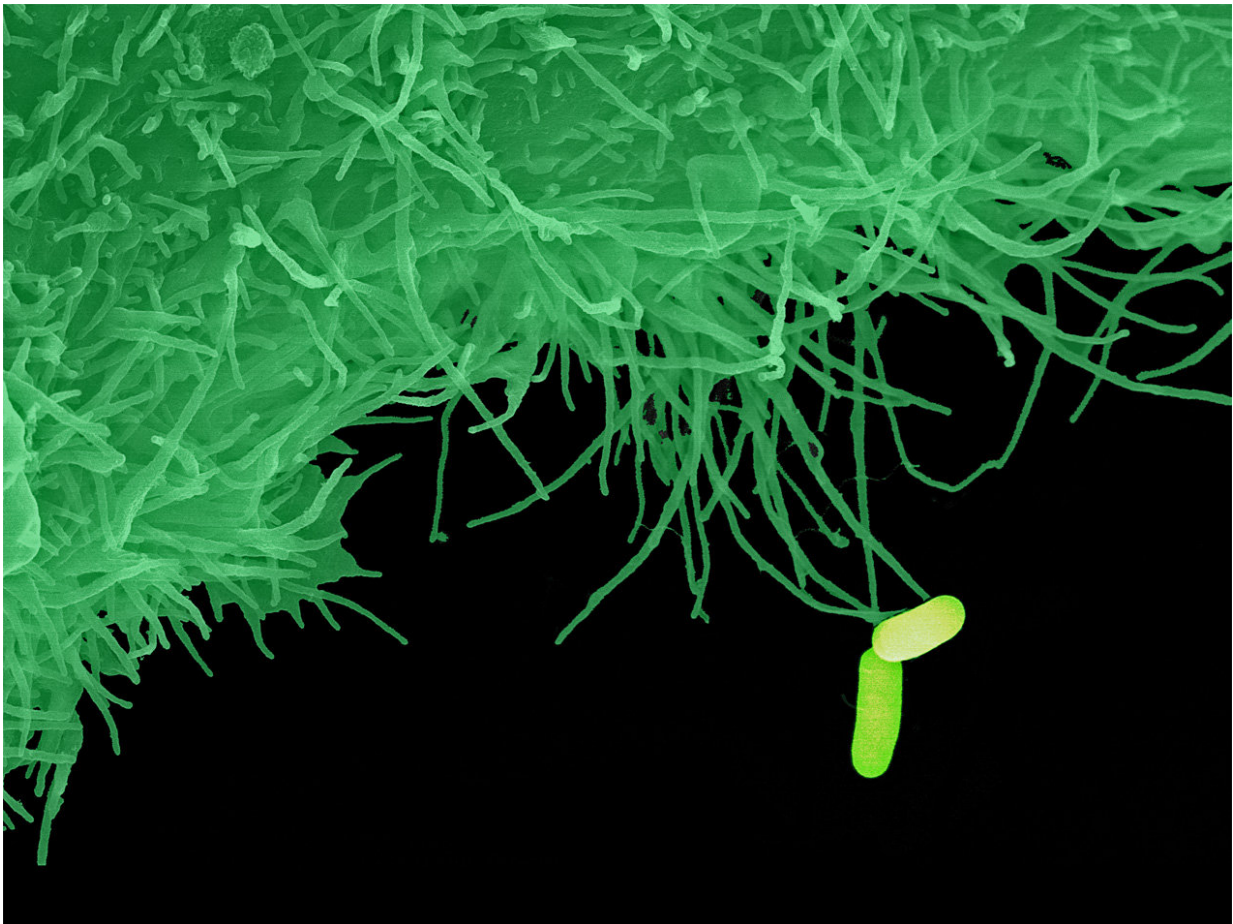


Typhoid outbreak—genetic cause of extensive drug resistance found

February 20 2018



Salmonella Typhi in Pakistan have developed greater drug resistance by acquiring a DNA plasmid encoding further antibiotic resistance genes from another bacteria. Credit: Dave Goulding, Wellcome Sanger Institute

The genetic cause behind a strain of typhoid's resistance to five classes of antibiotics has been uncovered by scientists at the Wellcome Sanger Institute and their collaborators at Public Health England and Aga Khan University, Pakistan. There is currently a major outbreak of typhoid fever in Pakistan, and there was a case in the UK following air travel, which has been isolated and treated. This study shows the typhoid strain causing the outbreak acquired an additional piece of DNA to become resistant to multiple antibiotics, including a third-generation antibiotic.

The results, published today (20 February) in *mBio* suggest that treatment options are running out for [typhoid](#), and there is an urgent need for preventative strategies including vaccines.

Typhoid fever is a bacterial infection caused by the bacterium *Salmonella enterica* serovar Typhi. It is highly contagious, and spreads through the human population in areas with poor water sanitation when contaminated food or water is consumed. Symptoms include fever, stomach pain, headache and constipation or diarrhoea and, if left untreated, it can become fatal.

Currently, an outbreak of drug-resistant typhoid is spreading through Pakistan and an emergency vaccination campaign is underway.

The outbreak began in November 2016, and was immediately recognised and reported to provincial [public health](#) authorities in Pakistan, where investigation into possible sources and control measures including use of a vaccine are ongoing. Public health alerts helped physicians recognise cases of typhoid that were resistant to ceftriaxone, an antibiotic reserved to treat multidrug-resistant infections. This strain was resistant to five [antibiotics](#) in total, a higher level of resistance than previously seen. The doctors treated the infections with the few remaining antibiotic options.



Clean water provision in Sindh, Pakistan. Currently there is an outbreak of extensively drug resistant (XDR) typhoid spreading through the region. Credit: Vicki Francis, Department for International Development

In the spring of 2017, collaborators Professor Rumina Hasan and Dr Sadia Shakoor from the Aga Khan University in Pakistan contacted the Wellcome Sanger Institute to genetically analyse the outbreak. Sanger Institute scientists performed whole genome sequencing of typhoid samples from Pakistan to investigate the [genetic cause](#) behind its high level of antibiotic resistance.

The team discovered that the typhoid outbreak was caused by strain H58, a strain known to be associated with multidrug resistance. When researchers looked further, they found this strain of H58 had gained an extra strand of bacterial DNA – a plasmid – that encoded for additional antibiotic resistance genes. The typhoid possibly picked up the plasmid from *E. coli*.

Scientists at Public Health England identified a strain of typhoid with the

same high levels of resistance from an individual in the UK who had recently returned from Pakistan. Genomic comparison revealed that it was identical to the outbreak strain, meaning the [outbreak](#) had reached the UK, where it has been isolated and treated.

More information: Elizabeth J. Klemm et al. Emergence of an Extensively Drug-Resistant *Salmonella enterica* Serovar Typhi Clone Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation Cephalosporins, *mBio* (2018). DOI: [10.1128/mBio.00105-18](https://doi.org/10.1128/mBio.00105-18)

Provided by Wellcome Trust Sanger Institute

Citation: Typhoid outbreak—genetic cause of extensive drug resistance found (2018, February 20) retrieved 24 April 2024 from <https://medicalxpress.com/news/2018-02-typhoid-outbreakgenetic-extensive-drug-resistance.html>

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