

Africa is worst hit by dual epidemic

The realization that it will be impossible to curb the spread of HIV/AIDS without tackling tuberculosis (TB) and vice versa has led to an upsurge in joint research, surveillance and treatment initiatives into the two diseases that are feeding off each other to devastating effect.

One-third of the estimated 40 million people living with HIV/AIDS are also infected with TB. In sub-Saharan Africa, the proportion is even higher. People infected with HIV are five to 10 times more likely to develop TB in a given year than those who are not, fuelling an upsurge in the TB epidemic which kills an estimated two million people worldwide a year.

“There were countries in Africa in the most horrendous situations of poverty and war, and yet TB rates were going down,” according to Dr Bernard Fourie, honorary scientist with South Africa’s Medical Research Council and former head of its TB research programme. “But since the late 1980s not one single country in sub-Saharan Africa has seen a decline.”

“This is undoubtedly because of HIV,” said Fourie, who worked in TB research for 30 years.

Africa is the worst hit region in terms of the impact of TB/HIV. In 2003, TB incidence fell in five of six

WHO regions but increased dramatically in many African countries. South Africa is one of the hardest hit nations.

The South African Medical Research Council forecasts that there will be 300 000 cases of TB this year and 30 000 deaths from it in the country — a fatality rate of 10% compared to one of 3–5% before the advent of HIV/AIDS. WHO said South Africa had 558 estimated cases of TB per 100 000 population in 2002, second only to Zimbabwe.

WHO’s ‘3 by 5’

Progress Report

published in January estimated that between 37 000 and 62 000 people out of the 837 000 South Africans needing antiretroviral medicines (ARVs) were actually receiving the treatment at the end of December — a coverage rate of 7%.

The problems faced by high burden countries such as South Africa have spurred the drive to tackle the dual epidemic with a coordinated response intended to draw on the strengths of the TB control strategy, DOTS, and the dynamism of the ‘3 by 5’ drive to get three million people with HIV/AIDS on antiretroviral treatment by the end of 2005.

Last September WHO launched a new internal HIV/TB Task Force to boost coordination between countries and encourage TB services and HIV/AIDS programmes to work more closely together.

The Task Force was launched at the annual conference of the TB/HIV Working Group of the Global Stop TB Partnership, which was held in Addis Ababa in September last year.

The conference, grouping 40 countries and agencies, concluded that

more needed to be done to implement WHO’s Policy on Collaborative TB/HIV Activities. (See box on p. 166.)

They agreed on the urgent need for more drugs, newer testing methods and more information on how best to treat TB/HIV dual infection and concluded that the DOTS treatment strategy for TB was essential, but not sufficient by itself.

“The top priority is strengthening of DOTS, but it is necessary to implement and scale up additional existing

interventions to prevent TB, such as chemoprophylaxis, and to diagnose TB more effectively by carrying out intensified case finding,” Dr Mario Raviglione, Director of WHO’s Stop TB Department told the *Bulletin*.

“The control of HIV is key for TB control as well. Thus, any measure should be attempted to prevent HIV infection and to treat it,” Raviglione said.

The meeting report called for better diagnostic tools to replace the smear microscopy test which was developed a century ago and is often too imprecise to detect TB in HIV-positive patients who show atypical symptoms.

“The long duration and high pill count of current TB drug regimens coupled with the spectre of increasing drug resistance require urgent development of new drugs,” the report said.

The TB/HIV Working Group also stressed the need for further research on toxic reactions and other interactions — such as reduced efficacy — between ARVs and TB drugs.

There are plans for trials sponsored by the Special Programme for Research and Training in Tropical

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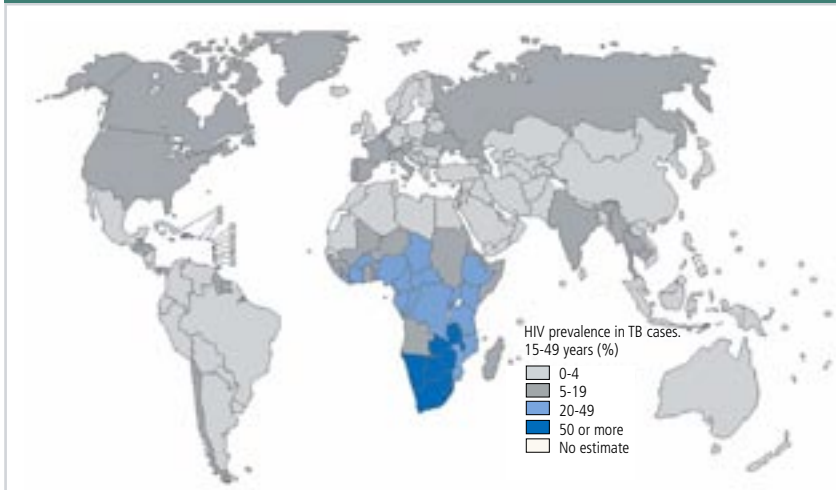
“We can’t fight AIDS unless we do much more to fight TB”.
Nelson Mandela, Bangkok, 14 July, 2004.



IFRC/Chris Black

Former South African president Nelson Mandela recalled at last year’s AIDS conference in Bangkok that he contracted TB in prison in South Africa. His impassioned appeal to the global community has since spurred efforts to fight TB, particularly in regions with a high burden of HIV/AIDS.

Estimated HIV prevalence in TB cases in 2003



Source: WHO

Diseases (TDR) to provide clinical evidence of efficacy, safety and concomitant use of TB and HIV drugs in co-infected patients in South Africa, the United Republic of Tanzania, Uganda and Zambia.

“African leaders must focus even more attention on TB as it is not only the major killer of HIV-infected people but a disease that is out of control on the African continent with incidence rates growing at up to 10% per year, despite all efforts made through implementation of DOTS,” Raviglione said.

He said that WHO was strengthening monitoring and evaluation systems and training capacity for the two diseases. WHO is also one of the partners in CREATE, the Consortium to Respond Effectively to the AIDS/TB Epidemic, which is studying new public health strategies in resource poor settings.

As part of the US President’s Emergency Plan for AIDS Relief, the US Centers for Disease Control and Prevention (CDC) has launched an initiative to help countries develop national TB/HIV surveillance systems. And there are hopes for an increase in resources for joint TB/HIV activities

from the Global Fund To Fight AIDS, Tuberculosis and Malaria.

But progress on the ground remains slow. In a report issued in December, Médecins Sans Frontières (MSF) said that — despite its pioneering role in treating HIV/AIDS patients in poor settings — only four of its 25 HIV/AIDS programmes in sub-Saharan Africa directly provide TB treatment. The charity is running a pilot project to combine TB/HIV treatment at one of its three clinics in the impoverished Cape Town suburb of Khayelitsha, where 2000 patients are receiving ARVs. The idea is that patients receive care for both TB and HIV in one clinic visit and staff develop expertise in managing both diseases. The

initial experience is promising, according to MSF spokeswoman Marta Darder.

About 60% of patients have a TB-related problem in the 90-bed medical ward at the GF Jooste Hospital, which deals with complex cases referred by day clinics in the deprived townships around Cape Town, South Africa. An estimated 50% are HIV-positive, according to Senior Specialist of ARV Services Dr Kevin Rebe.

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Dr Kevin Rebe, GF Jooste Hospital, Cape Town, South Africa.

The standard TB smear test is often negative in HIV patients, even if they have active TB, which can delay their entry into treatment under TB protocols. Results from more sophisticated techniques involving sputum culture can take up to eight weeks: a delay which can prove fatal. Given the continuing stigma of HIV, the majority of TB patients are reluctant to be tested for HIV, according to Rebe.

Treatment is even more problematic. WHO and national guidelines recommend that priority should be given to treating patients with the six-month course of TB treatment and then move on to ARVs. For patients with advanced clinical symptoms of AIDS, the alternative approach is to give a TB/HIV patient two months of TB treatment, and then to start the ARVs. But for really severely immunosuppressed patients (with a CD4 count of less than 50) the only option is to begin TB and HIV treatment simultaneously.

“We don’t like to do it,” said Rebe. “There is the pill burden of taking 10 or 11 tablets a day and the side-effects like nausea, vomiting, liver toxicity and peripheral neuropathy.”

What Rebe finds particularly frustrating is the lack of coordination between the TB and the HIV/AIDS programmes. He said that once a patient is diagnosed with TB, they are sent to a TB clinic with little further interaction with the HIV/AIDS specialists at the hospital.

“We have to start treating these two diseases together,” Rebe told the *Bulletin*. “TB is the most common opportunistic infection. It is the most common cause of death in a HIV-positive patient. It is the most common cause of hospitalization.” ■

Clare Nullis-Kapp, *Cape Town*

WHO’s Policy on Collaborative TB/HIV Activities recommends that governments develop a national TB/HIV policy and establish a mechanism to coordinate TB/HIV policy between countries. It also recommends the following measures:

- HIV surveillance of TB patients
- voluntary testing and counselling
- TB prevention and care in HIV/AIDS services
- HIV/AIDS prevention and care in TB services
- provision of antiretroviral therapy to eligible HIV-positive TB patients

Rotavirus vaccine introduction in Mexico sets precedent

When UK pharmaceuticals giant GlaxoSmithKline (GSK) launched Rotarix, a new rotavirus vaccine, in Mexico in January, it set a precedent. Spurred also by recent EU rules on drug licensing, other companies may follow suit.

The need for a rotavirus vaccine in Mexico became pressing after the only such vaccine to be launched, RotaShield was pulled from the market less than a year after its 1998 introduction when it became linked to bowel blockage or intussusception.

The recall of RotaShield, developed by US pharmaceuticals company Wyeth, held back the timetable for subsequent promising rotavirus vaccines, increasing the cost and testing period for a new product. Although the US Centers for Disease Control and Prevention (CDC) advised other countries to keep studying RotaShield, Wyeth stopped manufacturing it, making further trials impossible.

Pharmaceutical companies usually seek approval for a new product with the US Food and Drug Administration (FDA) or the EU's European Medicines Agency (EMA) even if the product is largely needed in developing countries. This approval can, in turn, be used in other countries, particularly developing countries with less established regulatory systems.

But seeking approval with the FDA and EMA can delay the entry of a new medicine or other pharmaceutical product in a country by up to 10 years. For rotavirus infection, where most of between 352 000 and 592 000 children who die annually of its effects live in the developing world, this could mean thousands of deaths before medication is available.

GSK said this is why it went straight to Mexican regulators, got approval in July 2004 and launched the vaccine officially in January 2005. The Mexican Ministry of Health is incorporating Rotarix into its infant immunization programme to prevent some 1000 annual deaths from rotavirus infection that occur in the country.

"We wanted to be in a country where there was a recognized medical need for the Rotarix vaccine, and we were successful in working with Mexican officials," said Patty Seif, a GSK spokeswoman based in Philadelphia. "Rotavirus isn't a big health issue in the US compared to the number of children in developing countries who

are dying from rotavirus. So there was a clear medical need."

Experts say it's logical for many reasons to go into a country like Mexico first. From the company's standpoint, a drug like Rotarix has greater profit potential in a developing country because the need, and thus the market, is greater. Although rotavirus is called a 'democratic virus', one that strikes children in every country, it kills an inordinate number of children in developing countries, where there is less access to treatment for diarrhoea.

GSK's direct entrance into Mexico avoided the 10–15 years it often takes for drugs to make their way from developed countries to the poorest countries. Dr Roger Glass, chief of the Viral Gastroenteritis Unit at CDC, said that it can take even longer for such medicines to become affordable.

In December 2004 GSK filed for regulatory approval for Rotarix in the European Union and expects approval soon, said Samantha Christey, a spokesperson for GSK in Belgium.

"Rotarix has been filed in more than 30 countries worldwide," Christey told the *Bulletin*. "Rotarix will be approved in many other Latin American countries in the course of 2005." She said GSK had not sought approval for Rotarix in the US.

Some experts argue that the regulatory authorities in a country like Mexico may be less rigorous. But vaccine advocates argue that the risk criteria in developing countries are different from those in developed countries. In the US, contracting rotavirus infection — which many children under five do — is unlikely to be fatal. In a less developed country an infected child is more likely to die. They argue that in that context a smaller risk of a bowel obstruction, such as the one that took RotaShield off the market, seems a small price to save thousands of lives.

"In a place like India where about 6% of the under-five deaths of

children are due to rotavirus, a vaccine would be a real lifesaver," said Glass. "If the risk [of bowel obstruction] was one in 10 000 or one in 30 000, you would save hundreds of lives in India before you would see a single intussusception event."

As developing countries strengthen their regulatory authorities, they may attract an increasing number of new drug licence applications.

"It's a strategy that will be very important in the future," said Ciro de Quadros, Director of International Programs with the Sabin Vaccine Institute, in Washington. "In the past, developing countries did not have national control authorities, [so] this could not happen."

Dr Liliana Chocarro, a WHO expert on regulatory matters, said that under new regulations in Europe the EMA will no longer license vaccines and other medicines that will not be marketed in the 25 EU member states. She said the development could spur companies to apply for licences in the countries where the drugs will be marketed.

"Perhaps we will see this happening more and more as new vaccines targeted for developing countries come up for licensing," Chocarro said. "More vaccines may be licensed first where the countries are going to use it, not where the vaccines have been manufactured."

Evan Simpson, spokesperson for the Rotavirus Vaccine Program (RVP), said that obtaining approval in the most developed country of a region — such as Mexico in Central America — could streamline approval in less developed countries of that region much the way US FDA approval streamlines this for other countries.

"The hope is that by introducing it in Mexico or Brazil, approval there will have a similar effect in Latin American countries as FDA approval," said Simpson, who is based in the US city of Seattle. "It's a little bit more piecemeal but hopefully a more rapid process." ■

Theresa Braine, *Mexico City*

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