamide</td>
</tr>
<tr>
<td>H: Isoniazid</td>
<td></td>
<td>Expert advice on dose</td>
</tr>
<tr>
<td>2–2.9 kg</td>
<td>½ tablet</td>
<td>½ tablet</td>
</tr>
<tr>
<td>3–3.9 kg</td>
<td>¾ tablet</td>
<td>¼ tablet</td>
</tr>
<tr>
<td>4–5.9 kg</td>
<td>1 tablet</td>
<td>¼ tablet</td>
</tr>
<tr>
<td>6–7.9 kg</td>
<td>1½ tablets</td>
<td>½ tablet</td>
</tr>
<tr>
<td>8–11.9 kg</td>
<td>2 tablets</td>
<td>½ tablet</td>
</tr>
<tr>
<td>12–14.9 kg</td>
<td>3 tablets</td>
<td>1 tablet</td>
</tr>
<tr>
<td>15–19.9 kg</td>
<td>3 ½ tablets</td>
<td>1 tablet</td>
</tr>
<tr>
<td>20–24.9 kg</td>
<td>4 ½ tablets</td>
<td>1 ½ tablets</td>
</tr>
<tr>
<td>25–29.9 kg</td>
<td>5 tablets</td>
<td>2 tablets</td>
</tr>
</tbody>
</table>
Regimen 3A: Uncomplicated TB with a low bacillary load for children >8-yo and adolescents

<table>
<thead>
<tr>
<th>Body weight (kg)</th>
<th>Intensive Phase (2 months) Treatment given 7 days a week</th>
<th>Continuation Phase (4 months) Treatment (DOT) given 7 days a week</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RHZE (150,75,400,275)</td>
<td>RH (150/75)</td>
</tr>
<tr>
<td>30-37 kg</td>
<td>2 tablets</td>
<td>2 tablets</td>
</tr>
<tr>
<td>38-54 kg</td>
<td>3 tablets</td>
<td>3 tablets</td>
</tr>
<tr>
<td>55-70 kg</td>
<td>4 tablets</td>
<td></td>
</tr>
<tr>
<td>&gt; 71 kg</td>
<td>5 tablets</td>
<td></td>
</tr>
</tbody>
</table>
Regimen 3B: Complicated TB, High bacillary load, retreatment cases. (e.g. extensive PTB, spinal/osteo-articular TB, abd TB, meningitis*).

<table>
<thead>
<tr>
<th>Weight kg</th>
<th>Intensive Phase 2 months</th>
<th>Continuation Phase 4 mos</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RH 60, 60</td>
<td>PZA 500 mg</td>
</tr>
<tr>
<td>2-2.9</td>
<td>½ tab</td>
<td>Expert advice</td>
</tr>
<tr>
<td>3-3.9</td>
<td>¾ tab</td>
<td>¼ tab</td>
</tr>
<tr>
<td>4-5.9</td>
<td>1 tab</td>
<td>¼ tab</td>
</tr>
<tr>
<td>6-7.9</td>
<td>1 ½ tab</td>
<td>½ tab</td>
</tr>
<tr>
<td>8-11.9</td>
<td>2 tab</td>
<td>½ tab</td>
</tr>
<tr>
<td>12-14.9</td>
<td>3 tab</td>
<td>1 tab</td>
</tr>
<tr>
<td>15-19.9</td>
<td>3 ½ tab</td>
<td>1 tab</td>
</tr>
<tr>
<td>20-24.9</td>
<td>4 ½ tab</td>
<td>1 ½ tab</td>
</tr>
<tr>
<td>25-29.9</td>
<td>5 tab</td>
<td>2 tab</td>
</tr>
</tbody>
</table>
Regimen 3B: retreatment cases for children >8-yo and adolescents

<table>
<thead>
<tr>
<th>Weight kg</th>
<th>Intensive Phase: 3 months</th>
<th>Continuation Phase: 5 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RHZE 150,75,400,275</td>
<td>RH 150,75 Ethambutol 400mg tab</td>
</tr>
<tr>
<td>30-37</td>
<td>2 tabs</td>
<td>2 tabs</td>
</tr>
<tr>
<td>38-54</td>
<td>3 tabs</td>
<td>3 tabs</td>
</tr>
<tr>
<td>55-70</td>
<td>4 tabs</td>
<td>3 tabs</td>
</tr>
<tr>
<td>&gt;70</td>
<td>5 tabs</td>
<td>3 tabs</td>
</tr>
</tbody>
</table>
Complicated TB: Individual drugs may be better – or not.

**Table 11.3: Recommended Doses For First-Line TB Drugs In Children**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg/kg)</th>
<th>Range (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid (H)</td>
<td>10</td>
<td>10-15</td>
</tr>
<tr>
<td>Rifampicin (R)</td>
<td>15</td>
<td>10-20</td>
</tr>
<tr>
<td>Pyrazinamide (P)</td>
<td>35</td>
<td>30-40</td>
</tr>
<tr>
<td>Ethambutol (E)</td>
<td>20</td>
<td>15-25</td>
</tr>
<tr>
<td>Streptomycin (S)</td>
<td>15</td>
<td>12-18</td>
</tr>
</tbody>
</table>
Response to TB Rx

- Younger children review monthly until 3 months
- Weight and resolution of symptoms
- Older children smear + sputum at 2 & 5 months (reg. 1) and 3 & 7 months (reg. 2)
- CXR not recommended as resolution slow
- If the child not responding NEED to INVESTIGATE FURTHER (? MDR, ? MAC, ?lymphoma)
Concomitant TB RX and ART

• Test all paediatric TB cases for HIV
• ART may be started 2 weeks after TB rx
• Watch for IRIS
• Remember to double dose the Kaletra or to add Ritonavir if child is on Aluvia/Kaletra and is started on TB rx
TB Rx and Kaletra

• Need to “boost” Kaletra (4:1 concentration lopinavir: Ritonavir)

Possibilities:

- Add Ritonavir to “boost” dose (1:1) – Best!!
- Double dose kaletra (use 600 mg/m2)
Indications for Steroids in TB

- TB meningitis
- TB pericarditis
- Mediastinal/hilar LAD obstructing the airways.
- Severely ill children with disseminated TB (miliary)
- IRIS (sometimes)
- The dosage is prednisone 1-2 mg/kg daily orally for 4-6 weeks added to the TB drugs. The dose can be tapered to stop over 2 weeks.
Documented TB exposure
Close contact with an adult or adolescent with pulmonary TB or child with smear-positive TB
Close contact is defined as any household contact or contact outside the household that is of sufficient duration and proximity to pose a high risk of infection.

Are there any current symptoms or signs suspicious of TB?
Cough, wheeze, fever, lethargy, fatigue, weight loss, or visible mass in the neck

No current symptoms or signs
Symptoms or signs present

Investigate for TB

Not TB
Follow up after 1-2 weeks
Child is well

TB diagnosed
Treat for TB
Enter into TB register

<5yrs or HIV-infected
≥5yrs and HIV-uninfected
Persistent non-remitting symptoms

INH for 6/12
No preventive therapy
Refer to hospital

Observe for symptoms
Evaluate / refer if symptoms indicative of TB
Baby Suzie

PHYSICAL EXAM

• She is failing to thrive with weight the same as on discharge, < -2 z-score
• Generalised LAD
• Scattered crepitations, left chest
• 3 cm hepatomegaly
• 2 cm splenomegaly
BABY SUZIE

LABORATORY RESULTS

• Her HIV DNA PCR result is positive
• CXR - Bronchopneumonic changes bilaterally, hilar LAD
• Mantoux non-reactive
• Gastric washings – negative for AFB’s, culture pending

• Pre-initiation lab results:
  - CD4% - 5%, CD4 - 276
  - Viral load - 300,000 copies/ml
  - FBC normal
## Does Suzie have TB??

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent LRTI</td>
<td>PPD negative</td>
</tr>
<tr>
<td>FTT</td>
<td>Gastric washings negative for AFB’s</td>
</tr>
<tr>
<td>Hilar adenopathy on CXR</td>
<td>No TB contact</td>
</tr>
<tr>
<td>HIV positive</td>
<td></td>
</tr>
</tbody>
</table>
Suzie is started on TB treatment

• She is given Rimcure 1 tablet daily
• Is this the correct management?
• Does she qualify for ART?
• When should we start ART?
• Which drugs?
• Do we need to make any changes to her ART regimen?
• What do we need to be cautious of if she starts ART?
Case 2 Simphiwe

• Simphiwe’s mother Dorothy was diagnosed with TB in her last month of pregnancy
• She is HIV positive and received ART for 2 months prior to his birth
• Her TB was diagnosed as she had a cough for 2 weeks, night sweats.
• Her geneXpert result was positive, sensitive to rifampicin
• How should we manage Simphiwe at birth and beyond?
Mom has TB

• Mom diagnosed in last 2 months of pregnancy or failed to convert to smear negative or has no documented smear conversion:
  - No BCG at birth
  - Needs TB treatment if TB cannot be excluded
  - Needs IPT if TB is excluded

• Give BCG
  - After IPT is completed if asymptomatic
  - If HIV infected give after IPT and after stable on HA^ART
Breastfeeding if Mom has TB

• HIV-uninfected mother on TB treatment should be encouraged to breastfeed
• HIV-infected mother should also be encouraged to BF exclusively (or formula feed exclusively) in line with national guidelines
• TB drug concentrations are too low to protect the infant from TB or to be toxic to the baby
Baby asymptomatic

• If continues to be asymptomatic, BCG administered after completion of the preventive treatment
• If baby HIV+ may delay BCG until on HAART and immune reconstituted
• Tuberculin available, test after 3 months of INH treatment
• TST negative and the mother sputum smear-negative, the INH can be stopped and the child given BCG vaccination
After exclusion of TB disease, INH prophylaxis should be given to:

- All children under 5 years of age and HIV-infected children (irrespective of age) in contact with an infectious case of TB (drug susceptible TB and MDR-TB)
- All children under 5 years of age with a positive Mantoux (10 mm in diameter or greater)
- All HIV-infected children, irrespective of their age, with a positive Mantoux (5 mm in diameter or greater)
Key Points

• Control of TB is a nation-wide priority
• Advocate for TB infection control (esp. workplace)
• Screen for TB at every medical encounter
• Must have a high index of suspicion to diagnose TB disease in children because investigations usually do not definitively diagnose TB
• ALWAYS double-dose Kaletra/Aluvia or add Ritonavir if child is on this drug as part of HAART
Thank You