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New drug-resistant TB strains could become widespread, says new study

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The emergence of new forms of tuberculosis could swell the proportion of drug-resistant cases globally, a new study has found. The finding raises concern that although TB incidence is falling in many regions, the emergence of antibiotic resistance could see virtually untreatable strains of the disease become widespread.

Australian researchers from the University of New South Wales and the University of Western Sydney have published the new finding in the latest issue of the Proceedings of the National Academy of Sciences.

Laboratory-based studies have suggested that antibiotic-resistant TB strains cause longer-lasting infections but with a lower transmission rate. Therefore, scientists have questioned whether drug-resistant TB strains are more likely than drug-sensitive strains to persist and spread - an important question for predicting the future impact of the disease.

One in three humans already carries the TB bacterium. Although it remains latent in most cases, the World Health Organisation (WHO) has estimated there were 9.27 million new cases of TB in 2007. There were 1.6 million TB-related deaths in 2005. Drug-resistant TB is caused by inconsistent or partial treatment, when patients do not take all their medicines regularly for the required period or because the drug supply is unreliable.

A research team led by UNSW's Dr Mark Tanaka used epidemiological and molecular data from *Mycobacterium* tuberculosis strains isolated

from Cuba, Estonia and Venezuela to estimate the rate of evolution of drug resistance and to compare the relative "reproductive fitness" of resistant and drug-sensitive strains.

"We found that the overall fitness of drug-resistant strains is comparable to drug-sensitive strains," says Dr Tanaka of the Evolution and Ecology Research Centre. "This was especially so in Cuba and Estonia, where the there is a high prevalence of drug-resistant cases."

The finding may reflect an inconsistency in drug treatment programs in these countries. Indeed, Estonia now has one of the highest rates of multi-drug resistance in the world. The intermittent presence of drugs and the resulting transmission of resistant strains would have let drug-resistant strains collectively spend more time within untreated hosts, allowing them to evolve ways to become more infectious and out-compete the drug-sensitive strains.

The study also reveals that the contribution of transmission to the spread of drug resistance is very high - up to 99 per cent - compared with acquired resistance due to treatment failure. "Our results imply that drug resistant strains of TB are likely to become highly prevalent in the next few decades," says UNSW's Dr Fabio Luciani, the study's lead author. "They also suggest that limiting further transmission of TB might be an effective approach to reducing the impact of drug resistance."

"Mathematical and statistical methods can add a lot of value to empirical data by allowing us to account for the processes behind them," says research co-author, Dr Andrew Francis from the University of Western Sydney. "In this case, we use samples of TB genotypes, together with information about drug resistance, to make inferences and predictions that wouldn't have been possible just a few years ago."

About tuberculosis

Tuberculosis is a contagious disease. Like the common cold, it spreads through the air. Only people who are sick with TB in their lungs are infectious. When infectious people cough, sneeze, talk or spit, they propel TB germs, known as bacilli, into the air. A person needs only to inhale a small number of these to be infected.

Left untreated, each person with active TB disease will infect on average between ten and 15 people every year. However, people infected with TB bacilli will not necessarily become sick with the disease. The immune system "walls off" the TB bacilli and it can lie dormant for years. When someone's immune system is weakened, the chances of becoming sick are greater.

Until 50 years ago, there were no medicines to cure TB. Now, strains that are resistant to antibiotics have emerged and about 1.7 per cent of cases worldwide have multi-drug resistant (MDR-TB) disease. In 2006, extensively drug-resistant tuberculosis (XDR-TB) emerged. XDR-TB is defined as MDR-TB plus resistance to any fluoroquinolone and at least one injectable agent: kanamycin, amikacin or capreomycin. The spread of XDR-TB globally has been fuelled by the HIV epidemic, inadequate public health systems, limited access to high-quality laboratory resources, and a neglect of infection control measures.

More information: The epidemiological fitness cost of drug resistance in Mycobacterium tuberculosis, Fabio Luciania, Scott A. Sisson, Honglin Jiangb, Andrew R. Francis, and Mark M. Tanaka, *PNAS* Public release date 10-Aug-2009

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