Chronic lung disease & TB in HIV-infected children

Ben Marais

www.sydney.edu.au/mbi
www.tbcre.org.au
Age 5yr old boy
Cough, fever, LOW + TB contact. TST = 12mm.
Clubbing, generalized lymphadenopathy
Pneumonia, LIP, TB ????????
Chronic lung disease

Pneumonia: recurrent acute - persistent/chronic
(S. pneumonia, H. influenza, viral)
- with parenchymal destruction
(S. aureus, K. pneumonias, M. tuberculosis)

Gastro-esophageal reflux (GER)
Lymphocytic interstitial pneumonia (LIP)
Malignancy (Kaposi’s, lymphoma)

• Bronchiectasis
• Cor pulmonale
Focus on TB
Children get TB where adults spread the disease
### Global Burden of TB - 2012

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Estimated Incidence (with Range)</th>
<th>Estimated Number of Deaths (with Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All forms of TB</td>
<td>8.6 million (8.3–9.0 million)</td>
<td>940 000 (1.3–1.6 million)</td>
</tr>
<tr>
<td>HIV-associated TB</td>
<td>1.1 million (13%) (1.0–1.2 million)</td>
<td>320,000 (300,000–340,000)</td>
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<tr>
<td>Multidrug-resistant TB</td>
<td>450,000 (300,000–600,000)</td>
<td>170 000 (100 000 – 240 000)</td>
</tr>
</tbody>
</table>

**Disease burden in children**

~1 million children with TB every year

*Source: WHO Global Tuberculosis Report 2013*

*Excluding deaths attributed to HIV/TB*

*Jenkins HE et.al. Lancet 2014*
TB and child survival/mortality

Underestimated among deaths from
- pneumonia
- malnutrition
- meningitis
- HIV

Relative importance likely to increase
- widespread vaccine roll-out (Hib, pneumo, rota)
- rise in DR-TB

Importance of tuberculosis control to address child survival

Stephen M Graham, Charalambos Sismanidis, Heather J Menzies, Ben J Marais, Anne K Detjen, Robert E Black

Tuberculosis commonly affects young children (<5 years) in countries that have high rates of child mortality.¹ The global public health focus to control tuberculosis has traditionally aimed to reduce transmission through early diagnosis and treatment. However, the control of tuberculosis in this important population remains an ongoing challenge due to the difficulty in diagnosing and treating tuberculosis in young children, particularly in resource-limited settings. Early childhood mortality from tuberculosis is not only associated with high case fatality rates but also with a significant impact on the overall childhood mortality rate. Therefore, efforts to control tuberculosis in young children are crucial for reducing overall child mortality in these settings.

¹ The global public health focus to control tuberculosis has traditionally aimed to reduce transmission through early diagnosis and treatment. However, the control of tuberculosis in this important population remains an ongoing challenge due to the difficulty in diagnosing and treating tuberculosis in young children, particularly in resource-limited settings. Early childhood mortality from tuberculosis is not only associated with high case fatality rates but also with a significant impact on the overall childhood mortality rate. Therefore, efforts to control tuberculosis in young children are crucial for reducing overall child mortality in these settings.
12yr old girl – admitted with “recurrent” pneumonia, worsening shortness of breath and cachexia (TB & HIV Dx missed)
Incidence of All TB / 100 000 Population: 1990-2004

Nunn P et al. JID 2007; Suppl 196: S5:14
TB - Age & Gender shift

HIV prevalence in general population:

- 3-4% 0-9y
- 25% 20-39y

Lawn SD et al. CID 2006; 42: 1040-7
Epidemic spread of MDR-TB
Children are affected

~ 32 000 children develop MDR-TB every year
All cases ever reported <2% of estimated annual burden

Jenkins HE et.al. Lancet 2014

Marais BJ et. al. JCM 2013; 51: 1818-25

Solid lines show a single loci-MIRU change, while dotted lines show 2 (black coloured) or more (grey coloured) changes. Circles show 12-loci MIRU international type (MIT) numbers and the color of the circles reflects the number of clinical isolates identified (N=71), illustrating unique (sky-blue) versus clustered isolates (deep blue, 2 to 5 strains; dark blue, 5 to 10 strains; brown, 10 to 20 strains; red, 20 strains and more). Additional colour groups demonstrate likely clusters with minimal strain variation.

www.sentinel-project.org
www.treatmentactiongroup.org/tb/publications/2013/we-can-heal
HIGHLY VARIABLE CLINICAL SEVERITY / RELEVANCE

INTRATHORACIC & EXTRATHORACIC DIVERSITY OF DISEASE

Highly variable clinical severity / relevance

Intra- & extra-thoracic
Age-related risk

% Immune compromised

Age in Years

<1 1to2 2to5 5to10 10to15

PTB
Disseminated

Marais. IJTLD 2004
**Time-related risk**

**Phase of disease**

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

HIV-infected - PERSISTENT RISK of re-activation & re-infection disease
3 month old boy - admitted to ICU
Pneumonia not responding to antibiotic Rx
No known TB contacts
Born prematurely (32/52) – 2 weeks in Kangaroo care unit
Another mother premature baby
Shared Kangaroo care unit / no subsequent contact
Long standing cough, especially post-pregnancy
Recently Dx with sputum sm+++ TB
3 month old baby of source case
Failure to thrive – culture confirmed TB
4/8 infants & 1 HIV-infected mother who shared Kangaroo care room Dx with TB within 6/12
Interdermal BCG Vaccine
BCG (unmasking IRIS)
Acute suppurative adenitis
3 weeks after HAART
BGC IRIS – distal disease
Gene Xpert positive
Mediastinal adenopathy
Distant (pulmonary) BCG disease
Increased risk disseminated disease

Hesseling et al, Clin Infect Dis 2006
Case

8 month old boy (Zambia)

Mother recently Dx with sputum smear-negative PTB
Found to be HIV-infected at the time
Household contacts not evaluated

Presents with persistent fever for 2 weeks
BUT Not acutely ill
  minimal coughing
  TST 0mm

Malaria considered most likely
CXR due to “exposure” history
Miliary TB – culture confirmed / HIV+
IRIS – following TB Rx and ART
Case

4yr old boy
HIV-infected, Not on ART

Previous close contact with a TB index case (uncle)
No preventive Rx

Intermittent cough for >4 weeks
No documented failure to thrive
Not acutely ill, as active as always
Pronounced parotid enlargement
Fingers clubbed
TST 0mm
Right hilar adenopathy
TB treatment initiated
Persistent symptoms after completing 6 months of TB treatment

CXR unchanged
Case

6yr old boy
HIV-infected, on ART but poorly adherent

Previous household contact with a TB index case
  2yrs ago
  treated for TB at this time – fully recovered

Persistent, non-remitting cough
Failure to thrive in the preceding 3/12
Less playful
No night sweats
2yr old girl – HIV+
Previously treated for cult+ TB 6 mo (HRZ)
5 months later again cult+ TB
TB recurrence

CAUSES TO CONSIDER

Relapse / Rx failure
- Poor adherence / incorrect regimen
- Drug-resistant TB
- Impaired drug absorption
- Insufficient Rx duration

Correct diagnosis

Re-infection