Drug Resistant Tuberculosis Global Crisis: Critical Role of NIAID/NIH

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Tuberculosis Facts:

• TB kills 2 million people every year (5000 every day) mostly adults between 15-54 years old

• 2 billion people are infected with TB worldwide

• 1 in 10 of these people will become sick with active TB

• 12 million people worldwide are co-infected with HIV & TB

• TB leads to a decline in productivity estimated at US$ 12 billion annually

• Workers may lose on average 3-4 months of their work time.
Drug Resistant Tuberculosis

• MDRTB -- Multidrug Resistant TB -- resistance to isoniazid and rifampicin, with or without resistance to other first-line drugs.

• XDRTB-- Extensively Drug Resistant TB – resistance to at least isoniazid and rifampicin, and to any fluoroquinolone, and to any of the three second-line injectables (amikacin, capreomycin, and kanamycin)
Tuberculosis drug resistance is growing...


CONTAGION
Why drug-resistant tuberculosis threatens us all

BY KRISTE BANK WITH PHOTOGRAPHS BY JAMES NACHTWEY
Forum on Drug Discovery, Development, and Translation
Institute of Medicine USA

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

Washington, DC
USA
Nov. 2008

The Emerging Threat of Drug-Resistant Tuberculosis in Southern Africa
Global and Local Challenges and Solutions

Pretoria, South Africa
March 2010

The New Profile of Drug-Resistant Tuberculosis in Russia
A Global and Local Perspective

Moscow, Russian Federation
May 2010

Facing the Reality of Drug-Resistant Tuberculosis in India
Challenges and Potential Solutions

Delhi, India
April 2011
International Workshop on Multi-Drug Resistant Tuberculosis

2013年1月14-18日 中国 北京

January 14-18, 2013 Beijing, China
Magnitude of Problem of MDRTB
Grossly Underestimated

Certain to exceed 500,000 new cases estimated to occur each year

Only half of 22 countries with highest TB burden participate in WHO MDR-TB survey

Surveys most often represent data at least four to five years old

Many countries’ data derived by modeling not surveillance

Few countries have capacity for testing susceptibility to second line drugs

Less than half of African Region population represented in surveillance data
Number Patients Receiving Treatment Small and Ineffective

Only ½ of 1% of new MDR-TB cases are treated each year (>5 million untreated over past decade alone, remain in the community, and continue to spread their resistant strains)

< 2% receiving verifiable, quality assured, second-line anti-TB drugs

Even in the small proportion of patients that are being treated, many are not receiving drugs that actually address their drug resistance profile, and therefore their treatment is ineffective.
Global Role of Person to Person Spread

• WHO: 74% of MDR TB cases globally arise from transmission rather than acquired resistance (WHO 2010 Drug-Resistance Report)

• China: 78% of MDR TB due to transmission (Zhao et al. NEJM 2012)

• Meta-analysis of 31 cohorts: 90% of XDR TB cases with no prior history of MDR TB treatment (Falzon et al. Eur Resp J in press)
NIAID Tuberculosis Research

- Basic research
- Epidemiology and natural history
- Drug, vaccine, diagnostics development
- Implementation of NIAID Research Agenda for MDR- and XDR-TB

Slide Source: A. S. Fauci
Critical/NIH Role of NIAID in Addressing the Threat of Drug

• Support of fundamental basic research, ie disease transmission and pathogenesis
• Support of translational and clinical research via partnerships with industry
• Support of product development SBIR
• Leveraging intellectual capital and resources, ie HIV/AIDS Clinical Trials Network and development of countermeasures for biothreats post 9/11 via contract resources
Eli Lilly & Company

Infectious Disease Research Institute (IDRI)
National Institute of Allergy and Infectious Diseases

Acadia Sinica

Jubilant Biosys
Merck and Company

Participants

Oversight from Board of Directors and Steering Committee
TB RESIST

International Genome Partnership

Collaborators
TB Drug resistant and related strains

Collaborators
Data Sharing and Release

Collaborators
Sequencing, Assembly, Annotation

Increase Knowledge Base
1000s TB genomes for genomic analysis to study and understand drug resistance

Data Analysis
Bioinformatic Tools
Algorithms – Predict Tools (IBM)
NIAID Large-Scale TB Genome Sequencing Project

- 2012 launch with international collaborators

- High-throughput, next-generation sequencing technology, bioinformatics analysis and tools
  
  - NIAID Genome Sequencing Center at Broad Institute & Bioinformatic Resource Center (PATRIC)

- Goal: Sequence 1000+ TB strains from human samples from Russia, Uganda, Korea, South Africa, and other countries
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.