TB Intensive
San Antonio, Texas
May 7-10, 2013

Epidemiology of TB
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• No conflict of interests
• No relevant financial relationships with any commercial companies pertaining to this educational activity
Tuberculosis Epidemiology
Global and the U.S.

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Tuberculosis Epidemiology

• TB is highly prevalent and poorly controlled in most of the world (it is a really bad problem)
• HIV co-infection and lack of resources are the engines driving the worldwide TB epidemic
• TB in the U.S. is increasingly a reflection of the worldwide TB epidemic
• Modern TB control programs are like fire departments and work really well if given adequate resources
TB IN THE WORLD*

*We don’t know the epidemiology of TB in most of the world with certainty. In most of the world TB is diagnosed on the basis if AFB smears without cultures, and treated without in vitro drug susceptibility results

Global Tuberculosis Control
WHO Report 2011

• In 2010 8.8 million (8.5-9.2 million) incident cases of TB
• 1.1 million (0.9-1.2 million) deaths HIV neg
• 0.35 million (0.32-0.39 million) deaths HIV associated
• India and China accounted for 40% of the world’s notified TB cases in 2010, Africa an additional 24%
• Approximately 13% of TB cases occur among HIV co-infected individuals
**Worldwide TB**
Lawn and Zumia, Lancet e-pub 3/18/11

- Approximately 12% worldwide TB caseload HIV-associated
- 4/5 HIV co-infected cases in subSaharan Africa
- In the worst affected countries of South Africa and Swaziland about 1% of the population develops TB each year (>50% TB cases HIV coinfected)

**Global Epidemiology of TB - 2009**

- 22 countries account for 80% of the worldwide burden
- 5 Countries with the largest number of incident cases:
  - India (1.6–2.4 million)
  - China (1.1–1.5 million)
  - South Africa (0.40–0.59 million)
  - Nigeria (0.37–0.55 million)
  - Indonesia (0.35–0.52 million)
- India alone accounts for an estimated one fifth (21%) of all TB cases worldwide
- China and India combined account for 35%
Global Epidemiology of TB - 2009

- Top 10 Countries with the highest NEW TB CASES per 100,000:
  - Worldwide 137
  - Swaziland 1,257 #56: India 168/100,000
  - South Africa 971 #78: China 96/100,00
  - Zimbabwe 742
  - Namibia 727
  - Botswana 694
  - Sierra Leone 644
  - Lesotho 634
  - Djibouti 620
  - Gabon 501
  - Timor Leste 498
  - Togo 446

All in Africa!

Global Tuberculosis Control
WHO Report 2011

- The absolute number of TB cases has been falling since 2006 (not rising slowly)
- TB incidence rates have been falling since 2002 (2 years earlier than estimated)
- Estimates of the number of deaths from TB each year have been revised downward.
- In 2009 there were almost 10 million children who were orphans as a result of parental deaths caused by TB.
Global Tuberculosis Control  
WHO Report 2011

• In China, between 1990 and 2010, prevalence rates were halved, mortality rates fell by almost 80% and TB incidence rates fell by 3.4% per year
• Worldwide, TB mortality rates have fallen by just over a third since 1990
• Between 1995 and 2010, 55 million TB patients were treated in programs that had adopted the DOTS/Stop TB strategy, and 46 million were successfully treated. “These treatments saved almost 7 million lives”.

Definitions of Drug Resistant Tuberculosis

• MDR TB: Resistant to INH and Rifampin
• MDR TB is the precursor of XDR TB
• XDR TB: MDR TB
  – PLUS
  – Resistance to any fluoroquinolone
  – Resistance to at least one of the following injectables:
    • Amikacin, Kanamycin, Capreomycin
Drug Resistant Tuberculosis
Creation of MDR & XDR TB

- The development of XDR TB results from TB control and treatment practices in most of the world that would not be acceptable in the United States
- Case identification and treatment response are based on AFB smears without confirmatory cultures or susceptibility testing.
- Retreatment for treatment failure not based on in vitro susceptibility studies, rather, on fixed retreatment regimens.

WHO Effort To Combat TB Backfires.

WSJ 11/24/12

- The World Health Organization’s long-standing strategy for fighting tuberculosis is showing deadly unintended consequences: By focusing for years on the easiest-to-cure patients, it helped allow TB strains to spread that are now all but untreatable by modern medicine.
- The WHO and a growing chorus of global health experts are now calling for a significant overhaul in the way nations with widespread drug-resistant TB combat the disease. It amounts to a de facto acknowledgment that the WHO's TB strategy, and the countries that use it, failed to adapt quickly enough as the disease formed more powerful, resistant strains.
National survey of drug-resistant tuberculosis in China
(Zhao et al NEJM 2012, 366; 2161)

- 2007 national survey of drug-resistant TB in China (“cluster randomized sampling” of 4000 cases)
- 5.7% new patients and 25.6% previously treated patients had MDR-TB
- Among all TB cases, 25% had resistance to INH, Rmp or both, 10% had MDR-TB
- 8% of MDR cases had XDR isolates
- Most cases due to primary transmission but patients with multiple previous treatments who received their last treatment in a TB hospital had the highest risk of MDR-TB


- 2008 an estimated 440,000 case of MDR-TB
- Among all TB cases, 3.6% estimated MDR-TB
- 50% of MDR-TB estimated in China and India
- 2008 an estimated 150K MDR-TB deaths
- In 27 high MDR-TB burden countries, 1% of new and 3% of previously treated TB cases underwent DST
Global Tuberculosis Control
WHO Report 2011

- Less than 5% of new and previously treated TB patients were tested for MDR-TB
- In 2010, 8/22 high burden countries did not have 1 microscopy center/100,000 population.
- Among 36 high burden and high MDR countries, 20 had less than 1 lab capable of performing culture and DST/5 million pop
- By 6/10, 26/145 countries eligible to purchase Gene Xpert technology had done so

Multidrug and Extensively Drug-Resistant TB: 2010
Global Report on Surveillance and Response
WHO

- Tajikistan
  - 16.5% MDR-TB among new TB cases
  - 61.6% MDR-TB among previously treated TB patients in one city and one district
Extensively drug-resistant TB: “There must be some kind of way out of here”
Cegielski 2010, CID; 50: S195

• “Unlike in affluent countries...the large majority of persons with MDR-TB worldwide do not receive a diagnosis and remain untreated. Sophisticated microbiology laboratories and complex combinations of expensive second-line drugs are not available to them, and the disease spreads unchecked.”

Multidrug and Extensively Drug-Resistant TB: 2010
Global Report on Surveillance and Response
2010 WHO MDR-TB Report

• It is estimated that 1.3 million MDR-TB cases will need to be treated between 2010 and 2015 at an estimated total cost of $16,000,000,000.
• The current level of funding in 2010 (from all sources) is less than $500,000,000.
Picking up the pace—Scale-up of MDR TB treatment programs
Keshavjee and Farmer NEJM 2010; 363: 1781

• Addressing the MDR TB epidemic will require critical transformation in 4 areas:
  – Diagnostics
  – Drug supply
  – Treatment implementation
  – Advocacy

Worldwide TB control 2012

• Overall, TB incidence is declining but:
• Current practices promote the emergence of drug resistant TB which is increasing in incidence
• Adequate treatment of MDR TB not currently feasible and which makes it an essentially fatal process
• Can improved TB diagnostics and therapeutics stop the MDR/XDR onslaught?
NBC.com 11/21/12

• 34 million people with AIDS 2011
• New HIV infected persons 2011: 2.5 million
  – 20% less than 2001
• Deaths attributable to AIDS 2011: 1.7 million
  – 2.3 million AIDS deaths 2005
  – 1.8 million AIDS deaths 2010

• “As HIV infections fall, UN says ending AIDS ‘feasible’ ”.

TB IN THE UNITED STATES
2012 United States TB Cases

9,951 TB cases reported in 2012
3.2 cases per 100,000 population
Decline of 6.1% from 2011 case rate

Reported new tuberculosis cases, by county — United States, 2010–2012
### 2012 TB Cases Reported by California, Texas, New York, and Florida

- California, Texas, New York and Florida reported more than 500 cases in 2012
- Accounted for 4,967 TB cases in 2012, approximately half for the United States
- Among the 441 counties in these four states, 136 (30.8%) did not report a new TB case from 2010–2012

### No. and Rate of TB cases and % Change

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>Rate</th>
<th>No.</th>
<th>Rate</th>
<th>% Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic</td>
<td>2999</td>
<td>5.8%</td>
<td>2793</td>
<td>5.2%</td>
<td>-9.1%</td>
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<tr>
<td>Asian</td>
<td>3156</td>
<td>21%</td>
<td>3043</td>
<td>19.8%</td>
<td>-5.6%</td>
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<tr>
<td>Black</td>
<td>2379</td>
<td>6.2%</td>
<td>2222</td>
<td>5.7%</td>
<td>-7.4%</td>
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<tr>
<td>White</td>
<td>1650</td>
<td>0.8%</td>
<td>1566</td>
<td>0.6%</td>
<td>-5.7%</td>
</tr>
<tr>
<td>Total</td>
<td>10524</td>
<td>3.4%</td>
<td>9951</td>
<td>3.2%</td>
<td>6.1%</td>
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</table>
Number and Rate* of TB Cases Among U.S.- and Foreign-born Persons, by Year Reported — United States, 1993–2012


<table>
<thead>
<tr>
<th>Country</th>
<th>No.</th>
<th>% Foreign born</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mexico</td>
<td>1303</td>
<td>21.0%</td>
</tr>
<tr>
<td>Philippines</td>
<td>768</td>
<td>12.3%</td>
</tr>
<tr>
<td>India</td>
<td>529</td>
<td>8.5%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>450</td>
<td>7.2%</td>
</tr>
<tr>
<td>China</td>
<td>351</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

US TB Rates 2011 to 2012

- US Born 1.5 to 1.4%
- Foreign Born 17.3 to 15.8%
- Foreign Born 1993-2011
  - -54%!
- US Born 1993-2011
  - -81%
- Overall 7.2% Coinfection with HIV
  - 25-44 12 HIV coinfection
In 2011, 1.6% (127 of 7,817) of culture-confirmed cases with susceptibility test results for isoniazid and rifampin had evidence of multidrug-resistant TB (MDR TB)

85.8% of MDR cases occurred among foreign-born persons

One case of extensively drug-resistant TB (XDR TB) reported in 2012

Data are updated as of 2/22/13 and are provisional.

Discussion

- 20th consecutive year of declines in TB cases and TB rates
- Geographic distribution of TB cases is heterogeneous
- Foreign-born persons and racial/ethnic minorities continue to be affected disproportionately
Worldwide TB and the United States

• Foreign born persons account for the majority of TB cases in the U.S.
• Foreign born persons account for the great majority of drug resistant and multi-drug resistant TB cases in the U.S.
• TB control resources:
  – Case finding/contact investigation
  – Rapid identification of drug resistant TB

Moving toward TB elimination: implementation of statewide targeted tuberculin testing in TN
(Cain et al, AJRCCM 2012, 186; 273)

• 2002-2006: 102,709 TST placed and read
• 9,090 + TST: 53% started treatment of whom 54% completed treatment (25% of total)
• Estimated 195 TB cases prevented over the 5 year study period
• The # of TST placed to prevent one TB case:
  – 150 for foreign born persons
  – 9,834 for persons without TB risk
• “Yield and cost-effectiveness are maximized by prioritizing foreign-born persons, a large population with high TB risk.”
1989 Advisory Council for the Elimination of TB (CDC DTBE)

- Goal: by 2010: < 0.1 case/100,000
- HIV/AIDS
- Worldwide TB Epidemic, Drug Resistance
- Variable $ Support and Infrastructure
- TB incidence in U.S. ↓ 80% since peak in early ’90’s
- What will be impact of declining TB control budgets and clinical competence on TB incidence?

Overseas Screening for Tuberculosis in U.S.-bound Immigrants and Refugees
Liu et al NEJM 2009, 360; 2406

- Improvements in overseas screening of immigrants and refugees:
  - Mycobacterial cultures
  - Drug-susceptibility testing
  - Directly observed therapy
  - TST for children 2-14 years
  - Shorter interval between screening and departure for the U.S.
Estimated Migrants “Entering” U.S.

- ~ 30,000,000
  - Non-immigrant visas
    - 27,907,139
  - Immigrants and refugees
    - 411,266
  - Undocumented migrants
    - ~ 275,000 ???

- N = ~ 59,000,000
  - 679,305


Entering the U.S. with Active TB

- Enter the U.S. as a tourist, for business, as a student or as a temporary worker, etc…
- Enter the U.S. illegally
- A classification on medications
- B1 classification with false negative smears
- B2 classification with false negative CXR
- “Asymptomatic” children, (immuno-compromised adults) with primary TB
TB Epidemiology: Bottom Line

• In the U.S. TB is increasingly a disease of persons born outside the U.S. Know the high risk immigrant populations in your area.
• In the U.S. TB disproportionately affects African-American, Hispanic and Asian/Pacific Island populations.
• In an era of diminishing resources, focus TB control efforts on high risk groups