The Global Tuberculosis Epidemic
Epidemiology, HIV/AIDS, and Multi-Drug Resistance

David Cohn, MD
Division of Infectious Diseases
University of Colorado School of Medicine

Global Health Course
November 13, 2012
Outline and Objectives

• Epidemiology of the global tuberculosis (TB) epidemic
• Role of HIV in fueling TB, especially in subSaharan Africa
• Extent and distribution of drug-resistant TB
• Selected global TB control efforts
TB
A Global Emergency

WHO Report on the TB Epidemic
Bush Sends Troops To West Nile

WASHINGTON, DC—Vowing to “exact justice for the taking of innocent American lives,” a determined and defiant President Bush deployed more than 14,000 ground troops to the West Nile Monday.

“My fellow Americans, an enemy from overseas has attacked us in our own land, waging biological warfare against us on our home soil,” Bush said in a nationally televised speech from the Oval Office. “We must send a strong message to our enemies in the West Nile region that this virulent aggression against America will not go unpunished; it will not stand.”

Bush’s decision to deploy troops came on the heels of three more West Nile virus deaths over the weekend—one in Louisiana and two in Illinois—bringing the national death toll to 51.

“These cowards want to bring down our very way of life,” Bush said. “They have sought to rob us of our ability to leave the house without repellent. But what they did not count on is the tremendous spirit and resolve of the American people. No one, be they man or mosquito, will dictate what we put or don’t put on our skin for protec-

Above: Bush outlines the details of Operation Deep Desert Off! to reporters.
THE LEADING INFECTIOUS KILLER OF ADULTS
Reasons for the Worsening TB Situation - 1990s

- Demographic factors
- HIV/AIDS epidemic
- MDR-TB
- Population movement, deteriorating social environment, famine, natural disasters
- Inadequate TB control efforts
  - Insufficient resources
  - Poorly managed national TB control programs
The Burden of Tuberculosis - 2011

- 8.7 million new cases - 22 high-burden countries account for ~82% of the cases, 38% in India and China
- 1.4 million deaths, 990,000 in HIV-negative, 430,000 in HIV-positive, 98% in the developing world
- Estimated 1.1 million new TB cases in persons co-infected with HIV (13%); 79% in Africa
- 3.7% of new cases have MDR-TB, 20% of previously treated cases
- Estimated 310,000 cases of MDR-TB among reported cases of TB - 27 high burden MDR-TB countries, 60% from India, China and Russian Federation

WHO, Global Tuberculosis Report, 2012
Estimated Numbers of New TB Cases by Country, 2007

WHO Report, Global TB Control, 2009

WHO Global Tuberculosis Report, 2012
Coexistence of TB and HIV Epidemics
Potential Interactions

Transmission of HIV to uninfected
(Blood, body fluids)

Affect pathogenesis of HIV infection

Increased morbidity and mortality

HIV Infection

Increased incidence and reactivation of TB

Unusual clinical manifestations

TB Infection

Transmission of TB to uninfected
(Airborne)
HIV Driving the TB Epidemic

Notification Rates (x100,000)

- Zimbabwe
- Kenya
- Malawi
- Tanzania
- Côte d’Ivoire

Years
HIV Seroprevalence in TB Cases
Africa, 1988-1997

Percent

Blantyre Malawi
Lusaka Zambia
Hlabisa S.Africa
Kampala Uganda
Abidjan Ivory Cst
Estimated HIV Prevalence in New TB Cases, 2011

WHO Global Tuberculosis Report, 2012
Causes of Death in HIV-Infected Patients from 257 Autopsies
Abidjan, Cote d’Ivoire, 1991

- Tuberculosis (36%)
- Pneumonia (13%)
- Toxoplasmosis (8%)
- Enteritis (4%)
- Other Diagnoses (<4% each)
Decreases in Incidence of TB in Patients on ART
South Africa, 1996-2005

Number (%) of HIV-infected TB patients on cotrimoxazole preventive therapy (CPT) and antiretroviral therapy (ART), 2004-2011

Tested HIV-positive

Number of TB patients (thousands)

WHO Global Tuberculosis Report, 2012
Estimated number of lives saved by implementation of TB/HIV interventions, 2005-2011

Scale-up saved total of 1.3 million lives

WHO Global Tuberculosis Report, 2012
Drug-Resistant Tuberculosis Definitions

- MDR TB (Multidrug-resistant TB) - Resistance to at least isoniazid and rifampin
- XDR TB (eXtremely drug-resistant TB) - Resistance to isoniazid and rifampin, and to any fluoroquinolone (levofloxacin, moxifloxacin), and at least one injectable 2nd-line drug (capreomycin, kanamycin, amikacin)
- Primary drug resistance - Patient is initially infected with a resistant strain of TB
- Acquired drug resistance - Patient develops drug resistance by not taking medications properly
Progress in Global Coverage of Data on Drug Resistance, 1994-2011

WHO Global Tuberculosis Report, 2012
Percentage of New TB Cases with MDR-TB, 2011

3.7% of cases

WHO, Global Tuberculosis Report, 2012
Percentage of Previously Treated Cases with MDR-TB, 2011

20% of cases
Extensively Drug-Resistant Tuberculosis (XDR-TB), 2005-2006
Outbreak of Drug-Resistant TB in HIV-infected Patients
KwaZulu Natal, South Africa, 2005-2006

• Over 15 months, sputum obtained from 1539 patients, 221 with MDR-TB, 53 with XDR-TB
• Of 475 consecutive patients with culture-confirmed TB, prevalence of 39% with MDR-TB and 6% with XDR-TB
• Of XDR-TB patients, 55% had never been treated for TB; 67% had recent hospital admission; of 44 tested for HIV, all were co-infected
• 52 of 53 XDR-TB patients died; median survival of 16 days (IQR, 6-37) from time of diagnosis
• Genotyping of XDR isolates; 39 of 46 were similar strains

Gandhi, Lancet 2006; 368:1575-80
Updated Figures from Tugela Ferry

From January 2005 to March 2007:

• 433 TB cases resistant to at least INH and RIF
  – 239 (55%) XDR-TB cases
    • 199 (84%) confirmed dead
  – 194 (45%) MDR-TB cases (not XDR-TB)
    • 119 (65%) confirmed dead

• Greater than 90% of MDR- and XDR-TB patients found to be HIV-infected

G Friedland 2007
Countries that had at least one case of XDR-TB by the end of 2011 (n=84)

Proportion of MDR-TB with XDR-TB is 9.0%
Directly Observed Treatment, Short-course
The WHO TB Control Strategy
“DOTS” (Directly Observed Therapy, Short Course)

- Government commitment to TB control
- Diagnosis by smear microscopy, mostly on self-reporting symptomatic patients
- Standardized short-course regimens with supervision and patient support
- Efficient system of drug supply
- Efficient recording and reporting system with assessment of treatment results
Number of countries implementing DOTS (out of a total of 212 countries), 1991-2006

WHO Report, 2008
## Directly Observed Short Course Chemotherapy of Smear-Positive Pulmonary TB, China 1991-1994

<table>
<thead>
<tr>
<th>No. patients</th>
<th>Cured</th>
<th>Died</th>
<th>Failed</th>
<th>Defaulted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td><strong>New cases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55,213</td>
<td>49,504 (89.7)</td>
<td>1297 (2.3)</td>
<td>1710 (3.1)</td>
<td>891 (1.6)</td>
</tr>
<tr>
<td><strong>Retreatment cases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57,629</td>
<td>46,728 (81.1)</td>
<td>2227 (3.9)</td>
<td>4696 (8.1)</td>
<td>1150 (2.0)</td>
</tr>
</tbody>
</table>

*2HRZS/4HR qO.D. (90 doses)
†2HRZSE/6HRE qO.D. (120 doses)

The Global Partnership to Stop TB

- established in 2000
- a global movement to accelerate social and political action to stop the spread of TB
- a network of international organizations, countries, donors (public and private sector), governmental and non-governmental organizations and individuals
- secretariat is housed in WHO
Global Plan to Stop TB launched in 2001
Advanced Plan in 2006 with 2015 goals
Updated at halfway point in 2010
Global targets

- by 2005
  at least 70% of people with infectious TB will be diagnosed (i.e. under the DOTS strategy) and at least 85% cured

- by 2015
  the global burden of TB disease (prevalence and deaths) will be reduced by 50% relative to 1990 levels (specifically, this means reducing prevalence to 155 per 100,000 and deaths to 14 per 100,000 per year by 2015)

- by 2050
  the global incidence of TB disease will be less than 1 case per million population
Components of the Global Plan

- Pursue high quality DOTS expansion and enhancement
- Address TB/HIV, drug-resistant TB, and the needs of poor and vulnerable populations
- Contribute to health system strengthening based on primary health care
- Engage all care providers
- Empower people with TB and communities through partnership
- Enable and promote research
## History of Global Approach to Drug-Resistant TB

- **1994**  
  WHO/IUATLD Global Anti-TB Drug Resistance Surveillance Project

- **1998**  
  DOTS-Plus

- **1999**  
  Stop TB Working Group on DOTS-Plus for MDR-TB

- **1999**  
  Negotiations with pharmaceutical industry to reduce prices of second-line drugs

- **2000**  
  Green Light Committee (GLC) organized

- **2000**  
  First DOTS-Plus project to assess feasibility and effectiveness of managing MDR-TB in resource-limited settings

- **2008**  
  WHO Guidelines for programmatic management of drug-resistant TB; updated in 2011
Xpert MTB/RIF Assay for Rapid Diagnosis of Drug-resistant TB - A Breakthrough
Progress in the Roll-out of Xpert MTB/RIF by July 2012
GLC approved DOTS-Plus Projects

Abkhazia
Azerbaijan
Bolivia
Costa Rica
Dominican Republic
Egypt
El Salvador
Estonia
Georgia
Haiti
Honduras
India
Jordan
Kenya
Kyrgyzstan
Latvia
Lebanon
Malawi
Mexico
Moldova
Nepal
Nicaragua
Peru
Philippines
Romania
Russia
Syria
Tunisia
Uzbekistan

GLC-approved DOTS-Plus projects

World Health Organization
StopTB Partnership
Good News:
- Major progress in reducing TB cases and deaths over past two decades
- TB mortality rate has fallen 41% since 1990
- Incidence rates and mortality are falling in all six WHO regions and in most of the 22 high-burden countries
- Increasing numbers of patients with TB have access to effective anti-TB treatment and related interventions such as CPT and ART
- Innovations in new diagnostics are being implemented; new drugs in the pipeline
Bad News:

- The global burden of TB remains enormous
- Surveillance data largely rely on estimates extrapolated from incomplete information
- 60% patients reported with TB do not know their HIV status
- 52% of HIV-infected patients with TB who know their HIV status are not on antiretroviral therapy
- Target of treatment success by 2015 for 75% of MDR-TB cases was reached by only 30 of 107 countries reporting outcomes (average 44%)
T.B. can be Cured!

Seek Early Treatment and take your Medicine Daily
Thank You!