BEWARE: EXTENSIVELY DRUG RESISTANT TYPHOID IN TRAVELERS


Posen and colleagues, utilizing data from Geosentinel and other sources, reviewed 17 cases of infection due to extensively drug resistant (XDR) Salmonella enterica serovar Typhi (XDR typhoid) in travelers. By definition, all isolates were resistant (although some were “intermediate/resistant”) to ampicillin, ceftriaxone (or cefotaxime), ciprofloxacin, and trimethoprim-sulfamethoxazole. Of 9 isolates tested against chloramphenicol, 8 were resistant and 1 was intermediate/resistant. All were susceptible to meropenem, and all 11 tested were also susceptible to ertapenem. Fifteen of 16 (93%) were susceptible to azithromycin. Three isolates were studied by whole genome sequencing, and all belonged to the H58 clade. All 33 resistance genes present in the reference XDR strain were detected as was the 84 kb reference plasmid p60006 carrying 6 resistance genes.

All patients for whom the information was available had visited family and friends (VFF) in Punjab or Sindh provinces or the Islamabad Capital Territory in Pakistan. The patients ranged in age from 9 months to 40 years (median age 7 years). After return from Pakistan, the infections were first identified in Canada in 10 cases, the United States and Spain (2 each), and 1 each in Italy, Australia, and Norway. Only 1 (7.1%) of the 14 for whom the information was available had received pre-travel typhoid vaccination.

All patients had fever, although diarrhea and abdominal pain were each reported by 12 (70.6%) and 10 (58.8%) had vomiting. Transition of initial antibiotic therapy to a carbapenem of azithromycin occurred after a median of 2 days (range 0–5 days). This change was in response to antimicrobial test results in 8 of 16 patients, to knowledge of travel to Pakistan in 6 of 16, and failure of initial therapy in 2 of 16.

Beginning with recognition of an outbreak of XDR typhoid in 2016 [1], the number of infections with this pathogen progressively increased in Pakistan, although there has been a recent decrease of reported cases in association with the coronavirus disease 2019 pandemic. The lack of microbiological diagnostics in many areas means that the number of cases undoubtedly far exceeds the number recognized. The outbreak beginning in 2016 was believed to have resulted from failure of effective treatment of potable water. The recent enormous flooding in Pakistan will result in use of contaminated water, and it seems likely that the number of cases of XDR typhoid will be on the increase once again.

It is necessary that clinicians and public health officials remain alert to the dangers represented by XDR typhoid. The lack of pre-travel vaccination seen in this report is typical of VFF and evidence that immigrant populations be educated and provided easy and inexpensive or free availability of vaccine.

Reference

WATERBORNE OUTBREAK OF EXTENSIVELY DRUG RESISTANT TYPHOID IN AN APARTMENT BUILDING IN CHINA


The emergence of extensively drug resistant (XDR) typhoid in Pakistan has led to large number of cases and put the world on alert [1]. A recent outbreak in Beijing demonstrates that XDR typhoid is not confined to Pakistan. Four residents of an apartment building in the countryside became ill and had positive blood cultures for XDR Salmonella enterica serovar Typhi. Stool sample screening of 106 residents of the apartment building detected the organism in 23 (attack rate 21.7%). Some of the 106 screened were from an adjacent building, but all of these were negative. All 23 developed symptoms between 22 January and 23 February 2022 and all were “effectively treated with ertapenem … and “most cases were recovered.”

The water to the apartment came from a “self-provided” village well and pumped from a nearby branch well to a storage tank on the roof from which water was distributed by gravity to each living space. Tap water from the room of each case patient sampled on 6 February had high coliform counts, but Salmonella was not recovered. Sampling 4 days later, however, resulted in the recovery of S. typhi from the outlet of a water storage tank. Control measures, including emphasis on the need for chlorination of drinking water, were implemented.

Susceptibility testing of the 4 isolates from the first cases as well as that from the storage tank outlet found that all were resistant to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, aztreonam, streptomycin, fluoroquinolones, third and fourth generation cephalosporins, and all produced extended spectrum β-lactamase. All 5 isolates were susceptible to meropenem, ertapenem, and azithromycin.

Whole genome sequencing determined that all 5 isolates were of ST1
and belonged to the H58 lineage. They each carried the same IncY plasmid that carried a gene cluster of a Type 4 secretion system, as well as 6 resistance elements and qnrS.

The authors, who were from the Beijing Center for Disease Prevention and Control, indicate that this was the first waterborne outbreak of XDR S. typhi infections in China. They point out the need for better management of water supplies, especially outside municipal areas. Despite investigation, they have not identified the origin and entry of the organism into China. It can be hoped that this event was, in fact, an isolated incident. Reports of cases of XDR typhoid in travelers from Pakistan provide a reason to maintain a high level of alertness [2].

**References**


**MONKEYPOX VIRUS 2022—MICROEVOLUTION, GENOMIC DELETIONS AND REARRANGEMENTS**


Isidro and colleagues examined the first 15 published sequences of monkeypox virus (MPXV) obtained from men in Europe who were part of the 2022 outbreak. All 15 belonged to the West African clade (clade II) and were genetically linked to MPX from an outbreak that occurred in Nigeria in 2017–18. A comparison with the 2017–18 sequence found that the 2022 MPX sequences diverged from the 2017–18 by a mean of 50 single nucleotide polymorphisms (SNP). This divergence was approximately 6–12 times greater than the expected 1–2 orthopoxvirus substitutions per year. Three of these substitutions have previously been associated with amino acid changes in glycoprotein B21, which is an immune target, whose alteration may facilitate immune evasion.

DNA viruses have a much lower frequency of SNP emergence than RNA viruses. As a consequence of identification of mutational bias and other factors, the investigators speculate, as have others, that this apparently accelerated MPXV evolution is the consequence of interaction with apolipoprotein B mRNA-editing catalytic polypeptide-like 3 (APOBEC3) [1]. APOBEC3, a cytosine deaminase, is upregulated in some viral infections and, by mediating viral genomic mutations, is an element of the intracellular innate immune system.

Separately, in the course of whole genome sequencing (WGS) of MPXV from a Minnesota patient’s lesion, Gigante and colleagues identified an absence of map reads relative to 2022 MPXV lineage B.1 reference sequence MA001. The absent map reads localized to a large region toward the right (3’) end and were associated with an overabundance of reads on the left-hand side toward the 5’ end of the genome. Reexamination of sequencing data from 206 MXPV samples from the United States led to the identification of an additional 6 genomes with similar read profiles, with all 7 (3.4%) having such gaps. Four of the 7 contained high-coverage plateaus (high-coverage sequencing allows identification of rare variants), all near the end of the genomes. All 7 cases associated with these MXPV sequences had had symptom onset from 8 June to 27 June of 2022.

The high-coverage regions at the terminus opposite to the deletions corresponded to duplicated genomic terminus. In 3 samples, deletions ranging from 2.3 to 15 kb but with evidence suggesting these were not just simple deletions but instead represented more complex rearrangements with terminal swapping rearrangements.

The genetic alterations described here indicate the need for continued surveillance. In addition to altering the pathogenicity of the virus and susceptibility to, for example, tecovirimat, potential future consequences of gene loss could negate the value of polymerase chain reaction (PCR) tests that target the missing DNA segment.

**Reference**


Published by Oxford University Press on behalf of Infectious Diseases Society of America 2022.
https://doi.org/10.1093/cid/ciac836