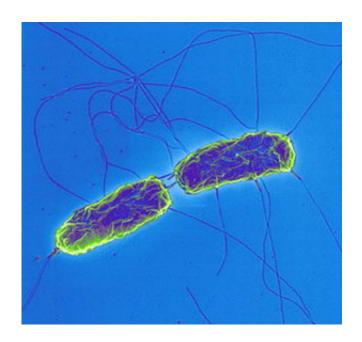


Antibiotic-resistant typhoid detected in countries around the world

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Salmonella Typhi. Image: Dr. Volker Brinkmann, MPI for Infection Biology

There is an urgent need to develop global surveillance against the threat to public health caused by antimicrobial resistant pathogens, which can cause serious and untreatable infections in humans. Typhoid is a key example of this, with multidrug resistant strains of the bacterium *Salmonella Typhi* becoming common in many developing countries. A landmark genomic study, with contributors from over two-dozen countries, shows the current problem of antibiotic resistant typhoid is driven by a single clade, family of typhoid bacteria, called H58 that has



now spread globally.

"The data was produced by a consortium of 74 collaborators from the leading laboratories working on typhoid and describes one of the most comprehensive sets of genome data on a single human infectious agent. It represents global co-operation in the scientific community at its best," says Dr Vanessa Wong, first author from the Wellcome Trust Sanger Institute. "Typhoid affects around 30 million people each year and global surveillance at this scale is critical to address the ever-increasing public health threat caused by multidrug resistant typhoid in many developing countries around the world."

The study shows the H58 clade of Typhi is displacing other typhoid fever strains that have been established over decades and centuries throughout the typhoid endemic world, completely transforming the genetic architecture of the disease. Multidrug resistant H58 has spread across Asia and Africa over the last 30 years, and created a previously underappreciated and ongoing epidemic through countries in eastern and southern Africa with important public health consequences.

Vaccination to prevent the disease is not currently in widespread use in these countries; instead the disease is controlled mainly through use of antimicrobial drugs. H58 Typhi is often resistant to the first-line antimicrobials commonly used to treat the disease, and is continuing to evolve as it spreads to new regions and populations, acquiring novel mutations providing resistance to newer antimicrobial agents, such as ciprofloxacin and azithromycin.

"Multidrug resistant typhoid has been coming and going since the 1970s and is caused by the bacteria picking up novel <u>antimicrobial resistance</u> genes, which are usually lost when we switch to a new drug," says Dr Kathryn Holt, senior author from the University of Melbourne. "In H58, these genes are becoming a stable part of the genome, which means



multiply antibiotic resistant typhoid is here to stay."

"H58 is an example of an emerging multiple drug resistant pathogen which is rapidly spreading around the world," says Professor Gordon Dougan, senior author from the Sanger Institute. "In this study we have been able to provide a framework for future surveillance of this bacterium, which will enable us to understand how antimicrobial resistance emerges and spreads intercontinentally, with the aim to facilitate prevention and control of typhoid through the use of effective antimicrobials, introduction of vaccines, and water and sanitation programmes."

The publication of this research in Nature Genetics coincides with the 9th International Conference on Typhoid and invasive Non-Typhoidal Salmonelloses held by the Coalition against Typhoid (CaT), where these results will be shared with the scientific community. The meeting brings together an international group of healthcare and public health experts, researchers and clinicians to focus on strategies to counteract the spread of typhoid in endemic countries.

"These results reinforce the message that bacteria do not obey international borders and any efforts to contain the spread of antimicrobial resistance must be globally coordinated," says Dr Stephen Baker, an author from The Hospital for Tropical Diseases, an Oxford University Clinical Research Unit in Ho Chi Minh City, Vietnam.

More information: Wong VK et al. (2015). Phylogeographic analysis of the dominant multidrug-resistant H58 clade of Salmonella Typhi identifies inter- and intra-continental transmission events. *Nature Genetics*. DOI: 10.1038/ng.3281



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