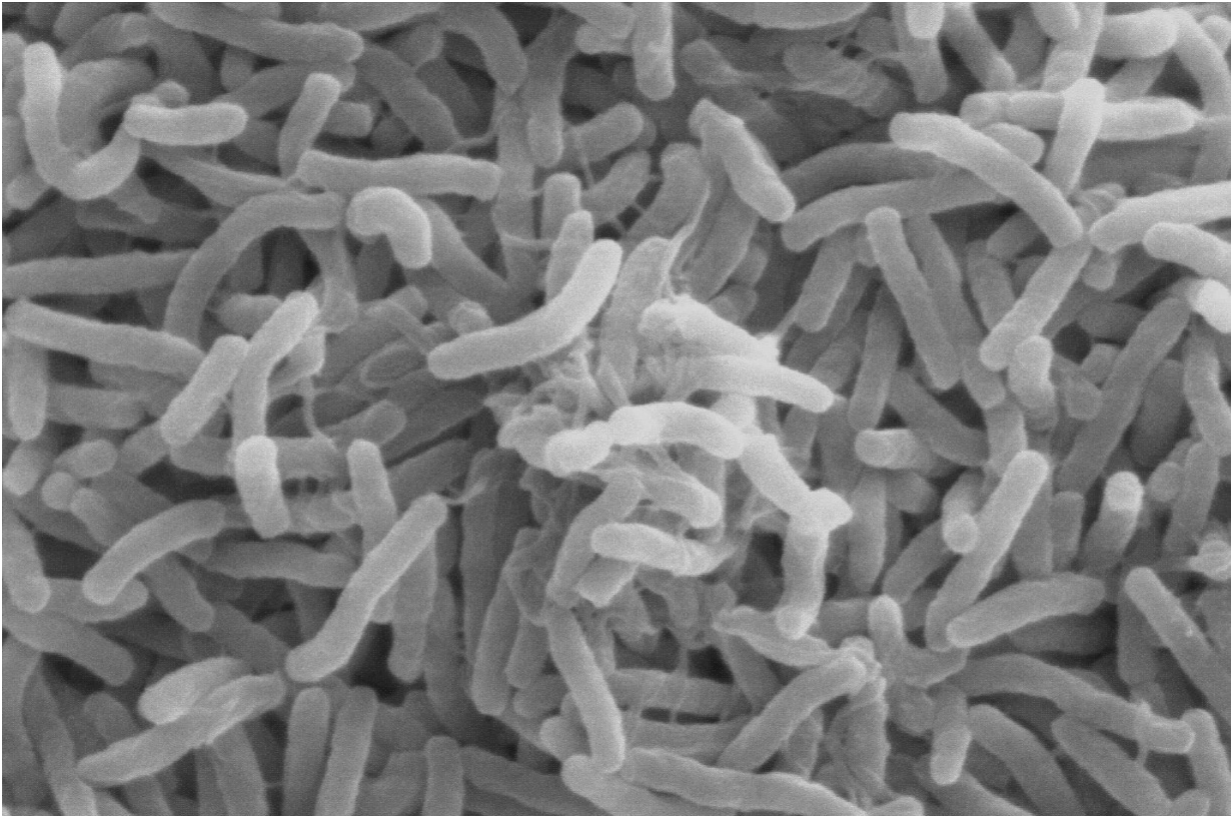


# Study reveals why highly infectious cholera variant mysteriously died out

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Scanning electron microscope image of *V. cholerae*. Credit: public domain

A new study reveals why a highly infectious variant of the cholera bug, which caused large disease outbreaks in the early 1990s, did not cause the eighth cholera pandemic as feared—but instead unexpectedly

disappeared.

The study analyzed samples of O139 *Vibrio cholerae*, a [variant](#) of the bacteria that causes [cholera](#), and discovered significant changes in its genome over time that led to its unexpected decline.

These [genetic changes](#) resulted in a gradual loss of antimicrobial resistance (AMR), and a change in the types of toxin produced by the cholera bug. In combination, these changes are likely to account for O139's failure to seed the eighth cholera pandemic.

The cholera bug is not currently monitored on a regular basis. Scientists say continuous monitoring of the genes underlying AMR and toxin production is key to keeping ahead of the cholera bug as it evolves. In particular, this will help to plan changes to vaccines and appropriate public health responses to prevent future cholera outbreaks.

The O139 variant of *Vibrio cholerae* was first detected in India in 1992. It quickly became dominant over the existing O1 variant and caused huge disease outbreaks in India and Southern Bangladesh.

The rapid spread of O139 across Asia surprised scientists, who feared it would cause the eighth cholera pandemic—and as a result cholera vaccines were modified accordingly. But for some reason that pandemic never happened: by 2015 the variant had largely declined, and the O1 variant established itself once again as a dominant strain. Until now, scientists have not understood why.

The study is published today in the journal *Nature Communications*.

"There's a real possibility that another cholera variant may emerge with the potential to cause large outbreaks, which could lead to the eighth cholera [pandemic](#). Continuous surveillance of the variants in circulation

is our best chance of preventing mass outbreaks," said Dr. Ankur Mutreja, in the University of Cambridge's Institute of Therapeutic Immunology and Infectious Disease, senior author of the study.

Cholera is a life-threatening infectious disease, usually caught by eating or drinking contaminated food or water. It only causes large outbreaks in places where hygiene and sanitation is poor, so is mainly restricted to the [developing world](#).

Cholera can also arise when water and sewage systems are disrupted due to war or natural disaster. Recent news reports have warned that the Ukrainian city of Mariupol, all but destroyed by weeks of Russian shelling, is now at risk of a major cholera [outbreak](#).

In the past 200 years, seven cholera pandemics have killed millions of people across the world; the seventh is still ongoing with large outbreaks in Yemen and Somalia. The dominant variant of *Vibrio cholerae*, the bacteria that causes cholera outbreaks today, is called O1 and arose in the 1960s—replacing all pre-existing variants.

The new study analyzed 330 samples of the cholera variant O139, taken between 1992 and 2015, to reveal two key changes in its genome that may have been the cause of its decline over three overlapping waves of disease transmission.

Before the O139 variant appeared, cholera was sensitive to many antibiotics. But O139 was resistant to these, which is likely to be the reason it became the dominant variant very quickly.

The study found that O139 had started out with several genes giving it resistance to antibiotics. But over time it gradually lost these genes. In tandem, the O1 variant gained [antibiotic resistance](#).

"When it first arose, the O139 variant of cholera had antimicrobial resistance. But over time this resistance was lost—while the pre-existing O1 variant gained resistance and re-established itself," said Mutreja.

The World Health Organization (WHO) estimates that globally there are 1.3 to 4.0 million cases of cholera, with 21,000 to 143,000 deaths, every year. There have been seven pandemics of cholera, all of which have been caused by O1 variant of *Vibrio cholerae*, with the first one documented in 1817.

**More information:** Thandavarayan Ramamurthy et al, *Vibrio cholerae* O139 genomes provide a clue to why it may have failed to usher in the eighth cholera pandemic, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-31391-4](https://doi.org/10.1038/s41467-022-31391-4)

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