ANTHRAX:

WHAT YOU NEED TO KNOW

Presented by the staff of the

AMERICAN COUNCIL ON SCIENCE AND HEALTH

Dr. Elizabeth M. Whelan, *President*

Dr. Gilbert Ross, *Medical and Executive Director*

Ashlee Dunston, *Assistant Director of Public Health*

Art Director:
Yelena Ponirovskaya

October 2003

AMERICAN COUNCIL ON SCIENCE AND HEALTH
1995 Broadway, 2nd Floor, New York, NY 10023-5860
Tel. (212) 362-7044 • Fax (212) 362-4919
URLs: http://www.acsh.org • http://www.HealthFactsAndFears.com
E-mail: acsh@acsh.org

THE AMERICAN COUNCILIN SCIENCE AND HEALTH (ACSH) APPRECIATES THE CONTRIBUTIONS OF THE REVIEWERS NAMED BELOW.

Donald A. Henderson, M.D., M.P.H.
Johns Hopkins Center for Civilian Biodefense Studies

John S. Parker, M.D.
Science Applications International Corporation

Marc Siegel, M.D.
New York University School of Medicine

TABLE OF CONTENTS

EXECUTIVE SUMMARY

In the post-Sept. 11 era of terrorism, the federal government has placed great emphasis on the potential threat posed by smallpox as a biological weapon. This stress on smallpox, however, raises a serious question: Are other, perhaps more serious bioterrorism agents – particularly anthrax – being given the attention they deserve?

Anthrax, in many respects, is an ideal bioweapon. It lends itself to aerosolization; its spores can be modified to "the ideal size" for causing lung infection; and the spores resist decontamination and persist in the environment for long periods of time. Further, the effective dispersion of an easily transportable quantity of anthrax spores could have the same devastating effect on a concentrated urban population as a nuclear device. We therefore neglect the threat of anthrax at our peril.

Weaponized anthrax could be disseminated over a large city by a piloted aircraft or unmanned drone equipped with spraying equipment. A spraying device also could be concealed in a moving vehicle or placed in a central location. Anthrax could even be spread throughout a building via its ventilation system. We have seen, with the anthrax-laced letters of 2001, that anthrax can even be spread through the mail. Food, too, could be contaminated. Water contamination probably presents less of a risk, but neither threat can be ruled out.

Early detection and treatment are key to survival following an anthrax attack. Otherwise, the disease, especially the inhalational form, is often fatal. Ciprofloxacin hydrochloride is the recommended initial antibiotic treatment for anthrax, although other antibiotics (e.g., doxycycline) are also effective when administered early on. There is also a licensed vaccine that is both safe and effective, but because it requires multiple doses over a prolonged period of time, an even better one is needed. The Bush administration's Project Bioshield intends to make new vaccines available quickly and also find new treatments and vaccines for a variety of bioterror agents, including anthrax.

INTRODUCTION

"Biological weapons are characterized by low cost and ease of access; difficulty of detection, even after use, until disease has advanced; unreliable but open-ended scale of predictable casualties; and clandestine stockpiles and delivery systems," the esteemed Rockefeller University biologist and Nobel laureate Joshua Lederberg told a Senate committee less than three weeks before the terrorist attacks of September 11th. "Per kilogram of weapon, the potential lives lost approach those of nuclear weapons, but less costly and sophisticated technology are required."[1]

Today's terrorists are not deterred from using such weapons of mass destruction for fear of in-kind retaliation. "While powerful nations maintain a degree of equilibrium through mutual deterrence and shared interests, less powerful elements may find in biological warfare opportunities to harm their enemies," Lederberg said, adding that "biological warfare is probably the most perplexing and gravest security challenge we face."

President George W. Bush shares this view. In a recent speech on the new Bioshield initiative, he said: "The attacks of September 11th, 2001 awakened America to the dangers of a new era. We face a different kind of threat than we were used to. On that morning, we saw the face of an enemy that will use any means to strike America – no matter how much destruction it causes, no matter how many innocent lives were lost. The kind of men who would seize planes filled with innocent people and crash them into buildings would not hesitate to use biological or chemical or nuclear weapons. They wouldn't hesitate at all."[2]

The question that now arises is whether the federal government, in conjunction with states and municipalities, is striking the right balance in developing responses to the myriad biological, chemical, and radiological threats we face.

Much, for instance, has been made of the potential threat to public health posed by the use of smallpox as a biological weapon. This is so, despite the fact that the last case of naturally-occurring smallpox was in 1977, and we do not know for certain that any nation or terrorist group has weaponized smallpox. Our new national policy now includes ordering smallpox vaccinations for the military and some other federal personnel located in high-risk areas overseas and also making the vaccine available on a voluntary basis to medical professionals, first responders, and certain microbiology laboratory workers.[3,4] While some concern is warranted, there is the risk that the emphasis on smallpox

could overshadow the dangers posed by other bioterror weapons, particularly anthrax.[5]

"SINGLE GREATEST BIOLOGICAL WARFARE THREAT"

We downplay the threat of anthrax at our peril. Anthrax's highly resistant spores could be dispersed as a small particle aerosol,[6] making them an ideal biological weapon.[7] And, as Secretary of State Colin L. Powell recently told the United Nations Security Council, "Less than a teaspoon full of dry anthrax in an envelope shut down the United States Senate in the fall of 2001."[8]

Indeed, according to experts at the U.S. Army Medical Research Institute of Infectious Diseases at Fort Detrick, Maryland, "Anthrax, in the minds of most military and counterterrorism planners, represents the single greatest biological warfare threat."[7]

A World Health Organization report published in 1970 estimated that 3 days after the release of 50 kilograms (kg) of anthrax spores along a 2-kilometer (or about a 1.24-mile) line upwind of a city of 500,000 population, some 125,000 infections would occur, producing 95,000 deaths.[9] "This number represents far more deaths than predicted in any other scenario of agent release," say the U.S. Army experts.[7]

Estimates of Casualties Produced by Hypothetical Biological Attack*

Agent	Downwind Reach, km	Number Dead	Number Incapacitated
Rift Valley fever	1	400	35,000
Tick-borne encephalitis	1	9,500	35,000
Typhus	5	19,000	85,000
Brucellosis	10	500	125,000
Q fever	>20	150	125,000
Tularemia	>20	30,000	125,000
Anthrax	>20	95,000	125,000

*Release of 50 kilograms by aircraft along a 2-kilometer line upwind of a population center of 500,000.

Source: World Health Organization[10]

In 2000, the RAND institute, a respected California-based think tank, held a symposium on the possible effects of a WMD. In a fol-

low-up report issued after the anthrax attacks of 2001, RAND experts concluded that a well-executed anthrax attack using 100 kg (220 lb) of weaponized anthrax spores had the potential to kill and sicken millions residing in any of California's large urban areas.[11]

The U.S. Congressional Office of Technology Assessment in 1993 analyzed the potential scope of even larger attacks.[12] It calculated that between 130,000 and 3 million deaths would follow the release of 100 kg of *Bacillus anthracis*, a lethality said to match that of a hydrogen bomb.[13]

Under ideal weather conditions, it is estimated that an aerial spray of anthrax along a line 100 kilometers (or about 62 miles) long could kill 50% of all persons exposed to the agent as far downwind as 160 km (or nearly 100 miles).[7] Additionally, in the 1960s, the U.S. military conducted a test near Johnston Atoll in the South Pacific in which a plane sprayed anthrax along a 32-mile line and found that the agent traveled more then 60 miles before losing its infectiousness.[13,14]

In this regard, it should be noted that President Bush has warned that spray devices could be used on unmanned aerial vehicles (UAVs) to dispense biological warfare agents. "A UAV launched from a vessel off the American coast could reach hundreds of miles inland," he said.[15] Powell similarly has noted that "UAVs outfitted with spray tanks constitute an ideal method for launching a terrorist attack using biological weapons."[16]

In fact, anthrax has already proven to be a threat in the United States. Shortly after the attacks on the World Trade Center and Pentagon, a number of envelopes containing *B. anthracis* spores were mailed to members of the news media and U.S. government officials, resulting in 11 cases of inhalational anthrax and 11 cases of cutaneous anthrax. Five persons with the inhalational form of anthrax died. The episode marked the first time that anthrax had been used in the United States as a bioterrorism weapon.[17]

WHAT IS ANTHRAX?

Anthrax is an acute infectious disease caused by the spore-forming bacterium *Bacillus anthracis*.[18] The incubation period for anthrax (i.e., the time between exposure and the appearance of clinical symptoms) is 1-7 days, with a range of up to 43 days.[6] Death typically occurs within 24-36 hours after the onset of severe symptoms.[19]

Anthrax, however, is not a contagious disease, meaning the illness is not transmitted from person to person.[6,20] Direct person-to-per-

son spread of anthrax, possibly via skin contact with someone contaminated with spores, is extremely rare, if it occurs at all.[6,18]

Anthrax is transmitted by inhalation, ingestion, or inoculation though the skin.[20] In a large-scale act of bioterrorism, the most likely means of anthrax transmission would be via an aerosol. Persons exposed to the aerosol thus would most likely show signs and symptoms of inhalation anthrax. Few, if any, persons would present symptoms associated with the GI (gastrointestinal forms) of the disease, except in the unlikely event that anthrax spores were used to taint foodstuffs.[6] Of course, if anthrax spores were again sent through the mail, some cases of cutaneous anthrax might occur as they did before.

Natural occurrences of the disease are rare in the United States. Anthrax most commonly occurs in such wild and domestic hoofed animals as cattle, sheep, goats, camels, and antelopes, but it can also occur in humans as a result of exposures to infected animals or infected animal products.[18]

Cutaneous (Skin) Anthrax: In this clinical form of the disease, the bacterium usually enters the body through a cut or skin abrasion. The first sign of infection is typically a bump, resembling a spider bite, which develops into a painless ulcer and eventually forms a black scab. (Anthrax is derived from the Greek word for "coal.") Other clinical manifestations of the disease include headache, fever, malaise, and swelling of the lymph nodes. The incubation period ranges from 1 to 12 days. If treated in time with antibiotics, skin anthrax is hardly ever fatal. Death has been reported in only 1% of treated cases but in 20% of untreated cases.[13,20,21]

Inhalation Anthrax: This is the most lethal form of the disease and is usually contracted by inhaling airborne anthrax spores.[22] The early symptoms may resemble the common cold or flu. Breathing may soon become difficult and the patient may go into shock. Inhaled anthrax can cause hemorrhage, edema (an accumulation of fluid), and necrosis (the death of tissue). Fluid often accumulates around the lungs and other chest structures, and can be seen on a chest x-ray. Meningitis (inflammation of the membrane that surrounds the brain and spinal cord) also may develop. The incubation period is 1 to 7 days, possibly ranging up to 60 days.[20]

Even with medical treatment, inhalation anthrax is often fatal: historically, the mortality rate has been approximately 90%. In the recent anthrax attacks, however, mortality was 45%, owing to modern improvements in urgent care.[6,21] It had been thought, based on animal studies, that it was necessary to inhale as many as 2,500 to 55,000

spores in order to produce a 50% fatality rate. Recent studies suggest that as few as 1 to 3 anthrax spores may be sufficient to cause infection and there is speculation – based on two of the deaths from the anthrax letters – that a fatal dose, in some individuals, may be quite low.[13]

Gastrointestinal Anthrax: The ingestion of anthrax spores can affect the pharynx (or throat) and the intestinal tract. Early symptoms include nausea, loss of appetite, vomiting, fever, sore throat, and swollen lymph glands. These may be followed by abdominal pain, vomiting of blood, and bloody diarrhea. The incubation period is 1 to 7 days. Gastrointestinal anthrax has been fatal in 25% to 60% of cases.[20,21]

From 1955 to 1999, according to the Centers for Disease Control and Prevention (CDC), 236 reported cases of anthrax – most of them cutaneous anthrax – were reported in 30 states and the District of Columbia. The last case of inhalational anthrax in the United States, before 2001, was in 1976. A California home craftsman died from infected yarn; *B. anthracis* was isolated from some of the imported yarns used by the patient. The last case of cutaneous anthrax, before 2001, occurred in North Dakota, in 2000.[23]

HOW IS ANTHRAX TREATED?

Anthrax is treatable with antibiotics, but the key to successful treatment is prompt administration of an antimicrobial at the first suspicion of illness. Since it is more likely that weaponized anthrax would be resistant to penicillin and tetracycline, treatment with the antibiotic ciprofloxacin hydrochloride (commonly referred to as Cipro) is recommended before antibiotic susceptibility data is available, although other antibiotics (e.g., doxycycline) are also usually effective once susceptibility is known. Treatment should be initiated early. If left untreated, anthrax can be fatal.[6] Cipro is approved by the FDA for use in patients who have been exposed to aerosolized anthrax spores.[24] The FDA has also approved doxycycline and penicillin G procaine for inhalational anthrax infection.

There also is a licensed vaccine (Anthrax Vaccine Adsorbed, BioThrax), but the stockpile is very limited. Most of the available production has been used to vaccinate military personnel or has been reserved for use by emergency personnel. The vaccine is not available on the open market.

THE WEAPONIZATION OF ANTHRAX

Anthrax spores are very stable – resisting sunlight, heat, and disinfectants – and thus can persist in the environment (e.g., soil or water) for years or even decades.[6,7,19] The spores' resistant properties, says the U.S. Army, "could be advantageous when choosing a biological weapon."[19] Anthrax spores also lend themselves to aerosolization,[i] which is one reason why inhalation is considered the most likely route of anthrax transmission in a bioterrorism attack.[6] At 2-6 microns in diameter, the spores are said to be "the ideal size" for impinging on human lower respiratory tract, thus optimizing the chance for infection.[7]

A primary means of attack might be the use of aerosol-delivery technologies over large outdoor areas.[13] Weaponized anthrax, for instance, could be dispensed as an aerosol cloud by a manned aircraft (such as a crop duster) or unmanned aircraft (drone) flying along a line upwind of a target area, a moving vehicle traveling along city streets, or a stationary spray device. It also could be disseminated inside buildings via central air ventilation systems.[19]

Turning anthrax into a bioweapon presents a challenge for terrorists, however. The manufacture and delivery of anthrax spores is made difficult because the spores have a tendency to clump. The milling process used to weaponize anthrax, moreover, imparts a static charge, making small anthrax particles hard to work with and increasing the likelihood that the spores, once released into the atmosphere, would soon bind to soil particles. Thus the chances that anthrax spores might pose a secondary aerosolization danger following an initial release are viewed as low.[7]

ANTHRAX IN HISTORY

Robert Koch, the German bacteriologist who established the bacterial cause of many infectious diseases, discovered the anthrax bacillus in 1876. The French chemist Louis Pasteur later confirmed the bacillus as the cause of anthrax and went on to develop a method of vaccinating sheep and cattle against the disease.[7,25]

Anthrax may have been a well-known disease afflicting cattle and humans even in ancient times. The fifth and perhaps the sixth of ten plagues visited upon the Egyptians in the Bible (Exodus 9:1-12) resemble the disease. The "Black Bane" that swept across Europe in the 1600s causing the deaths of animals and humans also was likely anthrax. Large outbreaks of the disease have occurred in more recent

times as well, including more than 6,000 cases in Zimbabwe in 1979-1980 and 25 cases in Paraguay in 1987.[7,25]

Research on anthrax as a biological weapon began over 80 years ago.[26] During World War II, Britain tested the use of anthrax as a weapon on the Scottish Island of Gruinard. The island was not decontaminated until 1987.[27] The U.S., too, produced biological weapons, including work on anthrax. But both Britain and the U.S. terminated their biowarfare programs in the late 1960s and early 1970s and destroyed any stockpiles in anticipation of an international treaty banning such weapons.

The Biological and Toxin Weapons Convention of 1972 banned such bioweapons as anthrax and required the destruction of existing stockpiles.[28] Some nations, however, continued to develop and manufacture these weapons even after the treaty went into enforcement in 1975.[13]

In 1995, the U.S. said 17 countries had biological weapons programs – specifically, Iran, Iraq, Libya, Syria, North Korea, Taiwan, Israel, Egypt, Vietnam, Laos, Cuba, Bulgaria, India, South Korea, South Africa, China and Russia. Russian leaders objected to the charge, insisting that they had terminated their biological weapons effort years before.[27] Iraq, on the other hand, admitted to the United Nations Special Commission in 1995 that it had produced and weaponized *B. anthracis*, among other biological warfare agents.[29]

More recently, the Center for Nonproliferation Studies at the Monterey Institute of International Studies in California estimated that at least 10 countries either have or possibly have active biological weapons programs. Among those believed to possess anthrax were Iran, Iraq, North Korea, and Syria.[30]

Russia, meanwhile, maintains that it is in full compliance with the 1972 convention banning biological and toxin weapons, but some experts are not so sure. Among them is Ken Alibek, former first deputy director of the Soviet bioweapons program, known as Biopreparat, who defected to the U.S. in 1992.

"Moscow has indeed shut down several large assembly lines for weapons, and dozens of Biopreparat production installations have been converted to pesticide plants or civilian biotechnology facilities. But the military plants are still off-limits to outsiders," he wrote in a *Wall Street Journal* article in 2000. Alibek further noted that many prominent Biopreparat officials remained in similar positions after the program was disbanded, raising suspicions about Russia's pledge to foreswear bioweapons development.[31]

THE SVERDLOVSK INCIDENT

On March 30, 1979, an invisible cloud of anthrax spores was accidentally released from a top-secret Soviet biological weapons production facility in the industrial city of Sverdlovsk (now Yekaterinburg or Ekaterinburg) at the base of the Ural Mountains, 845 miles east of Moscow. Known as Compound 19, the facility was the Soviet Union's busiest biological weapons production plant, operating around the clock to manufacture a dry anthrax weapon, Alibek explains in his book *Biohazard*. A faulty air filter resulted in the release of anthrax spores into the night air. The spores settled over the surrounding area.[32]

A few days later, night-shift workers at a ceramics factory nearby Compound 19 began to fall ill; all were reportedly dead within a week. Other Sverdlovsk residents also became ill. The outbreak lasted for a considerable time, with the last case reported on May 19.[32]

Soviet émigrés in the West soon reported that an explosion at Compound 19 caused the release of anthrax spores and resulted in many deaths. The Kremlin denied the reports, maintaining there had been a "natural outbreak" of anthrax among animals in the Sverdlovsk region and that some people had become ill after eating contaminated meat. The official Soviet version, however, did not square with the evidence of inhalational anthrax poisoning. In other words, people became ill after inhaling the spores and not after ingesting tainted food, as Soviet officials maintained.[32]

Boris Yeltsin, who later became head of the Soviet Union, was Sverdlovsk's Communist Party chairman at the time of the incident. In his 1990 autobiography, he said that the anthrax outbreak was caused by a "leak from a secret factory."[32] Yeltsin later blamed the deaths on the Soviet Union's germ warfare efforts.[33]

The estimated toll of dead and injured at Sverdlovsk varies even to this day. The Soviets said 96 persons had been stricken and 66 died.[32] However, a recent analysis finds that as many as 250 persons may have been infected and 100 died.[13,34]

ANTHRAX ATTACKS IN JAPAN AND THE U.S.

In 1992, a fanatical Japanese religious cult, Aum Shinrikyo, obtained what it believed was a virulent strain of anthrax.[35] As it turned out, the particular strain they acquired (Sterne 34F2) is non-lethal and was used for animal vaccination in Japan.[36] This strain does not pose a significant risk to humans.[13]

Nonetheless, in June 1993, cult members dispersed a liquid suspension of *B. anthracis* from atop their eight-story headquarters in Kameido, the Koto ward of Tokyo, using an industrial sprayer and a large fan. Cult members wore "moon suits" to protect themselves while feeding anthrax into a steam generator and then through the sprayer and fan over a four-day period. In July 1993, the cult twice used a compressor pump hidden in a truck to vent anthrax along the streets of downtown Tokyo. The attacks caused no injuries or deaths. The incidents indeed only came to light in subsequent court testimony by cult members and a retrospective investigation.[13,35]

In all, Aum members dispersed anthrax as well as what they thought was botulism at least eight different times in Tokyo to no effect.[37] The cult, however, did succeed in March 1995 in releasing Sarin gas, a deadly nerve agent, in the Tokyo subway system, killing 12 persons and injuring more than 1,000. Cult members had boarded several subway trains headed toward the heart of Tokyo and then used sharpened umbrellas to piece plastic bags containing liquid Sarin, which then leaked out and formed a toxic gas.[35,38]

The most notorious use of a biological agent in the United States was the mailing of the anthrax-laced letters in the fall of 2001. The envelopes containing *B. anthracis* spores, mailed to members of the news media and U.S. government officials, resulted in 22 cases of anthrax—11 cases of inhalational and 11 cases of cutaneous. Five of the inhalational cases were fatal.

The tainted mail was sent to addresses in Florida, New York, and Washington, D.C. Yet illness and death occurred not only at the offices targeted for bioterrorism but also along the path of mail and in other settings. All told, cases of anthrax infection were identified in residents of 7 states: Connecticut, 1 case; Florida, 2 cases; Maryland, 3; New Jersey, 5; New York, 8 (including a case in a New Jersey resident exposed in New York City); Pennsylvania, 1; and Virginia, 2. Twenty of the case-patients (or 91% of the total) were mail handlers or were exposed to worksites where contaminated mail was processed or received. *B. anthracis* was found in 4 powder-containing envelopes, 17 specimens from patients, and 106 environmental samples. Deaths occurred only in patients with inhalational anthrax. The case-fatality ratio for inhalational anthrax was 45%.[17]

How insidious a weapon was this? Consider the case of a 94-year-old female resident of Oxford, Connecticut, who become ill on Nov. 14, 2001 – 20 days after the second set of anthrax cases emerged.[17] Investigators found:

> No exposure to *B. anthracis* for this patient could be defined, despite extensive environmental sampling at her home and other sites. Environmental samples at the U.S. Postal Service Wallingford Mail Processing and Distribution Center in Wallingford, Connecticut, were positive for *B. anthracis*. The Wallingford facility received mail from the contaminated postal facility in Hamilton, New Jersey, and served as the primary source of mail delivered to the patient's home, suggesting cross-contamination of mail as a possible source of exposure. Postal sorting records indicated that an envelope had been processed in Hamilton on a high-speed sorter 15 seconds after one of the implicated envelopes sent to U.S. senators. That envelope had been delivered to an address 4 miles away from the residence of the Connecticut patient. The envelope was recovered and found to be positive for *B. anthracis*.[17]

The implications of these findings are clear: An act of bioterrorism using the postal system as its means of delivery poses serious health risks for anyone coming in contact with mail in neighboring regions and even the United States as a whole. The danger of cross-contamination in the postal system means that practically anyone could receive a contaminated piece of mail, whether or not he or she was the intended target. In the event that another such incident should occur, everyone ought to be on guard and take the appropriate precautions to reduce the risk of exposure to the bio-agent.

IDENTIFYING AND HANDLING SUSPICIOUS MAIL

Given the ongoing threat from anthrax, it is worth reprinting the CDC Health Advisory on how to recognize and handle a suspicious package or envelope:

IDENTIFYING SUSPICIOUS PACKAGES AND ENVELOPES

- *Inappropriate or unusual labeling*: excessive postage; handwritten or poorly typed addresses; misspellings of common words; strange return address or no return address; incorrect titles or title without a name; not addressed to a specific person; marked with restrictions, such as "Personal," "Confidential," or "Do not x-ray"; marked with any threatening language; or postmarked from a city or state that does not match the return address.
- *Appearance*: powdery substance felt through or appearing on the package or envelope; oily stains, discolorations, or odor; lopsided or

uneven envelope; or excessive packaging material, such as masking tape, string, etc.
- *Other suspicious signs*: excessive weight, ticking sound, or protruding wires or aluminum foil.
- If a package or envelope appears suspicious, DO NOT OPEN IT.

HANDLING OF SUSPICIOUS PACKAGES OR ENVELOPES

- Do not shake or empty the contents of any suspicious package or envelope.
- Do not carry the package or envelope, show it to others, or allow others to examine it.
- Put the package or envelope down on a stable surface; do not sniff, touch, taste, or look closely at it or at any contents that may have spilled.
- Alert others in the area about the suspicious package or envelope.
- Leave the area, close any doors, and take actions to prevent others from entering the area. If possible, shut off the ventilation system.
- Wash hands with soap and water to prevent spreading potentially infectious material to face or skin.
- Seek additional instructions for exposed or potentially exposed persons. If at work, notify a supervisor, a security officer, or a law enforcement official. If at home, contact the local law enforcement agency.
- If possible, create a list of persons who were in the room or area when this suspicious letter or package was recognized and a list of persons who also may have handled this package or letter. Give this list to both the local public health authorities and law enforcement officials.[39]

In addition, it is advisable to get into a routine of regular handwashing with soap and water. This is not only good hygiene; it also provides an extra layer of personal protection in the event of another anthrax outbreak.[40]

ANTHRAX VACCINE

A licensed vaccine (Anthrax Vaccine Adsorbed, BioThrax) is derived from a sterile culture fluid supernatant taken from an attenuated strain and therefore does not contain live or dead organisms. The vacci-

nation series consists of 6 doses (0.5 ml) at 0, 2, and 4 weeks, and then 6, 12, and 18 months, followed by yearly boosters.[18,19]

Contraindications for use of the vaccine include hypersensitivity reaction to a previous dose of vaccine and age (under 18 years of age or older than 65). Reasons for the temporary deferment of vaccination include pregnancy, active infection with fever, or a course of immune-suppressing drugs (e.g., steroids).[19]

While the vaccine is generally considered effective in preventing the onset of disease,[41] U.S. Army experts caution that "vaccine-induced protection could presumably be overwhelmed by extremely high spore challenge."[19]

The current anthrax vaccine, licensed by the FDA in 1970, is produced by BioPort Corp., Lansing, Michigan. In 1997, all U.S. military personnel (active duty and reserves) were required to receive the vaccine. With Food and Drug Administration (FDA) approval, more than 2 million doses of the vaccine were given to over 500,000 service men and women. The program was then halted after vaccine production was suspended while the manufacturing facility underwent renovations.[42]

The vaccine manufacturing plant was originally established and owned by the State of Michigan. In 1998, the vaccine was acquired by BioPort. Prior to the sale, the Department of Defense ordered a major renovation of the site. The State of Michigan ceased vaccine production in January 1998 as the upgrades were being made. The work was completed in 1999, and the FDA approved the renovated facility in late 2001, restoring the anthrax vaccine's availability.[42]

In June 2002, the Department of Defense resumed its Anthrax Vaccine Immunization Program (AVIP). However, because of supply limitations, vaccination was made mandatory only for military personnel in "higher threat areas," as well as some key Pentagon civilians and contractors.[43] The renewed program takes into account other national security considerations beyond the needs of military personnel. Therefore, a certain amount of the produced vaccine is being reserved for contingency use by other federal agencies. The Department of Homeland Security heads the planning effort for contingency use of the anthrax vaccine.[44] Still, anthrax vaccine stocks are very limited, and no vaccine is available on the open market.

In February 2003, President Bush announced the establishment of Project Bioshield for the research and production of "needed drugs and vaccines" to combat the threat of bioterrorism. The project's aim is quickly to make available "safer and more effective vaccines and treatments" against such biowarfare agents as smallpox, anthrax, botulinum

toxin, ebola, and plague.[2]

"In light of the new threats, we must now develop and stockpile these vaccines and these treatments," Bush said. "Right now, America must go beyond our borders to find companies willing to make vaccines to combat biological weapons. Two main drug therapies used to treat anthrax are produced overseas. We must rebuild America's capacity to produce vaccines by committing the federal government to the purchase of medicines that combat bioterror. Under Project Bioshield, the government will have the spending authority to purchase these vaccines in huge amounts, sufficient to meet any emergency that may come. Project Bioshield will give our scientific leaders greater authority and flexibility in decisions that may affect our security. Our labs will be able to hire the experts, get more funding quickly, and build the best facilities to accelerate urgently needed discoveries."[2]

There exists a persistent fear of anthrax vaccine, promulgated especially by anti-vaccine groups and claims of its association to "Gulf War Syndrome." These fears are unwarranted. A committee of the National Academies' Institute of Medicine has, in fact, called the current anthrax vaccine "safe and effective," although the committee's report added that it has certain drawbacks, including reliance on older vaccine technology and a six-dose vaccination schedule over 18 months.

Published March 2002 and titled *The Anthrax Vaccine: Is It Safe? Does It Work?* the report did not identify any unexpected short-term adverse reactions to the vaccine and found that the rates at which reactions occurred were similar to rates for other vaccines now in use for adults. Scientific data are limited on adverse health effects that might surface months or years following anthrax inoculations, it noted, but the available evidence does not confirm any long-term health risks among people who have received the vaccine. However, because no vaccine is 100% safe, the report called for the creation of systems to enhance long-term monitoring of health conditions that might be associated with any vaccine given to military personnel or others.[41,45]

"The anthrax vaccine should protect against even the inhalational form of the infection, but the lengthy vaccination schedule and the way the shots are physically administered make it far from optimal; it also is manufactured using older technologies that can be improved upon," said committee chair Brian L. Strom, a professor of biostatistics and epidemiology, medicine, and pharmacology and the director of the Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia. "The most prudent

course of action is to develop a new vaccine, given the nation's war against terrorism and the domestic attacks where anthrax was used as a deadly weapon. In the meantime, the current vaccine is sufficiently safe and effective to be useful."[45]

Vaccination alone is not enough to safeguard the American public from the likes of anthrax and other bioterror weapons, however. U.S. Army experts, writing in 1999, cautioned that the relatively short incubation period of inhalational anthrax and rapid progression of disease means "identification of the exposed population within 24 to 48 hours and employment of therapeutic and prophylactic strategies are likely to present a challenge."

"Good intelligence regarding the capabilities of terrorist groups, as well as heightened awareness of the threat on the part of clinicians, first responders, and public health personnel, remains a cornerstone of bioterrorism defense," they concluded.[7]

The Working Group on Civilian Biodefense, a CDC-endorsed multi-center consortium, issued a report in May 2002 entitled "Anthrax as a Biological Weapon, 2002." In this position paper, the group advocated the use of post-exposure anthrax vaccine for anyone in the vicinity of an anthrax release, for anyone involved in the clean-up or decontamination, and for laboratory workers who may be exposed (in combination with prolonged antibiotic therapy). Even pre-exposure vaccination "of some persons deemed to be in high-risk groups should be considered when substantial supplies of vaccine become available."[13]

Q's and A's

How would I know we were under attack from an anthrax weapon?

It is unlikely you would know. *B. anthracis* spores have no characteristic color, smell, or taste. They are also too small to be seen by the naked eye, although, as in the case of the anthrax-filled letters mailed in the fall of 2001, the spores might be mixed with a visible powder.[20] The covert release of a biological agent such as anthrax could, in most cases, take several days or weeks to become apparent.[46] One of the first indications of an anthrax outbreak (as was the case in Sverdlovsk) might be otherwise generally healthy individuals seeking emergency care who became acutely ill with fever and chest pain and died within one to two days of a rapidly progressing disease.

The U.S. has begun to position biological and chemical sensors in major cities around the country,[2] including New York.[47] The system, says the *New York Times*, uses advanced data analysis, adapted and test-

ed since the Sept. 11 attacks, and utilizes many of the U.S. Environmental Protection Agency's 3,000 air quality monitoring stations across the country. The air sensors will register any unusual quantities of a wide range of pathogens.[47] However, the first indication of an anthrax attack might not come until the stricken started turning up at emergency rooms and doctor's offices.

Are there dangers in taking Cipro, the recommended antibiotic treatment for anthrax, if I don't have anthrax or if the U.S. hasn't been attacked with bioweapons?

Overuse of antibiotics such as Cipro can have the unintended consequence of making bacteria more resistant and subsequently reduce the effectiveness of Cipro against other more common bacterial infections. A recent study, published in the *Journal of the American Medical Association*, indeed indicates that some types of bacteria have become less susceptible to the class of antibiotics that includes ciprofloxacin.[48]

Bacteria recovered from nearly 36,000 patients in intensive care units in 43 states and the District of Columbia between 1994 and 2000 revealed that the effectiveness of most fluroquinolone antibiotics in fighting off bacterial infections dropped by 6% or less over the period. The overall susceptibility to ciprofloxacin decreased steadily from 86% in 1994 to 76% in 2000. The study's authors concluded that the decline in effectiveness was "significantly associated with increased national use of fluoroquinolones."[48]

Are our national defenses adequate to protect us from an anthrax attack?

In spite of the grave dangers posed by biological weapons, the U.S. government has failed, until recently, to develop sufficient safeguards and adequately prepare for bioterrorism. Even the Bush administration admits the shortcomings. "Our approach to defend against biological threats has long been based on our approach to chemical threats, despite the fundamental differences between these weapons. The United States is developing a new approach to provide us and our friends and allies with an effective defense against biological weapons," the White House says in a recent report, *National Strategy to Combat Weapons of Mass Destruction*.[49]

Is there enough medicine and supplies to handle an anthrax attack in a large city?

Yes. The Strategic National Stockpile (SNS), formerly known as

the National Pharmaceutical Stockpile, provides 9 contingency supply sources that could be delivered anywhere in the country within 12 hours. On Sept. 11, for example, federal authorities deployed what is known as a "12-hour Push Package" of pharmaceuticals and medical supplies to New York and also sent a technical advisory team. Three out of the four non-military aircraft in U.S. airspace on the night of Sept. 11 were, in fact, carrying SNS assets and personnel to New York City.[50]

The Strategic National Stockpile is intended to ensure the availability and rapid deployment of life-saving pharmaceuticals, antidotes, other medical supplies, and equipment necessary to counter the effects of nerve agents, chemical agents, and biological pathogens. SNS is operated out of the Centers for Disease Control and Prevention but is jointly managed by the Department of Homeland Security and Department of Health and Human Services. It stands ready for immediate deployment to any U.S. location in the event of a bioterror attack.[51] These stockpiles are regularly rotated in cooperation with pharmaceutical manufacturers. Cities and states have been discouraged from buying and keeping reserves because of the limited shelf life of some of the products.

As part of the effort, Vendor Managed Inventory (VMI) packages would be delivered. These packages can be tailored to provide pharmaceuticals, vaccines, medical supplies, and/or medical products specific to the suspected or confirmed agent or agents used in an attack – including anthrax. A Technical Advisory Response Unit (TARU) also would arrive. These teams are comprised of pharmacists, emergency responders, and logistics experts, who would advise local authorities in an emergency.[51] However, it is worth noting that these "Push Packages" do not contain anthrax vaccine.

Is there a way to distinguish between early inhalation anthrax and the flu?

The Centers for Disease Control and Prevention provides the following answer:

> Early inhalational anthrax symptoms can be similar to those of much more common infections. However, a runny nose is a rare feature of anthrax. This means that a person who has a runny nose along with other common influenza-like symptoms is *far* more likely to have the common cold than to have anthrax.
>
> In addition, most people with inhalational anthrax have high white blood cell counts and no increase in the number of lymphocytes.

> On the other hand, people with infections such as flu usually have low white blood cell counts and an increase in the number of lymphocytes. However, it is recommended that people get flu shots annually. Knowing that a patient has had a flu shot would indicate that a bioweapon might be the cause of the illness, though still statistically quite unlikely compared with other infectious causes.
>
> Chest X-rays are also critical diagnostic tools. Chest X-rays have shown that all patients with inhalational anthrax have some abnormality, although for some patients, the abnormality is subtle. CT scans can confirm these abnormalities.[52]

Are there any adverse reactions to an anthrax vaccination?

Some vaccine recipients (i.e., up to 30%) may experience mild discomfort (e.g., tenderness, skin reddening, lumps, itching) at the site of injection for up to 3 days after an injection. A smaller number may experience moderate reactions, consisting of extensive swelling of the forearm and possibly limiting use of the injected arm for 1-2 days. Severe systemic reactions occur in fewer than 0.2% of recipients.[18,19] Women also experience more adverse reactions than men.[41]

If anthrax vaccination is recommended, should I get vaccinated if I'm pregnant? Also, what about antibiotic treatment for pregnant women?

Women who are pregnant or believe they might be pregnant should be vaccinated only if absolutely necessary.[18] And the FDA offers the following guidance on treatment with antibiotics:

> There have been no formal clinical studies of the safety and effectiveness of Cipro in pregnancy. However, based on available information, TERIS (The Teratogen Information System) has concluded that Cipro used during pregnancy is unlikely to cause physical defects to an unborn baby. But there is not enough information to say there is no risk. Guidelines for treating pregnant women with Cipro are limited. An expert panel, The Working Group on Civilian Biodefense, recommends that Cipro be used at usual adult doses to treat pregnant women exposed to anthrax. Pregnant women should always consult their health care provider before taking any medications.[53]

I'm joining the Armed Forces and was told I have to get vaccinated. Where can I get more information?

The Department of Defense recommends that servicemen and

women contact their chain of command on questions about the vaccine and its distribution. The Anthrax Vaccine Immunization Program in the U.S. Army Surgeon General's Office can be reached at 1-877-GET-VACC (1-877-438-8222) or at http://www.anthrax.osd.mil.

Should I be concerned about food being contaminated with anthrax? And what about drinking water?

While anthrax can be ingested, causing a gastrointestinal form of the disease, it is most unlikely that this method would be used by terrorists. However, the World Health Organization recently warned that a deliberate, concerted act of food terrorism could be "devastating."[54]

Some researchers have stressed the ease of distributing biological or chemical agents for the purpose of terrorism via food and water contamination.[55] The threat to food, though itself small, is much higher than that for drinking water. The effects of dilution, deterioration, and water treatment make an anthrax contamination of drinking water an extremely remote possibility.

"Although less effective as potable water threats, many [biological warfare agents] are potentially capable of inflicting heavy casualties when ingested," say experts at the U.S. Army Center for Health Promotion and Preventive Medicine, Aberdeen Proving Ground, Maryland. "Municipal water treatment facilities would be measurably less effective. Some replicating (infectious) agents and a few biotoxins are inactivated by chlorine disinfection; for others chlorine is ineffective or of unknown efficacy."[56]

Should I buy an anthrax test kit?

No. The kits are scams. Testing for anthrax requires sophisticated scientific equipment and training. It is not a project one conducts in a kitchen.

Should I prepare a "safe room" to protect myself against a possible anthrax attack?

While it is not recommended to make a "safe room" in anticipation of an anthrax attack, officials might require residents and workers to shelter in place following an aerosol release of a chemical, biological, or radiological agent. People will be instructed to seek shelter in interior rooms (with the fewest number of windows and doors), turn off the room's ventilation or air-conditioning system, and stay put until emergency assistance arrives or until you are instructed to leave. Of course, if anthrax spores were released indoors, such as occurred in the mail-

related 2001 episodes, this advice would not apply. For more information, consult www.ready.gov, the U.S. Department of Homeland Security's new information site.[57]

In the event of an anthrax attack, is there any possible scenario in which having a supply of surgical or other masks might offer some protection?

While protection of airways is an important step to take in the event of a chemical, biological, or radiological attack, the problem is that the currently available masks would not be very effective against anthrax. For example, the agent – in this case the anthrax spores – might be of such small molecular size that it would get through most masks. And most scenarios anticipate attacks with invisible or dust-like weapons, meaning that people probably would be unaware of their exposure to a toxic agent and thus have no reason to don a mask.

Masks like the N95 disposable respirator must be custom-fitted, and people have to be instructed in how to use them. Efforts are being made to develop a new type of respirator for use by the general public that would be effective against several chemical or biological agents. Until the devices become commercially available, the purchase of masks buys little more than a false sense of security.

I manage an office building. What should I do to prevent terrorists from contaminating the air system?

Reducing a building's vulnerability to bioterrorism, as well as chemical or radiological attack, requires a comprehensive approach, including prevention of access to outdoor air intakes and mechanical rooms. A building security assessment also should be performed. For a detailed discussion, consult *Guidance for Protecting Building Environments from Airborne Chemical, Biological, or Radiological Attacks*, published by the National Institute for Occupational Safety and Health (available online at http://www.cdc.gov/niosh/bldvent/2002-139.html).[58]

As a public official, what more should I being doing to prevent panic in the event of an anthrax or other bioterrorism attack?

Mass panic is always a possibility, but scientists at the Johns Hopkins Bloomberg School of Public Health completed a study in 2001 that showed if there were a large-scale bioterror attack, the American public could be counted on to respond quickly and efficiently. The findings discount the commonly held view that such an attack would result

in mass panic and social disorder. The authors warned, however, that failure to involve the public as a key partner in the medical and public-health response could hamper effective management of an epidemic and increase the likelihood of social disruption.[59]

"Ultimately," they said, "actions taken by nonprofessional individuals and groups could have the greatest influence on the outcome of a bioterrorism event. Five guidelines for integrating the public into bioterrorism response planning are proposed: (1) treat the public as a capable ally in the response to an epidemic, (2) enlist civic organizations in practical public health activities, (3) anticipate the need for home-based patient care and infection control, (4) invest in public outreach and communication strategies, and (5) ensure that planning reflects the values and priorities of affected populations."[59]

CONTACT INFORMATION

EMERGENCIES

General Public:

Contact the police and emergency services at 911 or the following:

New York City Department of Environmental Protection, Water-Watch Hotline, 888-H2O SHED (888-426-7433), http://www.nyc.gov/dep/

New York City Department of Health & Mental Hygiene, 877-692-3647, http://www.ci.nyc.ny.us/html/doh/

New York State Department of Health: 800-458-1158, http://www.health.state.ny.us

New York State Public Security Tips Hotline: 866-SAFENYS or 866-723-3697

U.S. Department of Agriculture Meat and Poultry Hotline: 800-535-4555

U.S. Food and Drug Administration emergency number: 301-443-1240

Healthcare Providers:

Centers for Disease Control and Prevention, Emergency Response Hotline (24 hours): 770-488-7100.

New York City Department of Health, Communicable Disease Program: 212-788-9830 (After hours, Poison Control Center: 212-764-7667)

New York State Department of Health, Communicable Disease

Control: 518-473-4436 (After hours, duty officer: 518-465-9720)

CHEMICAL/BIOLOGICAL INFORMATION

Centers for Disease Control and Prevention, Bioterrorism: 888-246-2675, or 404-639-3311, http://www.bt.cdc.gov

Federal Emergency Management Agency: 202-566-1600, http://www.fema.gov

Greater New York Hospital Association: 212-246-7100, http://www.gnyha.org/eprc/general/nbc/
National Institute for Occupational Safety and Health, 800-356-4674, http://www.cdc.gov/niosh

New York City Department of Health & Mental Hygiene, Bureau of Communicable Disease: 212-788-4204, http://www.ci.nyc.ny.us/html/doh/

New York State Department of Health: http://www.health.state.ny.us

Smallpox Vaccine Information, CDC National Immunization Hotline: 800-232-2522

U.S. Department of Homeland Security: http://www.dhs.gov/dhspublic/ or http://www.ready.gov/

NUCLEAR/RADIATION INFORMATION

Centers for Disease Control Public Response Source: 888-246-2675, http://www.cdc.gov

Energy Information Administration: 202-586-8800, http://www.eia.doe.gov

Federal Emergency Management Agency: 202-646-4600, http://www.fema.gov

Greater New York Hospital Association: 212-246-7100, http://www.gnyha.org/eprc/general/nbc/

Nuclear Regulatory Commission Radiation Protection and Emergency Response Program: 301-415-8200, http://www.nrc.gov

Radiation Emergency Assistance Center, Oak Ridge Associated Universities, 865-576-3131, http://www.orau.gov/reacts

U.S. Environmental Protection Agency: 212-637-5000, http://www.epa.gov/radiation

U.S. Department of Energy 800-dial-DOE, http://www.energy.gov

U.S. Department of Homeland Security: http://www.dhs.gov/dhspublic/ or http://www.ready.gov/

REFERENCES

1. Lederberg, Joshua, testimony before U.S. Senate Committee on Foreign Relations, Aug. 24, 2001, reprinted in "Biological Warfare," Emerging Infectious Diseases, Vol. 7, No. 6, Nov.-Dec. 2001.
2. Bush, George W., "President Discusses Measures to Protect the Homeland from Bioterorism: Remarks by the President on the Bioshield Initiative," White House transcript, Feb. 3, 2003.
3. Bush, George W., "Remarks by the President on Smallpox Vaccination," The White House, Dec. 13, 2002.
4. Whelan, Elizabeth M., "Smallpox Questions," the *Wall Street Journal*, Oct. 3, 2002.
5. Rotz, Lisa D., Khan, Ali S., et al., "Public Health Assessment of Potential Biological Terrorism Agents," Emerging Infectious Diseases, CDC, Vol. 8, No. 2, February 2002.
6. New York City Department of Health, Bureau of Communicable Disease, "Medical Treatment and Response to Suspected Anthrax: Information for Health Care Providers During Biological Emergencies," July 2000 Draft.
7. Cieslak, Theodore J., and Eitzen, Edward M., Jr., "Clinical and Epidemiologic Principles of Anthrax," *Emerging Infectious Diseases*, Centers for Disease Control and Prevention, Vol. 5, No. 4, July-Aug. 1999.
8. Powell, Colin L., "Remarks to the United Nations Security Council," transcript, U.S. Department of State, Feb. 5, 2003.
9. *Health Aspects of Chemical and Biological Weapons.* Geneva, Switzerland: World Health Organization, 1970.
10. *Health Aspects of Chemical and Biological Weapons.* Geneva, Switzerland: World Health Organization, 1970, reproduced in Christopher, George W., Cieslak, Theodore J., Pavlin, Julia A., Eitzen, Edward M. Jr., "Biological Warfare: A Historical Perspective," *JAMA*, Vol. 278, No. 5, Aug. 6, 1997, 412-417.
11. "Bioterrorism: Homeland Defense: The Next Steps," Conference Proceedings. Santa Monica CA: RAND Institute, 2000.
12. Office of Technology Assessment, U.S. Congress. *Proliferation of Weapons of Mass Destruction.* Publication OTA-ISC-559. Washington, DC: U.S. Government Printing Office, 1993.

13. Inglesby, Thomas V., O'Toole, Tara, et al., "Anthrax as a Biological Weapon, 2002: Updated Recommendations for Management," *JAMA*, Vol. 287, No. 17, May 1, 2002, 2236-2252.

14. Regis, E., *The History of America's Secret Germ Warfare Project*. New York, NY: Random House; 1999.

15. Bush, George W., "Statement by the President," transcript, The White House, Feb. 6, 2003.

16. Powell, Colin L., "Remarks to the United Nations Security Council," transcript, U.S. Department of State, Feb. 5, 2003.

17. Jernigan, D.B., Raghunathan, P.L., Bell, B.P., Brechner, R., et al. Investigation of bioterrorism-related anthrax, United States, 2001: epidemiologic findings. *Emerging Infectious Disease*, October 2002, 8.

18. Centers for Disease Control and Prevention, Division of Bacterial and Mycotic Diseases, "Anthrax: Frequently Asked Questions," October 2001.

19. U.S. Army Medical Research Institute of Infectious Diseases, *USAMRIID's Medical Management of Biological Casualties Handbook*, Fourth Edition, February 2001, 14-18.

20. Centers for Disease Control and Prevention, "Anthrax FAQ: Signs and Symptoms," November 2002.

21. Medical Society of the State of New York, "Public Health Emergencies – Anthrax: Ways to Cope with Anthrax and Other Bioterrorism Threats."

22. Centers for Disease Control and Prevention, "FAQ's about Anthrax," November 2002

23. Centers for Disease Control and Prevention, "Anthrax FAQ: History," November 2002.

24. U.S. Food and Drug Administration, "Cipro (Ciprofloxacin Hydrochloride) for Inhalation Anthrax: Information on Cipro for Consumers: Questions and Answers."

25. *The Columbia Encyclopedia*, Sixth Edition, 2001.

26. Christopher, G., Cieslak, T., Pavlin, J., Eitzen, E., "Biological warfare: a historical perspective," *JAMA*, 1997;278:412-417.

27. British Broadcasting Corp., "Anthrax Fact File: Biological Weapons and Anthrax," 2001.

28. Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction, opened for signature April 10, 1972 and entered into force March 26, 1975. Copy available from The Harvard Sussex Program on CBW Armament and Arms Limitation.

29. Zilinskas, R.A., "Iraq's biological weapons," *JAMA*, No. 278, 1997, 418-424.

30. Monterey Institute of International Studies, Center for Nonproliferation Studies, "Chemical and Biological Weapons: Possession and Programs Past and Present," April 9, 2002.

31. Alibek, Ken, and Handelman, Stephen, "Is Russia Still Preparing for Bio-Warfare?" the *Wall Street Journal*, Feb. 16, 2000.

32. Alibek, Ken, *Biohazard*. New York: Dell Publishing, 2000, 70-86.

33. Smith, R.J., "Yeltsin Blames '79 Anthrax on Germ Warfare Efforts," *Washington Post*, June 16, 1992, A1.

34. Brookmeyer, R., Blades, N., Hugh-Jones, M., Henderson, D., "The statistical analysis of truncated data: application to the Sverdlovsk anthrax outbreak," *Biostatistic*, No. 2, 2001, 233-247.

35. Smithson, Amy E., "Rethinking the Lessons of Tokyo," in Smithson, A.E. and Levy, L.E. (ed.), "Ataxia: The Chemical and Biological Terrorism Threat and the U.S. Response," Stimson Center Report.

36. Keim, Paul, Smith, Kimothy L., Keys, Christine, et al., "Molecular Investigation of the Aum Shinrikyo Anthrax Release in Kameido, Japan," *Journal of Clinical Microbiology*, Vol. 39, No. 12, December 2001, 4566-4567.

37. WuDunn, S., Miller, J., Broad, W., "How Japan germ terror alerted world," *New York Times*, May 26, 1998, A1, 6.

38. Olson, Kyle B., "Aum Shinrikyo: Once and Future Threat?" *Emerging Infectious Diseases*, CDC, No. 5, 1999, 513-6.

39. Centers for Disease Control and Prevention, "Updated Information About How to Recognize and Handle a Suspicious Package or Envelope," CDC Health Advisory, Oct. 31, 2001.

40. Boyce, John M., and Pittet, Didier, "Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force," *MMWR*, CDC, Oct. 25, 2002/51(RR16), 1-44.

41. Joellenbeck, Lois M., Zwanziger, Lee L., Durch, Jane S., and Strom, Brian L., eds., *The Anthrax Vaccine: Is It Safe? Does It Work?* Committee to Assess the Safety and Efficacy of the Anthrax Vaccine, Medical Follow-Up Agency, Institute of Medicine. Washington, D.C.: National Academies Press, 2002.

42. BioPort Corp., "History of the BioPort Vaccine Manufacturing Facility" and "Frequently Asked Questions About BioPort and the Anthrax Vaccine," 2003.

43. Wolfowitz, Paul, "Memorandum for the Secretaries of the Military Departments: Reintroduction of the Anthrax Vaccine Immunization Program (AVIP)," Office of Deputy Secretary of Defense, U.S. Department of Defense, June 28, 2002.

44. Anthrax Vaccine Immunization Program Agency, "Questions and Answers: AVIP Resumption," U.S. Department of Defense, 2003.

45. Institute of Medicine, "Anthrax Vaccine Is Useful, But Shortcomings Underscore Need for Replacement," press release, March 6, 2002.

46. World Health Organization, *Preparedness for the Deliberate Use of Biological Agents: A Rational Approach to the Unthinkable*. Geneva: World Health Organization, 2002.

47. Miller, Judith, "Threats and Responses: Biological Defenses; U.S. Deploying Monitor System For Germ Peril," the *New York Times,* Jan. 22, 2003, 1.

48. Neuhauser, Melinda M., Weinstein, Robert A., Rydman, Robert et al., " Antibiotic Resistance Among Gram-Negative Bacilli in U.S. Intensive Care Units: Implications for Fluoroquinolone Use," *Journal of the American Medical Association*, No. 289, 2003, 885-888.

49. The White House, *National Strategy to Combat Weapons of Mass Destruction*, December 2002.

50. Henderson, D. A., "The Science of Bioterrorism: HHS Preparedness," testimony before the Committee on Science, U. S. House of Representatives, Office of Public Health Preparedness, Department of Health and Human Services, Dec. 5, 2001.

51. Centers for Disease Control and Prevention, "National Pharmaceutical Stockpile," Dec. 18, 2002.

52. Centers for Disease Control and Prevention, "Anthrax FAQ: Anthrax and Influenza," December 2002.

53. U.S. Food and Drug Administration, "Cipro (Ciprofloxacin Hydrochloride) for Inhalation Anthrax: Information on Cipro for Consumers: Questions and Answers."

54. World Health Organization, *Terrorist Threats to Food: Guidance for Establishing and Strengthening Prevention and Response Systems*. Geneva: World Health Organization, 2002.

55. Khan, A.S., Swerdlow, D.L., Juranek, D.D. Precautions against biological and chemical terrorism directed at food and water supplies. *Public Health Reports*. Jan.-Feb. 2001, 116(1).

56. Burrows, W. Dickinson, and Renner, Sara E., "Biological Warfare Agents as Threats to Potable Water," Environmental Health Perspectives, Vol. 107, No. 12, December 1999.

57. Sorensen, John H., and Vogt, Barbara M., "Will Duct Tape and Plastic Really Work? Issues Related to Expedient Shelter-In-Place," Oak Ridge National Laboratory, August 2001.

58. National Institute for Occupational Safety and Health, *Guidance for Protecting Building Environments from Airborne Chemical, Biological, or Radiological Attacks,* DHHS (NIOSH) Pub. No. 2002-139, May 2002.

59. Glass, Thomas A., and Schoch-Spana, Monica, "Bioterrorism and the People: How to Vaccinate a City against Panic," *Clinical Infectious Diseases*, No. 34, 2002, 217-223.