A disease that is alive and kicking
Phyllida Brown

Tuberculosis – wasn’t that the disease that used to kill pale and interesting poets and novelists in nineteenth-century Europe? Yes – but if you thought TB was nothing more than a memory, wake up! The disease is alive and all too well, killing more people worldwide than any other infection including malaria and AIDS. Currently a third of the world’s population harbours the tubercle bacillus and is at risk for the disease, and 30 million people will die from TB over the next decade. These numbers could continue to increase with every passing year.

In the industrialized countries, TB is back with a vengeance after 35 years of decline. In New York, one of the worst-hit areas, the number of cases of the disease has risen by 150% since 1980. But it is in developing countries that the disease continues to exact its greatest toll – more than 95% of the eight million cases and three million deaths each year. Despite the clear successes of individual nations, TB was never really eliminated anywhere, and now it is creating new crises around the world.

So what has gone wrong? The answer, say researchers, is that we made a fatal mistake: we became complacent because we thought we had beaten tuberculosis. After the discovery of effective drugs between the 1940s and 1960s, the number of cases and deaths in the industrialized countries fell rapidly. The sanatoria were closed down, public health measures for TB control were dismantled, and medical researchers working on the disease moved into other fields. Funding for TB research fell to a mere trickle as few donors saw the need to continue. In the industrialized world, TB was presumed dead. Most health officials and scientists assumed that the developing world would subjugate the disease with equal ease using the new treatment programmes.

Both assumptions were wrong. TB treatments turned out to be less straightforward than originally supposed. TB drugs, though comparatively cheap, nevertheless represent a heavy burden on developing countries’ limited supplies of foreign exchange. Moreover, the complexity and demands of organizing effective treatment services have proven difficult for many countries.

Now, doctors are relying on antiquated – but still effective – diagnostic tools, since most research on TB stopped before the era of modern biotechnology. The TB bacterium, Mycobacterium tuberculosis, grows extremely slowly in culture and is so infectious that only certain laboratories are equipped to handle it. Using current methods, it can take at least two weeks to confirm TB and even longer to discover that a particular strain of the TB bacterium is resistant to a particular drug – by which time the sufferer may have already died.

Potential for rapid spread

While the world was complacent, a deadly mix of factors have combined to aid the spread of the disease. Poverty, economic recession, and malnutrition make populations more vulnerable to TB. Recent increases in human migration have rapidly mixed infected with uninfected communities. To this already explosive mixture has been added the human immunodeficiency virus (HIV), a potent and dangerous ally of the TB bacterium, so that a person infected with both the TB bacterium and HIV is much more likely to develop active tuberculosis than someone infected with the TB bacterium alone. WHO estimates that nearly five million people have already been infected with both microbes – setting the scene for a massive increase in TB cases in the coming years. In countries with a high prevalence of HIV infection, such as Malawi and Zambia, TB cases have risen sharply, sometimes more than doubling.
In addition, HIV creates particular problems for the diagnosis and treatment of TB. The skin test used to detect infection with TB is crude and basic, and often fails to work in people who are HIV-positive because it relies on measuring the response of the person's immune system. If the immune system is defective, it may not respond even though the person is infected. Furthermore, TB disease often has different clinical features in HIV-positive people. More sophisticated means of diagnosing infection in HIV-positive patients are being developed.

Treatment too is affected by HIV. For years in much of Africa, a drug called thiacetazone has been a mainstay of TB treatment. Although industrialized countries abandoned it some time ago, the drug has remained attractive to many developing countries because it is cheap. However, thiacetazone can cause severe and sometimes fatal reactions in an unacceptably high proportion of HIV-positive TB patients compared with HIV-negative patients, so doctors have warned against using it to treat TB in populations where HIV is widespread. Switching to safer drugs will cost countries money, but some doctors are adamantly that a drug that is unacceptable to the West is unacceptable worldwide. And patients are less likely to come for treatment if they have valid fears about the safety of medication.

More deadly than ever

While it was always important to avoid TB infection, the incentive has now increased dramatically because of the spread of "killer" strains that are resistant to more than one of the major drugs. These multidrug-resistant (MDR) strains have probably always existed as the result of random genetic mutations, but they remained rare until the 1980s when the scene was set in the USA for them to flourish and spread.

A survey in the USA at the beginning of the 1980s found that about 7% of all TB strains tested were drug-resistant. By 1992 in New York City, more than one-third of strains tested were resistant to one drug, and almost one-fifth were resistant to the two main drugs, rifampicin and isoniazid. A few strains resist almost all the known anti-TB drugs. So far in the USA, outbreaks of MDR tuberculosis have carried an extraordinarily high death toll: more than half of those known to have been infected with MDR strains have died. Most of these deaths have been among people who were also HIV-positive, so it is difficult to estimate the overall death rate from MDR tuberculosis. However, no one knows how many people with an intact immune system have also been infected with MDR strains.

Multidrug-resistant TB has been most intensively studied in the USA and information on its spread in developing countries is still limited. However, there is evidence that MDR strains are spreading in parts of southeast Asia and southern Africa. New studies suggest that these strains are being transmitted to people who were previously uninfected.

Leading TB researchers such as Dr Lee Reichman, President of the American Lung Association, believe that MDR tuberculosis gained a foothold in the USA because of poor treatment and the collapse of the public health system. The closure of the sanatoria was supposed to have been followed by a greatly improved service in community care. But money ran out in the 1970s, and community services were actually cut. Patients who failed to complete the long and cumbersome course of treatment were often not followed up, and incomplete or inadequate treatment was just what the drug-resistant mutant bacteria needed to encourage them. Today, many health authorities employ workers to supervise patients' treatment in order to ensure that the full therapy is finished.

Still a curable disease

Tuberculosis is a terribly debilitating disease and, if untreated, kills around half of those affected. People with TB suffer from weakness and exhaustion, profuse night sweats, chest pain and cough, sometimes with bloody sputum. Occasionally the bacteria spread to affect other tissues including the bone, bringing further disability. Fortunately, TB is still an avoidable, curable disease. With proper management, more than 95% of patients are cured. And treatment for TB costs less, in terms of the price for each year of life saved, than measles immunization. In stark contrast, the cost of ignoring TB could be catastrophic. In the USA alone, for example, which has only a tiny minority of the world's total TB cases, the direct and indirect costs of the TB epidemic since 1985 have been estimated at US$ 640 million already, with a projected loss of $2200 million by the end of the 1990s.

In the short term, scientists and politicians have their work cut out. More money for TB is desperately needed; better diagnostic technology and more acceptable, shorter treatment regimens will be essential. In the longer term, say health officials, countries must work to overcome the poverty that allows both TB and HIV to inflict such lasting damage on societies.