Report of the meeting of the WHO Global Task Force on XDR-TB

Geneva, Switzerland
9–10 October 2006

World Health Organization

WHO/HTM/TB/2007.375

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1. Background

In March 2006, the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention (CDC) reported extensively drug-resistant tuberculosis (XDR-TB)[1] as a serious, emerging threat to public health and TB control, raising concerns of TB epidemics with severely restricted treatment options that could jeopardize the gains made in global TB control. Furthermore, XDR-TB poses specific challenges to global control of HIV/AIDS and could compromise the progress already made in many countries towards universal access to HIV treatment and prevention.

In May 2006, the results of an outbreak of HIV-associated XDR-TB in Tugela Ferry, KwaZulu-Natal Province, South Africa, were presented at the PARTNERS[2] meeting in Atlanta, Georgia, USA.

In June 2006, WHO's strategic and technical advisory group for tuberculosis urged WHO to take immediate and effective action to address multidrug-resistant TB (MDR-TB) and XDR-TB in the African Region. Subsequently, in August 2006, the outbreak in Tugela Ferry was discussed at the XVI International AIDS Conference in Toronto, Canada.

From 7 to 8 September 2006, at an expert consultation meeting organized jointly by the South African Medical Research Council (MRC), WHO and CDC in Johannesburg, South Africa, international concerns about the emergence of XDR-TB were heightened by reports from KwaZulu-Natal Province of very high mortality rates in people co-infected with HIV and XDR-TB, beyond Tugela Ferry.

From 9 to 10 October 2006, the WHO Stop TB and HIV departments organized a meeting of the Global Task Force on XDR-TB at WHO headquarters in Geneva, Switzerland, in response to the XDR-TB emergency and as a follow up to the expert consultation (Annex 1).

More than 110 participants representing the most affected countries attended the meeting, together with global experts in TB control and MDR-TB management; HIV prevention, care and control; infection control and occupational health; communicable disease preparedness and response; advocacy, communication and social mobilization (ACSM); and representatives from bilateral and multilateral agencies and organizations (Annex 2).

[1] XDR-TB was initially defined as MDR-TB with further resistance to three or more of the six main classes of second-line anti-TB drugs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine and para-aminosalicylic acid).

[2] The PARTNERS project was funded by the Bill & Melinda Gates Foundation in 2000 to develop a replicable model for controlling MDR-TB in resource-limited settings. The grant supported a five-year collaborative effort between the Harvard Medical School, CDC, Partners In Health, the Task Force for Child Survival and Development, and WHO.

The objectives of the meeting were:

- To define key issues, make recommendations and propose urgent actions required in the next three to six months in the following areas:
    1. Management of XDR-TB suspects in settings of high and low HIV prevalence
    2. Programmatic management of XDR-TB and design of treatment regimens in HIV-negative and HIV-positive individuals
    3. The laboratory XDR-TB definition
    4. Infection control and protection of health-care workers, with emphasis on settings with high HIV prevalence
    5. Immediate activities and needs for surveillance of XDR-TB
    6. Advocacy, communication and social mobilization
- To develop plans for an appropriate response at the global level, and within countries, including designation of roles and responsibilities.

Dr Kenneth Castro, Director, Division of TB Elimination, CDC, USA, and Miss M.K. Matsau, Deputy Director-General, Strategic Health Programmes, Department of Health, South Africa, chaired the meeting. Dr Mario Raviglione, Director, Stop TB Department, WHO, opened the meeting by emphasizing that the management of drug-resistant TB is no longer an optional activity for countries but part of basic TB control, as outlined in the new Stop TB Strategy. XDR-TB has been identified in all regions of the world. Although a major concern in Eastern Europe, XDR-TB is now emerging in Africa among people living with HIV.

Mr Case Gordon, World Care Council, France, welcomed the participants on behalf of civil society and urged them to work with the global community and patients in the fight against XDR-TB.

The WHO Acting Director-General, Dr Anders Nordström, in addressing the meeting, stressed the urgency of critical actions to address the XDR-TB crisis. Such efforts are needed particularly in areas of high HIV prevalence. However, XDR-TB is a reminder of the longstanding need to strengthen TB control, and to build the necessary capacity in health services to respond to drug-resistant TB.

The first part of the meeting focused on the currently available data on XDR-TB and their implications for TB and HIV/AIDS control programmes. Following this introduction, representatives from three Southern African countries and four countries in Asia, Eastern Europe and Latin America presented their available data on MDR-TB and XDR-TB, MDR-TB management practices and availability of second-line anti-TB drugs. During the second part of the meeting, discussions were held in six working groups addressing each of the key issues listed above under the meeting objectives.

Discussions were held on the need for strengthening laboratory services to provide rapid drug susceptibility testing (DST) in resource-limited settings and on the urgent need for accelerated research and development of new tools. Finally, the meeting considered coordination with and collaboration among national authorities and international partners to fight MDR-TB and XDR-TB, and a proposed emergency plan of action to control XDR-TB.

2. Currently available data on XDR-TB and their implications for TB and HIV/AIDS control programmes

New WHO estimates suggest that 424 000 MDR-TB cases occurred in 2004 (95% confidence interval 376 000–620 000), or 4.3% of all new and previously treated TB cases.[1] In 2000, the Green Light Committee (GLC) was created to improve access to, and rational use of, second-line drugs. At the same time, GLC-approved pilot projects were launched to evaluate the feasibility and cost-effectiveness of managing MDR-TB in resource-constrained settings. At the beginning of 2006, the new *Stop TB Strategy*[2] and the *Global Plan to Stop TB, 2006–2015*[3] were launched. Both documents include MDR-TB management as a basic component of TB control; following their launch in May 2006, WHO published *Guidelines for the programmatic management of drug-resistant tuberculosis*.[4]

Dr Sarita Shah, Albert Einstein College of Medicine, USA, presented the first global compilation of XDR-TB data. In 2005, CDC, WHO and 25 supranational TB reference laboratories (SRLs) initiated a study to determine the extent to which resistance to second-line drugs had emerged among MDR-TB isolates. The data were published by WHO and CDC in March 2006 in an article in which XDR-TB was first defined.[5] The study analysed 17 690 isolates from 49 countries to reveal a prevalence of MDR-TB and XDR-TB of 20% and 2%, respectively. XDR-TB was identified in all regions but was most common in the Republic of Korea (15% of all MDR-TB isolates) and countries of Eastern Europe/western Asia (14% of all MDR-TB isolates). The total number and proportion of XDR-TB isolates observed worldwide increased from 5% of MDR-TB isolates in 2000 to 7% of MDR-TB isolates in 2004. The limitations of the study included variations in second-line DST by SRLs, concerns with the XDR-TB definition and significant sample biases. Prospective and population-based XDR-TB surveys are urgently needed.

Dr Paul Nunn, Coordinator, WHO TB/HIV and drug resistance team, presented XDR-TB as an emerging global threat. MDR-TB is the basis for XDR-TB. The highest rates of MDR-TB have been reported from countries of the former Soviet Union, where many countries report that 10% of new and 50% of previously treated TB cases have MDR-TB.[6] MDR-TB data are lacking from many parts of the world, including many countries in Africa, but several outbreaks of MDR-TB associated with HIV have been reported since 1990 in several locations including London, Milan and New York. The threat of XDR-TB is now present in all regions of the world, and people living with