

Multidrug-resistant and extensively drug-resistant tuberculosis (M/XDR-TB) pose major threats to public health. The rapid spread of these forms of TB is a matter of worldwide concern and constitutes a serious barrier to TB control. Drug-resistant TB is "manmade" and reflects poor treatment practices that may result from inadequate regimens, the poor quality of drugs, and failure to support patients' adherence to treatment. It is thus likeliest to develop in countries not, or not yet fully, implementing the Stop TB Strategy. Consequently, KNCV Tuberculosis Foundation continually advocates and ensures the integration of the programmatic management of drug-resistant TB according to the WHO guidelines and the Stop TB Strategy in all its partner countries.

#### **Facts and Figures**

In 2010, WHO estimated that 440,000 people develop MDR-TB annually and that over 150,000 deaths occur as a result of MDR-TB on a yearly basis. Worldwide, on average 5 percent of patients annually diagnosed with TB have MDR-TB, but the prevalence of MDR varies greatly across regions. MDR-TB requires costly, toxic, and very long treatment (up to twenty-four months). In addition, treatment success is low: approximately 60 percent in MDR-TB treatment programs. The availability and rational use of second-line drugs is very limited: Worldwide, only 18 percent of patients diagnosed with MDR-TB in 2010 received proper treatment with

second-line drugs. Improper management of MDR-TB has resulted in increasing numbers of XDR-TB cases. The latest estimate of the prevalence of XDR-TB among MDR patients is 5.4 percent. Currently, for

In MDR-TB (multidrug-resistant TB), the TB bacillus is resistant to at least isoniazid and rifampicin, the two most powerful drugs for first-line TB treatment. In XDR-TB, the TB bacillus is both multidrug-resistant and resistant to at least two of the most effective classes of second-line drugs used to treat MDR-TB, seriously reducing patients' chances of recovery.

many patients, the diagnosis of XDR-TB is equivalent to a death sentence, as evidence shows that even with the availability of all necessary drugs, less than 50 percent of XDR-TB patients can be cured (based on information published in Peru, Tomsk, and Latvia).

#### A Global Problem

Both MDR- and XDR-TB have been identified on all continents, but the problem is most pressing in South Africa and those countries making up the former Soviet Union (Eastern Europe and Central Asia). Here, the upsurge in M/XDR-TB has its roots in deteriorating public



health systems. Yet M/XDR-TB can also emerge in countries with effective TB control programs, owing for instance to inappropriate treatment practices implemented in the private sector. Migration has also resulted in the introduction of M/XDR-TB in countries with very low drug resistance levels among TB patients from the native

# What is KNCV Tuberculosis Foundation doing to curb MDR-TB and XDR-TB?

- As a member of the Global M/XDR-TB Task Force, we play a leading role in the international fight against M/XDR-TB.
- As one of the initiators of the Green Light Committee (GLC) mechanism, we aim to guarantee universal access to low-cost, qualityassured second-line TB drugs for M/XDR-TB treatment in all countries.
- We organize international training courses and conferences (such as KNCV/WHO training in the programmatic management of TB including M/ XDR-TB and the European Wolfheze meeting) in close collaboration with leading organizations in TB control.
- We actively support the control of M/XDR-TB in various countries and regions. We are currently involved in the roll-out of the programmatic management of drug-resistant TB in Vietnam, Indonesia, Kazakhstan, Ethiopia, Kenya, Nigeria, Namibia, and other countries.

- We strengthen PMDT in these countries through local capacity building by means of training in various PMDT aspects for health care staff in the civil and prison sectors.
- We advocate the integration of the programmatic management of M/XDR-TB within existing TB and TB/HIV control programs.
- We provide specialized technical assistance to countries for preparing, implementing, monitoring, and evaluating their M/XDR-TB programs.
- We contribute to the provision of quality-assured TB services for vulnerable groups, including children, migrants, and prisoners.
- We provide technical assistance in laboratory network strengthening and development, such as the introduction of new diagnostic methods (e.g., GeneXpert) and external quality assurance (EQA) systems.
- We advise and assist countries in assessing the risk of infection and in taking proper infection control measures.





population. Given the increasing trend toward globalization and international travel, all countries are at risk of outbreaks of M/XDR-

#### Programmatic Management of Drug-Resistant TB

Adequate treatment of both susceptible and drug-resistant TB is the most effective way to reduce the further emergence of acquired drug resistance. In addition, the transmission of M/XDR-TB can be reduced by the early diagnosis and treatment of M/XDR-TB and adequate infection control measures. For that reason, national TB control programs (NTPs) need to integrate the programmatic management of drug-resistant TB into routine activities and to link up with private providers, hospitals, and congregate settings such as prisons to ensure a comprehensive response to the



M/XDR-TB threat. **KNCV** Tuberculosis Foundation provides specialized training and technical assistance to NTPs for planning, implementing, monitoring, and evaluating all aspects the programmatic management of drug-resistant TB. We offer a compre-

hensive capacity-building

package, including operational and epidemiological research.

### **Infection Control Measures Can Save Lives**

M/XDR-TB is infectious just as drug-sensitive TB is. Infection control should thus be a part of any M/XDR-TB program with the aim of reducing transmission to contacts, particularly health-care staff. Proper infection control can save lives, particularly in settings with high levels of HIV co-infection. KNCV Tuberculosis Foundation assists NTPs in assessing the risk of infection and in taking proper measures in hospitals, congregate settings such as prisons, and at home during ambulatory treatment.

#### M/XDR-TB Control Is Impossible without Second-Line Drugs

One of the major problems in combating M/XDR-TB is the limited availability of second-line drugs. As one of the initiators of the GLC Mechanism, KNCV Tuberculosis Foundation stresses the urgent need of gearing up a quality-assured drug supply. We support countries in ensuring a quality-assured supply of TB drugs in both the public and the private sectors through public private partnerships (PPPs) and by providing technical assistance in the field of drug supply management.

#### **Improving Diagnosis and Treatment Capacity**

For M/XDR-TB control to be effective, it is imperative that NTPs be able to rely on a network of well-equipped, quality-assured laboratories for culture and drug susceptibility testing. Over the past few years, KNCV Tuberculosis Foundation has assisted countries such as Vietnam, Indonesia, and Botswana in building laboratory capacity

by training laboratory staff, funding lab equipment, and building lab infrastructure. In addition, we are supporting countries in introducing new rapid diagnostics that reduce the delays in diagnosing M/XDR-TB.

#### **Drug Resistance Surveillance and Surveys**

Surveillance is the routine collection and analysis of data on all TB cases detected. We assist countries in adapting recording and reporting systems so that they are in line with international standards for TB in general and M/XDR-TB. These data make it possible to monitor drug-resistant TB burden and trends, and are used for program planning and evaluation. If the country does not have the capacity to determine drug resistance routinely, we assist in surveys which will help people understand the magnitude of the problem of drugresistant TB.

#### Policy Development and Political Commitment

Together with other partners, KNCV addressed the alarming threat of M/XDR-TB which resulted in the May 2009 World Health Assembly (WHA) resolution urging all Member States to achieve universal access to the diagnosis and treatment of MDR-TB. The WHA called for extra emphasis on health system strengthening and coverage, human resources for health, the integration of TB infection control into national infection control policies, legislative frameworks for access to quality anti-TB drugs, and strategic planning and mobilization of the necessary funding. This followed the April 2009 ministerial meeting in Beijing attended by twentyseven high-burden M/XDR-TB countries.

#### MDR-TB control in the Netherlands

In the Netherlands between 1993 and 2010, 198 (1 percent) MDR-TB cases were notified, of which seven had an XDR-TB strain. A third of MDR-TB cases were identified during screening, mainly during immigrant screening. Only nine (5 percent) cases were caused by recent transmission in the Netherlands, and five (3 percent) had acquired MDR-TB after previous treatment for MDR or non-MDR TB in the Netherlands. In conclusion, the early identification of TB and MDR-TB disease through intensified and active case finding is one of the cornerstones of the TB control program in the Netherlands and limits the spread of the disease. At the same time, adequate treatment, guidance, and supervision remain essential to prevent acquired drug resistance.

## Regional PMDT Center of Excellence

With the support of KNCV, the Center of Excellence (CoE) for Training on PMDT in the East Africa Region in Rwanda was established in 2010. It focuses on:

- a field model for integrated programmatic TB/HIV control,
- including management of DR TB; - a well-functioning External Quality Assured (EQA) laboratory
- a system of multilevel training courses for all relevant staff;
- a regional group of experts, promoting up-to-date PMDT
- evidence-based policy development based on systematic surveillance and operational research.

KNCV will continue to support capacity-building activities for the CoE in Rwanda (with USAID / TB CARE I funding).

#### The following factsheets are available from KNCV Tuberculosis Foundation:

- Tuberculosis: Facts and Figures
- Tuberculosis and HIV/AIDS
- Tuberculosis: Poverty and Health Systems
- Tuberculosis in Europe
  Tuberculosis: MDR-TB and XDR-TB
- Prevalence Surveys and Tuberculosis
- Tuberculosis and ACSM All fact sheets can be downloaded from www.kncvtbc.nl

- Sources

  Towards universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis by 2015. WHO PROGRESS REPORT 2011, WHO/HTM/TB/2011.3

  "Global Tuberculosis Control 2011" WHO report, 2011. See also http://www.who.int/tb/publications/global\_report/en/index.html

  Multidrug and Extensively Drug-Resistant TB (M/XDR-TB): 2010 Global Report on Surveillance and Response, WHO/HTM/TB/2010.3

  "Prevention and Control of Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis of the Second Meeting of the WHO Task Force on XDR-TB, April 2008," WHO/HTM/TB/2008.403. See http://whqlibdoc.who.int/hq/2008/WHO\_HTM\_TB\_2008.403\_eng.pdf.

  Consolidated Action Plan to Prevent and Combat M/XDR-TB in WHO European Region 2011-2015.