

# US ricin attacks are more scary than harmful

But researchers hope that the incidents will renew development of stalled vaccines.

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The US Federal Bureau of Investigation (FBI) said on Wednesday that it has arrested a suspect in connection with three apparently ricin-contaminated letters sent to US politicians. The agency confirmed the discovery of a letter addressed to US President Barack Obama, one day after Congress's Capitol Police quarantined a letter sent to a Republican senator. A third was sent to an unnamed government official in Mississippi.

But the danger posed by such incidents may be relatively small, experts say.

Although [minute amounts of ricin can be lethal](#), it is difficult to process raw materials into the toxin's most dangerous form, a readily inhaled fine powder. That makes ricin unlikely to cause mass casualties, even though recipes to make it from castor beans are available on the Internet.



*Dinodia/Newscom*

Ricin is made from castor beans, which come from the castor oil plant.

There have been attempts to deploy ricin as a bioterror agent; for example, in 2003, letters found in South Carolina and Washington DC tested positive for the toxin. But few such incidents result in deaths, says Raymond Zilinskas, director of chemical and biological weapons non-proliferation at the Monterey Institute of International Studies in California. He thinks that the latest scare will probably not do serious harm because it is unlikely that the ricin is in the lethal powdered form.

"I can't imagine that ricin in an envelope is going to hurt anybody," says Zilinskas. "It's more likely remnants of a paste, intended to scare people."

## Better safe than sorry

The US government is still concerned about ricin, in part because the substance has been found in connection with people linked to suspected terrorist groups. The US National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, lists ricin in the second of three tiers of biological agents of concern, making it a lower-priority threat than smallpox or anthrax — but the government is still funding the development of vaccines and potential treatments.

That work has been slow. Ricin works by deactivating human ribosomes — parts of a cell that make proteins essential for life — in a way that is difficult for conventional drugs to neutralize. The best anti-toxin drugs work by binding tightly to the destructive part of the molecule, its active site, like a key fitting into a lock. That blocks the toxin's ability to damage a cell. But ricin has a relatively large and open active site that repels other molecules, so it is difficult to make small-molecule drugs that are a good fit.

That has prompted some researchers to look for larger protein molecules, called antibodies, that could block ricin's active site. A group led by Nicholas Mantis of the New York State Department of Health's Wadsworth Center in Albany has designed ricin antibodies, engineered plants to make them and tested them in mice. The antibodies saved animals treated up to 4 hours after ricin exposure<sup>1</sup>.

Mantis has licensed his antibodies to a biotechnology company for further testing, but he says that they will not be ready for use even in emergency situations until they have been tested in humans, which will take at least two years. Ultimately, antibodies may be most powerful in combinations that target multiple parts of the ricin molecule, says Mantis.

## Pre-emptive action

Ricin acts quickly, with symptoms appearing as early as 4 hours after exposure, so some researchers think that pre-emptively administered vaccines will be more effective than drugs in combating its effects. At least two ricin vaccines are now in the works, but their prospects are uncertain.

The US Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland, has developed a vaccine called RVEc, which

protected mice that were exposed to inhaled ricin.<sup>2</sup> The vaccine has also been tested in human volunteers, who subsequently developed antibodies to the toxin. But further human testing is needed, and it is not clear whether the Department of Defense will continue to fund the vaccine's development.

The other leading vaccine candidate, RiVax, is made by a company called Soligenix, based in Princeton, New Jersey. The vaccine was initially developed by Ellen Vitetta, an immunologist at the University of Texas Southwestern Medical Center in Dallas, and batches made by her group have been tested in animals. Those batches have also been found to be safe in healthy human volunteers, in whom they stimulated the production of antibodies.

### Money worries

But Soligenix has not yet tested the safety and effectiveness of its own batches of RiVax. The company's development efforts have slowed as a result of budget constraints at its funding agency, the NIAID, says Vitetta.

"It basically is not going anywhere," she says. "It's disappointing and upsetting." After an event such as the latest ricin mailings, "everyone wants to know where the vaccines are. Somebody has to think this work is important enough to fund us and let us finish it."

Soligenix's work on the vaccine is currently funded by a US\$9.4-million NIAID grant, but further testing in animals to prove the treatment's effectiveness would cost between \$20 million and \$40 million, says Chris Schaber, the company's president.

US budget woes have also threatened the country's bioterror response by [forcing cuts at the Strategic National Stockpile](#), a medical repository that buys and stores drugs and vaccines.

The situation was very different in the years immediately after the terrorist attacks on 11 September 2001 and subsequent anthrax mailings, when the development of anti-bioterror drugs [became a priority for the US government](#). But Schaber hopes that the ricin detected over the past two days will trigger renewed interest in funding biodefence work — at least for RiVax.

"You never want to see these unfortunate incidents, but the hope is that this puts a spotlight on our vaccine and the need to move it forward," says Schaber.

### Criminal investigation

In the meantime, the FBI's investigation into the letters addressed to Obama, Mississippi senator Roger Wicker and an unnamed Mississippi justice official continues. FBI special agents arrested a suspect on Wednesday in Corinth, Mississippi, said the Department of Justice.

Preliminary tests have identified granular substances enclosed in all three letters as ricin, but the FBI has said that such tests can be wrong. "Only a full analysis performed at an accredited laboratory can determine the presence of a biological agent such as ricin," the agency said in a statement. "Those tests are currently being conducted and generally take 24 to 28 hours."

At least two of the letters were postmarked in Memphis, Tennessee, according to an FBI intelligence bulletin obtained by the Associated Press (AP). Both missives contained the phrase, "To see wrong and not expose it, is to become a silent partner to its continuance," and both were signed, "I am KC and I approve this message," the AP reported.

It is not yet known whether more letters containing ricin have been sent. Congressional offices in Michigan and Arizona turned suspicious letters over to authorities on Wednesday, and Capitol Police combed two Senate office buildings after receiving reports of suspicious packages.

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### References

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