Module 9a

NTP MANAGEMENT AND CHILD TB
Child TB and NTP

- What is the usual pattern of child TB cases
- What is impact of HIV on child TB
- What is important to know about treatment of TB in children
- Why it is important to register and report child TB cases routinely
- Why is contact screening and management important
- How to include child TB activities within NTP and improve child TB management
TB disease in children: clinical epidemiology

• Most cases occur in young children (<5 years)
• Most disease occurs within 2 years after exposure/infection
  – The majority within 1 year

• Most cases in children are pulmonary TB
  – Smear negative or smear not done are the majority
  – Extrapulmonary TB is also common (around 25-35% of cases) and the type depends on age
  – Smear positive disease is usually in older children
The presentation of TB disease differs with age as older children have more mature and effective immune systems that eradicate or contain infection.

Infants and young children are particularly susceptible to severe, disseminated forms of TB as well as pulmonary TB.

The high risk of disease in young children is also the reason for contact screening and management.
National TB control data

- This slide could include recent data of TB control indicators from the National TB control programme
Childhood TB caseload: the example of Malawi in 1998

<table>
<thead>
<tr>
<th>Malawi NTP, 1998</th>
<th>numbers (proportion of childhood caseload)</th>
<th>proportion of total caseload</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total caseload</td>
<td>22,982</td>
<td>11.9%</td>
</tr>
<tr>
<td>Total childhood</td>
<td>2,739</td>
<td></td>
</tr>
<tr>
<td>0-5 years</td>
<td>1,615 (58.9%)</td>
<td>7%</td>
</tr>
<tr>
<td>5-14 years</td>
<td>1,124 (41.1%)</td>
<td>4.9%</td>
</tr>
<tr>
<td>Smear-positive PTB</td>
<td>127 (4.6%)</td>
<td>1.3%</td>
</tr>
<tr>
<td>Smear-negative PTB</td>
<td>1,804 (65.9%)</td>
<td>21.3%</td>
</tr>
<tr>
<td>EPTB</td>
<td>808 (29.5%)</td>
<td>15.9%</td>
</tr>
</tbody>
</table>
## Types of childhood EPTB disease

<table>
<thead>
<tr>
<th>Types of EPTB disease</th>
<th>Malawi NTP, 1998</th>
<th>PNG, 2005-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPTB cases</td>
<td>808</td>
<td>1097</td>
</tr>
<tr>
<td>Lymphadenitis</td>
<td>331 (41%)</td>
<td>342 (31%)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>101 (12%)</td>
<td>94 (9%)</td>
</tr>
<tr>
<td>Spinal</td>
<td>83 (10%)</td>
<td>41 (4%)</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>60 (7%)</td>
<td>12 (1%)</td>
</tr>
<tr>
<td>Abdominal</td>
<td>39 (5%)</td>
<td>173 (16%)</td>
</tr>
<tr>
<td>Miliary</td>
<td>34 (4%)</td>
<td>64 (6%)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>30 (4%)</td>
<td>257 (23%)</td>
</tr>
<tr>
<td>Bone disease</td>
<td>12 (1%)</td>
<td>15 (1%)</td>
</tr>
<tr>
<td>Not indicated/others</td>
<td>118 (14.6%)</td>
<td>99 (9%)</td>
</tr>
</tbody>
</table>
The diagnosis of TB can be made with confidence in the majority of children using careful clinical assessment.

It is difficult to confirm diagnosis of TB in many children but it is usually not so difficult to make a clinical diagnosis of TB in a child.
Child TB/HIV epidemiology

HIV epidemic

Large increase in TB cases in young adults

Increased number of child TB cases

HIV-infected children at risk of PTB because:

1. immune suppressed
2. more likely to be a contact of an adult with TB
HIV and TB in children

• HIV infected children at increased risk of exposure to TB

• HIV-infected at 20 times greater risk of TB disease than HIV-uninfected children

• Management of TB more complicated in HIV-infected children with significantly poorer outcomes

• Clinical diagnosis is more difficult especially for PTB as other HIV-related lung disease is common

• CPT and ART have a role in reducing TB-related death which is especially common within the first months following TB treatment
Treatment of TB in children

• Principles of treatment of TB in children are same as for adults
• Regimens are similar as for adults

• Children with TB usually respond well with symptomatic improvement during intensive phase and good outcome

• Dosages are calculated according to weight (not age)
• Weight is important for monitoring treatment response

• TB drugs are very well tolerated in almost all children
• The most important adverse event is hepatotoxicity
• Ethambutol can be safely used at recommended dosages in all ages including young children

• Register all children receiving anti-TB treatment
• Report treatment outcomes for children
Ethambutol efficacy and toxicity:
literature review and recommendations for daily and intermittent dosage in children
Use of ethambutol in children

- Ethambutol is recommended as fourth drug in intensive phase of first-line regimens in HIV and MDR endemic settings.
- Risk of toxicity is dose-related and related to duration of therapy.
- The risk of toxicity is **negligible** for children of any age when ethambutol is used at recommended dosages – especially when duration is limited to 2 months (as in first-line regimens).
- Ethambutol can be safely used at recommended dosages in all ages.
The 2006 guidelines listed regimens and drug dosages for children that were consistent with those used in adults.

There is increasing and consistent evidence that serum levels of drug are often low when these dosages in mg/kg are used.

Therefore, in 2010, drug dosages for children were revised.
Rapid Advice

Treatment of tuberculosis in children

These are the revised dosages for children up to 30 kgs:

- Rifampicin: 15 (10-20) mg/kg/day
- Isoniazid: 10 (10-15) mg/kg/day
- Pyrazinamide: 35 (30-40) mg/kg/day
- Ethambutol: 20 (15-25) mg/kg/day

Note also other revisions to recommendations in 2010:

1. Four drugs (RHZE) in intensive phase for all new cases in HIV endemic setting
2. No intermittent regimens in HIV-endemic setting
3. Streptomycin no longer recommended for first-line therapy
4. 12-month regimens for TBM and osteo-articular TB
Recent revision of recommended drug dosages: rationale and challenges

• Rationale for change
  – Consistent evidence that dosages need to be higher in mg/kg in young children (especially < 5 years) to achieve similar levels in the blood as for adults – and to achieve blood levels of drug considered high enough to provide optimal therapeutic effectiveness
  – Poor outcomes in some child TB cases (e.g. HIV-infected) raised possibility (theoretical, no evidence) that higher levels might mean better outcomes
  – Extensive review established that risk of toxicity remained very low if higher dosages are used

• Challenges
  – Current FDC preparations are not ideal for the new dosages – esp need for added isoniazid
  – Most FDCs have a ratio of R:H of 2:1 (e.g. R/H of 60/30) when it would be better to have 3:2 ratio
Recommended drug dosages should be consistent with national guidelines

*Insert drug regimens and dosages according to national guidelines*
WHO also now recommends that all cases of child TB should be registered and reported within age bands: 0-4 years and 5-14 years.
Treatment outcomes in children with TB

- Treatment outcomes should be routinely recorded and reported for child TB cases.

- Outcome categories are the same as for adult cases (although few child TB cases would meet the criteria for “cured”).

- Treatment outcomes are important data for monitoring & evaluation.

- There are few NTP data of treatment completion – but often poor in children.
<table>
<thead>
<tr>
<th>Available approaches to prevent TB in children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Improved case-finding and management</strong></td>
</tr>
<tr>
<td><strong>BCG</strong></td>
</tr>
<tr>
<td><strong>Contact screening and management</strong></td>
</tr>
</tbody>
</table>
Risk of TB disease following infection by age

## Studies of child contacts in Asian countries

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>No. of child contacts</th>
<th>Proportion with TB infection</th>
<th>Proportion with TB disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andrew et al</td>
<td>India</td>
<td>398</td>
<td>39 %</td>
<td>5.5 %</td>
</tr>
<tr>
<td>Narain et al</td>
<td>India</td>
<td>790</td>
<td>24 %</td>
<td>NR</td>
</tr>
<tr>
<td>Kumar et al</td>
<td>India</td>
<td>142</td>
<td>NR</td>
<td>3 %*</td>
</tr>
<tr>
<td>Singh et al</td>
<td>India</td>
<td>281</td>
<td>34 %*</td>
<td>3 %*</td>
</tr>
<tr>
<td>Rathi et al</td>
<td>Pakistan</td>
<td>151</td>
<td>27 %</td>
<td>NR</td>
</tr>
<tr>
<td>Salazar et al</td>
<td>Philippines</td>
<td>153</td>
<td>69 %</td>
<td>3 %</td>
</tr>
<tr>
<td>Tornee et al</td>
<td>Thailand</td>
<td>500</td>
<td>47 %</td>
<td>NR</td>
</tr>
<tr>
<td>Nguyen et al</td>
<td>Lao PDR</td>
<td>148</td>
<td>31 %</td>
<td>NR</td>
</tr>
<tr>
<td>Okada et al</td>
<td>Cambodia</td>
<td>217</td>
<td>24 %*</td>
<td>9 %*</td>
</tr>
</tbody>
</table>

* Data only for < 5 years; NR: not recorded

From Triasih R et al, J Trop Med 2012
Studies of child contacts in African communities

One-third to two-thirds of child household contacts of TB cases have evidence of TB infection i.e. TST positive

Incidence of TB disease among household contacts is very high – reported as >1,000 cases/100,000 population

Likelihood of infection is related to closeness/proximity of contact to and sputum smear positivity of index case

Risk of infection greatest when the index case is the child’s carer e.g. mother, grandmother

HIV-infected children are at increased risk of exposure to TB

Proportion of children with TB infection (positive TST) by degree of smear positivity of the source case
Kenyon TA et al, Int J Tuberc Lung Dis 2002

% of children with positive TST

<table>
<thead>
<tr>
<th>Degree of Smear Positivity</th>
<th>Male Index Case</th>
<th>Female Index Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>0+</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>1+</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>2+</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>3+</td>
<td>35</td>
<td>40</td>
</tr>
</tbody>
</table>
Increased risk of TB exposure among young children in HIV-endemic countries

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Notification Rates per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td>25</td>
<td>100</td>
</tr>
<tr>
<td>35</td>
<td>150</td>
</tr>
<tr>
<td>45</td>
<td>200</td>
</tr>
<tr>
<td>55</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td></td>
</tr>
</tbody>
</table>

Tanzania NTLP / IUATLD. Progress Report 1996; No. 36

From: Reider HL. Interventions for TB control and elimination. IUATLD publication 2002
Why is contact screening important?

1. Opportunity to prevent TB-related morbidity and mortality in children and HIV-infected individuals

2. Opportunity to increase case-finding and earlier treatment of undiagnosed active TB cases
Why is child contact screening important?
Prevent child morbidity and mortality

• The prevalence of TB infection is high among child contacts

• Child household TB contacts had significant increase risk of all-cause mortality compared to children living in non-TB households in same community
  – If mother had TB, 8-fold increase: MRR 7.82 (95% CI 2.1-30)
    AF Gomes et al, Thorax 2011

• Missed opportunities for IPT were common (71%) in at-risk children that later presented with confirmed TB disease
  – 81% were <3 years of age, 25% had disseminated TB and 5% died
  – TB source case was the mother or father in 74/156 (47.4%) children
    K Du Preez et al, Ann Trop Paediatr 2011
Why is contact screening important? 
Increased case-finding

- The prevalence of TB infection and disease is high among contacts
  - All TB cases 4.5% (95% CI 4.3-4.8)
  - Confirmed cases 2.3% (95% CI 2.1-2.5)
  - Latent TB infection 51.4% (95% CI 50.6-52.2)

- TB prevalence significantly higher by active case finding in household contacts (1735/100,000) than with passive case finding (191/100,000)

- Incidence of TB disease among contacts was 603 per 100,000 (95% CI 370-830)
  PC Hill et al, PLoS ONE 2008
  and in same community, prevalence of TB cases was 1518 per 100,000 among 2174 contacts of 317 adults with smear-positive PTB
Most studies of IPT efficacy have been done in adults such as below.

Studies have included children and the efficacy of IPT for preventing disease in children infected with TB and not HIV-infected is over 75%.

IPT needs to be given for at least 6 months duration to be this effective.

From: Reider HL. Interventions for TB control and elimination. IUATLD publication 2002
Symptom-based screening of child contacts is recommended by WHO

Guidance for national tuberculosis programmes on the management of tuberculosis in children
Adapted from the WHO 2006 guidance: note that HIV-infected children that are contacts with no evidence of active disease should receive IPT irrespective of age.

Child in close contact with a case of sputum smear-positive TB

Less than 5 years

Well

Preventive Therapy

If becomes Symptomatic

Symptomatic*

Evaluate for TB disease

If becomes Symptomatic*

5 Years and Over

Symptomatic*

Well

No Treatment

Well

*S symptomatic: If TB is suspected, refer to local guidelines on diagnosis of childhood TB

*Also consider if the mother or primary caregiver has sputum smear-negative pulmonary TB

* Isoniazid 10/mg/kg daily for 6 months

* Unless the child is HIV-infected (in which case isoniazid 10/mg/kg daily for 6 months is indicated)
Management of child contacts

- **Decentralise**: symptom-based screening provides opportunity to undertake an integrated family-based approach in the community around the source case receiving DOT rather than requiring referral to health facility for all cases.

- **Adherence**: to IPT for 6 months is a major challenge.

- **Enhanced case-finding**: Note that symptom-based screening also aims to identify symptomatic contacts of any age for investigation for possible TB disease.
Management of child contacts

List close contacts

• What is the age of the contact?
• Is the contact HIV-infected?
• Does the contact have any symptoms suggestive of TB?

Checklist of main symptoms

• Persistent cough for more than 2 weeks
• Weight loss or failure to gain weight
• Persistent fever for more than 1 week and/or night sweats
• Fatigue, reduced playfulness, less active
Management of child contacts

Criteria for contacts to receive IPT

- No active TB disease – no symptoms suggestive of TB
  AND
- At high risk of disease following TB exposure
  • < 5 years
  • HIV-infected

<table>
<thead>
<tr>
<th>Management of contacts</th>
<th>Response</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic</td>
<td>TB treatment</td>
<td>Register</td>
</tr>
<tr>
<td>Sputum smear positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>Refer</td>
<td>Refer</td>
</tr>
<tr>
<td>Sputum smear-negative or not available</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic and high risk</td>
<td>IPT</td>
<td>IPT register</td>
</tr>
<tr>
<td>Asymptomatic and not high risk</td>
<td>No treatment</td>
<td>Advise to return if symptoms develop</td>
</tr>
</tbody>
</table>
## Sample contact screening register

<table>
<thead>
<tr>
<th>Name</th>
<th>Age (years)</th>
<th>TB symptoms (Y/N)</th>
<th>Anti-TB treatment (Y/N)</th>
<th>Isoniazid preventive therapy (Y/N)</th>
<th>TB registration number</th>
<th>Treatment outcome</th>
<th>HIV status$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ For young children under 15 years of age, the tuberculin test is optional.
Burundi, Kenya, Rwanda, Tanzania, Uganda, Zambia, Zimbabwe

Included emphasis on child TB

Participants devised and agreed on 10 action points for including child TB in NTP activities
Childhood TB and NTPs

1. Develop and adapt child TB guidelines
2. Operationalise child TB guidelines
3. Identify child TB champion
4. Focal person for child TB at NTP – working group
5. Training – provide child TB training and incorporate into ongoing training related to TB and TB/HIV
6. Incorporate child TB into annual plans and 5-year strategic plan
7. Incorporate child TB into budget
8. Include child TB data in routine reporting and reviews
9. Operational research to determine constraints and barriers
10. Research aimed to improve child TB and contact management
Child TB training for paediatricians or trainees – clinicians, researchers and/or teachers – held each year in Cape Town since 2007

Ideal for child TB champion within NTP or national child TB steering group.
Clinical and training tool

Aimed at peripheral/district health worker

Up-to-date with current guidelines

Management algorithms

Includes TB in HIV-infected

Desk-guide for diagnosis and management of TB in children
Child TB, NTP and operational research

Priorities in Operational Research to Improve Tuberculosis Care and Control

GOAL SETTING
- SPECIFIC
- MEASURABLE
- ATTAINABLE
- RELEVANT
- TIME-BOUND
Operational research is a critical tool

- Identify barriers
- Identify main management issues
- Identify OR priorities
- Advocacy
- Implementation
- Monitoring progress

Operational research course for NTP staff held by IUATLD annually
Roadmap for TB in children
Figure. Interventions that target stages of the continuum in children from susceptibility to disease and outcome.
“There are many contributions which the pediatrician can make to a TB control program.

First the negativism about tuberculosis so prevalent in pediatrics must be overcome...”

*Edith Lincoln, 1961*