

Slow-growing TB bacteria point the way to new drug development

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The discovery of a large number of slow-growing *Mycobacterium tuberculosis* bacteria, which cause tuberculosis (TB), in the lungs of TB patients could be an important step forward in the design of new anti-TB drugs.

Until now it was thought that *M. tuberculosis* bacteria in the lungs of TB patients were rapidly multiplying. However recent research by Dr Simon Waddell and colleagues from St George's University of London and the University of Leicester, using gene chips to look at how TB bacteria behave in different environments, revealed that the tuberculosis bacteria in the sputum (phlegm coughed from the lungs) of TB patients resemble bacteria that are growing very slowly or hardly at all. This has caused concern, as slowly growing bacteria are non-responsive to treatment with isoniazid, one of the main antibiotics used to treat TB. This may be the reason why it takes six months to treat pulmonary TB successfully, whereas most bacterial infections are treated in days. This prolonged treatment often leads people to stop taking their medicines early or only to take them intermittently, which can cause relapses and the emergence of antibiotic resistance.

"Our observations imply that either a large number of the infecting bacteria in the lungs are not multiplying rapidly as previously suggested; or the bacteria are adapting by not growing when they are coughed from the lungs into the air," said Dr Waddell, presenting his findings at the Society for General Microbiology meeting at Harrogate today (Monday 30 March).

"We need to find out how bacteria respond during infection and after drug treatment to understand how bacteria become tolerant to antibiotics. This will provide alternative opportunities for the development of better drugs that the world desperately needs to combat the growing health threat of TB."

Tuberculosis kills around 1.7 million people each year, equating to 4,500 deaths a day, or someone dying of TB every 19 seconds. Approximately one third of the world's population are infected with tuberculosis bacteria (~2 billion people), of which around one in ten will develop active disease. Current antibiotic treatment for *M. tuberculosis* involves a minimum of 3 drugs over a 6-month period (isoniazid, rifampicin and pyrazinamide for 2 months, followed by isoniazid and rifampicin for a further 4 months). Multidrug-resistant TB (MDR-TB), resistant to two front line drugs, and extensively-drug resistant TB (XDR-TB), resistant to at least two front line drugs and two others, have recently become major clinical problems. It is estimated by the WHO (World Health Organisation) that there are around 500,000 new cases of MDR-TB per year, and 40,000 new cases of XDR-TB. The need for new drugs to treat TB is greater now than ever.

Source: Society for General Microbiology

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