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What the Pentagon doesn't want you to know about the anthrax vaccine

By Kent Miller, Times Staff Writer

The Defense Department is on the verge of having to further curtail or altogether suspend its anthrax vaccination program because of dwindling supply.

With only about 32,000 doses now in stock, defense officials say, and shots continuing at a rate of about 5,000 doses a month, the supply will run out by the end of September.

Defense Secretary Donald Rumsfeld has asked for a review of the vaccination policy, but will "make no snap decisions," according to his spokesman, Rear Adm. Craig Quigley. He "wants to understand the facts behind the vaccine" before taking any action.

But while supplies run down and Rumsfeld studies the issue, prosecutions of service members who refuse the shots continue. Perhaps the most celebrated of these is the case of Air Force Capt. John Buck, the first military doctor to refuse the shots. He is to be court-martialed May 15 at Keesler Air Force

Base, Miss. Other cases continue to wind their way through the courts.

While the Pentagon's foes on the anthrax issue have primarily been service members, others are beginning to join the fray. Connecticut Attorney General Richard Blumenthal wrote to Rumsfeld and Dr. Bernard Schwetz, acting deputy commissioner of the Food and Drug Administration, March 21, urging them to abandon the anthrax vaccination program or make it voluntary.

Blumenthal has standing in the debate, he said, because his state could bear responsibility if its guardsmen get sick as a result of the vaccinations. "Unfortunately, and directly contrary to law, the [vaccine] is being administered to military personnel under threat of imprisonment, loss of pay and discharge," Blumenthal wrote. "In effect, the military is forcing its personnel to serve as human guinea pigs for an unlicensed drug that has not been proven to be safe or effective."

Blumenthal and other critics of the Anthrax Vaccine Immunization Program, known as AVIP, say the Pentagon and the Food and Drug Administration are hiding information about the safety and efficacy of the vaccine and violating the individual rights of service members by continuing the program.

Here's what they say the Pentagon doesn't want you to know:

DoD officials have themselves called the vaccine inadequate

The Pentagon was concerned about the vaccine's inadequacies long before the immunization program began.

The first anthrax vaccine was developed in the 1950s to protect sheep handlers from contracting cutaneous anthrax, which enters the body through the skin. But no vaccine has ever been tested against aerosolized or "inhalational" anthrax - the form used in biological weapons - in humans.

Indeed, as early as 1985, military officials were seeking a different vaccine to protect troops against exposure to airborne anthrax. The Army solicited bids that year to develop a new anthrax vaccine from the biologics industry.

"There is an operational requirement to develop a safe and effective product which will protect U.S. troops against exposure [to] virulent strains of Bacillus anthracis," it said in an official request for proposals.

"There is no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent."

The FDA concluded independently in 1985 that the anthrax vaccine's "efficacy against inhalation anthrax is not well documented."

And in 1989, Assistant Defense Secretary Robert W. Barker wrote to Sen. John Glenn, then chairman of the Senate Committee on Governmental Affairs, saying "current vaccines, particularly the anthrax vaccine, do not readily lend themselves to use in mass troop immunization." Barker cited problems including a higher-than- desirable rate of adverse reactions to the shots and the "lack of strong enough efficacy against infection by the aerosol route of exposure."

The vaccine's effectiveness against inhaled anthrax is unknown

A 1994 report by the Senate Veterans Affairs Committee concluded that the vaccine could not be expected to protect troops against airborne anthrax.

"Unfortunately, when anthrax is used as a biological weapon, it is likely to be aerosolized and thus inhaled," the report said. "Therefore, the efficacy of the vaccine against biological warfare is unknown. ... The vaccine should be considered investigational when used as a protection against biological warfare."

As an investigational drug, the vaccine would require informed consent each time a shot is administered. Military officials fear the extra work involved, however, and worry that too many troops might choose not to accept the shots.

Another Senate report, "Unproven Force Protection," released in February 2000 by the Senate Committee on Governmental Reform, also criticized the inoculation program. Mandatory vaccination "expands and distorts the use of invasive, dated medical technology to address perceived weaknesses in detection technology and external physical protection against biological attack," the report said. "Born of a post-Gulf War panic over apparent weaknesses in chemical and biological warfare defenses, the AVIP is an unmanageably broad military undertaking built on a dangerously narrow scientific and medical foundation."

The report criticized Pentagon medical leaders for responding to questions "with an excess of faith but a paucity of science."

The anthrax threat is real, but overstated

Anthrax worries reached their height in 1990 during Operation Desert Shield. Defense intelligence experts knew Iraq had been trying to develop germ warfare agents, and Saddam Hussein was believed to have anthrax in his stockpile of unconventional weapons. Most British troops and about 150,000 U.S. troops were given anthrax vaccines.

When the U.S.-led coalition ground offensive began in early 1991, however, strong winds blowing toward the Iraqi lines all but eliminated any incentive Iraqi commanders might have had to use bio-weapons against allied forces.

Today, the defense intelligence community reports U.S. forces face an increasing risk of exposure to the hostile use of biological weapons. But the exact nature of that threat is not clear. In a July 1999 opinion piece in the Washington Post on domestic defenses against biological and chemical warfare, then-Defense
Secretary William Cohen asserted that "at least 25 countries, including Iraq and North Korea, now have - or are in the process of acquiring and developing - weapons of mass destruction." A year later, in an opinion article in this newspaper, Cohen downgraded that estimate, saying "at least 10 countries are developing anthrax as a weapon."

Then, in December 2000, the Pentagon decided to suspend shots for service members going to Korea. Officials said then that North Korea was not an imminent threat for anthrax attack.

In a 1997 television appearance, Cohen held up a 5-pound bag of sugar and said the bag, if filled with anthrax spores, was enough to wipe out half the population of Washington, D.C. But government experts later wrote in Archives of Internal Medicine, a medical journal, that Cohen had overstated the effect by 100 times.

The vaccine has never been clinically tested on humans

Air Force Reserve Maj. Thomas Rempfer was in the Air National Guard in 1998 when he and fellow pilot Maj. Russell Dingle were tasked by their commander to research the vaccine and develop questions and answers for Air Guard leaders. Their research led them to conclude the vaccine wasn't safe, and not long after,
both resigned their Guard commissions. (Ironically, they were later able to join the Air Force Reserve.)

In a December meeting with Army Times reporters and editors, Rempfer pointed out that the only controlled clinical tests of the vaccine on humans actually involved a different vaccine.

His documentation shows that Dr. Philip Brachman, who was then chief of the Investigations Center at the Public Health Service's Communicable Disease

Center in Atlanta, conducted the first human field trials of anthrax vaccine at four goat-hair processing mills from 1955 to 1959. His findings were published in 1962. But the vaccine he used was developed by Merck Sharpe and Dohme, the giant pharmaceutical company.

The vaccine now used by the military was granted to the U.S. Army in 1965.

And according to an April 1999 report by the General Accounting Office, the current vaccine differs from the vaccine used in the Brachman study in three ways:

** The manufacturing process changed when the Michigan Department of Public Health was granted a license and began producing vaccine for the military.

** The strain of anthrax that Merck used to grow the original vaccine was not the same strain used to grow the military's vaccine.

** The ingredients in the vaccine were changed to increase the yield of the protective component of the vaccine.

The military's vaccine was used in a 1960s study conducted at a mill in Talladega, Ala., but the results were not published. A 1969 memorandum from the licensing oversight board stated: "The lack of cases of anthrax in an uncontrolled population of approximately 600 persons in the Talladega mill can hardly be accepted as scientific evidence for efficacy of the vaccine."

Still, a license was granted for the military's vaccine in 1970 without data on its effectiveness. The approved package insert refers to the Brachman study, which predated the military's vaccine.

The manufacturer did not notify the FDA of key changes

The manufacturing of a drug is controlled by both a product license, which establishes the chemical composition of the drug, and a site license, which controls the procedures used to operate the product line.

BioPort Corp. and its predecessor, Michigan Biologic Products Institute (which received the license originally held by the Michigan Department of Public Health) have failed to keep the FDA informed of key changes they were making, changes that could have affected their licenses.

The Food and Drug Administration has documented numerous violations in the manufacturing of the vaccine. Blumenthal's letter to Rumsfeld characterizes these as relating to "organization and personnel, buildings, facilities, equipment controls, laboratory controls and records and reports."

Reports in 1996 and the three following years all found problems.

For example, Blumenthal noted, four major pieces of equipment used to formulate the vaccine were used without prior FDA approval, as required by law. "The new equipment was made of stainless steel and was not glass-lined, as the originals were."

Blumenthal noted other errors: "Some lots of the vaccine were not properly labeled, a potential violation of federal law, and one lot's shelf life was extended after it had expired."

In 1998, three former employees of the Michigan Biologic Products Institute filed a grievance with the state's Civil Service Hearings Division seeking a portion of the profits from the sale of the vaccine. During a hearing in March 2000, Dr. George Burgoyne, one of the three, testified that after the Defense Department showed increased interest in the vaccine in the late 1980s, changes had to be made so larger quantities of the vaccine could be produced. The production changes included additional filters and a new container in which to grow the bacteria.

Dingle, the Air Force reservist, explained the issue. "Before the Gulf War, 7,500 doses was the largest batch they had made," he said. But as Iraqi President Saddam Hussein became more menacing in the Gulf, the Pentagon "saw the need for more vaccine because the United States had sold [anthrax] spores, equipment and technology to the Iraqis."

Defense officials needed 300,000 doses immediately, but up to that time, the lab had only made 70,000 doses total.

But while the changes increased production capacity, the FDA was never notified, as required by law.

And in February 1998, just one month before the first troops began receiving shots under the mandatory vaccination program, the FDA found that "the manufacturing process for anthrax vaccine is not validated."

Military officials knew they needed to amend the license

In October 1995, a group of military medical experts gathered in Falls Church, Va., to discuss modifying the FDA license so the anthrax vaccine could be administered in fewer doses and so it could be approved for inhalational anthrax.

According to official minutes from the meeting, Brig. Gen. Walter Busbee, joint program manager for biological defense, said the six-dose schedule was a key issue for the Joint Chiefs of Staff and then-Secretary of Defense William Perry.

He noted that a tour of duty in areas like Korea was 13 months, and the six-shot regimen needed to produce full immunity took 18 months.

Col. Arthur Friedlander, chief of the Bacteriology Division of the Army's Medical Research Institute for Infectious Diseases, offered a possible solution. He said the original series of six doses was established in the 1950s, but later studies of rhesus monkeys showed the military's vaccine was effective in much smaller doses than required by the label, according to notes from the meeting.

When the monkeys received just two shots, 100 percent of them survived exposure to airborne anthrax four to nine months later and 88 percent survived when exposed two years after the shots, he said. When the monkeys received just one dose, 100 percent survived exposure to airborne anthrax administered six weeks later.

Lt. Col. Phillip Pittman, chief of special immunizations at the Army medical institute, said Gulf War research suggested that two doses followed by annual boosters appeared to provide sufficient protection.

The group then discussed the need to get the manufacturer to apply to the FDA for a change in the license, so they could change the required regimen.

But when they realized that such a change would automatically put the vaccine in the experimental category - an "investigational new drug," in the parlance of the FDA - they took pause.

"Several participants expressed concern over putting the vaccine back into IND status," according to meeting minutes.

In 1996, after the license was transferred to Michigan Biological Products Institute, the institute filed the application with the Food and Drug Administration.

That request is still pending.

The mandatory vaccination program may be illegal

Connecticut Attorney General Blumenthal says there are four reasons why the anthrax immunization program is illegal:

** "The anthrax vaccine has not been proved safe or effective for its intended use in that [it] has never been licensed for protection against inhalational anthrax.

** "The vaccine is not being manufactured in accordance with either its site license or product license.

** "The vaccine is not being administered according to the license.

** "Since the vaccine has not been tested on humans, there is no basis for concluding that it is safe and effective."

Because of these deviations, the military's use of the vaccine must be considered experimental, Blumenthal said. Under federal law, citizens of the United States, including service members, can only be given an experimental drug when they are fully informed of the risks and benefits and provide their informed consent.

Rempfer, Dingle and others argue that defense officials' decision to file the IND application is proof they recognized that they wanted to use the vaccine for a purpose and at a dosage that fell outside of the scope of the license.

Pentagon officials deny that.

Such changes normally would trigger classification of the vaccine as an investigational new drug. Any service member asked to take it would first have to be told of the advantages and risks, then given the choice whether or not to take it. In theory, that was how the vaccine was supposed to have been administered during the Gulf War. In practice, many commanders just told their subordinates to line up and take their shots.

Executive Order 13139, signed by then-President Clinton in September 1999, says the Defense Department cannot give investigational new drugs to service members without their informed consent, except in times of national emergency.

"Waivers of informed consent will be granted only when absolutely necessary," the executive order says.

According to the relevant portion of U.S. law - Title 10, Section 1107 of the U.S. Code - only the president may grant waivers for investigational new drugs.

Further, the law says, a waiver may be granted "only if the president determines, in writing, that obtaining consent is not feasible, is contrary to the best interests of the member or is not in the interests of national security."

"The current IND process requires the submission of controlled studies proving that the drug is safe and effective for the proposed new use," Blumenthal wrote in his recent letter to Rumsfeld. No such studies have been conducted on the AVA (anthrax vaccine adsorbed, the official name of the drug). Furthermore, such
controlled studies of a new drug pursuant to an IND application cannot be conducted on human subjects without their informed consent."

The Pentagon chose, however, to use a different approach to the matter. In a March 4, 1997, letter, Dr. Stephen C. Joseph, assistant secretary of defense for health affairs, sought FDA permission to use the vaccine to protect U.S. troops "against the threat of an Iraqi biological warfare attack with anthrax."

"While the package insert for this vaccine is nonspecific as to the route of

exposure, DoD has long interpreted the scope of the license to include inhalation anthrax," he wrote to the FDA's lead deputy commissioner of food and drugs, Dr. Michael Friedman. "... Please advise whether the FDA has any objection."

In a carefully worded response, Friedman noted the "paucity of data regarding the effectiveness of anthrax vaccine for prevention of inhalation anthrax." But despite the lack of proof of effectiveness, the use of the vaccine for that purpose "is not inconsistent with the current label," he wrote.

Blumenthal's letter addresses this point: "In his very short letter, with the stroke of the pen, Dr. Friedman wiped out 10 years of DoD analysis and 25 years of FDA law designed to protect the safety and well-being of the citizens of the United States."

The Defense Department insists that today's vaccine meets FDA approval, and FDA officials have testified to that effect before Congress. Still, lawyers who argue against the anthrax vaccine say these statements are "informal opinions," not the official position of the FDA.

"What we need is a waiver of informed consent" from the president, said Air Force Reserve Lt. Col. John J. Michels Jr., a judge advocate general who defended Maj. Sonny Bates, the highest ranking officer to refuse the anthrax shots.

President Bush did that during the Gulf War, he added.

Defense officials "have gone through a great deal of effort to preclude the commander in chief from assuming his legal responsibilities under federal law for waiving service members' [rights to] informed consent," Michels said. "We just don't know why."

Staff writers Vince Crawley and Deborah Funk contributed to this report.