BIOTERRORISM

DOD Retreats on Plan for Anthrax Vaccine

The Pentagon's first comprehensive effort to protect troops against a potential bioweapon is under heavy political and regulatory fire

Anthrax bacterium, once the deadly scourge of goat-hair workers, has become the bane of the U.S. defense establishment. Without infecting a single soldier, it has created a logistical headache for the Pentagon, as military contractors have fallen far short of supplying a vaccine that will protect all troops and be acceptable to health authorities. Last week military officials were forced to beat a hasty retreat in their current efforts, raising the hackles of legislators who already had serious doubts about the program.

Two years ago, Defense Secretary William Cohen launched the world's most ambitious anthrax vaccination effort. Responding to reports that several countries, including Iraq and North Korea, are capable of using anthrax as a bioweapon, Cohen gave the go-ahead for a program to inoculate 2.4 million men and women in uniform. But in hearings before the Senate and House on 12 and 13 July, Department of Defense (DOD) officials acknowledged that short supplies are forcing a drastic reduction in the effort, although they called it only a "temporary refocus." DOD is cutting back the number of shots given per month from 74,000 to 14,000, and unless authorities release vaccine now held in quarantine—which seems unlikely—supplies will run out in 6 to 10 months.

"We are in a pickle," said Representative Steve Buyer (R–IN), chair of the House Armed Services personnel subcommittee. Adds Senator John Warner (R–VA), chair of the Senate Armed Services Committee, "We have to find out what went wrong. But I think our main thrust, focus, and energy has got to be ... to figure out how we can get out of this problem."

Closed for repairs

The anthrax vaccination program was thrown into disarray by a complex set of political and technical demands. The vaccine protocol was set by federal authorities in 1970—a time when the main concern was protecting textile mill workers and veterinarians. The approved label says the vaccine must be given in six shots over 18 months, with annual boosters. But current supplies—produced by a single facility in Michigan—are not adequate to meet this regime. In fact, the Michigan facility has been closed for renovation since January 1998, although its preexisting stocks were used by DOD to begin inoculation of about 455,000 people.

Defensive jab. Only 56,000 of 2.4 million troops have been fully immunized with a six-shot anthrax vaccine.

CREDIT: M. SULLIVAN/AP

Only 56,725 of them have received the full six-shot regimen, however, and only 160,000 approved doses remain available. The dwindling stocks are being reserved for people going to South Korea and Kuwait, considered high-risk zones. That means that many who received the first injection will be left with uncertain protection.

The task of describing this snafu to Congress fell to Rudy de Leon, undersecretary of defense. He and other high-ranking DOD officials met sharp questioning from critics such as Representatives Walter Jones (R–NC) and Chris Shays (R–CT). Jones claims that hundreds of service members are opting to quit rather than take the shots or face a court martial for refusing to be vaccinated. The shortage, he said last week, "casts doubt on the stability and integrity of this already controversial program." Shays has focused on possible immunological side effects, including Gulf War syndrome, arguing that the entire vaccine program is based on "a paucity of science." In March, the House Government Reform Committee endorsed Shays's report, demanding that vaccination be suspended until "DOD obtains approval for use of an improved vaccine." But that, say researchers, could mean a wait of up to 7 years. Now, vaccine shortages may bring about a suspension.

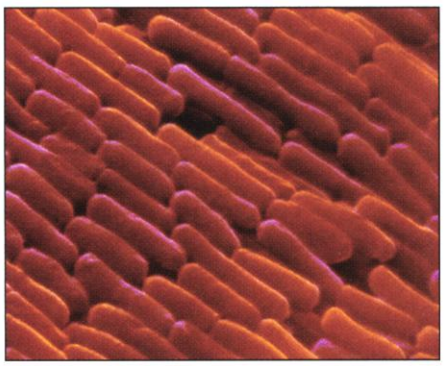
De Leon admitted that the Pentagon has a problem with supply but insisted that the vaccine is safe and effective. The Food and Drug Administration (FDA) agrees. But even staunch Pentagon supporters who have kept out of the anthrax flap—such as Warner—are growing concerned. Warner, who called it "one of the toughest issues I've seen in 22 years," said he may seek new funding of "solutions to the vaccine supply problem."

The shortage occurred after the Pentagon bet all its vaccine money on one horse: the BioPort Corp. of Lansing, Michigan. BioPort stepped onto the scene in 1997 to rescue the faltering Michigan Biologic Products Institute, owned by the state of Michigan. The institute was the sole producer of anthrax vaccine in the United States. Michigan had taken over after a private firm had bailed out in the 1960s. Big companies weren't interested, de Leon explained, because the anthrax vaccine is a nuisance to make and doesn't yield much profit.

But BioPort saw an opportunity. William Crowe Jr., the former chair of the U.S. Joint Chiefs of Staff, brought together the technical staff of the Michigan plant and a businessman involved in the United Kingdom's military vaccine work, Fuad El-Hibri. (The U.K.'s anthrax production line has been down for 3 years for renovation, too. Israel reportedly is developing an independent anthrax vaccine line, but the project is just starting.) With these investors, BioPort purchased the anthrax facility from Michigan for $25 million in September 1998.

By then, however, the project was headed for trouble. FDA inspectors said the plant didn't meet modern production standards and began taking steps in 1997 to revoke its license. After BioPort took over, some lots were approved for use, but others were set aside because test data were questionable. Meanwhile, BioPort began to renovate the plant.

Unfortunately, the new company didn't have enough money to cope with all the regulatory issues and the rapidly growing demand for vaccine. As its chief executive officer, El-Hibri, told the House Armed Services personnel subcommittee on 13 July:



Deadly object. Anthrax spores, shielded by a tough shell, can survive for years in soil before germinating.

"We encountered challenges substantially beyond what we anticipated." El-Hibri said it was a shock, for example, when DOD denied a cost-plus-profit contract and demanded a fixed-price agreement.

Pentagon negotiators won a short-term bargain when BioPort agreed to sell each dose for $2.26 to $4.36. But that price left the company with no income to pay for the necessary renovations, a Defense auditor said. In response to emergency pleadings from BioPort, DOD raised the contract price to more than $10 per dose last year and gave BioPort an advance of $18.7 million, new equipment, and regulatory consulting help. Even so, federal auditors testified last week, BioPort still can't afford new capital investments.

No stock answers

Two problems stand in the way of getting BioPort's vaccine to the troops: FDA has not approved BioPort's supplemental license to operate the renovated production line, and the company can no longer produce valid test results for preexisting vaccine stocks. El-Hibri testified last week that about 800,000 doses of anthrax vaccine remain in the stockpile. Some of these quarantined reserves have passed sterility and purity tests, but not a test for potency. BioPort's chief scientific officer, Robert Myers, says the problem came to his attention in June, when he learned that graduated dilutions of vaccine given to guinea pigs were not yielding corresponding levels of protection against anthrax as they should. The company has assembled an expert panel to figure out what went wrong. No one can say when, or whether, the stocks will be released.

Nor can anyone predict when, or if, the production line will begin running. U.S. military officials had counted on getting it going before the end of the year, a schedule that FDA official Kathryn Zoon called "optimistic." She estimated it could take "6 to 12 months" to clear outstanding issues.

Members of Congress asked whether people with fewer than six shots would need to start over again. Zoon said FDA has no data on how delays might affect the vaccine's efficacy, but that FDA "would have no objection" if DOD decides to postpone some shots. Zoon added that FDA has seen no significant side effects of the anthrax vaccine. FDA's voluntary reporting system has registered only 1404 adverse reactions so far for nearly 2 million shots. This ratio is "toward the low end" of the spectrum, according to Zoon.

The Pentagon hopes to ease the production problem by finding a second vaccine supplier that would share BioPort's exclusive license as well as create a dedicated government-owned vaccine production facility, an idea the department rejected several years ago. DOD is also gearing up efforts to develop a new-generation vaccine based on a genetically engineered recombinant anthrax protein.

None of these initiatives will ease the anthrax vaccine supply crunch this fall, however. "These are not immediate fixes," de Leon confessed. Still, the changes prompted by this fiasco could give vaccinemakers the tools they need the next time the Pentagon attempts to protect troops against a potential bioweapon.

–ELIOT MARSHALL

CONSERVATION BIOLOGY

When Protecting One Species Hurts Another

Plans to protect the grizzly bear in Montana are not helping endangered fish there. Biologists are grappling with how best to save both

SWAN VALLEY, MONTANA—If grizzly bears dream, they might dream of Swan Valley. Streams brocade the valley floor, rich with fish and surrounded by greenery: horsetail, cow parsnip, and berry-bearing shrubs. Together, they provide a cornucopia of foods that bears crave when they descend the mountains in the spring. As if to prove the bounty of the valley, Dave Mattson digs a slender green shoot of sweet cicely from the earth, peels back the outer layer of its root, and chews the exposed inner root. "Bear food," he says.

The valley is also home to at least a dozen species of native fish, including the threatened bull trout and the declining westslope cutthroat trout. But rarely, if ever, have the conservation needs of both grizzly and fish been considered together.

Mattson, a grizzly biologist with the U.S. Geological Survey, and Chris Frissell, a fish biologist with the University of Montana's Flathead Lake Biological Station, have set out to change that. The two biologists recently completed a singular study of western Montana, including the Swan Valley, in which they compared the habitat needed to conserve both grizzly bears and fish. In particular, they wanted to see whether providing habitat for one wide-ranging species would protect the other—the so-called umbrella effect. This study, reported at last month's meeting of the Society for Conservation Biology,* came up with a sobering conclusion: There is limited overlap between prime grizzly habitat and that of threatened fish in the region, and grizzly conservation programs in Swan Valley may even be hurting the fish.

Mattson and Frissell's work—the first to look specifically at the combined needs of a large terrestrial species and several aquatic species—reflects an emerging approach to large-scale conservation that spurns a rigid focus on a single species. It "is a huge step forward," says J. Michael Scott, a conservation biologist at the University of Idaho, Moscow. "It's an extremely useful tool for ranking areas for conservation."

To calculate the overlap between ideal areas for both bear and fish, Mattson and Frissell independently ranked habitat quality for both species using preexisting information on species distributions, introduced species (especially fish), habitat productivity, human population density, and road den-

Two for one? Frissell (left) and Mattson compared ideal habitat for grizzlies and fish in Montana and found limited overlap.

* 9 to 11 June, Missoula, Montana.

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