TB EPIDEMIOLOGY: IMPACT ON CHILDREN

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Robert Koch 1843-1910
Discovered *M. tuberculosis* 1882
TB deaths in England and Wales
The global burden of TB in 2008

Estimated number of cases

9.37 million
(range, 8.9–9.9 million)

Estimated number of deaths

1.3 million*
(range, 1.1–1.7 million)

HIV-associated TB
1.4 million (15%)
(range, 1.3–1.6 million)

Multidrug-resistant TB (MDR-TB)
0.5 million

*excluding deaths among HIV+ people
High-burden countries (HBCs)

- 22 countries responsible for ~80% of TB morbidity and mortality worldwide
- 8 of 22 HBCs are in Africa (Nigeria, Ethiopia, South Africa, Kenya, DR Congo, Tanzania, Uganda, Mozambique)
- Other countries not ‘HBC’ due to smaller population but high incidence reflects TB burden (e.g. Zambia)
“The world’s biggest killer and the greatest cause of ill health .... is listed almost at the end of the ICD. It is given code Z59.5 - extreme poverty”.

(Br Med J 1996;313:65)

- “A deterioration in the control of TB thus immediately hurts the youngest generation”

(Rieder, 1997)
TB incidence rates & socio-economic level, New York, 1973
(SE level estimated on the basis of education, occupation and income)
Key transitions in TB transmission

Susceptible → Exposed → Infected → Diseased → Infectious → Sick
Accessed care → Recognized → Diagnosed → Treated → Completed → Cured

Each transition has a measurable probability
Probability varies with the situation

(Don Enarson)
RELEVANCE OF PEDIATRIC TB

• Indication of epidemic control (sentinel surveillance): failure of health systems

• Recent transmission: DR, genotypes

• Unique spectrum and severity of disease

• Opportunity: study of distinct phenotypes (TBM)

• Preventable: epidemic control, IPT, vaccines

• Childhood TB as sentinel Event
RISK

- Different risks for infection and disease
- Factors influencing risk:
  - Organism
  - Host
  - Environment
Key Transitions in tuberculosis

Who Gets Infected?

From Rieder Epidemiologic Basis of Tuberculosis Control
Key Transitions in tuberculosis

Who Gets Infected?

Percent infected

Bedfordshire 1948-1952
Rotterdam 1967-1969
Saskatchewan 1966-1971

Van Geuns HA, Bull Int Union Tuberc 1975;50:107-21
Tuberculous Infection Among Children by Type of Contact and Bacteriologic Status of Index Case, British Columbia and Saskatchewan, 1966 - 1971

Early case detection essential to limit transmission

Transmission

Bacterial Load

![X-ray image]

Graph showing percentage of negative cases over visits.

Diagnosis

- Smear +
- Smear ++
- Smear +++

Treatment Begins

Cure (Smear -)

Transmission

0 20 40 60 80 100

Diag D1 D3 W1 W2 W4 M2 M3 M6

Visit

% Negative

75%

Courtesy, Rob Warren
Risk of Infection

- Determined by exposure to infectious case
- Mediated by duration of infectiousness
- Variable numbers of infections per infectious case
- Young TB patients more likely to infect children sharing households
Measuring Infection

- Annual Risk of TB Infection Survey (ARTI)
  - Declining in industrialized countries
  - Stable in some areas
  - Increasing in some parts of Sub-Saharan Africa
NTP response to children exposed to TB = contact tracing

- Numerous studies on household contact tracing studies
- Limited data on how often contacts are traced in NTP
- Malawi – hospitalised adults
  - 21% informed about childhood screening
  - In 12% some of the children were screened

*Int J Tuberc Lung Dis 2002;6:362-364*
• TB notification rate children 0-14 years: 620/100 000
• Annual risk of infection: 3.5%
<table>
<thead>
<tr>
<th>COMPONENTS</th>
<th>ITEMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td>Two</td>
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<td>X</td>
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</tbody>
</table>

*46 children were excluded from principal component analysis due to missing data values.*
<table>
<thead>
<tr>
<th>COVARIATES</th>
<th>AGE GROUP ANALYZED</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>3 months to 15 years</td>
<td>3 months to 5 years</td>
<td>6 years to 15 years</td>
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<td></td>
<td>(N=350)</td>
<td>(N=254)</td>
<td>(N=96)</td>
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<td></td>
<td>Unadjusted</td>
<td>Adjusted</td>
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<td>Adjusted</td>
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<tr>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
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<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
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</tr>
<tr>
<td><em>M. tb</em> contact score</td>
<td>1.51 (1.32 - 1.73)</td>
<td>1.54 (1.33-1.78)</td>
<td>1.74 (1.45-2.09)</td>
<td>1.76 (1.45-2.12)</td>
<td>1.21 (0.96-1.52)</td>
<td>1.20 (0.96-1.52)</td>
<td></td>
</tr>
<tr>
<td>Age in months</td>
<td>1.01 (1.008-1.019)</td>
<td>1.02 (1.008-1.039)</td>
<td>1.00 (0.98-1.012)</td>
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<tr>
<td>Prior <em>Tb</em> treatment</td>
<td>1.97 (0.606-6.403)</td>
<td>2.30 (0.439-12.024)</td>
<td>1.57 (0.29-8.47)</td>
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*Baseline measure of *M. tb* infection: infected defined if two of three test of infection (TST, QFT-IT, T-SPOT.TB) were positive

Mandalakas, in progress
Risk of TB progression

Rieder H Epidemiological basis for TB control

RISK OF DISEASE PROGRESSION IN CHILDREN

- **Young age**
  - 43% of **infants** (children < 1 year)
  - 25% of children aged one to five years
  - 15% of **adolescents**

- **Recent infection (1-2 years):** children with close contact

- Malnutrition

- HIV
## IMPACT OF HIV

<table>
<thead>
<tr>
<th>Number of TB cases per 100 0000 population (95% CI)</th>
<th>All infants</th>
<th>HIV-uninfected infants</th>
<th>HIV-infected infants</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB incidence</td>
<td>83.1 (73-94)</td>
<td>65.9 (57-75)</td>
<td>1596 (115-2132)</td>
<td>24.2 (17-34)</td>
</tr>
</tbody>
</table>

*Hesseling, Clin infect Dis, 2009*
TB IN CHILDREN: CONTINUUM OF TB INFECTION AND DISEASE: WHAT DO WE WANT TO PREVENT, DIAGNOSE AND TREAT?

Exposure

>60% children 0-5 with TB disease have household/close TB exposure

Infection

Limited Disease

Severe disease

Disseminated Disease and death
Exposure

Infection

Limited Disease

Severe disease

Disseminated disease and death

Age

HIV

Environmental factors, strain, nutrition, genetics
Global TB emergency DOTS programme launched

- TB declared a global emergency in 1993
- Targets for TB control first formulated at 44th World Health Assembly 1991
- Initial performance targets
  - detect 70% of new smear+ cases
  - successfully treat 85% of cases
1995-2008: 15 years of progress
DOTS/Stop TB Strategy

- 36 million patients cured in 1995-2008
- Up to 7 million deaths averted, compared to non-DOTS treatment
- Case fatality rate halved from 7.6% to 4%
- Cure rate at its highest ever (87% in 2007-8)
- But….TB incidence declining much more slowly than predicted
Global TB Control Global Targets

2015: Goal 6: Combat HIV/AIDS, malaria and other diseases

Target 8: to have halted by 2015 and begun to reverse the incidence of TB ....

Indicator 23: Reduce, prevalence and deaths associated with TB

Indicator 24: Increase proportion cases detected/cured under DOTS

2015: 50% reduction in TB prevalence and deaths

2050: elimination (<1 case per million population)
1. Pursue high-quality DOTS expansion
2. Address TB-HIV, MDR-TB, and needs of the poor and vulnerable
3. Contribute to health system strengthening
4. Engage all care providers
5. Empower people with TB and communities
6. Enable and promote research
TB prevalence and mortality

On track everywhere except for Africa

Prevalence (all)

<table>
<thead>
<tr>
<th>Rate per 100,000</th>
<th>1990</th>
<th>1995</th>
<th>2000</th>
<th>2005</th>
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<tbody>
<tr>
<td>300</td>
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<td>250</td>
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<td>200</td>
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<tr>
<td>150</td>
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</table>

Mortality (excl. HIV)

<table>
<thead>
<tr>
<th>Rate per 100,000</th>
<th>1990</th>
<th>1995</th>
<th>2000</th>
<th>2005</th>
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<tbody>
<tr>
<td>40</td>
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<td>20</td>
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</tbody>
</table>
Incidence: All TB / 100,000 Population: 1990-2004

Nunn P et al. JID 2007; Suppl 196: S5:14
Global estimate: about 1.4 million TB/HIV cases and half a million TB/HIV deaths a year

HIV prevalence among TB cases

FIGURE 2
Estimated HIV prevalence in new TB cases, 2008

HIV prevalence in new TB cases, all ages (%)
- 0-4
- 5-19
- 20-49
- ≥50
- No estimate
Policy on collaborative TB/HIV activities
WHO recommendations

Establish TB/HIV collaborative mechanisms
- Coordination and joint planning at all levels
- Conduct surveillance of HIV prevalence among TB cases
- Monitor and evaluate collaborative TB/HIV activities

Decrease burden of TB among PLHIV (the "3 I’s")
- Intensified TB case finding
- Infection control (health care and congregate settings)
- INH preventive therapy

Decrease burden of HIV among TB patients
- Provide HIV testing and counselling
- Introduce HIV prevention methods
- Introduce co-trimoxazole preventive therapy
- Ensure HIV/AIDS care and support
- Introduce ARVs
The lower the Gross National Income, the higher TB incidence.
## Multi-dimensional efforts required

### Core TB sphere
- Coherent pursuit of StopTB Strategy by TB programmes
- Focus on early case detection and high cure rates
- Facing TB/HIV and MDR-TB
- Measuring impact
- Engaging non-state sector and communities

### Health system & policies
- Abolishing financial barriers (UHC)
- Facing human resources crisis
- Laboratory strengthening
- Drug quality and rational use
- Infection control
- Planning, governance, management
- TB/HIV service integration & PAL
- Linkages with NCD

### Development sphere
- Social protection; housing & urban planning; nutrition/food security; migration; labor
- Refugees; crises response
- Human rights agenda
- Poverty reduction strategies

### Research sphere
- Advocating for growth in basic research, R&D and operational research
- Supporting rapid transfer of technology
Increasing Burden of TB in Cape Town, SA

**Table:**

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of TB notifications</th>
<th>Population size</th>
<th>TB notification rate, cases/100,000 persons&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TB re-treatment rate, %&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Estimated prevalence of HIV infection, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>32</td>
<td>5518</td>
<td>580</td>
<td>3</td>
<td>6.3</td>
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<tr>
<td>1997</td>
<td>42</td>
<td>6429</td>
<td>653</td>
<td>21</td>
<td>8.9</td>
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<tr>
<td>1998</td>
<td>67</td>
<td>7339</td>
<td>913</td>
<td>7</td>
<td>11.6</td>
</tr>
<tr>
<td>1999</td>
<td>74</td>
<td>8250</td>
<td>897</td>
<td>20</td>
<td>14.2</td>
</tr>
<tr>
<td>2000</td>
<td>90</td>
<td>9161</td>
<td>982</td>
<td>17</td>
<td>16.5</td>
</tr>
<tr>
<td>2001</td>
<td>142</td>
<td>10,071</td>
<td>1410</td>
<td>15</td>
<td>18.4</td>
</tr>
<tr>
<td>2002</td>
<td>150</td>
<td>10,982</td>
<td>1366</td>
<td>18</td>
<td>19.9</td>
</tr>
<tr>
<td>2003</td>
<td>175</td>
<td>11,892</td>
<td>1472</td>
<td>22</td>
<td>21.1</td>
</tr>
<tr>
<td>2004</td>
<td>188</td>
<td>12,803</td>
<td>1468</td>
<td>24</td>
<td>21.9</td>
</tr>
</tbody>
</table>

<sup>a</sup> P = .007, by test for trend.

<sup>b</sup> P = .073, by test for trend.
Increasing incidence of TB

HIV prevalence in general population:
- 3-4% 0-9y
- 25% 20-39y

Lawn SD et al. CID 2006; 42: 1040-7
BURDEN OF TB IN CHILDREN

- **Global**: 2 billion latently infected, 8.8 million new cases
- >75% in 22 high-burden countries
- Estimated 10% among (inaccurate estimates)
- International and domestic problem
- Limited surveillance: challenges in diagnosis
- Limited programmatic emphasis (prevention and diagnosis)
- Diagnostic challenges
- Infection and disease both relevant entities

www.who.int
Notifications among children, countries reporting age-disaggregated data, 2010

Estimated at least 6% of global notifications are among children

BUT: high levels of under-reporting of cases thought to exist e.g. due to lack of linkages between NTPs and paediatricians

WHO 2011 Global TB report www.who.int
Notifications among women, countries reporting cases disaggregated by sex, 2010

- ~38% cases notified globally are among women

Variation by region – higher percentage of cases among women in Africa and EMR

WHO Global TB report 201
www.who.int
“MISSING CASES IN CHILDREN”

- South Africa study (TBM) among children < 15 years:
  - Only 56% of cases were registered
  - 16% of all cases in register contained errors
  - Incorrect diagnosis, double notification, clerical error

- Surveillance study:
  - Only 87.8% of children treated for TB were recorded in register
  - Most severe cases not recorded and reported


*Marais et al Int J Tuberc Lung 2006; 10(3):259-263*
Lung Disease Identified At Necropsy In Zambian Children

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>HIV positive (N=180)</th>
<th>HIV negative (N=84)</th>
<th>Odds ratio (95%C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyogenic pneumonia</td>
<td>41%</td>
<td>50%</td>
<td>0.7 (0.4-1.2)</td>
</tr>
<tr>
<td>PCP</td>
<td>29%</td>
<td>7%</td>
<td>5.3 (2.1-15.7)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>18%</td>
<td>26%</td>
<td>0.6 (0.3-1.2)</td>
</tr>
<tr>
<td>CMV</td>
<td>22%</td>
<td>4%</td>
<td>7.7 (2.3-40.0)</td>
</tr>
<tr>
<td>Interstitial pneumonitis</td>
<td>8%</td>
<td>18%</td>
<td>0.4 (0.2-0.96)</td>
</tr>
<tr>
<td>Other</td>
<td>24%</td>
<td>16%</td>
<td>-</td>
</tr>
</tbody>
</table>

Millennium Development Goals

1. Eradicate extreme poverty and hunger
2. Achieve universal primary education
3. Promote gender equality and empower women
4. Reduce child mortality
5. Improve maternal health
6. Combat HIV/AIDS, malaria and other diseases
7. Ensure environmental sustainability
8. Global partnership for development
Millennium Development Goals - TB

5 targets
- 2005 – detect 70% of new smear+ cases
- 2005 – successfully treat 85% of these cases
- 2015 – halve and begun reversing incidence
- 2015 – halve TB prevalence
- 2015 – halve TB deaths

Application to children, women and families
THANK YOU

“A generation of children free of tuberculosis”