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Researchers keep mum on botulism discovery

Publishing all the scientific details might show terrorists how to create a bioweapon.

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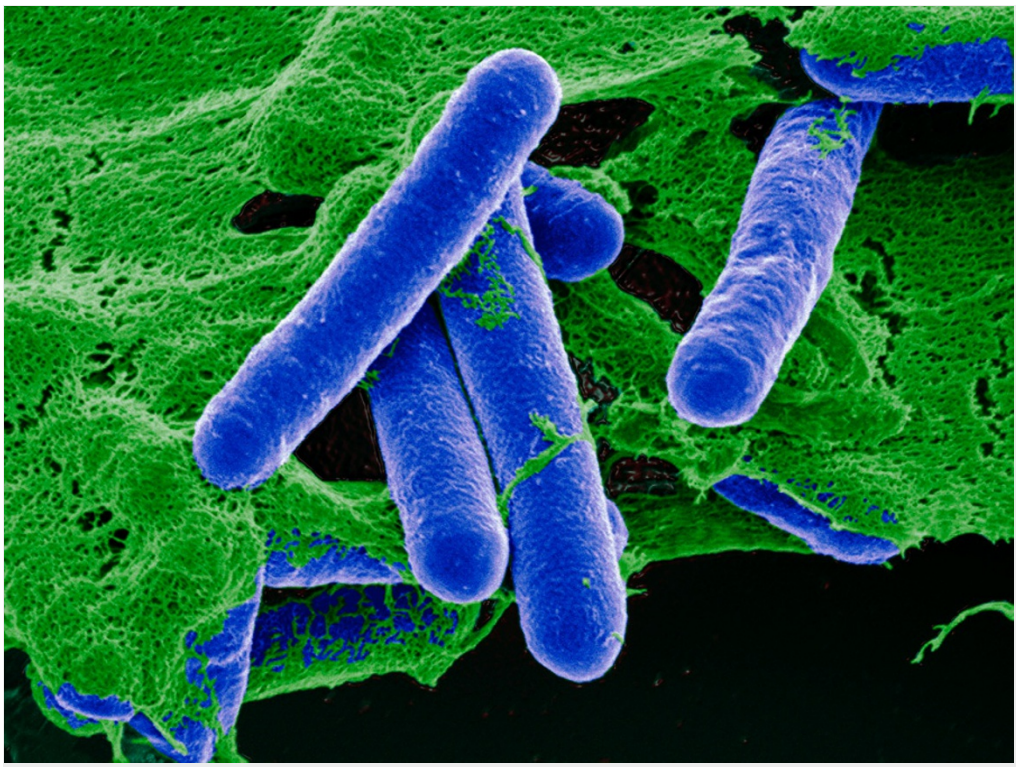

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The toxin from *Clostridium botulinum* (the bacteria shown here in a coloured scanning electron micrograph) is considered the most deadly in nature: a single gram could kill more than one million people.

Scientists have discovered a new strain — the first in 40 years — of *Clostridium botulinum*, the bacterium that is ultimately responsible for causing botulism. And although they have reported their findings in a scientific journal, the investigators have taken the extraordinary step of withholding key details of the discovery. That's because the toxins made by *C. botulinum* are the most dangerous known to humankind and currently there is no antidote for a toxin generated by the new strain. The fear is that malevolent organizations or rogue governments might use the information to reverse engineer their own version of the new bug, making it a potent and real bioterrorism threat.

C. botulinum toxin is high on the list of feared biological weapons because minute quantities can fatally paralyze people who swallow or breathe it. It is known or suspected to have been part of bioweapon programs in countries such as the Soviet Union, Iran, Iraq, North Korea and Syria, and was used, fortunately ineptly, in Tokyo in the early 1990s by the Japanese cult Aum Shinrikyo before they turned to the nerve agent sarin.

A consensus statement on *C. botulinum* toxin as a biological weapon published in 2001 in *JAMA: The Journal of the American Medical Association* calculated that "a single gram of crystalline toxin, evenly dispersed and inhaled, would kill more than one million people."

Until now there have been seven known strains of the bacterium; the toxins they make are labelled A through G. There are antidotes for those, but each antitoxin neutralizes only the specific toxin against which it is made, and none works against the new toxin that has been dubbed H.

Until an antidote can be developed, the scientists who discovered the strain — employees of the California Department of Public Health

— have decided not to release the genetic blueprints of either the new strain or the H toxin. The bacterium was isolated from a patient who had developed botulism but, fortunately, did not die.

The findings are described in two papers that were published in the *Journal of Infectious Diseases (JID)*[1]. The senior author, *C. botulinum* expert Stephen Arnon, was not available for interview. But Gilberto Chavez, deputy director of the Center for Infectious Diseases in the California Department of Public Health, said in an email interview that development of an H antitoxin requires additional work by many partners and suggests that even partial publication of the information will speed the effort.

Like many scientific journals, the *JID* normally requires authors to include genetic sequences in their papers in order that other scientists can attempt to replicate and build on the research. Deputy editor David Hooper says Arnon had already conducted discussions with a number of federal government agencies about the idea of holding back the sequence data before he approached the journal to see if they would publish the finding.

US government agencies consulted included the National Institutes of Health, the US Army Medical Research Institute of Infectious Diseases, and the US Centers for Disease Control Office of Public Health Preparedness and Response's Division of Select Agents and Toxins.

Arnon "was trying to be very careful and thoughtful because of the biothreat consequences," says Hooper, who notes that the journal would have been uncomfortable about taking this approach but for the opinions of the government agencies that weighed in on the publication plan. He says the journal had a number of discussions about whether publishing redacted work was an appropriate thing to do. "We decided it was important enough to let the scientific community know." The journal plans to add the sequence data to the scientific record later, once an H antitoxin is made.

The situation creates a sharp counterpoint to a debate that ignited in international scientific circles around two years ago. That was when leading influenza scientists in the US and the Netherlands attempted to publish details of how they had genetically engineered H5N1 "bird flu" virus to spread among ferrets, mammals that often serve as a proxy for people in influenza research. To date, wild H5N1 viruses do not transmit this way.

At that time, the NIH's National Science Advisory Board for Biosecurity (NSABB) — an expert panel that advises the US government — recommended that the mutations that rendered the viruses more easily transmissible be withheld from publication. Making the information public was in effect publishing a recipe for a pandemic virus that could be unleashed on the world by terrorists or overly ambitious scientists working in laboratories without adequate biosecurity conditions, the group argued.

Months of debate ensued, involving the World Health Organization and US government agencies. Many argued that rules governing the publication of sensitive information — known as export controls — made it clear that the studies could be published in full or not at all, but they could not be published in a redacted form. (Hooper says the documentation that flowed from Arnon's discussions with the government did not raise concerns about export controls.)

In March 2012 the NSABB withdrew its recommendation about the H5N1 research and the flu articles were published in full in a few weeks later. David Relman is a member of the NSABB who opposed full publication of the contentious flu studies. He applauds the California group's handling of the *C. botulinum* papers. "In my book, they did the right thing. And I think it's important to say that we don't think or hope or expect that this sort of situation is going to arise often, because I certainly wouldn't want to see authors and journals redacting bits of information willy-nilly or frequently. But I do think this is a really unusual circumstance," says Relman, an infectious diseases specialist at Stanford University and the Veterans Affairs Palo Alto Health Care System in California.

But that view is not shared by Ron Fouchier, a Dutch virologist who was the senior author of one of the H5N1 papers. Fouchier's view is that — with very few exceptions — science must be shared openly. And he believes Arnon and his co-authors could have held off publishing these papers until the H antitoxin was made. He notes the articles were submitted to the journal in May and the California laboratory probably had the information for a few months before that. "Why rush now? Why not wait another two months until you have the antisera, then you publish? You release all the information at once," says Fouchier, with Erasmus Medical Center in Rotterdam.

Chavez says publishing even a little information was important for the diagnosis, treatment and control of botulism. But Fouchier argues that laboratories elsewhere that are trying to type *C. botulinum* strains will not be able to spot the new strain if they encounter it by using the information in these papers.

References

1. Barash, J. R. & Arnon, S. S. *Journal Infect. Dis.* http://dx.doi.org/10.1093/infdis/jit449 (2013).