



## **Extensively Drug-Resistant Tuberculosis (XDR-TB): Immediate U.S. Action is Required**

The Infectious Diseases Society of America (IDSA) and the HIV Medicine Association (HIVMA) are gravely concerned over the recent emergence of strains of so-called “extensively drug resistant tuberculosis,” or XDR-TB. Transmitted through the air, these strains are resistant to nearly every TB drug. The World Health Organization (WHO) has called XDR-TB “virtually untreatable.” First documented in 2006<sup>1</sup>, XDR-TB now has been found in 28 countries including the United States.<sup>2</sup> There are few committed resources to track its spread globally.

In the early 1990s, New York City spent approximately \$1 billion to quell an outbreak of multi-drug resistant tuberculosis (MDR-TB) in that city. **The United States once again is at serious risk and, at present, is particularly vulnerable to an XDR-TB outbreak due to recent 14 percent funding cuts at the Centers for Disease Control and Prevention’s (CDC) Division of TB Elimination. These funding cuts have been passed on to state and local TB programs, placing fragile community initiatives in grave jeopardy.** CDC-funded TB clinical research consortiums also have been impacted. **At highest risk are populous, TB-endemic nations such as China, India and the Russian Federation, as well as impoverished nations including those of Sub-Saharan Africa.**

IDSA, a national medical society representing approximately 8,400 infectious diseases physicians dedicated to patient care, research and domestic and global public health, and HIVMA, a national society housed within IDSA and representing 3,600 HIV physicians and caregivers, call upon the U.S. Congress to take immediate, comprehensive action to address the XDR-TB threat.

### **A dangerous, new twist on an age-old threat: Defining XDR-TB**

**Tuberculosis** is an ancient scourge, found in all countries and spread through the air to close contacts. Globally, TB infects nearly 9 million new people per year, and annually accounts for greater than 2 million deaths. Standard cases of TB can be controlled through a six-month course of medications, although rigorous programs are required to ensure patients are compliant.

**Multi-drug resistant TB (MDR-TB)** emerged in the early 1990’s and was defined as occurring when the TB bacteria had developed resistance to isoniazid and rifampicin, the two most powerful or “first line” anti-TB drugs.<sup>3</sup>

**XDR-TB** is highly drug-resistant not only to first line anti-TB drugs, but also to second line oral (fluoroquinolones) and even injectable drugs (capreomycin, kanamycin, and/or amikacin).<sup>4</sup>

#### **A global threat:**

- In 2004, there were about 424,000 new cases of MDR-TB<sup>5</sup>. Transmission of XDR-TB could be expected to eventually reach this scale unless action is taken.
- Resistant strains are posing a threat to highly populous, TB-endemic nations such as India and China, as well as the former Soviet countries.

<sup>1</sup> In CDC’s *Morbidity and Mortality Weekly*, Vol. 55, No. 11; March 24, 2006

<sup>2</sup> Including U.S., Canada, Japan and Norway; [http://www.who.int/tb/xdr/xdrmap\\_feb\\_en.pdf](http://www.who.int/tb/xdr/xdrmap_feb_en.pdf)

<sup>3</sup> <http://www.who.int/tb/xdr/faqs/en/index.html>

<sup>4</sup> <http://www.who.int/tb/xdr/faqs/en/index.html>

<sup>5</sup> MDR-TB rates ranged up to 14 percent of all TB cases in some countries, in a 79-country study; Epidemiology of antituberculosis drug resistance (the Global Project on Anti-tuberculosis Drug Resistance Surveillance): an updated analysis, *The Lancet* 2006 Dec 16;368(9553):2142-54

- XDR-TB is highly fatal to HIV-positive individuals, because of their suppressed immune systems. An August 2006 South African study found that 52 of 53 patients with XDR-TB died within 25 days of their diagnosis; most or all were co-infected with XDR-TB and HIV.<sup>6</sup> XDR-TB poses a major threat to AIDS-endemic countries and hard-hit areas including in the U.S.
- Major reference laboratories in TB-endemic countries presently are not equipped to identify resistance to many anti-TB drugs, hindering proper diagnosis.

**An imminent threat to U.S. citizens:**

- According to the Advisory Council for the Elimination of Tuberculosis (ACET) in an urgent letter to Department of Health and Human Services Secretary Leavitt<sup>7</sup>, dated December 14, 2006, XDR-TB poses “an imminent airborne biological threat” to the U.S.
- XDR-TB already is present in the United States. Four percent of all MDR-TB cases in this country fit the definition of XDR-TB. U.S. HIV patients are at particular risk.
- Increased global trade as well as travel and migration of individuals from TB endemic countries places the United States at further risk of an XDR-TB epidemic. More than half of U.S. TB cases occur among foreign-born persons.
- Hospitalizing additional XDR-TB infected patients will tax already strained infection control efforts and place health care workers and patients at significant risk.

**ID Physicians’ Prescription for XDR-TB: Congress must reverse recent TB program funding cuts as well as provide additional long-term resources for targeted activities.**

In the 1990s, Congress responded to the MDR-TB crisis by strengthening funding for TB prevention and control programs, laboratory infrastructure, and programs supporting adherence to therapy. These improvements led to a drastic reduction in domestic TB cases. A reinigorated and sustained response again is urgently needed to strengthen:

- ***Research & development of countermeasures (vaccines, drugs, and rapid diagnostics)***  
XDR-TB must become a funding priority under the new Biomedical Advanced Research and Development Authority within the Department of Health and Human Services. Further, \$350 million in new funding is needed for CDC’s and the National Institutes of Health’s (NIH) research efforts to support preclinical and clinical evaluation of new vaccines, drugs and diagnostics as well as for operational, basic, translational, and clinical (TB Trials Consortium and TB Epidemiology Studies Consortium) research.
- ***TB control efforts within the U.S.***  
Funding for TB prevention and control must increase substantially in order to address this new, emerging threat. As a starting point, IDSA supports the ACET recommendation of \$252.4 million for CDC’s Division of Tuberculosis Elimination.
- ***Global TB programs***  
\$400 million is needed to scale up treatment efforts (especially in developing countries), strengthen laboratories and infection control practices, and provide access to drugs, commodities and services, via the U.S. Agency for International Development, CDC, WHO and the “Stop TB” initiative, and to support public-private partnerships working to develop TB diagnostics, drugs and vaccines. Furthermore, IDSA supports \$275 million for the TB component of the U.S. contribution to the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), and supports increased funding for the GFATM overall in part to help combat HIV-TB co-infection.

**For more information:** Contact Julie Hantman, MPH, IDSA, at [jhantman@idsociety.org](mailto:jhantman@idsociety.org).

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<sup>6</sup> Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa, *The Lancet* 2006 Nov 4;368(9547):1575-80

<sup>7</sup> Letter from ACET Chair Michael Fleenor to DHHS Secretary Michael Leavitt, December 14, 2006