Harmful hospital bacteria evolved 'in response to modern diets'

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Clostridioides difficile is a form of bacteria that typically infects patients in hospital environments after they have received antibiotic therapy that has upset the bacterial balance in their guts. New research explains how this bacterium is evolving and suggests new ways forward in prevention and therapy.

C. diff. may have evolved in line with the evolution of human diets, researchers find.

Clostridioides difficile (formerly known as *Clostridium difficile*) are a leading cause of bacterial infections in hospitals.

C. diff. caused nearly 50,000 infections in just 1 year in the United States alone, according to 2015 estimates from the Centers for Disease Control and Prevention (CDC).

The CDC also call *C. diff.* "a major health threat." This is because of the severity of symptoms that accompany the infection, particularly diarrhea and nausea, and because it is very difficult to treat. As many as 15,000 deaths likely result from *C. diff.* infections in the U.S. each year, say the CDC.

New research from the Wellcome Sanger Institute, the London School of Hygiene & Tropical Medicine, and other research institutions now offers more explanations as

to how *C. diff.* have adjusted so well to hospitals and other environments and why they have become so hard to eradicate.

In the study, the team analyzed the genetic makeup of *C. diff.* after having collected samples from various hosts and environments. The results, which appear in *Nature Genetics*, explain how these bacteria have evolved and continue to evolve.

The study authors suggest that their findings may also indicate new ways forward in the prevention and treatment of *C. diff.*

Mapping *C. diff.*'s genetic evolution

For their study, the researchers sequenced and compared the DNA of 906 strains of *C. diff.* Of these, they isolated 761 strains from humans, 166 from animals, including dogs, horses, and pigs, and 29 strains from different environments.

The samples came from 33 countries, though most — as many as 465 — came from the United Kingdom.

After analyzing the DNA of all their bacterial samples, the researchers made an intriguing discovery: *C. diff.* is still evolving and has separated into two species. One has adapted to easily permeate hospital environments and infect human hosts.

"Our large-scale genetic analysis allowed us to discover that *C. diff.* is currently forming a new species, with one group specialized to spread in hospital environments," explains joint first author Nitin Kumar, Ph.D.

"This emerging species has existed for thousands of years, but this is the first time anyone has studied *C. diff.* genomes in this way to identify it. This particular bacteria was primed to take advantage of modern healthcare practices and human diets before hospitals even existed," he goes on to note.

The team observed that this species — which they call *C. diff.* clade A — accounted for approximately 70% of the samples that they had collected from individuals who had been admitted to the hospital.

The researchers also found that *C. diff.* clade A showed changes in the genes that drive the metabolism of simple sugars, which gave the scientists an idea that the bacteria might thrive in hosts whose diets were rich in sugar.

An experiment in mice demonstrated that this hypothesis was correct — bacteria belonging to clade A were better able to colonize animals that had consumed a diet enriched with sugar.

The research team also observed that *C. diff.* clade A had differences in the genes that drive spore formation, which made them more resistant to common ways of combatting bacteria in hospitals, namely powerful disinfectants.

C. diff. evolved with human diets

According to further analyses, *C. diff.* clade A emerged approximately 76,000 years ago, and it started to further differentiate and evolve around the year 1595. This species is still evolving and adapting, the researchers warn.

"Our study provides genome- and laboratory-based evidence that human lifestyles can drive bacteria to form new species so they can spread more effectively," notes senior author Trevor Lawley, Ph.D.

Not only that, but laboratory experiments suggest that these stubborn bacteria evolved to thrive in bodies primed on modern diets rich in sugar.

While these findings show how *C. diff.* has become such a major threat to healthcare, they may also point to the way forward in preventing these bacteria from infecting vulnerable individuals, the researchers argue.

"We show that strains of C. diff. bacteria have continued to evolve in response to modern diets and healthcare systems and reveal that focusing on diet and looking for new disinfectants could help in the fight against this bacteria."

Trevor Lawley, Ph.D.

"This largest-ever collection and analysis of *C. diff.* whole genomes, from 33 countries worldwide, gives us a whole new understanding of bacterial evolution," adds co-author Prof. Brendan Wren.

"It reveals the importance of genomic surveillance of bacteria. Ultimately, this could help understand how other dangerous pathogens evolve by adapting to changes in human lifestyles and healthcare regimes, which could then inform healthcare policies," he suggests.