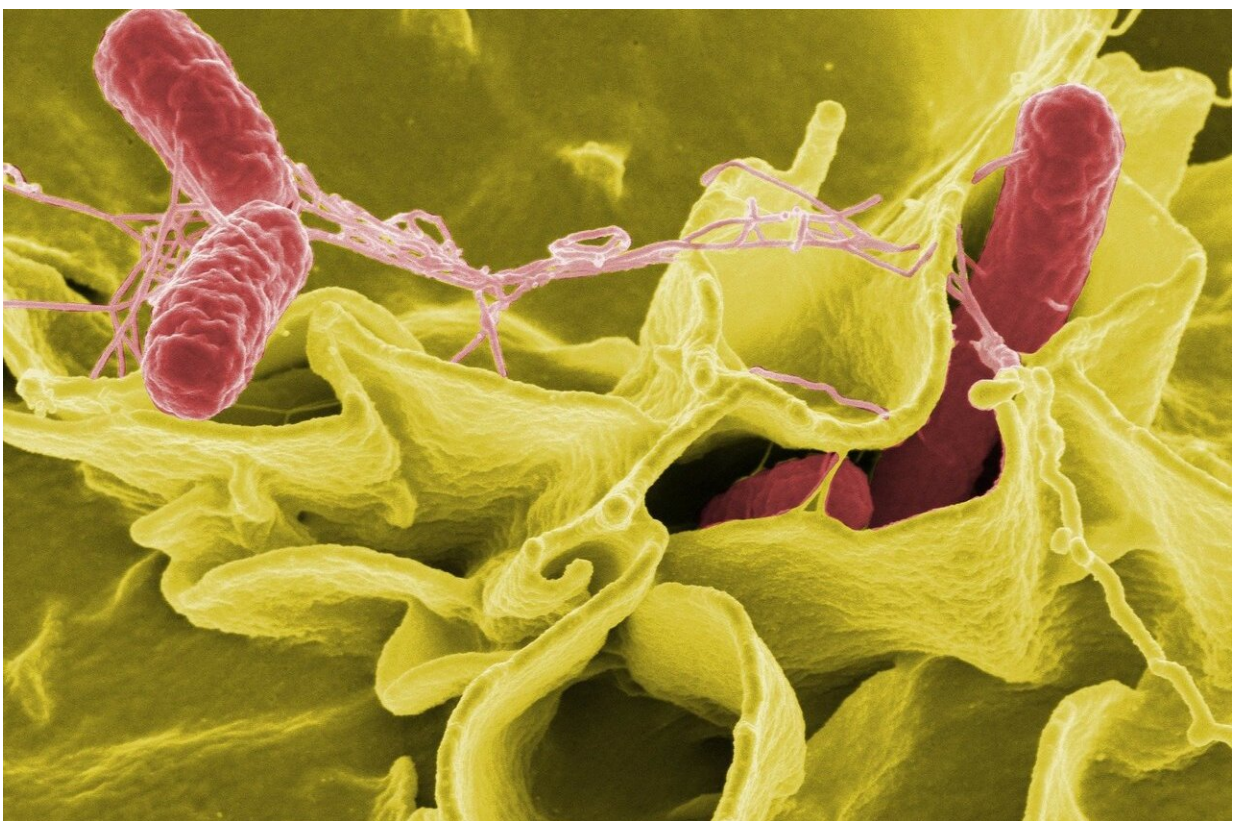


# Bloodstream infections in central Africa caused by strains of *Salmonella* resistant to nearly all drugs

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*Salmonella* bacteria (red) cause up to a million deaths a year worldwide and there is a need for effective vaccines. New work from UC Davis shows how salmonella-specific T-cells can be stimulated to take up residence in the liver, ready to quickly fight off the infection. Credit: Rocky Mountain Laboratories, NIAID, NIH

The first extensively drug-resistant (XDR) strains of *Salmonella Typhimurium*, a pathogen which is responsible for millions of bloodstream infections per year in sub-Saharan Africa, have been identified in the Democratic Republic of Congo (DRC). Drug-resistance has increased in successive groups of *S. Typhimurium* over time. These new strains are resistant to all but one of the commonly available drugs in the DRC, with one sample showing reduced susceptibility to this final antibiotic.

The study, published today (19 September 2019) in *Nature Communications*, was conducted by researchers from the Institute of Tropical Medicine (ITM) in Antwerp, the Institut National de Recherche Biomédicale (INRB) in the DRC, the Wellcome Sanger Institute, the University of Cambridge and their collaborators. The findings suggest that *S. Typhimurium* has evolved in sub-Saharan Africa in the past decades and continues to do so. A multifaceted approach will be needed to track and control the spread of XDR *Salmonella*, including further microbiological and genomic surveillance.

Most *Salmonella* infections result in symptoms associated with food poisoning. While unpleasant, symptoms are not life-threatening in the vast majority of cases. But in sub-Saharan Africa, *Salmonella* such as *S. Typhimurium* can cause infections of the blood, known as invasive non-typhoidal *Salmonella* (iNTS) infections.

Every year, iNTS infections are estimated to affect 3.4 million people and result in 681,316 deaths globally, of which the majority are caused by *S. Typhimurium*. The containment and treatment of iNTS infections in places like the DRC is complicated by limited access to healthcare, infrastructure challenges and weakened immunity, with children under five years of age particularly at risk.

It is known that iNTS infections in sub-Saharan Africa are dominated by

a type of *S. Typhimurium* known as ST313, which is associated with [antibiotic resistance](#). Two groups of ST313 (named lineage I and II) split off independently and subsequently spread over the African continent. Antibiotic resistance has been growing over time, with lineage II now the primary cause of iNTS infections.

Now a global research partnership is working to understand how *Salmonella* ST313 continues to evolve and develop drug resistance. Working on blood samples collected in DRC hospitals from people with suspected bloodstream infections, researchers from the INRB and ITM observed antibiotic resistance levels never seen before in *S. Typhimurium* causing bloodstream infections, including resistance to the antibiotic azithromycin—a drug normally held in reserve in case others prove ineffective.

To better understand these findings these strains were genome sequenced and analysed, including bioinformatics analyses and laboratory experiments at ITM and the Wellcome Sanger Institute, and machine learning analyses at the Centre for Genomic Pathogen Surveillance (CGPS). Analysis of these *S. Typhimurium* genomes identified a new subgroup that is branching off from ST313, named lineage II.1. Estimated to have emerged in 2004, this new group exhibits extensive drug resistance (XDR).

Dr. Sandra Van Puyvelde, first author of the study from the Institute of Tropical Medicine and Visiting Scientist at the Wellcome Sanger Institute, said: "All antibiotic resistance genes contributing to 'XDR' are present on the same plasmid. This is worrying because a plasmid is a mobile genetic element that could be transferred to other bacteria. While accumulating more antibiotic resistance, we discovered that the novel *Salmonella Typhimurium* line is also showing further genetic and behavioral changes which suggest ongoing evolution of the bacteria towards bloodstream infections."

The researchers also studied the way *S. Typhimurium* is adapting to an invasive "lifestyle," moving away from the forms of *Salmonella* that cause gastrointestinal illness towards the types that cause dangerous invasive [bloodstream infections](#) in sub-Saharan Africa. In addition to lab experiments, the samples were tested with a machine learning algorithm designed to look for characteristic patterns in the DNA of *Salmonella* that indicate the potential to cause dangerous invasive infections.

Dr. Nicole Wheeler, a bioinformatician at the Centre for Genomic Pathogen Surveillance, based at the Wellcome Sanger Institute, said: "In the lab we've observed changes in this new group of *Salmonella Typhimurium* that we've seen in other invasive [salmonella](#). What's interesting as a bioinformatician is that we've been able to pick up these changes using machine learning. The hope is that in the near future we'll be able to deploy machine learning in a more predictive role to help control the emergence and spread of [drug-resistant](#) strains of bacteria such as *S. Typhimurium*."

INRB and ITM have established bloodstream infection surveillance in the past ten years which has been pivotal in the early detection of the XDR *S. Typhimurium*.

Professor Octavie Lunguya of INRB in the DRC, said: "We isolated the *Salmonella Typhimurium* from patients in hospitals across the Democratic Republic of Congo during our bloodstream [infection](#) surveillance activities. It is now crucial that we closely monitor the bacteria and their progression."

Professor Gordon Dougan, from the University of Cambridge, said: "Studies like this are unique as we are making the bridge between the most important health issues observed in hospitals across the world with in-depth biological research for which we apply cutting edge technologies. Collaborations like this are key and will be important in the

future to gain further insights on emerging diseases."

**More information:** Sandra Van Puyvelde et al. An African Salmonella Typhimurium ST313 sublineage with extensive drug-resistance and signatures of host adaptation, *Nature Communications* (2019). [DOI: 10.1038/s41467-019-11844-z](https://doi.org/10.1038/s41467-019-11844-z)

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