PRECEPTIONS vs REALITIES

IOM (Institute of Medicine) of US National Academies of Science

“Addressing the Threat of Drug-Resistant Tuberculosis: A Realistic Assessment of the Challenge”

Washington, DC, November 5, 2008
STEMMING THE TIDE OF MULTIDRUG-RESISTANT TUBERCULOSIS:

MAJOR BARRIERS TO ADDRESSING THE GROWING EPIDEMIC

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WASHINGTON DC
NOVEMBER 5, 2008
“The Emerging Threat of Drug-Resistant Tuberculosis in Southern Africa”

Pretoria, South Africa
March 3-4, 2010
IOM/Russian Academy Medical Sciences

“The New Profile of Drug Resistant TB: A Global and Local Perspective”

Moscow, May 26-27, 2010
IOM/Indian National Science Academy & Indian Council of Medical Research

“Facing the Reality of Drug-Resistant Tuberculosis in India”

Delhi
April 18-19, 21, 2011
COMMON THEMES
Magnitude of Problem  Grossly Underestimated

Certain to exceed 500,000 new cases estimated to occur each year!!!!
Until 2006, it was assumed drug resistant strains too weak to achieve human-to-human transmission. Therefore, infection control was not a public health priority.
BARRIERS TO ACCESS RESULTING FROM SECOND LINE DRUG SUPPLY CHAIN:

• Bottlenecks in Procurement,
• Unreliable Demand Forecasting
• Issues in Distribution of High Quality Drugs
PEDIATRIC MDR/XDR: A SILENT EPIDEMIC

- **South Africa** – Gary Reubenson (*2008 140 culture confirmed cases*)
- 85% no previous TB treatment
- None with history of adult MDRTB contact
- 49% HIV +
- 30% mortality
Number Patients Receiving Treatment Small and Ineffective

• <1/2 of 1% newly diagnosed patients have been treated since 2000.

• Even in the small proportion of patients that are being treated, many are not receiving drugs of high quality or that actually address their drug resistance profile, and therefore their treatment is ineffective.
Point of Care Diagnostic for MDR/XDR TB Must be Given Absolute Highest Priority, ie the Polio Approach

Enhancing laboratory capacity may improve surveillance but not likely to impact individual patient treatment and thus failure to impact epidemic spread of drug resistant strains.

Unrealistic to think in countries where there are currently fewer than one laboratory per 10 Million population (which is the case in most high-burden countries), that sufficient resources and time are available to scale up quickly enough to have a major impact upon rapid diagnosis and treatment, especially given that most patients are in remote settings.

Recently introduced diagnostics and those in late stage development increase speed and sensitivity but unfortunately they still require laboratory infrastructure.

Technology for detection of MDR and XDR-TB at point of care is available but requires further development and evaluation.
<table>
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<th>KZN</th>
<th>Nr of cases</th>
<th>Incidence</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>TB</td>
<td>120,000</td>
<td>1,200 / 100,000</td>
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<tr>
<td>MDR</td>
<td>2,800</td>
<td>30 / 100,000</td>
<td>2.5% of all TB</td>
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<tr>
<td>XDR</td>
<td>270</td>
<td>3 / 100,000</td>
<td>10% of MDR</td>
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<tr>
<td>TDR</td>
<td>240</td>
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<td>88% of XDR</td>
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<table>
<thead>
<tr>
<th>Paediatric</th>
<th>Nr of cases</th>
<th>Incidence</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>TB</td>
<td>17,000</td>
<td>520 / 100,000</td>
<td>14% of all cases</td>
</tr>
<tr>
<td>MDR</td>
<td>153</td>
<td>4 / 100,000</td>
<td>5.5% of all cases</td>
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<tr>
<td>XDR</td>
<td>9</td>
<td>0.2 / 100,000</td>
<td>3.5% of all cases</td>
</tr>
<tr>
<td>TDR</td>
<td>7</td>
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Need for Urgency:

Currently there are no consistent policies to deal with patients whose TB is untreatable.

What we do know is that proof that disease in these patients is untreatable may take months during which time they may spread their resistant organisms to family members and others in the community, including health care workers.
Treatment of Totally Drug Resistant TB (TDR)

• Even under the best of circumstances, 30 to 40% of cases of XDRTB are untreatable with existing drugs. Do they represent TDR?

• Currently there are NO good data on TDRTB. We all know it exists but no one systematically looks for it and no one talks about it. One of the most urgent needs is to get accurate data so we can realistically address the challenge.

• Treatment of drug sensitive TB requires a cocktail of 3 or more antibiotics. “Successful treatment of XDR and TDR TB requires not one or two new antibiotics but 3-4 new classes of antibiotics simultaneously thus representing a HUGE technical and financial challenge.”
Putting Challenges into Perspective: The Realities of Drug Discovery

• 90% failure rate from target identification to regulatory approval

• 50% failure approval rate even in Phase III. Thus to get a single new drug the pipeline must be full at each stage.

• Average time for drug discovery and development from target ID to approval 10-14 years (probably considerably longer for TB due to follow-up).

• Average costs for a single new drug from discovery to approval and not including post-launch surveillance for adverse events, manufacturing compliance, drug delivery, etc = >$1.5 billion (probably higher for TB due to lack of infrastructure, point of care diagnostics, surrogate markers)
Realities of New TB Drug Development:

Technical and financial challenges in development of new drugs are so large that no one government, institution, or company has enough resources or expertise to adequately address the challenges. To put it in perspective, the total R&D budget for large companies on average across therapeutic areas is $2-3 billion with average launch of a single new product of 1 in 4 years. **Total global investment in TB drug R&D, including the Gates Foundation, in 2009 was $176 million.**
Public Perception Does Not Match the Realities

- TB remains a problem but we have drugs to successfully treat it. Some countries have almost eliminated it using existing tools. It is a disease restricted to those living in poverty.

- Only 500,000 new cases of MDR-TB per year which is not large compared to other unmet medical needs besides these are caused by inappropriate treatment, lack of patient compliance, and impure drugs

- No worries, MDR/XDR TB are not spread from person to person, or if so, it is a low risk due to lack of fitness of resistant strains
Key Messages...

• Failure to acknowledge the new realities of drug resistant TB and to act rapidly will be catastrophic for many countries and will greatly jeopardize the public health of all others (immigration and international travel).

• We must start communicating the realities of drug resistant TB and translating the data we do have into policies commensurate with the magnitude and urgency of the challenges we face.

January 16-18, 2013
WHY THE BRICS?

• >50% WORLD’S POPULATION RESIDE IN BRICS COUNTRIES

• >80% OF WORLD’S MDRTB, BASED UPON CURRENTLY AVAILABLE DATA

• BRICS ARE THE EMERGING ECONOMIES. HEALTH = WEALTH

• DEMONSTRATED SUCCESS ONCE DETERMINED: WORLD CUP SOCCER GAMES (SOUTH AFRICA, 2007; OLYMPICS (BEIJING); OLYMPICS (BRAZIL, 2016)

• POLITICAL WILL EXISTS: China as an example (China CDC, MOH, SFDA)
#1. COLLABORATE AND COOPERATE FOR DEVELOPMENT OF CAPACITY AND INFRASTRUCTURE TO REDUCE PREVELANCE AND INCIDENCE OF MDRTB THROUGH: INNOVATION FOR NEW DRUGS/VACCINES, AND DIAGNOSTICS AND PROMOTION OF CONSORTIA OF TB RESEARCHERS
#2. COLLABORATE ON CLINICAL TRIALS OF DRUGS AND VACCINES, STRENGTHENING ACCESS TO AFFORDABLE MEDICINES AND DELIVERY OF QUALITY CARE
#3. COOPERATE ADOPTING AND IMPROVING SYSTEMS FOR NOTIFICATION OF TB PATIENTS, AVAILABILITY OF ANTI-TB DRUGS AT FACILITIES BY IMPROVING SUPPLIER PERFORMANCE, PROCUREMENT SYSTEMS AND LOGISTICS AND MANAGEMENT OF HIV-ASSOCIATED TB IN THE PRIMARY HEALTH CARE SYSTEM.
WHY THE BRICS?

MAGNITUDE OF THE PROBLEM AND URGENCY REQUIRED DEMAND THAT THE BEST AND BRIGHTEST YOUNG INVESTIGATORS ARE FULLY ENGAGED AND PASSIONATE ABOUT ACHIEVING SUCCESS.