Forgotten But Not Gone: The Global Epidemiology of TB

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TB Historical Permutation

- 17th - 18th centuries TB took 1 in 5 adult lives
- 1850 - 1950 one billion people died of TB
- This decade 2010-2020
  - 300 million new infections
  - 90 million new cases
  - 30 million deaths
- More people died from TB last year than any year in history

The Global Burden of TB - 2013

<table>
<thead>
<tr>
<th>Estimated number of cases</th>
<th>Estimated number of deaths</th>
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<tbody>
<tr>
<td><strong>All forms of TB</strong></td>
<td></td>
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<tr>
<td>9 million</td>
<td>1.5 million*</td>
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<tr>
<td>(8.6–9.4 million)</td>
<td>(1.3–1.6 million)</td>
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<td>(830 cases per 100,000 pop.)</td>
<td>(800,000 – 1000,000)</td>
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<td><strong>HIV-associated TB</strong></td>
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<td>1.1 million (13%)</td>
<td>360,000</td>
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<td>(1.0–1.2 million)</td>
<td>(400,000–460,000)</td>
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<td>480,000</td>
<td>210,000</td>
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<tr>
<td><strong>Multidrug-resistant TB</strong></td>
<td></td>
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<tr>
<td>3.5% new, 20.9% prev. treated</td>
<td>210,000</td>
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<tr>
<td>(350,000–610,000)</td>
<td>(180,000–290,000)</td>
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<tr>
<td>out of ~12 million prevalent TB cases</td>
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<tr>
<td><strong>Childhood TB</strong></td>
<td></td>
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<tr>
<td>550,000</td>
<td>80,000**</td>
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<td>(470,000–640,000)</td>
<td>(54,000 – 97,000)</td>
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* 6% of the total burden
* Excluding deaths attributed to HIV/TB
** Excluding deaths attributed to TB/HIV

Source: WHO Global Tuberculosis Report 2014
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Emergence of “worst-case” TB scenarios

- Co-infection between TB and HIV
- Multidrug-resistant TB (MDR-TB)
  - Resistance to isoniazid and rifampin – the 2 most powerful anti-TB drugs
- Extensively-drug resistant TB (XDR-TB)
  - MDR-TB plus resistance to any fluoroquinolone and at least 1 second-line injectable (AMI, KAN, CAP)
- Totally Drug Resistant TB (TDR-TB)
  - Resistant to all anti-TB drugs

The Global Burden of TB/HIV

- 1/3 of 33 million people living with HIV/AIDS co-infected with TB (>10 million people)
- Without treatment, 90% will die
  - HIV and TB form a lethal combination, each speeding the other's progress
- TB is the leading cause of death among HIV-positive people (up to 50% of all patients worldwide)

Co-Existence of HIV & TB infection

Risk of Active TB

- 10% per lifetime
- 10% per year
- 0.0017% per year
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WHO TB/HIV Policy: 12 Point Policy Package

- Mechanism for integrated TB and HIV services
- Activities to reduce TB burden in PLHIV
- Activities to reduce HIV burden in TB patients

MDRTB/XDR-TB - The Big Problem!

- 480,000 new MDR-TB cases estimated annually with 210,000 deaths
- XDR-TB in 100 countries; 9.0% MDR cases have XDR
- 25% of estimated MDR-TB cases detected
- 44-58% (overall 48%) successfully completed treatment
- About 85% of the global MDR-TB burden found in 27 countries

Sources: Global TB Report, 2014
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Use of One Drug Knowingly or Unknowingly

- Sensitive bacilli killed
- Resistant bacilli multiply unimpeded
- Resistant bacilli become dominant

Pathogenesis of Drug Resistance

*Never add a single drug to a failing regimen*
Cost of a single MDR-TB case in the U.S. ranges from $28,217 - $1,278,066

Source: Rajbhandaw SS et al, IJTD 2004:204

Why Do We Have Drug Resistance?

- Inadequate treatment
  - Incorrect regimen (lack of drugs or knowledge)
  - Poor adherence
- Treatment failure / relapse with drug resistant TB
- Transmission of drug resistant TB

Unsexy Tuberculosis

- Concern and attention re: XDR-TB is appropriate, but skips the more important message
- XDR-TB, MDR-TB, and drug-sensitive tuberculosis are all the same disease
- The only difference is that MDR-TB is drug-sensitive tuberculosis modified by inappropriate treatment or drug taking, and XDR-TB is MDR-TB thus modified
- We need to recognize that there are 8,700,000 new active drug-sensitive cases of tuberculosis globally that could be feeding drug resistance
- It might be a less sexy concept, but they all must be appropriately treated with current strategies (as well as new diagnostics, drugs, vaccines, and proper infection control measures) to avoid preventable MDR-TB and XDR-TB, which are always lurking
- Preventing active, drug-sensitive tuberculosis, or treating it properly, should be everybody’s priority; it is the only way to prevent MDR-TB and XDR-TB

Reichman, LB. The Lancet, 2009
Inadequacies in Physician Practices

Major recurring practice delays in diagnosis and errors in treatment resulting in:
- Increased risk and likelihood of disease transmission
- More advanced and complicated disease
- Lengthened hospital stays
- Increased medical costs
- Development of MDR-TB and XDR-TB
- Development of TDR-TB?

International Standards for TB Care

All persons with otherwise unexplained cough lasting for 2-3 weeks or more should be evaluated for tuberculosis.
International Standard for TB Care: Diagnosis
Microbiological evaluation (smear ± culture) is essential for all patients (including children, extra-pulmonary, and persons with radiographic abnormalities).

International Standard for TB Care: Treatment
The provider is responsible for prescribing an adequate regimen and ensuring adherence.

International Standard for TB Care: Treatment
A patient-centered, individualized approach to treatment should be developed for all patients. A central element is direct observation by a treatment supporter.
Where Are The Missing Cases?

They are not detected due to poor laboratory capacity

Where Are The Missing Cases?
At home, if services are not accessible

Where Are The Missing Cases?
In other un-connected public systems (prisons)
Where Are The Missing Cases?

In the private sector

The Patient’s Charter for Tuberculosis Care

- Companion document to International Standards
- Initiated and developed by patients from around the world
- Outlines rights and responsibilities of people with tuberculosis
- Affirms that empowerment is catalyst for effective collaboration of the patient with health providers and authorities
Patient's Rights

You have the right to:
- Care;
- Dignity;
- Information;
- Choice;
- Confidence;
- Justice;
- Organization;
- Security

Source: Patient's Charter for TB Care, 2006

Patient's Responsibilities

You have the responsibility to:
- Share information;
- Follow treatment;
- Contribute to Community Health;
- Show Solidarity

Source: Patient's Charter for TB Care, 2006

Reported TB Cases in the United States, 1982-2013*

Historically low 9,582 Cases
Rate 3.0/100,000

Impact of HIV Epidemic, Poverty, Homelessness, Failure of Public Health Infrastructure

*Updated as of June 11, 2016
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US Response to 1990’s MDR Epidemic – Turning the Tide

- Strong public health advocacy to obtain increased funding from Congress
- Rebuilt the weakened infrastructure for TB services and research
- Implemented routine drug susceptibility testing with liquid media
- Implemented and monitored infection control precautions in healthcare and congregate settings
- Strengthened public-private partnerships
- Supported centers of excellence
- National Institute of Health’s 5-10 year investment in TB academic awardees
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2013 U.S. TB
- 9,582 TB cases
- 3.0 cases per 100,000 population
- Decline of 3.6% from 2012 case rate
- Decline of 64.1% from 1992

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TB at a Crossroad of Global TB Control
- US domestic decline of TB since prior to development of drugs
- US resurgence of TB during the 1980s and 1990s, largely due to neglect
- Massive and effective response
- TB on the radar screen domestically
- TB on the radar screen internationally

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BUT TB Remains a Global Killer

Why does TB still infect one-third of the world’s population and remain a global health threat despite the fact that highly cost-effective drugs are available to eradicate it?
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Challenges in TB Control

- Insufficient financial and human resources
- Inadequate healthcare infrastructure
- Weak laboratory capacity and lack of new rapid diagnostic tools
- Lack of new drugs that would cure TB in a shorter time
- Lack of effective vaccine that would prevent TB
- Poor use of infection control in healthcare settings
- HIV and MDR/XDR threats
- Minimal social mobilization for TB control and minimal population awareness → stigma

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Why Do We Need New Drugs To Treat TB?

- Shorter overall treatment duration
- Lower relapse rates
- Development of regimens with fewer adverse effects, particularly less hepatotoxicity
- Development of regimens that can be given easily and safely in combination with antiretroviral therapy
- Development of regimens that are effective in treating MDR-TB/XDR-TB
- Development of regimens that are effective and non-toxic in childhood TB
Drugs in clinical development:
- Heart Disease and stroke: 299
- COPD: 54
- Antibacterials and antivirals: 89
- Cancer: > 900 (includes vaccines)
  - Lung Cancer: 121
- HIV/AIDS: 70
- Diabetes: 221
- Anti-tuberculosis: 5-8
- Anti-malarials: 6

Leading causes of global mortality:
1. Ischemic heart disease
2. Stroke
3. COPD
4. Lower respiratory infection
5. Lung cancer
6. HIV/AIDS
7. Diarrhea
8. Road traffic
9. Diabetes
10. Tuberculosis
11. Malaria

The Few Remaining Cases
- With DOTS and case management along with funding, interest and involvement in developing new tools and strategies for combating TB we have taken care of the easy ones and…
- Expertise decreases
- Funding decreases
- Innovative Initiatives are de-emphasized or even forgotten
Several key challenges persist:
- Many vulnerable people do not have access to affordable services of sufficient quality.
- Technologies for diagnosis, treatment, and prevention are old and inadequate.
- Multi-drug resistant tuberculosis is a serious threat in many settings.
- HIV/AIDS continues to fuel the tuberculosis epidemic, especially in Africa.
- Other risk factors and underlying social determinants help to maintain tuberculosis.

Updated 2012

Defaulter and Motivation
“...to default is the natural reaction of normal, sensible people: The person who continues to swallow drugs or have injections with complete regularity in the absence of encouragement and help from others is the abnormal one.”

-Bull IUAT 1972; 47:68-75
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Lessons from Andrew Speaker

- TB has not gone away, it remains with us, highly prevalent and transmissible
- Anybody can get tuberculosis, not only poor people, minorities, or the foreign-born
- TB anywhere is TB everywhere
- All resistant TB, MDR and XDR TB is preventable by proper TB diagnosis and treatment
- Good public health is a silent secret, but when there is a small glitch, it becomes major news
- We desperately need new tools for TB diagnosis and treatment
- You don't want to sit on an airplane for 8 hours next to an untreated coughing person with any kind of TB, be it drug sensitive, MDR or XDR

INFORMATION LINE
1-800-4TB-DOCS (482-3627)
globaltb.njms.rutgers.edu