Bioterrorism threat becomes reality

As *Nature Medicine* went to press, the number of people in the United States who had tested positive for exposure to anthrax had risen to 10—one of whom has died. Anthrax spores have been sent to victims in the mail and appear as white powder. The events are almost certainly acts of bioterrorism.

Two victims in Florida developed inhalation anthrax, a rare but deadly form of the disease. The spinal fluid of the man who died was cloudy and contained a high titer of immune cells in addition to rectangular rods of bacilli. One woman and a baby in New York have developed cutaneous anthrax after the spores entered their bodies through lesions in the skin. They are being treated with antibiotics and are expected to survive. So far no cases of gastrointestinal anthrax, which is acquired by eating infected meat, have been reported.

AP Photo/Steve Mitchell

FBI agents decontaminate offices in Florida

Scientists hope genetic fingerprints from the anthrax samples will provide clues to the source, says Steven Block, a biophysicist at Stanford University and a member of JASON, a scientific group that advises the military on sensitive national security problems. There are over 1,000 strains of anthrax, and if the infections were caused by one of the more common strains, the genetic sample will not be useful in pinpointing a source.

Primarily a disease of hoofed animals, anthrax becomes deadly when dormant spores of the organism *Bacillus anthracis* enter the body. Once inside, the bacteria produce a three-part toxin comprising a protective antigen, a lethal factor and an edema factor. Symptoms develop as the three combine to penetrate and destroy cells. The antibiotic ciprofloxacin can stop the process, but only during the brief window between exposure and infection. Sales of ciprofloxacin, produced by Bayer, have risen sharply.

The US Food and Drug Administration (FDA) approved an anthrax vaccine in 1970, but its efficacy in humans is uncertain. At the present time the Michigan-based biotechnology company, Bioport, is licensed to make an anthrax vaccine but only supplies the military, and production of vaccine batches is presently delayed because the company has been cited by the FDA for quality control problems.

Tinker Ready, Boston

Smallpox vaccine development quickened

The United States Health and Human Services Secretary, Tommy Thompson, last month requested that the United Kingdom biotechnology company, Acambis, speed up its development of a new smallpox vaccine amid the threat of bioterrorism attacks. Around 140,000 vials of existing vaccine are in storage at the US Centers for Disease Control and Prevention (CDC), each with doses for 50–60 people, and an additional 50–100 million doses are estimated to exist worldwide. However, this vaccine is considered unclean as it is made using cow tissue.

On 20 September, Acambis signed an exclusive $343 million deal with the CDC for initial production of a 40 million dose stockpile of the new vaccine and annual production of additional vaccine until 2020. Prior to 11 September, Acambis was scheduled to produce the vaccine for clinical trials next year, with licensing set for mid 2004, but the company is scaling up operations and aims to license the vaccine within two years.

The financial spokesperson for Acambis, David Yates, says, "The old vaccine did not meet 21st century health and safety requirements and we won a contract from the US government based on our technology. We are a relatively small company but are able to quickly scale-up operations with our subsidiary OraVax in Cambridge, Massachusetts." OraVax will be responsible for production in live-cell cultures and preclinical and clinical testing of the vaccine.

The company—which is also producing a West Nile virus vaccine for the US government—will not comment on the scientific details of the deal for security reasons. However, earlier reports from the company state, "the new smallpox vaccine will be based on the same vaccinia virus strain that was licensed in the US and used for routine immunization against the disease prior to its eradication."

Smallpox is caused by the highly infectious variola virus, and symptoms include a physically disfiguring blistering of the skin, which is deadly in 30% of cases, accompanied by pain and fever. The disease was eradicated globally in 1980 following a mass immunization campaign orchestrated by the World Health Organization (WHO), and the variola virus is now stored officially at only two research centers, the CDC and the Russian State Center for Research on Virology and Biotechnology in Koltsovo.

The WHO had advocated destruction of remaining stocks of variola virus by June 30th 1999, but fortunately, the World Health Assembly voted for a temporary retention of samples "up to and not later than 2002" for the purpose of research into antiviral agents and improved vaccines (*Nature Med*. **5**, 474; 1999). The present climate of anthrax bioterrorism may now see that decision reconsidered.

In a January 1999 paper written for a WHO working group on orthopoxvirus infections, Donald Henderson, who directed the WHO's smallpox eradication campaign and is now at the Johns Hopkins University Center for Civilian Biodefense wrote, "The deliberate reintroduction of smallpox into the population would be an international crime of unprecedented proportions. A spreading, highly lethal epidemic in an essentially unprotected population, with limited supplies of vaccine, no therapeutic drugs, and with shortages of hospital beds suitable for patient isolation is an ominous specter."

As few as 50–100 cases would invoke large-scale, perhaps national emergency control measures. But a September report from the US General Accounting Office called the nation's planning "insufficient," saying that the public health infrastructure, including hospitals and emergency response teams, were not prepared to deal with the mass casualties from a terrorist act. And non-governmental medical experts told Congress at a 9 October hearing on Capitol Hill that US medical facilities and healthcare workers are largely unprepared for such an attack.

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