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Common antibiotic found useful in accelerating recovery in tuberculosis patients

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Bottle of Doxycycline Capsules of the antibiotic doxycycline spill from a medication bottle. Oral antibiotics, such as doxycycline or amoxicillin, are often prescribed after exposure to tickborne Lyme disease. Credit: NIAID

Globally, an estimated 10 million people develop tuberculosis (TB) each year and the disease remains a leading cause of death from a single

infectious agent. Standard short-course anti-TB treatment still requires a regimen of at least six months of antimicrobial drugs, and drug-resistant TB is an increasing public health threat. Even after the traces of TB disease are quashed, patients often suffer from significant sequelae, such as lung scarring. TB survivors have approximately three to four times greater mortality than their local population.

In pulmonary TB, the most common form of active TB disease, the Mycobacterium tuberculosis bacteria causes the formation of sites of high bacterial load, known as cavities. These cavities are poorly penetrated by TB drugs. After TB treatment is complete, there is likely to be tissue damage within the lungs that can lead to further lung problems such as permanent respiratory dysfunction leading to difficulty in breathing, stiffness in the lungs and bronchiectasis, which can make people cough up blood.

Researchers from NUS Yong Loo Lin School of Medicine's Infectious Diseases Translational Research Program have discovered that the use of a common antibiotic, doxycycline, in combination with TB drug treatment, reduces the size of lung cavities and accelerates markers of lung recovery.

In the Phase 2 double-blind trial conducted at the National University Hospital and TB Control Unit, the treatment was found to be safe, with side effects similar to patients on placebo pills. The study shows promise in delivering a new standard-of-care which can potentially prevent long term complications and the study team is seeking funds for a fully-powered larger scale Phase 3 trial to verify these findings.

"Pulmonary TB patients tend to suffer from lung damage after TB, which is associated with mortality, and poorer quality of life. Doxycycline is a cheap and widely available antibiotic that can decrease lung damage, and potentially improve quality of life for these patients,"

said Assistant Professor Catherine Ong, Principal Investigator of the study and member of the Infectious Diseases Translational Research Program (TRP) at NUS Medicine. The study findings were published in the *Journal of Clinical Investigation*.

Professor Paul Tambyah, who was also involved in the study and is Deputy Director of the Infectious Diseases TRP commented, "While we have been able to successfully treat most cases of TB for the last few decades, we have seen many people suffer the complications of the lung damage from the original TB infection. If this common drug, doxycycline, can help prevent the complications of "Long TB" (to use a term currently in vogue), this will really help a lot of patients in Singapore and worldwide."

The Infectious Diseases TRP aims to provide a holistic, patient-centric approach to infectious diseases that are relevant to Singapore and the region. The Program focuses on programmatic research areas including pathogen evolution and transmission, host-microbe interactions and vaccine and therapeutics development.

More information: Qing Hao Miow et al, Doxycycline host-directed therapy in human pulmonary tuberculosis, *Journal of Clinical Investigation* (2021). DOI: 10.1172/JCI141895

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