

Lives could be saved from tropical disease with new rapid test

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Globally, more than half of patients die after infection with the neglected tropical disease, melioidosis, often before they are diagnosed. A new rapid test could save lives by diagnosing patients in hours rather



than several days taken by current bacterial culture methods, meaning they receive the correct antibiotics faster.

The test uses CRISPR to detect a genetic target that is specific to Burkholderia pseudomallei, the bacterium that causes melioidosis, with 93 percent sensitivity. It was developed by researchers at the Mahidol-Oxford Tropical Medicine Research Unit (MORU), Chiang Mai University, Vidyasirimedhi Institute of Science and Technology (VISTEC) in Thailand, and the Wellcome Sanger Institute in the UK.

The results, published in *Lancet Microbe*, mean more lives could be saved from melioidosis with a rapid, easy-to-use diagnostic test that could be rolled out globally.

Melioidosis is a neglected tropical disease that is estimated to affect 165,000 people worldwide each year, of whom <u>89,000 die from the disease</u>. It is caused by the bacterium Burkholderia pseudomallei, which lives in soil and water in tropical and <u>subtropical regions</u> and enters human bodies via inoculation through skin abrasions, ingestion, or inhalation.

It is difficult to diagnose melioidosis as symptoms vary from localized abscess or pneumonia to acute septicemia or may present as a chronic infection. As a result of this, and the locations of isolated communities in rural areas that it mostly affects, the disease remains hugely underreported.

Currently, melioidosis is diagnosed in patients after bacterial samples are cultured, which takes three to four days. In Thailand, approximately 40 percent of <u>patients with melioidosis</u> die, many of whom die within the first one to two days following admission to hospital, while waiting for a diagnosis.



There is no licensed vaccine for melioidosis, but patients can be effectively treated with intravenous antibiotics—ceftazidime or carbapenem—during the first intensive phase of treatment. However, current practices often involve initially treating patients with a range of unnecessary antibiotics to target the various symptoms the disease produces, which can waste time and resources.

In a new study, the team set out to develop a new rapid test to reduce the time taken to diagnose and treat patients with melioidosis correctly.

The researchers identified a genetic target specific to B. pseudomallei by analyzing over 3,000 B. pseudomallei genomes, most of which were sequenced at the Sanger Institute. They searched for conserved regions of the genome and screened the targets against other pathogens and human host genomes to ensure their chosen target was specific to B. pseudomallei.

Their test, called CRISPR-BP34, involves rupturing <u>bacterial cells</u> and using a recombinase polymerase amplification reaction to amplify the bacterial target DNA for increased sensitivity. Additionally, a CRISPR reaction is used to provide specificity, and a simple lateral flow 'dipstick' read-out is employed to confirm cases of melioidosis.

To assess the efficacy of the test, the team collected clinical samples from 114 patients with melioidosis and 216 patients without the disease at Sunpasitthiprasong Hospital, a hospital in northeast Thailand where melioidosis is endemic. The CRISPR-BP34 test was then applied to these samples.

The new test showed enhanced sensitivity at 93 percent, compared to 66.7 percent in bacterial culture methods. It also delivered results in less than four hours for urine, pus, and sputum samples and within one day for blood samples. This is a significant improvement over the current



bacterial culture diagnostic method, which typically takes three to four days.

This new rapid diagnostic test will enable health professionals to prescribe the correct antibiotics faster, meaning fewer patients will die while waiting for a diagnosis. While saving precious time, the new test will also save resources and money, with fewer unnecessary antibiotics prescribed and less time for patients in the hospital.

In the next steps for the team, they are currently designing randomized clinical trials to show the effectiveness of these tests in hospital settings. Plus, members of the team will begin investigating the role of human genetics in susceptibility and immune response to melioidosis infection.

Dr. Claire Chewapreecha, co-lead author at the Mahidol-Oxford Tropical Medicine Research Unit (MORU), Thailand, and Wellcome Sanger Institute International Fellow, said, "Working in rural Thailand has many limitations. But we have shown that limitations breed innovation, and what succeeds here can succeed anywhere."

"I am so proud of the team behind this new, robust, rapid diagnostic test for melioidosis, and I hope that it can potentially be used anywhere in the world to get the right treatments to patients faster, ultimately saving lives."

Dr. Somsakul Wongpalee, co-lead author at Chiang Mai University, Thailand, said, "We carefully designed the rapid <u>diagnostic test</u> based on CRISPR-BP34, with a robust algorithm, and tested its performance in vitro. We are thrilled that the CRISPR-BP34 test demonstrates outstanding diagnostic efficacy when tested on clinical samples, showcasing its potential to significantly impact patient outcomes and potentially save lives in the near future."



Professor Nick Thomson, senior author and Head of Parasites and Microbes at the Wellcome Sanger Institute, said, "This research is a testament to international collaboration and how the application of genomics at scale leads to clinical intervention. Using a genetic target mined from a bank of thousands of bacterial genomes, the team was able to produce an incredibly sensitive test that is specific to the bacterium behind melioidosis. I look forward to seeing the clinical impacts of this research."

Professor Nick Day, senior author and Director of the Mahidol-Oxford Tropical Medicine Research Unit (MORU), Thailand, and the Wellcome Trust Thailand Asia and Africa Programme, said, "Melioidosis has been neglected despite its <u>high mortality rate</u> and high incidence in many parts of Asia. Early diagnosis is essential so that the specific treatment required can be started as soon as possible. The new rapid diagnostic tool developed through this collaboration has the potential to be a gamechanger."

More information: Claire Chewapreecha et al, Benchmarking CRISPR-BP34 for point-of-care melioidosis detection in low-income and middle-income countries: a molecular diagnostics study., *The Lancet Microbe* (2024). DOI: 10.1016/S2666-5247(23)00378-6

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