

Diagnosis: hope

It's one of the world's most neglected, yet most devastating, diseases. Is effective treatment for TB in sight at last? By Andrew Jack

The search goes on: studying a DNA-based TB vaccine at the Pasteur Institute

THE DIRECTOR OF Tanzania's tuberculosis programme, Said Egwaga, holds out a handful of the indigestibly large, brightly coloured tablets that his patients are required to take each day. Add in the anti-retroviral drugs for the many who are also infected with HIV, he jokes, and "it's a full meal in itself".

But one problem is that many of those with TB – an ancient scourge that still kills 1.7m people globally every year – do not eat regular meals. Many suffer initially from the disease of poverty; even if they can afford the regular trips from remote rural areas to a clinic for diagnosis and treatment, they do not have the nutrition essential to assist their recovery.

Another problem is evident behind Dr Egwaga, where the small staff in a dusty, decrepit ward of one of Dar es Salaam's main hospitals are clearing up after an exhausting day of consultations. There is a severe lack of funding in those developing countries that shoulder the greatest burden of TB.

A third problem is the crude and outdated tools that he and his colleagues around the world must work with. At the Dar es Salaam clinic, staff use the same technique for diagnosing TB first developed 100 years ago: they mix dye with sputum coughed up by patients on a slide, for analysis under a microscope, despite the inaccuracies of the method – and the limited protection from cross-infection afforded by hand-washing and fresh air to kill the bacteria.

Even in richer countries with more sophisticated, expensive diagnostics, there has been no new vaccine launched for 80 years to improve on the very limited protection of BCG given in early childhood. And for 40 years there has been no new drug breakthrough to reduce the burden of multiple pills, given daily over a minimum of six months.

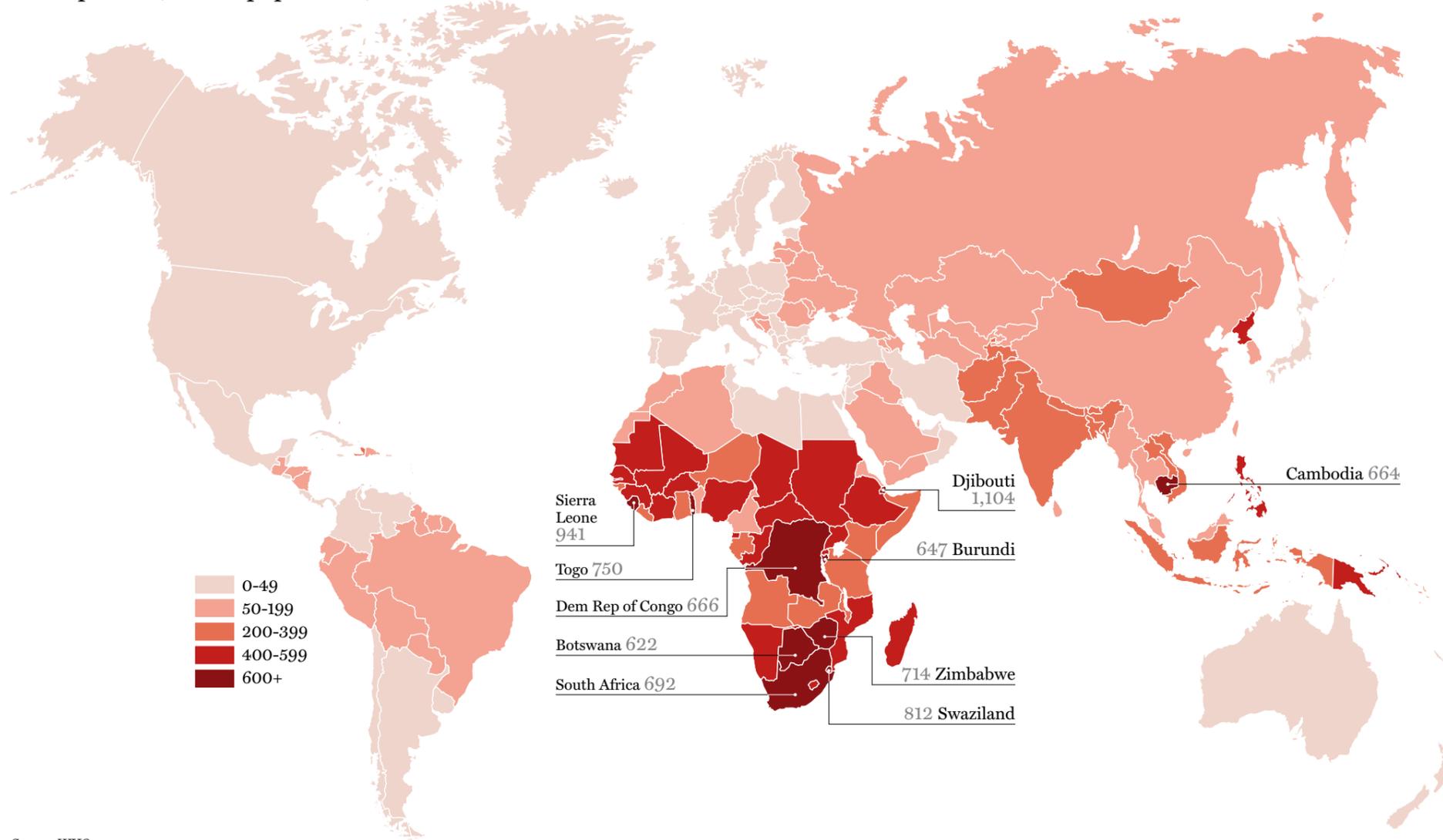
All combined, these challenges have helped create a resurgent threat to global public health, as many people who are infected go undetected and untreated; and those who are treated struggle to follow cumbersome drug regimes, while their doctors lack the ability to identify treatment failures quickly and prescribe alternative medicines.

The result is a continued growth in infections to more than 9m new cases annually, an estimated 500,000 of which are multi drug-resistant TB (MDR) and extremely drug-resistant TB (XDR), the spectre first identified in South Africa in

PHOTO: SCIENCE PHOTO LIBRARY

Prevalence of TB

Cases per 100,000 of population, 2007



Source: WHO

2005. This variant, which is extremely difficult to treat, has since been observed in more than 50 countries.

There are many reasons for sluggish progress, starting with the considerable scientific challenges. As Professor Brigitte Gicquel from the Pasteur Institute in Paris described in an interview in the Bulletin of the World Health Organisation recently, even the slow growth of the TB bacteria itself threatens advances.

“It can take two years to complete an experiment,” she said. “That’s compared with just three weeks for a

There are 9m new cases diagnosed annually, while the spectre of extremely drug-resistant TB has been observed in more than 50 countries

disease such as cholera. When it comes to publishing, you have to submit studies in small pieces, which isn’t very attractive to prestigious journals – so the research isn’t very attractive for ambitious young scientists. The costs are also higher ... because there’s less financial return, industry

makes less of an investment in the first place.”

HIV has generated enormous resources, research and reform over the past three decades, partly because of commercial appeal and public advocacy by rich, vocal patients. TB’s concentration in poor adults in poor countries

has struggled to capture the imagination of western funders or whet the appetite of for-profit companies.

Even research into malaria, another long-neglected “killer” disease, has been reinvigorated with fresh funding, tapping into a stronger vein of sympathy in the developed world. That may reflect the continued threat of infection to western travellers and soldiers; the image of children as the greatest victims; and the lure of relatively simple tools – nets and potent new drugs – to tackle the parasite. At last June’s Pacific Health Forum, an annual health issues gathering in Seattle, one session was even dedicated to the lessons TB campaigners should learn from malaria’s recent success.

But the same conference also offered

some fresh prospects for optimism, not least in simply focusing on the disease and bringing together an unprecedented number of pharma and diagnostics companies with non-profit researchers and policymakers.

PETER SMALL, SENIOR programme officer at the Gates Foundation, says: “Ten years ago there was a small, chaotic group of researchers – we were in this death spiral. Now there is a more virtuous circle with a sense of urgency, exciting science, regulatory clarity and some very smart people thinking about the issues.”

These views are shared by Mel Spigelman, head of the TB Alliance, a Gates-funded, non-profit drug-development

partnership. “We’re on the verge of a quantum leap,” he says. “We have the beginnings of a critical mass of new drugs in development in ... the TB drug landscape. We can actually now envision a new treatment paradigm.”

This summer Tibotec, a subsidiary of Johnson & Johnson, became the latest pharmaceutical company to join forces with his organisation, offering joint development and pledging affordable pricing on TMC207, the most advanced of a series of new and promising experimental drugs that are now under test for TB.

Spigelman sees the possibility of its approval by regulators within three years, while other prototype drugs in combination could reduce standard TB treatment by two-thirds (ie to just two months) within five or six years. That would ease the burden on patients enormously, boosting cure rates and reducing the incidence of drug resistance.

IN DIAGNOSTICS, A NEWER generation of more sophisticated, reliable and affordable tests are closer still. Timescales are longer for vaccines, but Jerry Sadoff, head of the Aeras Global TB Vaccine Foundation, says: “There is a broad array of promising incentives and other measures on the horizon to accelerate TB vaccine R&D.”

Mario Raviglione, director of the Stop TB department at the World Health Organisation, also veers towards optimism, stressing not only the prospect of new diagnostics and drugs but also of better implementation of existing therapies:

Prospects for optimism include a new focus on the disease among pharma companies, working alongside policymakers and non-profit researchers

“Forty million people have now been treated and cured.” And as a proportion of the world’s still-rising population, infection rates have begun to tail off too. He also points to a new recognition, among countries such as China and Brazil, of the problem of drug-

resistant TB, and a willingness to act, whether through domestic funding or efforts to strengthen cheaper and easier-to-take formulations of drug therapies.

Raviglione’s continuing concerns include the need for more funding; a more flexible attitude by regulators to new drug trials and approvals; and the need to clamp down on TB prescriptions by private doctors that do not comply with the latest scientific conclusions.

Paul Sommerfeld, chairman of TB Alert, a UK-based charity, remains more cautious. He warns that, should the current costly trials for new tools fail, there are few fallbacks. He also sees large gaps remaining in the need to integrate medical services for TB with those for HIV, as the two infections increasingly co-exist. And he argues that few funds yet match the rhetoric about increasing community engagement to boost awareness and detection of TB.

He points wistfully to the vast amount of money, attention and progress given in just three months to the apparently mild pandemic flu virus, with its genome mapped, and plans for widespread vaccination well advanced. “Why doesn’t TB gather that kind of attention? It kills 1.7m people a year and it’s curable.” ■



Pricking the conscience: the battle against TB needs more effective vaccines

PHOTO: PANOS

GRAPHIC: RUSSELL BIRKETT