Epidemiology of Tuberculosis: Global and Local

McGill Tuberculosis Course
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Objectives

Participants will be able to:

• Describe key features of current TB epidemiology, at the global and local level
• Identify major determinants of trends in TB incidence globally, and in Canada
• Identify key elements of global and Canadian TB control strategies
Case 1

- 32 y.o. male refugee claimant from DR Congo presented to RVH ER with herpes zoster involving left V1 distribution, with probable bacterial superinfection
- Wife known to be HIV-infected
- Hospitalized, confirmed HIV+ with CD4 ~70
- Minor hemoptysis; sputum induction performed
Case 1

- Found to have smear-negative, culture-positive pulmonary TB
- Sensitive to all first line anti-TB drugs
- Treated successfully with microbiologic cure
- HAART instituted with excellent response

Case 2

- 20 y.o. Peruvian-born male, in Canada for several years
- No past medical history of any kind
- Presented with sudden onset severe chest pain and dyspnea ~one week after returning from visit to Peru by airplane
Case 2

• Culture-positive on pleural fluid, BAL
• Found to have MDR-TB i.e. probable primary MDR
• Hospitalized for over 3 months with bronchopleural fistula
• Still on complex treatment regimen

Case 3

• 43 y.o. Quebec-born female
• No past medical history of any sort
• Referred to MCI clinic for persistent cough of several months duration
• Minor fatigue, weight loss
Case 3

- Immediately admitted to hospital
- 3+ smear positive on spontaneous sputum
- TB sensitive to all
- No clear exposure history; HIV-negative
- Prolonged hospitalization (> 3 months) as slow to clear sputum
- Ultimately cured
“I thought TB had disappeared”

- 2007: WHO estimated 9.3 million new cases, vs. 8.3 million cases in 2000 and 6 million cases in 1990
- 55% in Asia, 31% in Africa
- Overall global incidence 137 per 100,000 annually, down from peak 142 in 2004
- 1.3 million deaths in HIV-negative individuals, 450,000 deaths in HIV-positive individuals (~25% of all deaths in HIV-infected persons)

**FIGURE 1.2**
Estimated TB incidence rates, by country, 2007

**TABLE 1.2**
Estimated epidemiological burden of TB, 2007

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence 1000</th>
<th>smear-positive</th>
<th>smear-negative</th>
<th>initiality</th>
<th>reinfection</th>
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<tbody>
<tr>
<td>India</td>
<td>18000</td>
<td>982</td>
<td>168</td>
<td>873</td>
<td>305</td>
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<td>1328300</td>
<td>1306</td>
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<td>290</td>
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<td>245</td>
<td>392</td>
<td>109</td>
<td>174</td>
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<tr>
<td>South Africa</td>
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<td>25</td>
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<td>Cambodia</td>
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<tr>
<td>Afghanistan</td>
<td>27145</td>
<td>96</td>
<td>165</td>
<td>21</td>
<td>76</td>
</tr>
</tbody>
</table>

FIGURE 1.8
Global rates of TB incidence, prevalence and mortality, including in people with HIV, 1990–2007
Incidence (all forms, including HIV)
Prevalence (all forms, including HIV)
Mortality (including HIV)

FIGURE 1.9
Africa high HIV
Africa low HIV
Central Europe
Eastern Europe
High income countries
Eastern Mediterranean
Latin America
South-East Asia
Western Pacific
Limitations

- Reported TB cases (notifications) account for a variable proportion of all TB cases depending on the country
- Notifications will increase with improvements in diagnosis and reporting, regardless of underlying true incidence
- Notifications will decrease when national TB control programs worsen
- Total TB cases (reported + unreported) must therefore be estimated indirectly from other data e.g. prevalence surveys, annual risk of infection surveys, mortality data, extrapolation from “DOTS areas” etc.
- Substantial implications for program quality indicators
Major Determinants

- Basic elements of TB control e.g. diagnosis, consistent and appropriate treatment
- Health system infrastructure e.g. national control programs, public vs. private providers etc.
- General socioeconomic and health status, tobacco, alcohol
- HIV
- Drug resistance
- Obviously all these are interrelated

Figure 3. A. Case report rates of new sputum smear (ss)-positive tuberculosis (TB) cases per 100,000 population in 25 departments of Peru, plotted on a log, scale. B. National case report rates of all new TB cases (●), new pulmonary cases (●), and new smear positive cases (O). Lines were fitted by regressions for the years 1996–2000.

Suarez et al, JID 2001
Table 3. Results of multivariate linear regression analysis of Models 1–3: adjusted estimated effect (95% CI) of the specific parameter in the specific model on the change in TB incidence rate/100,000, between 1990 and 2005.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Model 1***</th>
<th>Model 2**</th>
<th>Model 3*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in life expectancy (per 1-year increase in life expectancy between 1990 and 1995)</td>
<td>-7.8 (-11.2 to -4.3)**</td>
<td>1.0 (-0.5 to 4.4)*</td>
<td>-1.3 (-2.3 to -0.3)**</td>
</tr>
<tr>
<td>Change in mortality in children aged &lt;5 years (per 1/10000) increase in mortality among children aged &lt;5 years between 1990 and 1995</td>
<td>9.00 (4.1 to 13.9)**</td>
<td>0.05 (-0.1 to 0.2)**</td>
<td>0.06 (0.2 to 0.0)**</td>
</tr>
<tr>
<td>Change in measles vaccination coverage (per 1% increase in measles vaccination coverage over period 1990–2005)</td>
<td>1.1 (-0.2 to 2.4)**</td>
<td>0.30 (-0.0 to 0.6)**</td>
<td>0.35 (-0.0 to 0.7)**</td>
</tr>
<tr>
<td>Change in GDP per capita (per 1% increase in GDP between 1990 and 2005)</td>
<td>1.1 (1.0 to 2.4)**</td>
<td>0.30 (-0.0 to 0.6)**</td>
<td>0.35 (-0.0 to 0.7)**</td>
</tr>
<tr>
<td>HIV prevalence in 2005 (per 1% higher HIV prevalence)</td>
<td>-0.9 (-1.8 to 0.02)</td>
<td>-0.9 (-1.8 to 0.07)</td>
<td>-0.5 (-2.0 to 0.1)</td>
</tr>
</tbody>
</table>

Oxlade et al, *IJTL* 2009
HIV

- Strongest known risk factor for TB disease
- Increases risk of progression/reactivation of latent TB infection by 100-fold or more
- To date, impact on global epidemiology most evident in sub-Saharan Africa, but concern re unknown magnitude of HIV-TB coinfection notably in India
Drug Resistance

• In 2007, the estimated number of cases of multi-drug resistant TB was 511,000
• 3.1% of all new TB cases and 19% of retreatment cases were multi-drug resistant
  – Defined as resistance to isoniazid AND rifampin, with or without resistance to other antibiotics
• A marker of treatment program quality
• Poor prognosis, treatment complexity and expense
Figure 1.6: Countries with the highest numbers of estimated MDR-TB cases, 2007. Horizontal lines denote 95% confidence intervals. The sources of estimates to drug resistance surveillance surveys (DRS, in red) or modelling (in grey).

Figure 2: Countries or settings with multidrug-resistant TB prevalence higher than 6.0% among new cases, 2002–2007.

**Figure 8:** Prevalence of multidrug-resistant TB among new and previously treated cases in the WHO Region of the Americas, 2002–2007.

**Table 2.2**

Technical elements of the DOTS strategy

- **Case detection through quality-assured bacteriology**
  - Case detection among symptomatic patients self-reporting to health services, while sputum smear microscopy and culture are used for diagnosis in some countries, but direct sputum smear microscopy should still be performed for all suspected cases.

- **Standardized treatment with supervision and patient support**
  - Standardized short course chemotherapy using regimens of 6-8 months for at least all confirmed smear-positive cases. Good case management includes directly observed treatment (DOT) during the intensive phase for all new smear-positive cases, during the continuation phase of regimens containing rifampicin and during the entirety of anti-TB treatment regimen. In countries that have consistently documented high rates of treatment success, DOT may be reserved for a subset of patients, as long as cohort analysis of treatment results is provided to document the outcome of all cases.

- **An effective drug supply and management system**
  - Establishment and maintenance of a system to supply all essential anti-TB drugs and to ensure no interruption in their availability.

- **Monitoring and evaluation system, and impact measurement**
  - Establishment and maintenance of a standardized recording and reporting system, allowing assessment of treatment results (see Table 2.7).
Table 2.1
Component of the Stop TB Strategy

1. Pursue high quality DOTS expansion and enhancement
   a. Secure political commitment, with adequate and sustained financing
   b. Ensure early case detection, and diagnosis through quality-assured bacteriology
   c. Provide standardized treatment with supervision, and patient support
   d. Ensure effective drug supply and management
   e. Monitor and evaluate performance and impact

2. Address TB-HIV, MDR-TB, and the needs of poor and vulnerable populations
   a. Scale up collaborative TB-HIV activities
   b. Scale up prevention and management of multidrug-resistant TB (MDR-TB)
   c. Address the needs of TB contacts, and of poor and vulnerable populations, including women, children, prisoners, refugees, migrants and ethnic minorities

3. Contribute to health system strengthening based on primary health care
   a. Help improve health policies, human resource development, financing, supply, service delivery and information
   b. Strengthen infection control in health services, other congregate settings, and households
   c. Upgrade laboratory networks, and implement the Practical approach to lung health (PAL)
   d. Adapt successful approaches from other fields and sectors, and foster action on the social determinants of health

4. Engage all care providers
   a. Involve all public, voluntary, corporate and private providers through Public-Private mix (PPM) approaches
   b. Promote use of the International Standards for TB Care (ISTC)

5. Empower people with TB, and communities through partnership
   a. Pursue advocacy, communication and social mobilization
   b. Foster community participation in TB care
   c. Promote use of the Patients Charter for TB Care

6. Enable and promote research
   a. Conduct programme-based operational research, and introduce new tools into practice
   b. Advocate for and participate in research to develop new diagnostics, drugs and vaccines
TB Control

- Continued implementation and expansion of the basic DOTS strategy
  - Target 70% case detection, 85% treatment success
- Strengthen basic TB control programs

**FIGURE 2.2**
DOTS coverage by WHO region, 2007. The red portion of each bar shows DOTS coverage as a percent of the population. The numbers in each bar show the population (in millions) within (red portion) or outside (gray portion) DOTS areas.
Other Aspects of TB Control

- Improved diagnostics
- Better selection of drug treatment regimens
- Treatment of MDR-TB: Green Light Committee
- New drugs, vaccines

TB in Canada

Figure 2: Tuberculosis cases and incidence rates – Canada: 1987-2007

Ellis et al, Public Health Agency of Canada
Ranked tuberculosis incidence in Canada – provinces/territories: 2007

<table>
<thead>
<tr>
<th>Reporting province or territory</th>
<th>Abbreviation</th>
<th>Incidence rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nunavut</td>
<td>Nu.</td>
<td>98.2</td>
</tr>
<tr>
<td>Northwest Territories</td>
<td>N.W.T.</td>
<td>34.5</td>
</tr>
<tr>
<td>Saskatchewan</td>
<td>Sask.</td>
<td>10.9</td>
</tr>
<tr>
<td>Yukon</td>
<td>Y.T.</td>
<td>9.2</td>
</tr>
<tr>
<td>Manitoba</td>
<td>Man.</td>
<td>8.8</td>
</tr>
<tr>
<td>British Columbia</td>
<td>B.C.</td>
<td>6.4</td>
</tr>
<tr>
<td>Ontario</td>
<td>Ont.</td>
<td>5.1</td>
</tr>
<tr>
<td>Alberta</td>
<td>Alta.</td>
<td>3.2</td>
</tr>
<tr>
<td>Quebec</td>
<td>Que.</td>
<td>3.9</td>
</tr>
<tr>
<td>Newfoundland and Labrador</td>
<td>N.L.</td>
<td>1.1</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>N.S.</td>
<td>0.7</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>N.B.</td>
<td>0.7</td>
</tr>
<tr>
<td>Prince Edward Island</td>
<td>P.E.I.</td>
<td>0.9</td>
</tr>
<tr>
<td>CANADA</td>
<td></td>
<td>4.7</td>
</tr>
</tbody>
</table>

Figure 6
Tuberculosis incidence rate by age group and sex – Canada: 2007
TB in the Foreign-Born

- Data consistently demonstrate parallel between incidence rates in countries of origin and incidence rates following arrival in destination country
- Incidence highest during the first years after arrival
  - Recently acquired infection
  - “Stressors” associated with migration?
- Disproportionately affects young adults
Drug Resistance in 2007

Of 1,188 Canadian cases with drug resistance data:
- 94 (8%) mono-resistance to first line drugs (82 INH), plus 6 INH/ethambutol
- 10 (0.8%) MDR-TB
- 1 (0.08%) XDR-TB
Montreal

- 123 reported active TB cases in 2007; maximum was 209 in 1994
- Corresponding decrease in incidence from 11.6 to 6.4 per 100,000
- Consistently ~80% of cases involve foreign-born persons

DSP Montréal-Centre, Bureau de surveillance épidémiologique


Elements of Canadian TB Control

- Successful completion of appropriate treatment for active TB
- Contact investigation, with suitable treatment of latent TB infection
- Screening of new immigrants and refugees for 1) active TB; 2) “high-risk” latent TB i.e. “inactive TB”
- Improved diagnosis and contact investigation among Aboriginals and other high-risk subgroups
Key Messages

• TB remains a global epidemic and public health emergency
• There are a number of reasons for this:
  – Basic TB control infrastructure
  – Limitations of current diagnostic tools and treatment
  – HIV
  – Drug resistance
  – General health and socioeconomic conditions
• Successful control will clearly require more than “basic DOTS”

Key Messages

• Relative to global incidence, TB in Canada is extremely rare
  – Incidence in Canada is clearly decreasing
  – TB is concentrated in several population subgroups including foreign-born, Aboriginals, those with “inner city risks”
  – We see the impact of global phenomena locally