

Researchers look at the spread of dysentery from Europe to industrializing countries

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Researchers have found that a bacterium that emerged centuries ago in Europe has now been spreading globally into countries undergoing rapid development and industrialization. Unlike other diarrheal diseases, this one is unlikely to be resolved by providing access to clean water. As developing countries become more industrialized the numbers of infections with dysentery-causing *Shigella flexneri* are known to decline, associated with improved health, lifestyle and perhaps most importantly access to clean water, but the incidence of another form of the dysentery-causing bacterium, *Shigella sonnei*, actually increases.

The team pinpointed that *S. sonnei* was first established in Europe just a few centuries ago, but in the last few decades has spread to the rest of the world. They also found that a key factor in the spread of this pathogen was a rise in multidrug resistance - the ability to survive exposure to a wide array of antibiotics. Because *S. sonnei* is easily transmitted and has high levels of <u>drug resistance</u>, the researchers suggest that drug treatment and better <u>sanitation</u> alone will not be sufficient for controlling the disease. <u>Vaccine development</u> will be crucial.

<u>Dysentery</u> is a disease primarily associated with <u>developing countries</u> and more than one million people, mostly young children, are estimated to die from dysentery caused by Shigella each year. Whilst most people have heard about dysentery, few know about the bacteria that causes it, Shigella. This is because it is relatively understudied and little is known about their <u>population structure</u> or its origins. Traditionally, *S. flexneri*



has been the most common form of Shigella <u>bacterium</u> to cause dysentery in developing countries with *S. sonnei* more prevalent in <u>industrialized countries</u>. Yet, this is beginning to change with *S. sonnei* becoming increasingly common as developing countries rapidly industrialize.

"Although *S. sonnei* is a relatively new species of bacterium, during its spread it has diversified into an array of different distinguishable clones or strains found right across the world," says Dr Kathryn Holt, first author from the University of Melbourne. "This is hard to see using traditional methods, but by sequencing the genomes of over 100 different forms of the bacteria, we were able to get a glimpse into its past and really start to understand how it is evolving and moving around the world."

"We compared the *S. sonnei* family tree and geographical locations of the different strains to determine when and where this bacterium first emerged and why it has become such a problem in industrialized countries with increasing access to clean water. Traditionally we associate dysentery with contaminated water and lack of <u>industrialization</u>."

To investigate why the bacterium was spreading so effectively, the team looked at the *S. sonnei*'s genetic evolution and found that only a few types of genes were selectively evolving over time, particularly those involved with drug resistance. This suggests that a major driver in the spread of this bacterium was its apparent ability to become resistant to drug treatment.

"Since *S. sonnei* originated, we found there have been three, independent, yet closely related lineages that have spread. The two most recent lineages have been continually evolving to become increasingly resistant to antimicrobials," says Dr Stephen Baker, a senior author from



the Oxford University Clinical Research Unit in Vietnam. "Our data is consistent with antibiotic resistance as being a main driver of the spread and persistence of *S.sonnei* around the world, stressing that <u>antibiotics</u> are not a long-term solution for the elimination of this global health problem."

Despite the fact *S. sonnei* and *S. flexneri* are closely related they have very different surface antigens or coats that interact with the human immune system. S. sonnei has only one type of outer coat, while *S. flexneri* has many, all of which look very different from that of *S. sonnei*. It has been speculated for some time that *S. sonnei* acquired its outer coat from another bacterium that is commonly found in contaminated water, *Plesiomonas shigelloides*.

Both *S. sonnei* and *P. shigelloides* have an identical outer coat. It is believed that when a person is exposed to contaminated water containing *P. shigelloides*, there is an immune cross reaction and the body builds a natural immunity against *S. sonnei*. This theory may explain why the incidence of *S. sonnei* increases following economic development and improvements to water quality, and is consistent with the patterns of global spread described in the current report.

"One of the Millennium Development Goals is to improve drinking water and reduce water borne diseases, an undeniably important aim," says Professor Nicholas Thomson, lead author from the Wellcome Trust Sanger Institute. "This may have the unforeseen result of increasing the incidence of *S. sonnei* dysentery in transitional countries.

"Our research emphasises the importance of a vaccine against *Shigella*. The combination of increased incidence and antibiotic resistance of *S. sonnei*, means that a vaccine will be increasingly important for the long-term control and prevention of dysentery."



More information: 'Out of Europe: The recent global dissemination of Shigella sonnei' *Nature Genetics*, August 5 2012. DOI: 10.1038/ng.2369

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