Three items in this issue of the Journal review past and current topics regarding the cause and prevention of anthrax infection in humans. In Voices From the Past, Fee and Brown discuss the groundbreaking work of John Henry Bell on occupational anthrax among woolsorts in Bradford, England, after wool and hair were introduced from abroad in the middle of the 19th century. Bell, in a 1878 report—also presented in Voices From the Past—recommended measures during the 1880s and 1890s to prevent what had become known as "woolsorts' disease." These measures, initially voluntary, were finally adopted as official policy by the British Home Office in 1899. Deaths from anthrax declined rapidly, but control measures were less than fully effective because of the persistence of anthrax spores and because of economic pressures to continue the work with contaminated wool.

Nass, in her commentary, discusses the conflicts raging about current use of a vaccine to prevent human anthrax. She describes the use of anthrax vaccine on military personnel by the US Department of Defense during the Persian Gulf War, with inadequate attention to adverse reactions, and since 1998 as a required immunization for military personnel. The vaccine was also recently offered by the Centers for Disease Control and Prevention (CDC) to postal workers and others who had been exposed to anthrax spores in the mail.

A TANGLED TALE

Midway between these episodes of human infection with anthrax, in the 1950s, Brachman and his colleagues, at what was then known as the Communicable Disease Center, conducted a controlled trial of a version of the anthrax vaccine and found it effective in preventing cutaneous anthrax in woolen mill workers.

On the basis of this trial, a similar vaccine was approved by the US Food and Drug Administration (FDA) for prevention of human cutaneous anthrax, and it has been used to immunize a number of workers in contact with animal skin and hides, as well as many others, including veterinarians. In the original trial, the number of cases of inhalation anthrax at the mill where the trial was conducted was insufficient for determining the vaccine's efficacy in preventing inhalation anthrax.

Purposeful infection of humans with inhalation anthrax to test the efficacy of the vaccine would clearly be unethical, but some nonhuman animal experiments have suggested that the vaccine may prevent inhalation anthrax, and the vaccine has been used by the Department of Defense for that "off-label" purpose. During the Persian Gulf War, because of fear that anthrax would be used against US troops as a biological weapon, thousands of US military personnel were immunized with the vaccine despite the absence of any evidence that the troops had been exposed to anthrax spores.

The immunizations were given without informed consent, and adequate records of the number of personnel receiving the vaccine or of adverse reactions they suffered were not maintained. In 1997, the Department of Defense ordered the immunization of all US military personnel despite advice from a number of sources that the immunization was of unproven efficacy against inhalation anthrax and that its potential for causing adverse effects was incompletely known.

Again, there was no evidence that troops had been exposed to anthrax and informed consent was not obtained. Although a passive system of reporting adverse reactions was in place, an active system of eliciting information about adverse reactions—which the military could easily have instituted—was not initiated.

The Governing Council of the American Public Health Association approved a policy statement in 1999 calling on the Department of Defense "to delay any further immunization against anthrax using the current vaccine or at least to make immunization voluntary," but immunization was not suspended until the stocks of the vaccine had been almost exhausted. The FDA had required the sole manufacturer of the vaccine to suspend production after inspections revealed repeated instances of poor manufacturing practices.

In the most recent episode of this tangled tale, anthrax spores were disseminated by mail in the United States, resulting in 5 deaths from inhalation anthrax.
among a total of about 20 confirmed cases. The spores had been finely milled and treated with chemicals to prevent clumping, permitting them to become airborne when the envelopes were opened. The spores also apparently escaped from the sealed envelopes, infecting those who handled the envelopes and contaminating several mail distribution centers and mail sorting machines. Postal workers in those centers were subjected to the potential risk of acquiring the disease, a risk of a very different type of exposure to “occupational anthrax” than Bell had described more than a century earlier.

In the most recent exposures, antibiotic treatment—unknown, of course, in Bell’s time—proved effective against cutaneous anthrax and against inhalation anthrax when the treatment was begun early after infection. Continuation of the treatment for some months was recommended because of the unknown lifespan of the spores. Because some of the people who were treated suffered adverse reactions to the antibiotics and discontinued the treatment; because the long-term effects of the antibiotics treatment are not known; because of the persistence of the spores in mail centers and sorting machines; and because of the unknown duration of the spores’ viability among humans exposed to them, the CDC offered—rather than recommended—the vaccine to postal workers and others who were known to be, or might have been, exposed to the spores.7

(This use of the vaccine is viewed by the FDA as “experimental,” owing to its postexposure use and shortened course (only 3 initial doses), and for this reason the CDC did not advise those who were exposed or potentially exposed to take the vaccine. Rather, the CDC simply offered the vaccine to those who were provided with information about it and were willing to sign an informed consent form relieving the US government of any liability for occurrence of adverse reactions.)

**WHEN WILL THEY LEARN?**

Thus, over the course of more than a century, the emphasis on prevention of occupational exposure to anthrax has shifted from protection of woolsorters to protection of mail sorters. That the efficacy of immunization for prevention of human inhalation anthrax and the risks of adverse effects of immunization are still imperfectly known is inexcusable. Had the Department of Defense taken its responsibilities more seriously, there would have been ample opportunity to learn about the nature and extent of the adverse effects and possibly about the efficacy of the current vaccine. Pressures to use the current vaccine (perhaps driven in part by the fact that the vaccine was being produced in a facility that had been purchased by a consortium headed by a former chairman of the Joint Chiefs of Staff) might have been resisted until more was known about the risks of infection with inhalation anthrax and the risks of the vaccine. Many military personnel might thereby have been spared adverse consequences of immunization, and those who refused the required immunization might have been spared the forced termination of their military careers. And the dangerous effects on public health in the United States that have risen from the mandatory use of an unproven vaccine and from the political pressures placed on the leadership of the US Public Health Service and of the CDC might have been avoided.8

Perhaps even more important, the original source of the “weaponized” anthrax spores used in the recent dissemination is believed to have been a US military laboratory, rather than the animal hides with which John Henry Bell had been concerned.9 Had those engaged in weaponizing anthrax in military laboratories, originally as an offensive weapon and since 1972 purportedly for “defensive” purposes, paid more attention to strengthening the verification regime of the Biological Weapons Convention10,11 and less attention to developing even more powerful anthrax weapons, the most recent cases of human anthrax might have been prevented. Bell, had he been alive a century after his efforts to end anthrax infection among woolsorters, might have asked, as Pete Seeger did in his 1956 song “Where Have All the Flowers Gone”: “When will they ever learn, when will they ever learn?”

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1. Fee E, Brown TM. John Henry Flowers Gone”: “When will they ever learn, when will they ever learn?”

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