# TB–THE KILLER

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Medicins Sans Frontiers (MSF) has sounded alarm bells about the current tuberculosis (TB) crisis which has reached emergency proportions, and which the standard World Health Organisation (WHO) policy is unable to cope with.

According to MSF, the recent outbreak of extensive drug-resistant tuberculosis (XDR-TB) represents an emergency requiring the WHO to devise drastically new approaches, as relying on standard WHO TB strategies will be fatal.

To respond to the XDR-TB outbreak, WHO will need to get newer drugs to patients as soon as possible by ensuring accelerated development of new drugs already in clinical trials. Existing TB drugs and diagnostics are not adequate.

An MSF report, "Development of New Drugs for TB Chemotherapy", launched at the press conference, finds that none of the TB drugs currently in development, however promising, will be able to drastically improve TB treatment in the near future.

With nine million people developing active tuberculosis every year and 1.7 million deaths annually, TB is far from under control. HIV infection dramatically increases the risk of developing active tuberculosis and is driving the TB epidemic in Africa. The situation is exacerbated by the increasing emergence of extensively drug-resistant TB.

Directly Observed Therapy (DOT), as promoted by the WHO to improve compliance for the difficult and long-lasting regimen, is demanding for patients, labour intensive for health staff and is compromised in settings where health services are poorly accessible, said MSF.

Analysing the current TB drug pipeline, the MSF report noted that there are simply not enough promising compounds in the pipeline compared to the pipeline for other diseases that predominantly affect the wealthy countries. Also, many of the compounds in the pipeline today are derivatives of existing ones.

The report also noted that most of the funding to neglected disease research and development (R&D) is still philanthropic, with governments only contributing 16% to product development partnerships' engagement in drug development.

Gillies said that TB has been a health catastrophe for a number of years. It has been very difficult to treat in the Western world - treatment takes about six months and diagnostic tests are not very good. When it comes to the developing world, it is much more difficult. The diagnostic tests that are available today are well over 100 years old.

On top of that, there is multi-drug resistant TB, which is resistant to a number of drugs. Instead of the normal six-month treatment, multi-drug resistant TB takes about 18-20 months to treat. Also, the drugs used to treat this form of TB are quite toxic and often they don't succeed anyway, he added.

Gillies attributed the present situation to the fact that there has been very little research and development on TB in the last 40-50 years. The drug pipeline was

completely closed down in the last 30-40 years mainly because TB patients do not live in countries that are a reasonable market for pharmaceutical research.

Gillies, however, noted that there has been an increase in research and development in the last few years mainly through philanthropic organisations such as the Global Alliance for TB Drug Development (largely funded by the Bill and Melinda Gates Foundation), and the drug pipeline has been restarted. But he said that 'we are still a long way to treating normal TB and even further away to treating multi-drug resistant TB'.

MSF is asking for leadership from the WHO in the major health crises of today, especially TB. Gillies stressed that the WHO cannot delegate this responsibility but it has to take it onto itself, especially when it comes to R&D into new tools and medications. "This is what we desperately need," Gillies said.

Dr Tido von Schoen-Angerer, Director of the MSF Campaign for Access to Essential Medicines, said that there are only a few promising drugs currently in the pipeline. There are only six drugs for TB in clinical development whereas there are around 150 for cardiovascular diseases.

There must be more investment in R&D for TB, and this cannot only be through philanthropic effort. Stronger engagement is required by governments. According to MSF, with 450,000 new cases of drug-resistant TB globally each year, resistance to drugs is a problem that is growing at a rapid pace. Multi-drug resistant tuberculosis (MDR-TB) is a form of tuberculosis resistant to at least the two principal first-line drugs rifampicin and isoniazid.

The Global XDR-TB Task Force convened by the WHO in October 2006 has defined extensively drug-resistant tuberculosis (XDR-TB) as a form of tuberculosis resistant not only to rifampicin and isoniazid, but also to certain second-line drugs (at least one fluoroquinolone and one of the three injectable drugs kanamycin, amikacin or capreomycin).

MSF said that XDR-TB is particularly alarming in the context of HIV, as people who are co-infected with HIV/AIDS could die before test results can confirm their drug resistance. Using standard drugs to treat XDR-TB without knowing whether there is drug resistance could effectively condemn a patient to death.

According to Dr Francoise Louis, MSF TB and HIV/AIDS advisor: "Business as usual would be a disaster when it comes to treating XDR-TB. XDR-TB has the potential to be devastating in places where HIV/AIDS is widespread. But trying to treat XDR-TB with the tools we have today would be like trying to put out a forest fire with a garden hose." :

To respond to the XDR-TB outbreak, said MSF, the WHO will need to get newer drugs to patients as soon as possible by working with regulatory agencies and pharmaceutical companies to ensure fast-track clinical development and availability of new drugs for "compassionate use".

The WHO will also need to push to accelerate the development of more easy-to-use tests. This will require the WHO to take a lead and not simply delegate responsibility to product development partnerships.

According to MSF, the emergence of XDR-TB is a reflection of how the WHO approach to TB has failed, particularly by neglecting R&D into urgently needed new drugs and diagnostics that could help reduce the nearly two million TB deaths each year.

The drugs in today's standard TB treatment were developed in the 1950s and 1960s and the most commonly used TB test was developed over a century ago and manages to detect TB in only about half of the cases. In addition, existing TB drugs and tests are even less adapted for use in people who also have HIV/AIDS.

According to MSF, it is seeing an increasing number of cases of multi-drug resistant TB (MDR-TB) among the 17,000 patients it treats in over 94 projects in 44 countries.

MSF also said that patients who are undergoing treatment for MDR-TB face long and arduous treatment lasting up to two years, much of which is often spent hospitalised in isolated wards. The drugs are very toxic, cause a wide range of side effects and are very expensive, costing up to US$15,000 per treatment course.

The emergence and rapid spread of XDR-TB in high HIV prevalence settings represent a major threat to global health. The phenomenon is a demonstration of the limitations of TB control programmes, which have been relying on outdated tools for TB diagnosis and treatment, MSF said.

The immediate responses of the public health community must not focus solely on strengthening control programmes. It is also urgent to mobilise all necessary resources for the rapid delivery of new drugs and diagnostic tools.

It is also crucial that the drug pipeline be filled with compounds that act through novel mechanisms that are able to target novel molecular targets, in order to avoid cross-resistance with drugs currently in use, said MSF.

Currently, there are a few new promising candidate drugs in the clinical phase of development. There is an urgent need for innovative thinking in the field of clinical trials for new TB drugs, in order to speed up the development of these new drugs and accelerate their delivery to patients.

Also, rapid, reliable and field adapted diagnostic tools for TB and drug resistant forms of TB are an integral part of treatment strategies and urgently need to be developed, MSF said. ✍✍✍

*—Third World Network Features*