Creating Political Will to Fight Drug-Resistant TB: Lessons from AIDS Activism

by Mark Harrington

Treatment Action Group
www.treatmentactiongroup.org

Institute of Medicine
Forum on Drug Discovery, Development, and Translation
Beyond XDRTB: Preparing for the Inevitable Rise of Totally Drug Resistant TB
5 November 2008
Washington, D.C.
What is missing in the fight against DR-TB?

- Data
- **Diagnosis**
- DRS and DST
- **Drugs**
- Delivery
- **Dollars**
- Determination
- **Demand**
- **Demonstrations!!!**
Missing Data

- Most countries neither report on nor treat most persons with DR-TB;
- True incidence and prevalence of DR-TB not well defined (epidemiology and surveillance);
- Most cohorts incomplete, unpublished, and/or non-validated;
- Rigorous randomized evidence for the standard of care nonexistent – no RCTs for MDR-TB treatment even began until 2006-07 (Tibotec, Otsuka).
Missing Diagnosis

- Smear microscopy detects ~19% of TB cases globally; at best it would detect ~40%, less in children and the HIV+.
- The recent deployment of complex expensive technology ill-suited to resource poor settings is hailed as a breakthrough but will remain far from those most at need.
- TB diagnostics research funding is an anemic 6% of NIH TB R&D and only 11% of global TB R&D.
- Target(s) for a point-of-care (dipstick) remains to be characterized.
Developing an Agenda to Expedite Development of Point-of-Care Assays for Diagnosing Active TB Disease in Resource-Poor Settings

6-7 April 2008
Cambridge University
Cambridge, UK

co-sponsored by

AIDS and Rights Alliance for Southern Africa
&
Treatment Action Group
TB Dipstick: a top priority for improving TB/HIV care

“There is a need for focused and relevant research and development, with top priorities for improving TB/HIV care being the development of a single, point-of-care rapid test for TB – something akin to the finger prick test for HIV.”

-- Anthony D. Harries
Robert Koch Memorial Lecture
38th Union Conference, Cape Town 2008
IJTLD 12(3):241-249
The Ideal TB Test

One- or two-step test that fulfills the following:

- Is sensitive and specific to *M. tuberculosis*
- Can be easily performed at rural health clinics
- Provides immediate easy to interpret results
- Diagnoses pulmonary and extra-pulmonary TB
- Works in immunocompromised and HIV+ patients
- Identifies resistance to at least INH and RIF, but preferably also to FQ and injectable agents
## TB diagnosis and the role of POC assays

<table>
<thead>
<tr>
<th>Location</th>
<th>Current practice</th>
<th>Dipstick</th>
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<tbody>
<tr>
<td>Referral hospital</td>
<td>Physician, specialist physicians Culture, CXR, Microscopy HS delay = 8 (0-45) days*</td>
<td>• No delay- Lives saved!!</td>
</tr>
<tr>
<td>District hospital</td>
<td>Physician, Clinician, lab technician CXR, Microscopy</td>
<td>• Can be done by any HCW at any level- HR advantage</td>
</tr>
<tr>
<td>Health centres</td>
<td>Clinician, nurse, lab technician Microscopy</td>
<td>• Less need for infrastructure and technical expertise</td>
</tr>
<tr>
<td>Health post/clinic</td>
<td>Clinician, nurse, HA No diagnosis- only referral</td>
<td>• Simplify TB prevention and infection control</td>
</tr>
<tr>
<td>Community/ home</td>
<td>CHW, Rx supporters, patients No diagnosis - Referral possible Pt delay =21 (7-49)days**</td>
<td>• Patients can diagnose themselves</td>
</tr>
</tbody>
</table>

\* IJTL D 2008 : 392-396

\** IJTL D 2006; 10:422-28
Conclusion

A dipstick diagnosis of latent TB infection and active TB disease using easily-obtained specimens (urine, saliva and blood spots) will revolutionise TB control efforts, save millions of lives, enhance access to TB services and will facilitate the elimination of TB as a public health problem.
A New TB POC Initiative

Project-Managed Specification-Based RFA on TB POCs

Advocacy
Larger Bio-Marker Effort for Active Disease
Platform Development
Clinical Specimen Bank

Basic Research for TB Diagnostics
Reagent Facility
Missing Drugs

- 2nd line and salvage drugs for DR-TB are weak, toxic, ill-characterized, expensive, and hard to produce and distribute;
- TB drug development has stagnated since the 1960s;
- Only five new compounds are in the clinic; statistically, only 1-2 of them is likely to make it to full approval;
- Far too few drugs are in the pipeline to revolutionize treatment for either drug-sensitive or drug-resistant TB;
- Neither the background regimen nor how to use the new drugs with it is yet well-defined and there is no clinical trials infrastructure available to carry out the needed strategy trials.
Missing Delivery

- Despite strong evidence for its effectiveness, community based outpatient treatment for DR-TB is only available at a handful of sites;
- Many countries still focus on institutionalization in settings which increase the risk of transmission, reduce health care worker morale, violate the rights of people with DR-TB who want to be treated and to live in a humane fashion, and are prohibitively expensive;
- An over-emphasis on isolation for DR-TB patients as a method to prevent transmission of DR-TB is the equivalent of an overemphasis on abstinence as a method to prevent transmission of HIV;
- Countries fail to use and expand existing human resources to provide ongoing follow-up and treatment support for people with DS- and DR-TB;
- There is a need for trained doctors, nurses, community health workers, treatment supporters, and laboratory technicians;
- TB care providers need to be paid.
Missing Dollars

• Globally spending on TB R&D increased by just six percent ($26M) from $429M in FY06 to $455M in FY07;
• Domestically investment in TB R&D is almost stagnant due to flat NIH budgets since 2005 which given inflation are actually down by 20% in real dollars;
• In 2007, NIH invested $2.9 billion in HIV research compared with only $157 million on TB research, despite the fact that TB kills almost as many people globally as HIV (and kills many people with HIV);
• Lack of investment in TB R&D reflects a fundamental lack of political will and a failure of political leadership.
TB R&D Investment by Category (2007)
$455,490,794

- Basic Science: $116,264,867 (25.5%)
- Drugs: $153,185,276 (33.6%)
- Vaccines: $59,990,919 (13.2%)
- Diagnostics: $52,488,075 (11.5%)
- Operational: $37,335,233 (8.2%)
- Unspecified: $36,226,424 (8.0%)

Total: $455,490,794

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<td>$40,608,898</td>
<td>$31,441,835</td>
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TB R&D Funding by Donor Sector (2007)

- Philanthropy: 30.9%
- Private: 12.1%
- Public (overall): 57.0%
- International Development Agencies: 15.7%
Basic Science
$116,264,867
Diagnostics
$52,488,075

- Gates: 39.2%
- US CDC: 17.8%
- NIAID: 16.2%
- EC F6/7: 14.6%
- Company Y: 3.4%
- USAID: 3.1%
- DGIS: 2.2%
- Sequella: 1.3%
- Other ICs, NIH: 1.3%
- SA MRC: 0.9%
- Brazil: <0.1%
- KNCV: <0.1%
- Other ICs, NIH: 1.3%
Drugs
$153,185,276
Vaccines
$59,990,919

Gates 49.5%
NIAID 25.0%
DGIS 15.8%
Other ICs, NIH 1.2%
Max Planck 2.2%
DGIS 15.8%
Wellcome 0.5%
Danida 0.6%
Sida 0.3%
UK HPA 4.5%
US CDC 0.4%
Wellcome 0.5%
Danida 0.6%
Sida 0.3%
DGIS 15.8%
Gates 49.5%
NIAID 25.0%
DGIS 15.8%
Wellcome 0.5%
Danida 0.6%
Sida 0.3%
DGIS 15.8%
Gates 49.5%
NIAID 25.0%
Operational Research
$37,335,233
## TB Research Investors: 2007 vs. 2006 and 2005

(change in rank; change in amount invested; % change)

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<td>119,772,018</td>
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<td>US Centers for Disease Control &amp; Prevention (CDC)</td>
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<td>17,852,744</td>
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<td>US other Institutes &amp; Centers, NIH</td>
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<td>12,767,399</td>
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<td>23</td>
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<td>Dafpharme International Ltd</td>
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<td>25</td>
<td>Swedish International Development Cooperation (SIDA)</td>
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<td>1,145,691</td>
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<td>26</td>
<td>Brazil (Amparo/Conecta)</td>
<td>171,481</td>
<td>27</td>
<td>4,019,631</td>
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<td>Russian TB Institutes</td>
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<td>2,772,000</td>
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<td>KNCV Tuberculosis Foundation</td>
<td>36,720</td>
<td>29</td>
<td>193,556</td>
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<td>29</td>
<td>Korean Institute of Tuberculosis</td>
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<td>30,000</td>
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<td>30</td>
<td>30,000</td>
<td>30</td>
<td>0.0%</td>
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</table>

| 31        | NIA Research Institute for Tuberculosis, Japan Anti-TB Association | 11,308 | 9 | 359,039 | 57 | 0.0% | 100.0% |
| 32        | Rockerfeller Foundation | 0 | 0 | 0 | 0 | 0 | 0 |
| 33        | Thailand Ministry of Public Health | 0 | 0 | 0 | 0 | 0 | 0 |
| 34        | Swiss Agency for Development and Cooperation | 0 | 0 | 0 | 0 | 0 | 0 |
| 35        | ** Institute Pader | 3,365,300 | 10 | 0.0% | 100.0% |
| 36        | UK Medical Research Council (MRC) | 3,31,397 | 13 | 0.0% | 100.0% |
| 37        | India NHRC Research Council (NHRC) | 6,321,667 | 16 | 0.0% | 100.0% |
| 38        | Irish Aid | 752,307 | 20 | 0.0% | 100.0% |
| 39        | Canadian Institute of Health Research | 3,297,307 | 22 | 0.0% | 100.0% |
| 40        | Global Fund to Fight AIDS, Tuberculosis and Malaria | 1,534,293 | 26 | 0.0% | 100.0% |
| 41        | All India Institute of Medical Sciences (AIIMS) | 1,298,064 | 30 | 0.0% | 100.0% |
| 42        | ** US FDA | 651,224 | 32 | 0.0% | 100.0% |
| 43        | China CDC National Tuberculosis Reference Laboratory | 620,000 | 33 | 0.0% | 100.0% |
| 44        | ** Amsa Biological | 395,547 | 36 | 0.0% | 100.0% |
| 45        | ** ELF Life Foundation | 0 | 0 | 0 | 0 | 0 | 0 |
| 46        | France Ministry of Foreign Affairs Cooperation France | 152,821 | 41 | 0.0% | 100.0% |
| 47        | ** Intern | 527,563 | 14 | 0.0% | 100.0% |
| 48        | ** NIV/C.G. NL | 0 | 0 | 0 | 0 | 0 | 0 |

** TOTAL | 455,496,794 | 422,166,680 | 368,315,024 |
Missing Determination

- The picture globally demonstrates a lack of political will, urgency, leadership, vision, and determination to address the problem.
- Unlike HIV and malaria, TB has no US Presidential Initiative;
- Unlike HIV Universal Access, the WHO/Stop TB *Global Plan to Stop TB 2006-2015* fails to set universal access targets and will not – even if fulfilled – reverse the TB pandemic in Africa or in Europe, the continents most badly affected by HIV/TB and by DR-TB respectively.
- Unlike HIV, there is little grassroots activism against TB.
Missing Demand

• The comparisons with the response to the HIV pandemic reveal that the missing elements include grassroots activism creating demand, research of significant scale and ambition to create new and more effective tools to combat the disease, political pressure to mobilize resources, political leadership to demand results, and ultimately a failure of human solidarity.

• Urgent needs include activism at all levels, massively increased scientific investment, strong political leadership, and massively increased resources to diagnose, treat, prevent, and ultimately eliminate TB.
Missing Demonstrations!!!

“Thereal change comes from the bottom up, not from the top down.”

-- President-Elect Barack Obama, 2008
Twenty years ago this October, 1,500 AIDS activists from around the USA surrounded the headquarters of the U.S. Food & Drug Administration in Rockville, Maryland, to demand that the FDA revolutionize its regulatory approach to the testing and approval of new drugs for AIDS. That demonstration was successful beyond our wildest dreams and we are living with its consequences still. Indeed, I and many thousands of others might not be living today had it not been for the unprecedented activism spawned by the AIDS epidemic over two decades ago.
ACT UP Storms the NIH

21 May 1990
Demand Accountability
What is Needed

• A US Presidential Initiative to Stop TB, integrated within OGAC and the President’s Malaria Initiative, in a State Department Level Office of AIDS, TB, and Malaria, or in a new Department for Global Development Office of Global Health;

• An emergency effort to develop a cheap, simple, sensitive and specific TB point-of-care (dipstick) test.

• Massive scale up of basic, applied, and operational research on TB.

• At least $2 billion per year in funding for TB research and development.
What is Needed (2)

• A revised and rewritten *Global Plan to Stop TB* which includes full funding for true universal access to TB prevention, care, treatment, and cure – including extrapulmonary TB, HIV/TB, DR-TB, and pediatric TB.

• A new commitment by the World Health Organization (WHO) to 1) cease bureaucratic infighting over ‘health sector strengthening’/primary health care’ versus ‘priority diseases’ and 2) to integrate universal access for HIV, TB, and other priority diseases into a plan to achieve comprehensive and universal primary health care for all.

• Meaningful political leadership at the national level in all countries worldwide to universal access and ultimately TB elimination.

• Strengthen community based science and policy literacy to enable affected communities to participate effectively in the fighting TB.
Treatment Action Campaign (TAC) March Against TB

Cape Town, November 2007
Acknowledgments

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Shreemanta K. Parida, Max-Planck Institute for Infection Biology, Berlin, DE
Javid Syed, TB/HIV Project Director, Treatment Action Group, New York, NY, USA
Martine Usdin, Campaign for Access to Essential Medicines, MSF, Paris, FR

ARASA, Cambridge University, CD4 Initiative, Gates Foundation, MSF, Partners in Health, Stop TB/World Health Organization