Module 1

EPIDEMIOLOGY OF CHILDHOOD TB
Burden of TB in children

- Tuberculosis (TB) in children is common wherever TB is common in adults i.e. TB endemic settings
- TB is an important cause of illness and death in children in many TB endemic countries
- At least 550,000 children become ill with tuberculosis (TB) each year.
- Up to 80,000 HIV-uninfected children die of TB every year*.
- 70–80% of children with TB, have the disease in their lungs (pulmonary TB). The rest are affected by TB disease in other parts of the body (extrapulmonary TB).
- There were over ten million orphans due to parental TB deaths in 2010.
- An understanding of the risks for infection and disease due to TB in children is critical for improved diagnosis and preventive management
- The HIV epidemic has increased the burden of childhood TB and the clinical challenges
- The main benefit of neonatal BCG is protection against severe disseminated TB in children
The proportion of cases among children may be different in countries for which age-disaggregated data were not available. However, this is becoming less of a problem as the reporting of cases disaggregated by age has been improving and the number of countries not reporting age-disaggregated data was low in 2013.

TB-related deaths in children are underrepresented in this report because TB-related deaths in children are often attributed to HIV or pneumonia or malnutrition.
Figure 1. Percentages of the tuberculosis caseload

The percentage of the tuberculosis caseload made up by children <15 years of age in relation to the incidence of tuberculosis/100,000 population and the population pyramids typical of an (A) developed and a (B) developing community.
National TB control data

• This slide could include recent data of TB control indicators from your National TB control programme or regional data
CALL TO ACTION for CHILDHOOD TB

Read the Call in French, Read the Call in Russian

Sign the Call to Action

We, participants gathered at the ‘International Childhood Tuberculosis Meeting’ held March 17-18, 2011 in Stockholm, Sweden recognize that:
Childhood TB and public health

• Public health approach: Proper identification and treatment of infectious cases will prevent childhood TB

• Child TB historically afforded a low priority by NTPs:
  – Diagnostic difficulties
  – Usually not infectious
  – Limited resources
  – Lack of recording and reporting

But .....  
- this disregards the impact of TB on childhood morbidity and mortality

- child TB reflects recent TB control

- infected children become adults with disease
Pathogens found in lungs from autopsy studies of African children

<table>
<thead>
<tr>
<th>Causes of pneumonia</th>
<th>HIV-infected N=473</th>
<th>HIV-uninfected N=338</th>
<th>Total N=811</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial</td>
<td>238 (50%)</td>
<td>132 (39%)</td>
<td>370 (46%)</td>
</tr>
<tr>
<td>PcP</td>
<td>145 (31%)</td>
<td>11 (3%)</td>
<td>156 (19%)</td>
</tr>
<tr>
<td>CMV</td>
<td>121 (26%)</td>
<td>7 (2%)</td>
<td>128 (16%)</td>
</tr>
<tr>
<td>M. tuberculosis</td>
<td>50 (11%)</td>
<td>27 (8%)</td>
<td>77 (9%)</td>
</tr>
<tr>
<td>Co-infection</td>
<td>98 (21%)</td>
<td>5 (1.5%)</td>
<td>103 (13%)</td>
</tr>
</tbody>
</table>

Combined data from 7 autopsy studies from five TB endemic countries shows that tuberculosis is a common diagnosis in children dying with lung disease including HIV-uninfected children.
Studies from many TB endemic settings consistently show that BCG protects against severe disseminated forms of TB in children and leprosy.
Risk factors for TB infection and disease in children

For TB infection

• Contact with source case
  – Closeness of contact
  – Duration of contact

• Source case
  – Smear positivity
  – Cavities on CXR

• Increased exposure
  – Living in high TB endemic communities
  – Children of families living with HIV
Risk factors for TB infection and disease in children

For TB infection
- Contact with source case
  - Closeness of contact
  - Duration of contact
- Source case
  - Smear positivity
  - Cavities on CXR
- Increased exposure
  - Living in high TB endemic communities
  - Children of families living with HIV

For TB disease
- Young age
  - Especially 0-2 years
- HIV infection
  - Risk of infection and disease
- Other immunosuppression
  - Malnutrition
  - Post-measles
- Not BCG vaccinated
  - Risk of disseminated disease
The risk of infection with tuberculosis (as measured by TST) is greatest if the contact is close and with a case of sputum smear-positive disease.
Infection with TB can occur from contact with a sputum smear-negative source case but it is less common than from smear-positive cases.

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

## 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
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
Risk of TB disease following infection by age

Percentage distribution of TB disease by age group:

- **<1 year**: High risk
- **1 to 2 years**: Moderate risk
- **2 to 5 years**: Low risk
- **5 to 10 years**: Very low risk
- **10 to 15 years**: Minimal risk

Note: The diagram indicates the percentage of cases for PTB and disseminated TB.
Incidence by age when TB was first diagnosed

TB disease in children

- 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 and the type depends on age
  - Smear positive disease is usually older children
# Childhood TB caseload: Malawi 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></td>
</tr>
<tr>
<td>Total childhood</td>
<td>2,739</td>
<td>11.9%</td>
</tr>
<tr>
<td>0-4 years</td>
<td>1,615 (59 %)</td>
<td>7%</td>
</tr>
<tr>
<td>5-14 years</td>
<td>1,124 (41 %)</td>
<td>4.9%</td>
</tr>
<tr>
<td>Smear-positive PTB</td>
<td>127 (5 %)</td>
<td>1.3%</td>
</tr>
<tr>
<td>Smear-negative PTB</td>
<td>1,804 (65 %)</td>
<td>21.3%</td>
</tr>
<tr>
<td>EPTB</td>
<td>808 (30 %)</td>
<td>15.9%</td>
</tr>
</tbody>
</table>

### Types of childhood EPTB disease in 2 endemic settings

<table>
<thead>
<tr>
<th></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>Pericardial</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>

Child TB data and NTP

- The burden of TB in children at a national or global level is uncertain.

- The burden of TB in children is an important indicator of ongoing transmission within the community.

- Children with TB are often not registered with or reported by NTP - but should be.

- Important data include age, TB disease type, HIV status and treatment outcomes.
The challenge of HIV and TB/HIV

- Increased caseload of child TB
- Greater difficulty with diagnosis
- Poorer response to TB treatment
- Drug interactions
- Implementation of the “three I’s”
TB/HIV epidemiology

Estimated Incidence of Tuberculosis per 100,000 Population in African Countries in 1990 and 2005.
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
The TB notification rate and notification rate of smear-positive disease rose in Malawi in the wake of the worsening HIV epidemic.

Childhood tuberculosis notifications in Blantyre district, Malawi, increased 8-fold from 1986 to 1995 as the TB epidemic worsened.

Increased risk of TB exposure among young children in HIV-endemic countries
Child TB and TB/HIV

- Risk of culture-confirmed TB is far higher in HIV-infected than in HIV-uninfected children
  

- TB risk is higher in HIV-infected children with low CD4% < 15% compared to HIV-infected children with higher CD4%
  
  Elenga N et al, Pediatr Infect Dis J 2005

- Mortality significantly higher in HIV-infected especially if not receiving ART
Impact of HIV on TB treatment outcome

HIV infection was associated with a very poor outcome from TB in children in the pre-HAART era

<table>
<thead>
<tr>
<th>Country</th>
<th>Complete recovery HIV+</th>
<th>Complete recovery HIV-</th>
<th>Mortality HIV+</th>
<th>Mortality HIV-</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>65%</td>
<td>95%</td>
<td>15%</td>
<td>0%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Jeena et al 1994</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cote d’Ivoire</td>
<td>23%</td>
<td>3%</td>
<td>23%</td>
<td>3%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mukadi et al 1995</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>63%</td>
<td>97%</td>
<td>16%</td>
<td>0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Espinal et al 1994</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethiopia</td>
<td>55%</td>
<td>73%</td>
<td>38%</td>
<td>6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Palme et al 2002</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Three “I”s for TB control

1) Intensified Case Finding
2) INH Prevention Treatment (IPT)
3) Infection Control

….and a fourth?

Integration

of TB/HIV including maternal TB/HIV
of other health services such as maternal child health/IMCI
Maternal TB/HIV impact

• TB in pregnancy or post-partum is common especially in HIV-infected women

• Associated with maternal mortality

• Associated with LBW and poorer infant outcomes

• Associated with risk of TB and of HIV transmission
Child TB data and NTP

• Children diagnosed and treated for TB should be routinely registered, recorded and reported

• Important information includes age, TB type, HIV status and treatment outcome

• Such data are important for M&E as well as informing training activities, drug procurement, strategic plans etc.

• NTP should have a designated child TB working group that oversees and facilitates child TB activities
A few points to keep in mind......

- Tuberculosis (TB) in children is common wherever TB is common in adults i.e. TB endemic settings
- TB is an important cause of illness and death in children in many TB endemic countries
- An understanding of the risks for infection and disease due to TB in children is critical for improved diagnosis and prevention
- The HIV epidemic has increased the burden of child TB and the clinical challenges
- The main benefit of neonatal BCG is protection against severe disseminated TB in children
- NTP should register and report all child TB cases!
Revision and self-assessment

List three important risk factors for TB exposure and infection

(3 marks)

List three important risk factors for developing TB disease if infected

(3 marks)

True or False: (4 marks)
1. The risk of infection for children has been reduced in the HIV endemic setting
2. Extrapulmonary TB is usually more common than pulmonary TB in children
3. Careful contact history is an important diagnostic tool in young children with suspected TB
4. Neonatal BCG immunisation has limited protective efficacy against TB in children