Scientific Facts on

Drug-resistant Tuberculosis

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GreenFacts

Level 2 - Details on Drug-resistant Tuberculosis

This Digest is a faithful summary of the leading scientific consensus report produced in 2008 by the World Health Organization (WHO):
"Anti-Tuberculosis Drug Resistance in the World"

The full Digest is available at: https://www.greenfacts.org/en/tuberculosis/

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1. What is tuberculosis and why is it a concern?


TB can be treated with antibiotics.
Source: TB Global drug Facility

Tuberculosis (TB) is a pulmonary bacterial infectious disease that spreads through the air. When people who are sick with TB in their lungs cough, sneeze, talk or spit, they propel TB germs into the air, and a person needs only to breathe in a small number of these to be infected.

Overall, one-third of the world's population is currently infected with the TB bacillus, the bacterium that causes tuberculosis. However, most of these people infected with TB will never become sick or infectious as their immune system keeps the infection in check.

People with a weakened immune system have a greater chance of becoming sick with tuberculosis, particularly if they are also infected with HIV. TB is one of the major causes of death in people who are HIV-positive, and HIV is the most important factor responsible for the rise of TB in Africa since 1990.

The proportion of people in the general population who become sick with tuberculosis each year is stable or falling worldwide but, because of population growth, the absolute number of new cases is still increasing. In 2005, South-East Asia had the largest number of new cases but the highest proportion of new cases and TB-related deaths was found among the African population. About 1.6 million people worldwide died from tuberculosis that year.

Although antibiotics to cure TB have only been available for the past 50 years, forms of tuberculosis that are resistant to the major anti-TB drugs have emerged worldwide. Drug-resistant tuberculosis is caused by inconsistent or incomplete treatment, when doctors prescribe the wrong treatment or when patients do not take all their medicines regularly for the required period.

Multidrug-resistant tuberculosis (MDR-TB) is a dangerous form of tuberculosis that is resistant to at least isoniazid and rifampicin, the two most powerful "first-line" anti-TB drugs. Usually, multidrug-resistant tuberculosis can be cured with long treatments of "second-line" drugs, but these are more expensive than first-line drugs and have more adverse effects.

When the rate of multidrug resistance in an area is high, it becomes increasingly difficult to control tuberculosis. This threat is even more serious because of the emergence of **extensively drug-resistant tuberculosis (XDR-TB),** particularly in settings where there are many patients who are also infected with HIV. XDR-TB is caused by strains of the disease resistant to both first- and second-line antibiotics. This confirms the urgent need to strengthen TB control.

In 2006, The WHO launched the Stop TB Strategy, a new approach that aims at halting the progression of tuberculosis by 2015, and to eliminate it as a public health problem by 2050. The six components of the Stop TB Strategy are:

- Pursuing expansion and enhancement of the TB control approach launched by WHO in 1995 (the so-called DOTS strategy).
- Addressing TB/HIV, MDR-TB and other challenges.
- Contributing to health system strengthening.
- Engaging all care providers.
- Empowering people with TB, and communities.
- Enabling and promoting research.

This text is a summary of: WHO, Fact sheet N°104, Revised March 2007 [see http://www.who.int/mediacentre/factsheets/fs104/en/print.html]

2. What is the Global Project on Anti-tuberculosis Drug Resistance Surveillance?

Keeping track of the patterns of drug-resistant tuberculosis throughout the world is difficult. Firstly, the data available are limited because some countries, particularly countries with a high TB burden, do not have enough laboratories to conduct tests, or systems to keep track of TB cases. Secondly, the quality of drug susceptibility tests is not consistent and needs to be better ensured, particularly for resistance to second-line anti-tuberculosis drugs.


A network of supra-national laboratories supports the national laboratory network.
Source: Pierre Virot

The Global Project on Anti-tuberculosis Drug Resistance Surveillance was set up in 1994 by the WHO, the International Union Against Tuberculosis and Lung Disease and other partners. Its aims are to estimate the levels of resistance to anti-TB drugs throughout the world and see how these change with time, to develop plans to prevent and tackle drug resistance and to evaluate the progress of these plans.

The project assembles a network of 26 "supra-national reference laboratories" (SRLN) that give practical and technical support to over 150 national laboratories worldwide. The supra-national laboratories are the backbone for surveillance and since 1994, the Global Project has collected data on resistance to first-line anti-TB drugs from areas representing almost half of the world's TB cases. The main priorities for the network are to cope with the demand for laboratory services and to obtain regular funding.

New methods have been developed that can diagnose MDR-TB quickly, and although they have not yet been fully validated, some countries are already using them to identify cases of MDR-TB. If successful, these new methods would be extremely helpful to gather more information on drug-resistance. At the moment there are no quick methods that can detect resistance to second-line drugs.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf],
Fourth Global Report (2008), Chapter 4: Discussion, Overview (p. 78), Chapter 4: Discussion, SRLN (p. 87-89)

3. What are current trends in drug-resistant tuberculosis?

3.1 How many people are affected by drug-resistant tuberculosis?

It is estimated that 1 to 1.5 million people worldwide are living with multidrug-resistant tuberculosis. In 2006, one in every 20 of all new cases of tuberculosis was multidrug-resistant. Of the nearly half a million people who became ill with multidrug-resistant tuberculosis, 50% were in China and India, and 7% in the Russian Federation.


TB Patients in a prison in Tbilsi, Georgia.
Source: Agnes Montanari

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, Global estimates (p.87)

3.2 How do trends vary from region to region?

The lowest levels of drug-resistance are in Western and Central Europe, followed by Africa and the Americas. The Eastern Mediterranean and South East Asia are moderately affected, followed by the Western Pacific. Eastern Europe reports the highest proportions of drug-resistance.

There are important variations within the WHO regions, particularly in the Eastern Mediterranean, the Western Pacific, and the European regions. For example, there is much less drug-resistant TB in Western and Central Europe than in Eastern Europe. In all regions, there are some countries where the results are very different from the average.

Data on the evolution of the occurrence of tuberculosis and drug-resistance show different trends. For example, the proportion of multidrug-resistant tuberculosis (MDR-TB) among new TB cases is decreasing rapidly in Hong Kong, China and the United States while it appears to be stable in Thailand, Viet Nam, in three Baltic countries and in many countries with a low TB burden.

In South Korea and in Peru, TB cases are declining, although at a slower pace than before, and the number of cases of multidrug resistant tuberculosis is increasing. In Peru this is probably caused by weaknesses in tuberculosis control. In South Korea, the results could be due to a better surveillance system that is now detecting cases that would not have been detected in the past.

In some parts of the Russian Federation, the overall number of new TB cases is not as high as in previous years but the proportion of new cases that are multidrug-resistant is increasing very rapidly.

At present it is not possible to estimate global trends because there is very little information on trends from high burden countries.

Data on trends can be misleading. For instance, an improvement in testing would detect previously unreported cases and therefore lead to an apparent increase in multidrug-resistant tuberculosis. An increase in the reported proportion of drug resistance in a population could also be due to a better control programme that cures more TB cases overall, but cannot cure resistant forms of the disease. Therefore, when evaluating the trends, it is important to interpret the data carefully, to consider additional information and to take into account any changes in TB control programmes that could affect the data.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, Magnitude and trends (p.81-82)

3.3 How common is extensively drug-resistant tuberculosis?

Extensively drug-resistant tuberculosis (XDR-TB) is more expensive and difficult to treat than multidrug resistant tuberculosis (MDR-TB) and outcomes for patients are much worse because the treatment options are limited. Therefore, it is important to know how many cases of XDR-TB there are and how they are distributed.

The available data on XDR-TB have several limitations. Firstly, the quality of the tests for resistance to second-line drugs is not sufficiently ensured as most tests were not carried out by supranational reference laboratories. Secondly, second-line drug susceptibility testing is not available in most countries because of its significant cost. Therefore, in most settings

only MDR-TB cases were tested for resistance to second-line drugs, which may limit the accuracy of the estimates of the levels of XDR-TB.

Despite these shortcomings, data indicate that XDR-TB is widespread with 45 countries having reported at least one case. However, no conclusions can be drawn about the total number of cases worldwide because most of the information available is from countries that report few TB cases.

Japan and South Korea have reported high rates of XDR-TB but these may be overestimates because the test population was not representative. The Philippines might also be heavily affected. In Africa the problem of XDR-TB may be less, except in South-Africa. In the countries of the former Soviet Union, where drug resistance is widespread a very high proportion of cases of MDR-TB are XDR-TB.

Data from many parts of the world is still sparse, highlighting the need for a strengthening of the global capacity for diagnosis and surveillance of resistance to second-line drugs.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, XDR-TB (p. 83-85)

4. Why do HIV and tuberculosis form a lethal combination?

HIV-TB patient in Thailand. Source: Thiery Falise

See also our AIDS Digest. [see https://www.greenfacts.org/en/aids/index.htm]

Tuberculosis can be very difficult to detect in people who are HIV-positive. Tests to detect tuberculosis are often negative in people infected with both HIV and TB, which can cause delays in the diagnosis. In addition, people infected with dormant tuberculosis bacteria can quickly become sick with tuberculosis when their immune systems are weakened by HIV. This, together with the difficulty of treating both diseases at the same time, has led to high death rates in people living with TB and HIV.

Tuberculosis is one of the opportunistic infections closely associated with HIV and there have been many outbreaks of drug-resistant forms of tuberculosis in places where large numbers of HIV-positive patients are in close contact with each other such as some hospitals and prisons. However, information on how tuberculosis is transmitted in these particular settings cannot be used to predict the spread of drug-resistant tuberculosis in the general population. This is an important point because people infected with both HIV and tuberculosis develop the disease quickly and, if they are infected with MDR-TB, they could start an outbreak of drug-resistant tuberculosis.

There are two main reasons why HIV and drug-resistant tuberculosis may be associated: HIV infection or its treatment could result in poorer absorption of anti-tuberculosis drugs or in acquired resistance to these medicines. In addition, HIV-infected patients and drug-resistant tuberculosis patients may have similar risk factors such as history of hospitalization. It is also possible that HIV infected patients may be more susceptible to infection once exposed, although no data support this.

The main obstacle to understanding the association between HIV and drug-resistant tuberculosis is the lack of data available. In Ukraine and Latvia, there is a high proportion of MDR-TB and an emerging HIV epidemic that is becoming more generalized in the population. The data gathered in these two countries will be crucial not only to find the right treatment for the patients, but also to help understand how HIV may affect the spread of drug-resistant tuberculosis in the region. The development of infection control measures

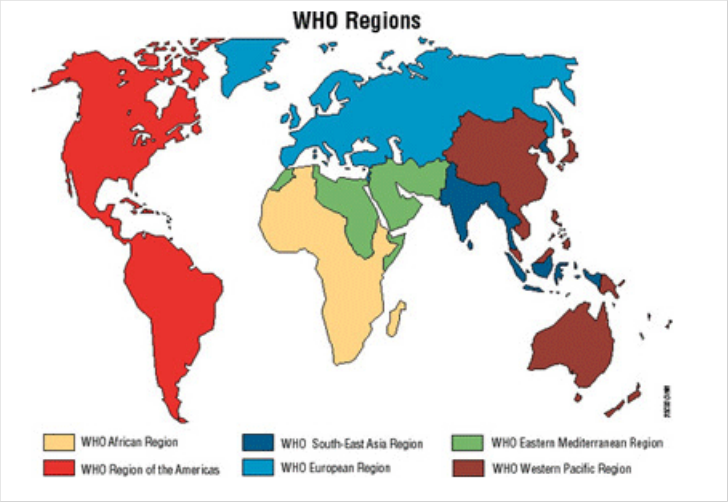
as well as diagnostic screening tools to rapidly identify drug resistant TB are a priority, for all countries, but particularly for those with high prevalence of HIV or MDR-TB.

From a global perspective, patients would benefit if tests for HIV and TB were carried out at the same time.

Additional studies will be needed to understand the association between HIV and drug-resistant tuberculosis at the population level.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, Drug resistance and HIV (p. 85-87)

5. What is the status of drug-resistant tuberculosis in the different WHO regions?



5.1 The African WHO Region


The number of new TB cases in India is very large. Source: Gary Hampton

In Africa, the proportion of cases of multidrug-resistant tuberculosis (MDR-TB) is relatively low at 2.2%. It is estimated that in 2006, approximately 67 000 new cases of MDR-TB emerged in the region, with almost 90% of these cases emerging in areas where HIV is widespread.

The lack of adequate laboratory facilities in most African countries makes it very difficult to detect tuberculosis in people who are also infected with HIV. It is also not clear how drug-resistant tuberculosis spreads in areas where HIV infection is common. Given the high rates of HIV infection in some parts of Africa and the lack of laboratories, current figures could underestimate the true burden of MDR-TB in the region.

It is difficult to identify trends of infection in the region as there are only very few surveys available. Preliminary data from Botswana showed that drug resistance is increasing and the results from a further survey will be very important to understand the trends in drug resistance in countries with high rates of HIV. In terms of extensively drug-resistant tuberculosis (XDR-TB), South Africa has recently reviewed its laboratory database and found that 5.6% of multidrug-resistant samples collected over a four year period were in fact extensively drug-resistant. However, these results are not part of a formal survey.

Several countries in the region have nationwide surveys under way or have plans to start them soon, and some of these will include testing for resistance to second-line drugs. Tanzania is evaluating the use of new methods capable of detecting multidrug resistance quickly. If successful, these would be useful to gather information over a wider area and to study trends.

The most critical factor in addressing drug resistance in African countries is the lack of laboratory infrastructure and transport networks that can diagnose drug-resistant tuberculosis quickly. Most countries in the region are far from reaching the targets for multidrug-resistance testing set in The Global Plan to Stop TB 2006-2015. However, there are plans to upgrade national laboratory networks in most countries and to set up at least three new Supra-national Reference Laboratories in addition to the two existing ones.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, WHO Regions, African region (p. 90-92)

5.2 The North and South American WHO Region

The proportion of drug-resistant tuberculosis among TB cases is low in America as a whole. However, some countries are more heavily affected than others.

In North America, Canada has low proportions of drug-resistant tuberculosis and the number of new cases has decreased every year since 1997. In the USA, tuberculosis is declining and multidrug-resistance even faster.

In South America, there were an estimated 12,070 new cases of MDR-TB in 2006, with Peru alone accounting for about a third of these and Ecuador and Brazil for about an eighth each. This may likely be due to weaknesses in the management of TB cases and in the entire health system in Peru, particularly in the years 2003 and 2004. The proportion of drug-resistant tuberculosis among the general population is low in Argentina, Uruguay and Cuba.

In Brazil and in Mexico there are nationwide surveys under way that test for multidrug-resistance and HIV. A repeat survey in the Dominican Republic is ongoing and Panama also has plans for a nationwide survey.

Currently there are five Supranational Regional Laboratories in the region with plans to expand the network to one or two additional laboratories over the next two years. Many countries have plans to upgrade laboratory networks, and there is more demand for laboratories that can detect resistance to second-line drugs.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, WHO Regions, Region of the Americas (p. 93-94)

5.3 The Eastern Mediterranean WHO Region

The information available on drug resistance in the Eastern Mediterranean WHO region has improved significantly since 2002 although it is still limited.

It is difficult to gather information in the region for two reasons. Firstly, many countries are involved in conflicts and struggle to provide even basic health care so they do not have the resources to collect data on drug resistance. Secondly, laboratory infrastructure is poor in many countries of the region.

Approximately 5.4% of all cases of tuberculosis in the region are multidrug-resistant. In 2006 there were approximately 25,000 new cases of multidrug resistant tuberculosis (MDR-TB), and more than half of these were in Pakistan.

The proportion of MDR-TB among new TB cases is low in Morocco, Lebanon and Oman, but higher in Yemen and Jordan. Jordan, Lebanon, and Oman reported very high proportions of resistance among retreated cases, although the results are not very reliable due to small sample sizes.

Currently, there is only one reference laboratory in the region, but two more could be set up. Pakistan has expanded its laboratory services widely and has plans to do a nationwide survey and to start a programme to treat multidrug-resistant tuberculosis. Iran has been planning a second nationwide survey for several years, but has not yet carried it out. Libya, Saudi Arabia and Somalia will start preparation for drug resistance surveys in 2008. Sudan has recently begun a survey.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, WHO Regions, Eastern Mediterranean Region (p. 95-96)

5.4 The European WHO Region

The proportion of cases of tuberculosis that are multidrug-resistant varies widely between Western and Central Europe, where it is only 1.5%, and Eastern Europe and the Central Asian countries, where it is as high as 22.6%.

In most of Western and Central Europe, there is little drug-resistance both in absolute and in relative terms. Israel is an exception and has the highest proportion of resistance in the region. However, most cases of multidrug-resistant tuberculosis (MDR-TB) in Israel were likely to have been infected abroad before immigrating to Israel. Importantly, almost all countries in Western and Central Europe are now linked to a supra-national reference laboratory and the quality of the drug resistance testing and the correctness of the test results are monitored independently.

Countries of Eastern Europe and Central Asia have reported the highest proportions of resistance to anti-tuberculosis drugs in the world and an estimated 80,057 MDR-TB cases emerged in the area in 2006. One of the main factors responsible for this could be the economic crisis that followed the disintegration of the USSR in 1991. This resulted in the deterioration of the health sector and had a devastating effect on the well-being of the population. Other important factors could be the failure of many countries to follow standard procedures to deal with tuberculosis and the spread of drug-resistant tuberculosis in prisons.

In the Baltic countries, the proportion of people diagnosed with TB each year is falling and trends in drug-resistance among new cases appear to be relatively stable. This decline in tuberculosis over the last 10 years is a result of economic growth, investment in health and improved TB control, particularly in Latvia and Estonia, and to a lesser extent in Lithuania. In all three countries, social problems among TB patients, such as alcohol, psychoactive drug abuse and homelessness, have a negative impact on treatment outcomes.

In the Russian Federation, the proportion of people who become ill with tuberculosis is relatively stable and is falling in some areas. In two areas that have provided reliable trend data, However, the number and the proportion of cases that are drug-resistant are increasing considerably despite strong and improving TB control programs, and the reason for this is not clear. While the results from these areas cannot be extrapolated to the country as a

whole, they suggest that extraordinary measures will have to be taken if MDR-TB is to be reduced in the population.

Currently, all countries in this sub region are linked to a supra-national regional laboratory with the exception of Turkmenistan and Bulgaria. Several countries are starting or planning national drug resistance surveys. Appropriate MDR TB treatment is becoming available in more and more countries, but additional investment will be needed to meet the targets set out in the Global Plan.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, WHO Regions, Eastern Europe (p. 97-101)

5.5 The South East Asia WHO Region

The South East Asia WHO region is home to a number of countries that have a high burden of tuberculosis, with India alone accounting for close to two million cases. Though the proportion of cases of multidrug-resistant tuberculosis (MDR-TB) among new TB cases in the region is moderate, the overall number of cases of MDR-TB is considerable. In 2006, approximately 150,000 people became ill with MDR-TB, with three quarters of them living in India.

In five of the six countries that reported data since 2002, the proportion of multidrug resistance among new cases was lower than 3.0% but in Myanmar it was 3.9%, which accounted for over 4000 cases in 2006. Despite these results and the lack of resources, Myanmar has made some progress in TB control.

Levels of drug resistance appear to be moderate in Indonesia, low in Bangladesh and exceptionally low in Sri Lanka where all cases that do not respond to standard treatment are tested for drug-resistance, and multidrug resistance is managed by the public sector. Nepal also shows low levels of drug resistance. .

Recent results from India show low to moderate proportions of multidrug resistance among new cases but considerably higher proportions among those previously treated for tuberculosis. Many such "retreatment" cases are thought to be managed by the private sector and there is concern that, unless the public sector takes up drug-resistance management rapidly, an increasing number of MDR-TB cases will be managed by an unregulated private sector which has access to second-line drugs that are of variable quality. Extensively drug-resistant tuberculosis (XDR-TB) has also been reported in the country.

North Korea could be affected by multidrug-resistance more heavily than other countries in the region. It has developed plans to improve its laboratory capacity to test for resistance but the main obstacle to achieve this goal is lack of sustainable funding.

All countries in the region with the exception of Thailand have identified the upgrading, expansion and quality assurance of their laboratory network as their primary requirement to scale up MDR-TB control.

Unlike the other countries in the region Thailand has an extensive and well developed network of laboratories, some capable of performing tests for resistance to second-line drugs. However, laboratory services are not centralized and many are managed by the private sector, which makes it is difficult to maintain high levels of performance. All MDR-TB patients are managed in the public sector but practices do not follow international guidelines.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, WHO Regions, South-East Asian Region (p. 101-105)

5.6 The Western Pacific WHO Region

In 2006, there were over 150,000 new cases of multidrug-resistant tuberculosis (MDR-TB) in the Western Pacific, which represents 6.7% of all cases of tuberculosis in the region. Almost 85% of MDR-TB cases emerged in China. Besides China, the worst affected countries among those that have reported data are Viet Nam and the Philippines.

Data from three provinces in North Eastern China show proportions of multidrug resistance among new TB cases as high as 7.3%, but these are much lower in the cities of Beijing and Shanghai. China has the second highest level of resistance in the world and the extent of resistance to second-line drugs is currently unknown. Although there are plans to expand MDR-TB treatment, China is not on target to meet the goals set for 2011.

Data from Viet Nam suggest that multidrug resistance has not increased over the past 10 years while resistance to any one drug has actually decreased. In 2006, the proportion of MDR-TB was 2.7% among new TB cases but it was much higher among previously treated cases (19, 3 %).

In the Philippines, 4.0% of new TB cases and 20.9% of previously treated cases were MDR-TB in 2004. The Philippines have had a long-running programme to manage multidrug-resistant tuberculosis that is now expanding and is performing well. However, the high proportion of resistance to some second-line drugs and the emergence of extensively drug-resistant tuberculosis (XDR-TB) require careful monitoring.

Trends are available from Hong Kong and South Korea. In both places, the proportion of TB cases in the population has decreased , although it has been relatively stable in the past few years in South Korea. In Hong Kong multidrug resistance has been declining fast, while in South Korea there has been a gradual but significant increase in MDR-TB among new cases.

Available data on XDR-TB show that the highest proportion among MDR-TB is found in Japan followed by Hong Kong. Where absolute numbers of MDR-TB are low, XDR-TB may not represent a significant obstacle for TB control However, in countries with many cases of MDR-TB and widely available second-line drugs, such as China and the Philippines, monitoring of resistance to second-line drugs will be crucial.

China is the only country in the Western Pacific with a significant number of laboratories able to test samples for drug resistance. The region has five very active Supranational Reference Laboratories and there are plans to add one more over the next year. However, to cope with the demand, it may be crucial to forge links with the private sector.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, WHO Regions, Western Pacific Region (p. 105-109)

6. Why is it difficult to gather information on drug-resistant tuberculosis?


Traditional skin tests do not detect drug resistance. Source: Greg Knobloch

In order to gather information on drug-resistant tuberculosis it is necessary organize surveys and repeat them. This requires sufficient laboratories capable of performing drug resistance tests, staff to interview and classify the patients, and a transport network to send samples for analysis to different laboratories inside and outside the country. These facilities are not available in all countries, particularly those where relatively large proportions of the population are affected. It would also be desirable to have large samples of patients classified in sub-categories according to their previous treatment history, to test patients for HIV and to perform second-line drug resistance tests. All these come at great additional expense and workload. That is why surveys tend to be repeated infrequently.

In order to limit the number of samples, current survey methods are based on smear positive cases. Since many HIV co-infected TB cases are smear negative, this approach may underestimate drug resistance among those infected with both HIV and TB. In addition, surveys tend to focus on new cases and to exclude prevalent cases and patients in the private sector. Including these cases would substantially increase the cost and the workload of the surveys, and the improvement in results may not be worth it.

It must also be borne in mind that the current survey methods do not allow to reliably differentiate between primary and acquired resistance.

In order to gather more data and determine trends in countries with a high TB burden, surveys must be simplified. One option could be the use of new, rapid methods to test drug resistance, such as the one being evaluated in a study in Tanzania. Although these rapid tests would only be useful for measuring resistance to one or two anti-TB drugs, the testing would not require specialized laboratories or the transport of infectious samples. Where resources are limited, the priorities are to detect multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). Samples could be tested first for resistance to first-line drugs and the ones that give positive results could be tested subsequently for resistance to second-line antibiotics. Alternatively, all samples could be tested for extensive drug-resistance from the outset.

To assess trends in drug resistance over time, patients could be classified by treatment history on a routine basis and a certain number of samples could be tested each month. The process would be even simpler and more effective if the tests could be done at the time of consultation. All patients diagnosed with MDR-TB would be further screened for XDR-TB and enrolled on treatment.

It is important to realize that different information is gathered for different purposes: to know the extent of the disease and its evolution over time, to monitor and improve the tuberculosis programmes or to answer research questions. Many countries are conducting several surveys at the same time to address each of these questions.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Chapter 4: Discussion, Survey methods (p.79-81) See also Chapter 2: Methods &Executive summary: background and methods

7. Conclusions

7.1 Magnitude and trends of drug-resistant tuberculosis


Patients need to be registered into a suitable treatment programme. Source: Gary Hampton

In 2006, approximately half a million new cases of multidrug resistant tuberculosis (MDR-TB) emerged in the world. China and India are estimated to carry 50% of the global burden of cases, and the Russian Federation is estimated to carry a further 7%.

Globally, MDR-TB makes up 4.6% of all cases of tuberculosis but, in some parts of the former Soviet Union, this proportion exceeds 35%. The patients in these countries have forms of tuberculosis that are resistant to a wide range of drugs, with the highest rates of extensively drug resistant tuberculosis (XDR-TB) in the world.

China has the second highest proportion of MDR-TB among TB cases but, in absolute terms, it has the highest number of MDR-TB cases in the world. The high proportion of drug-resistant TB among new cases in China suggests a concerning level of transmission of drug-resistant forms of TB.

In most countries where cases of TB are relatively few, the absolute numbers of cases of drug-resistant tuberculosis as well as the proportions of resistance are stable. Trend results are good in Hong Kong where MDR-TB is falling faster than tuberculosis. In Peru and in South Korea, tuberculosis is declining but MDR-TB is increasing. In Peru this could be due to a weakening in the control of the disease but in South Korea it may be due to changes in the surveillance method and not reflect a true worsening of the situation.

In the Baltic countries, tuberculosis is declining and levels of MDR-TB are relatively stable. However, in parts of the Russian Federation drug-resistance is rising rapidly, both in absolute numbers and in terms of proportion among new TB cases. Tuberculosis control is improving but there is a large pool of long-term cases that continues to fuel the epidemic. Current efforts to control the disease will have to be accelerated to have any impact in what appears to be a growing epidemic of drug-resistant tuberculosis.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Executive Summary: Conclusions, Magnitude of drug resistant TB &Trends (p.16-18)

7.2 Extensively drug-resistant tuberculosis (XDR-TB)

Extensively drug-resistant tuberculosis (XDR-TB) can only be treated with a handful of drugs and these are more expensive and have worse side-effects than those used to treat multidrug-resistant tuberculosis (MDR-TB).

Extensively drug-resistant tuberculosis is widespread and 45 countries have reported at least one case. There is a significant problem within countries of the former Soviet Union, where cases of XDR-TB are high both in absolute and in relative terms. Levels of resistance to second-line drugs are also high in Japan and South Korea, and moderate in South Africa.

Elsewhere, in Africa, levels of extensively drug-resistant tuberculosis seem to be low. XDR-TB is likely to emerge as a result of inappropriate use of second-line anti-tuberculosis drugs, but these drugs are not yet widely used in the region

In order to understand the extent and the pattern of extensively drug-resistant tuberculosis throughout the world, all countries need to increase their efforts to measure resistance to second-line anti-tuberculosis drugs.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Executive Summary: Conclusions, XDR-TB (p.18)

7.3 Drug-resistant tuberculosis and HIV

There is a significant association between HIV and multidrug-resistant tuberculosis (MDR-TB). A major reason for this association might be environmental: people become infected with both HIV and MDR-TB in places where patients are in close contact with each other such as health care facilities and prisons. Improving infection control in these settings may be critical to reducing the number of people infected with both HIV and multidrug-resistant tuberculosis.

People who have both infections at the same time are likely to die from TB unless they are diagnosed and treated quickly. This is a great concern for countries without sufficient testing facilities.

It is extremely important to develop methods that can detect drug-resistant tuberculosis quickly, particularly for HIV infected patients.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Executive Summary: Conclusions, MDR and HIV (p.19)

7.4 Survey coverage and methods

Monitoring of drug resistance should be part of routine surveillance, but this requires culture and drug susceptibility testing to be the standard of diagnosis. Since many countries do not yet have these facilities, surveys are important to determine the extent of the drug resistance problem. Survey coverage and reliability of data are increasing, but major gaps remain. For instance, it is very difficult to determine trends in most high burden countries.

The largest obstacle is the lack of laboratory capacity. Testing for resistance to second-line drugs is not available in most countries and it has been difficult to introduce HIV testing as part of the general care for tuberculosis. Supranational reference laboratories will continue to provide testing for resistance while countries develop their own national facilities.

New methods to detect and monitor drug-resistant tuberculosis are being developed. Special studies are necessary to answer questions such as the risk factors for acquiring drug-resistant tuberculosis, or how the disease is transmitted in different populations.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Executive Summary: Conclusions, Coverage and methods (p.19-20)

7.5 Tuberculosis control and drug-resistant tuberculosis

The main priority for all countries is to prevent the development of drug resistant tuberculosis but all cases that emerge have to be treated properly.

Some countries need to develop ways of detecting and treating drug-resistant cases quickly. This is particularly important in countries with high proportions of anti-tuberculosis drug resistance, countries with high absolute numbers of multidrug-resistant tuberculosis (MDR-TB), and countries with a TB population heavily co-infected with HIV.

New drugs to treat multidrug-resistant tuberculosis are urgently needed.

To control MDR-TB there needs to be a coordinated effort from all countries. The three priority areas include improvements in infection control measures to prevent transmission, expansion of testing services to detect cases quickly, and community involvement to ensure patients get tested and take all their drugs regularly. Most importantly, all patients must be registered in a suitable treatment programme.

This text is a summary of: WHO, Anti-Tuberculosis Drug Resistance in the World, Fourth Global Report (2008) [see http://www.who.int/tb/publications/2008/drs_report4_26feb08.pdf], Executive Summary: Conclusions, TB Control and drug resistant TB (p.20)

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