

# Chapter 19

## THE U.S. BIOLOGICAL WARFARE AND BIOLOGICAL DEFENSE PROGRAMS

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### SUMMARY

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## INTRODUCTION

Biological agents have been used in war for centuries. After World War I, Major Leon Fox, Medical Corps, U.S. Army, prepared a lengthy report<sup>1</sup> that concluded that biological warfare was no longer a concern because of the development of modern sanitary procedures. However, as he wrote, the Japanese were already developing an offensive biological warfare program involving an extensive list of biological agents, capable of causing diseases such as anthrax, tularemia, plague, botulinum, smallpox, glanders, and typhoid.

The United States conducted a second review of the potential of biological warfare during 1941 and 1942 and implemented its program to develop biological weapons in 1943. The biological warfare program of the United States was conducted under military auspices and was characterized during its early years by a high degree of secrecy and controversial testing programs. By the 1960s, U.S. scientists had clearly established that the development of biological weapons was feasible and that their use on the battlefield could be effective.

The purpose of the U.S. program in the early years was to deter the use of biological agents

against the United States and its military forces, and to retaliate only if deterrence was unsuccessful. The program was characterized by an aggressive offensive and defensive research and development effort that would be modified to one based on maintaining a strong defense against biological agents.

When the biological warfare program was established, the United States was fighting World War II on two fronts. After the war ended, the Cold War developed and our security was still threatened. The United States maintained an active offensive biological warfare program until it unilaterally renounced the use of biological weapons in two National Security Memoranda in 1969 and 1970. The United States ratified the Biological Weapons Convention in 1975. Although capabilities of the world's military forces have changed significantly in the years following the disestablishment of the U.S. biological warfare program—and despite the Biological Weapons Convention—a biological warfare threat still exists; therefore, the United States maintains a program for medical defense against biological warfare agents.

## A SECRET BIOLOGICAL WARFARE PROGRAM

In 1941, Secretary of War Henry L. Stimson asked the National Academy of Sciences to evaluate the feasibility of biological warfare. The academy concluded that biological warfare was feasible and recommended that steps be taken to reduce U.S. vulnerability and also to conduct research to explore the offensive potential of bacteriological weapons. In April 1942, Stimson recommended to President Franklin D. Roosevelt the creation of a civilian advisory group that would coordinate governmental and privately owned institutions in a biological warfare effort.<sup>2,3</sup> (What he did not tell Roosevelt was that the Army Chemical Warfare Service had begun its own biological warfare research in 1941.)

The idea of biological weaponry was controversial, since little was known about the predictability or effectiveness of biological weapons in wartime. President Roosevelt approved the plan in 1942, and the War Reserve Service, headed by George W. Merck, was established and attached to the Federal Security Agency, a New Deal agency of the Department of Agriculture. The War Reserve Service started out in mid 1942 with a budget of \$200,000. Secret work began under Merck's direction at 28

American universities, including Harvard, Stanford, and other top schools. This agency received consultative advice from national scientific committees and organizations, including the National Academy of Sciences and the National Research Council.

The War Reserve Service also empowered the U.S. Army's Chemical Warfare Service to greatly expand its efforts in regard to biological weapons. The army's efforts were better funded than those of the War Reserve Service: in 1942 and 1943, the Chemical Warfare Service received millions of dollars to build research facilities. Several locations were selected for the army's biological research, with the main headquarters at Camp Detrick, Frederick, Maryland, a small National Guard airfield (designated Fort Detrick in 1956). The army also made plans to build a manufacturing plant near Terre Haute, Indiana, and built a 2,000-acre field test site on Horn Island in Pascagoula, Mississippi. It is ironic that much of the United States's biological warfare effort during World War II was in response to a perceived threat from Germany, when in fact the Japanese were much more actively building their biological warfare capability.<sup>2</sup>

In the spring of 1942, President Roosevelt and British Prime Minister Winston Churchill announced policies limiting the use of biological weapons to retaliation only, closely paralleling previous decisions, such as the Geneva Protocol of 1925, on the limited use of chemical weapons. But these new policies did not prevent the United States and Great Britain from beginning to amass arsenals of biological weapons.<sup>4</sup> By 1943, the research center and pilot plant at Camp Detrick employed approximately 3,800 military and 100 civilian personnel. In 1944, Dugway Proving Ground, Utah, was established to replace the Mississippi site, and the production plant was constructed near Terre Haute, Indiana.<sup>2</sup>

The United States exchanged information with Great Britain and Canada, two other nations concerned about the biological warfare threat, but the general public was unaware of a biological warfare program in the United States until 4 months after the war was over. During World War II, the United States worked primarily on anthrax and botulism; however, brucellosis, psittacosis, tularemia, and glanders were also studied. There was also considerable work on agents for use against plants, and records show that there were plans drawn up to decimate Japan's rice crops.<sup>2</sup>

At the end of World War II, construction and testing slowed to a stop, and the effort on biological warfare development was largely limited to research. The production plant in Indiana was sold to the Charles A. Pfizer Company for commercial use. Although the highly classified program was initially defensive, and closely tied with the chemical weapons program, research continued on developing an independent retaliatory capability using various disease agents.

### The Secret Program Is Acknowledged

Since 1937, Japan had conducted a large biological warfare program, including human testing, at its Unit 731 in Manchuria.<sup>5</sup> After the war, the United States granted amnesty to Japanese scientists who had participated in the research; however, a condition of the amnesty was full disclosure of research information. Two scientists from Camp Detrick, Dr. Edwin Hill and Dr. Joseph Victor, went to Japan in 1945 and interviewed 22 scientists. They learned that many of the classical biological warfare agents had been studied, and that approximately 1,000 autopsies had been performed in Unit 731, most of these on humans who had been exposed to anthrax. They also learned that the Japanese had stockpiled

400 kg of anthrax spores, which were to be used in a specially designed fragmentation bomb.

In January 1946, the War Department made public for the first time the fact that the United States had been conducting biological warfare research and testing. The press release emphasized the high priority placed on safety:

In all work on biological warfare carried on in the United States, extreme care was taken to protect the participating personnel from infection. Many new techniques were devised to prevent infection and proved highly successful. Hospitals and dispensaries were maintained at all installations, staffed with both Army and Navy personnel and were equipped to treat accidental infections. As the result of the extraordinary precautions taken, there occurred only sixty cases of proven infection caused by accidental exposure to virulent biological warfare agents which required treatment. Fifty-two of these recovered completely; of the eight cases remaining, all were recovering satisfactorily. There were, in addition to the sixty proven cases, 159 accidental exposures to agents of unknown concentrations. All but one of these received prompt treatment and did not develop any infection. In one instance, the individual did not report exposure, developed the disease, but recovered after treatment.<sup>3(vol 1, p1-4)</sup>

Mr. Merck, the head of the War Reserve Service, in his final report<sup>6</sup> to the secretary of war noted that although remarkable achievements had been made, the potential of biological warfare had by no means been completely measured. He recommended that the program be continued on a sufficient scale to provide an adequate defense.

In 1948, the Research and Development Board (then under the secretary of defense), which had been given the responsibility to supervise the governmental research program, requested an evaluation of biological agents as weapons of sabotage. The Committee on Biological Warfare was formed, and the Baldwin Report<sup>7</sup> prepared by the committee stated that the United States was particularly vulnerable to covert attack with biological agents. It also stated that the current research and development program was "not now authorized to meet the requirements necessary to prepare the defensive measures against special [biological warfare] operations."<sup>7(p1)</sup>

The Baldwin Report recommended<sup>7</sup> that

- means be developed to detect and identify biological warfare agents;
- methods be developed for decontamina-

tion, protection, prophylaxis, and treatment; and

- methods be assessed for dissemination of biological agents, with emphasis on application to special operations.

Specifically recommended were research programs, such as the testing of “innocuous organisms”<sup>7(p7)</sup> in ventilation systems, subway systems, and public water supplies. This guidance influenced several subsequent administrations over the next 20 years, and the United States conducted a sequence of highly classified scientific tests on unknowing populations throughout the country, with agents and materials believed to be nonpathogenic. In fact, not until early 1977 was the extent of the military biological weapons testing program publicly disclosed before Congress.<sup>3,4</sup>

The biological warfare research program in the early 1940s and 1950s involved antipersonnel, anticrop, and, for a brief period, antianimal studies.<sup>8</sup> Field trials included open-air vulnerability testing, and contamination of public water systems with live organisms such as *Serratia marcescens*. Covert programs were conducted by the Central Intelligence Agency. Pathogenic organisms were also tested in Florida and the Bahamas in the 1940s. Chemical anticrop studies evaluated defoliation and crop destruction. Explosive munitions tests with pathogens were begun in 1949.

In 1950, the first open-air tests with biological simulants were conducted in various locales, one of which was off the coast of Norfolk, Virginia. This was followed by limited zinc cadmium sulfide dispersal tests in Minneapolis, Minnesota, and St. Louis, Missouri, in 1953; and *Bacillus subtilis* var *niger* dispersal in the New York City subway system in 1966.<sup>3,4</sup> The Special Operations Division at Camp Detrick conducted much of the research on possible methods of covert attack and sabotage, and many environmental studies—often without informing local or state governmental agencies or the general population.

Between 1948 and 1950, several reviews were conducted by the Research Review Board of the biological, chemical, and radiological warfare programs. Recommendations included the creation of a specific biological warfare production facility, continued field tests with biological warfare agents and munitions, and expansion of the overall program. In 1949, an enclosed, 1-million-liter steel test sphere was built at Camp Detrick, and biological warfare explosive munitions tests with agents were begun (Figure 19-1).



**Fig. 19-1.** These workers are standing outside the “8-Ball,” a 1-million-liter sphere used for testing static aerosols of biological agent preparations during the United States’s offensive biological warfare program. The building enclosing the 8-Ball and its supporting infrastructure were destroyed by fire in 1974. The sphere remains today as a historical monument at Fort Detrick, Frederick, Maryland. Photograph: Public Affairs Office, Fort Detrick, Frederick, Md. circa 1968.

During the early 1950s, Major General George E. Armstrong, The U.S. Army Surgeon General (1951–1955) became concerned about medical defense issues. Lieutenant Colonel Abram S. Benenson, a medical officer from the Walter Reed Army Institute of Research, was appointed medical liaison with the biological warfare laboratories at Fort Detrick. A joint agreement was signed, and beginning in 1953, studies on medical defense against biological weapons were conducted cooperatively by the Chemical Corps and the U.S. Army Medical Department. In 1954, a congressionally approved medical volunteer program, designated “Project Whitecoat,” was established after a series of meetings with representatives of the General Conference of the Seventh-Day Adventist Church and The Surgeon General, U.S. Army.

## Field Testing in the United States

The Korean War, which began in June 1950, added justification for continuing the biological warfare program, when the possible entry of the Soviet Union into the war was feared. Concerns over the Soviet Union were justified, for the Soviet Union would pronounce in 1956 that chemical and biological weapons would, indeed, be used for mass destruction in future wars.<sup>9</sup> In October 1950, the secretary of defense approved continuation of the program, based largely on the Soviet threat and a belief that the North Korean and Chinese communists would use biological weapons.<sup>10</sup>

The first large-scale aerosol vulnerability test was conducted in the San Francisco Bay area in September 1950, using two species of bacteria (*Bacillus globigii* and *Serratia marcescens*) and fluorescent particles. Various *Bacillus* species were used in many experiments because of their spore-forming capabilities and their similarities to *Bacillus anthracis*. *S. marcescens* was used because its red pigment made it readily identifiable. What was unexpected was the increased number of cases of *Serratia* infections over the next few years in communities that had been sprayed earlier with the organisms.<sup>4</sup> The military considered the situations coincidental, but many civilian physicians believed them to be directly related. Other limited-scale field tests with pathogenic organisms were conducted at Dugway Proving Ground, Utah. Antianimal studies were conducted at Eglin Air Force Base, Florida.

The biological warfare research facilities at Camp Detrick were expanded, and a biological warfare production facility was created at Pine Bluff Arsenal, Arkansas, in 1951. The first limited, biological warfare retaliatory capability was achieved when an anticrop bomb was developed, tested, and placed in production for the U.S. Air Force. Anticrop-agent production sites were carefully selected for safety with the coordination and approval of the U.S. Department of Agriculture. This marked the first peacetime biological weapons production by the United States.<sup>11</sup>

By 1954, the Pine Bluff laboratory produced *Brucella suis* (the causative agent of brucellosis, also called undulant fever) and *Francisella tularensis* (tularemia, or rabbit fever). Hardware for antipersonnel biological cluster bombs was delivered to Pine Bluff for filling with *Brucella suis* to support air force requirements. By 1955, the accelerated program was producing stocks of *B. suis* and *F. tularensis* as bio-

logical warfare agents. While many of the efforts involved military researchers, others from the Public Health Service, other Federal departmental agencies, and civilian scientific institutions were also involved in the research.

The general public was uninformed of these ongoing studies, especially the environmental and open-air experiments that were being conducted. A controversial environmental test occurred in 1951, when army researchers deliberately exposed a disproportionate number of black citizens to the fungus *Aspergillus fumigatus*, to see if African Americans were more susceptible to such infection, like they were already known to be to coccidioidomycosis (*Coccidioides immitis*). Some in the scientific community believed that such knowledge would assist in preparing defenses against a more virulent form of this fungus. Similarly, in 1951, unsuspecting workers at the Norfolk Supply Center, Norfolk, Virginia, were exposed to crates contaminated with *A. fumigatus* spores.

Needless to say, there was a public outcry several years later when much of this information was released, and the biological warfare research program would be forever tainted as operating within "clouds of secrecy."<sup>4</sup> The first lawsuit against the U.S. government was filed by family members of an individual who had died, allegedly as a result of the San Francisco experiments in 1950. The court decided that the U.S. government could not be sued (under the Federal Tort Claims Act), since the decision to spray *S. marcescens* was a part of national defense planning. Several of the organisms (such as *S. marcescens* and *A. fumigatus*), which were considered at one time to be innocuous, are now recognized to cause infections in humans, on occasion. Immunocompromised or debilitated persons appear to be at greatest risk. Early experiments conducted with such organisms involving subjects or populations who were unaware of the ongoing experiments may have posed a health risk to highly susceptible persons.

During the two decades following the second World War, laboratories for biological and chemical warfare research continued to increase in size, and programs were expanded with a multi-million dollar budget. The Fort Detrick research program was complemented by contractual civilian institutions; for example, Ohio State University was tasked with making vaccines. Human volunteers were used in many of the studies. Vaccines against diseases, such as Q fever and tularemia, were developed.

## AN EXPANDED DEFENSE PROGRAM

With expansion of the biological warfare retaliatory program, the scope of the defensive program was nearly doubled. Data were obtained on personnel protection, decontamination, and immunization. Early detection research produced prototype alarms for use on the battlefield, but progress was slow, apparently limited by technology.

The U.S. Army Medical Unit, under the direction of The U.S. Army Surgeon General, began formal operations in 1956. One of the Unit's first missions was to manage all aspects of Project CD-22, the exposure of volunteers to aerosols containing a pathogenic strain of *Coxiella burnetii*, the etiologic agent of Q fever. The volunteers were closely monitored and antibiotic therapy was administered when appropriate. All volunteers recovered from Q fever with no adverse aftereffects. One year later, the Unit submitted to the U.S. Food and Drug Administration an Investigational New Drug application for a Q fever vaccine.

The United States was now accumulating invaluable data on personnel protection, decontamination, and immunization; and, in the offensive program, on the potential for mosquitoes to be used as biological vectors. A new Department of Defense Biological and Chemical Defense Planning Board was created in 1960 to establish program priorities and objectives. Preventive approaches toward infections of all kinds were funded under the auspices of biological warfare. As concern increased over the biological warfare threat during the Cold War, so did the budget for the program: to \$38 million by fiscal year 1966.

The U.S. Army Chemical Corps was given the responsibility to conduct biological warfare research for all of the services.<sup>3</sup> In 1962, the responsibility for the testing of promising biological warfare agents was given to a separate Testing and Evaluation Command. Depending on the particular program, different test centers were used, such as the Deseret Test Center at Fort Douglas, Utah, the headquarters for the new biological and chemical warfare testing organization. In response to increasing concerns over public safety and the environment, the Testing and Development Command implemented a complex system of approval of its research programs that included the U.S. Army Chief of Staff, the Joint Chiefs of Staff, the Secretary of Defense, and the President of the United States.

During the last 10 years of the offensive research and development program, many scientific advances were made that proved that biological warfare was clearly feasible, although dependent on careful planning, especially with regard to meteorological conditions. Large-scale fermentation, purification, concentration, stabilization, drying, and weaponization of pathogenic microorganisms could be done safely. Furthermore, modern principles of biosafety and containment were established at Fort Detrick that have greatly facilitated biomedical research; still today, these are copied throughout the world. Arnold G. Wedum, M.D., Ph.D., a civilian scientist who was Director of Industrial Health and Safety at Fort Detrick, was the leader in the development of containment facilities (Figure 19-2).



**Fig. 19-2.** Technicians in Class III hood lines are seen working with preparations of biological agents at Fort Detrick, Frederick, Maryland, circa 1968, when the United States had an offensive biological warfare program. The completely enclosed hood lines provide total containment of hazardous organisms. Hoods were maintained at a pressure negative to ambient by constantly drawing air out through high-efficiency particulate air (HEPA) filters. Workers wore heavy rubber gloves to access material inside the hoods. Photograph: Public Affairs Office, Fort Detrick, Frederick, Md.

During the 1960s, the country experienced a philosophical change, and attention was now directed toward biological agents that could incapacitate but not kill. In 1964, research programs involved staphylococcal enterotoxins capable of causing food poisoning. Research initiatives also included new therapy and prophylaxis. Pathogens studied included the agents causing anthrax, glanders, brucellosis, melioidosis, plague, psittacosis, Venezuelan equine encephalitis, Q fever, coccidioidomycosis, and a variety of plant and animal pathogens.<sup>10,12</sup>

Particular attention was directed at chemical and biological detectors during the 1960s. The first devices were primitive field alarms to detect chemicals. Although the development of sensitive biological warfare agent detectors was at a standstill, two systems were, nonetheless, investigated. The first was a monitor that detected increases in the number of particles sized 1 to 5  $\mu\text{m}$  in diameter, based on the assumption that a biological agent attack would include airborne particles of this size. The second system involved the selective staining of particles collected from the air. Both systems lacked enough specificity and sensitivity to be of any practical use.<sup>8</sup>

But in 1966, a research effort directed at detecting the presence of adenosine triphosphate (a chemical found only in living organisms) was begun. By using a fluorescent material found in fireflies, preliminary studies indicated that it was possible to detect the presence of a biological agent in the atmosphere. The important effort to find a satisfactory detection system continues today, for timely detection of a biological attack would allow the attacked force to use its protective masks effectively, and identification of the agent would allow any pretreatment regimens to be instituted.

The army also experimented with and developed highly effective barrier protective measures against both chemical and biological agents. Special impervious tents and personal protective equipment were developed, including individual gas masks even for military dogs.

During the late 1960s, funding for the biological warfare program decreased temporarily, to make up for the accelerating costs of the Vietnam War. The budget for fiscal year 1969 was \$31 million, decreasing

to \$11.8 million by fiscal year 1973. Although the offensive program had been stopped in 1969, both offensive and defensive programs continued to be defended. John S. Foster, Director of Defense Research and Engineering, responded to a query by Congressman Richard D. McCarthy:

It is the policy of the U.S. to develop and maintain a defensive chemical-biological (CB) capability so that our military forces could operate for some period of time in a toxic environment, if necessary; to develop and maintain a limited offensive capability in order to deter all use of CB weapons by the threat of retaliation in kind; and to continue a program of research and development in this area to minimize the possibility of technological surprise.<sup>13(pp153-154)</sup>

On 25 November 1969, President Nixon visited Fort Detrick to announce a new policy on biological warfare. In two National Security Memoranda,<sup>14,15</sup> the U.S. government renounced all development, production, and stockpiling of biological weapons and declared its intent to maintain only small research quantities of biological agents, such as are necessary for the development of vaccines, drugs, and diagnostics.

Ground was broken in 1967 for construction of a new, modern laboratory building at Fort Detrick. The building would open in phases during 1971 and 1972. With the disestablishment of the biological warfare laboratories, the name of the U.S. Army Medical Unit, which was to have been housed in the new laboratories, was formally changed to U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) in 1969. The institute's new mission was stated in General Order 137, 10 November 1971 (since superseded):

Conducts studies related to medical defensive aspects of biological agents of military importance and develops appropriate biological protective measures, diagnostic procedures and therapeutic methods.<sup>16</sup>

The emphasis shifted away from offensive weapons to development of vaccines, diagnostic systems, personal protection, chemoprophylaxis, and rapid detection systems.

## A COMPREHENSIVE MEDICAL BIOLOGICAL DEFENSE PROGRAM

In response to President Nixon's decision in 1969, all antipersonnel biological warfare stocks were destroyed between 10 May 1971 and 1 May 1972. The

laboratory at Pine Bluff Arsenal, Arkansas, was converted to a toxicological research laboratory, and was no longer under the direction or control of the

Department of Defense. Biological anticrop agents were destroyed by February 1973. Biological warfare demilitarization continued through the 1970s, with input provided by the U.S. Department of Health, Education and Welfare; Department of the Interior; Department of Agriculture; and the Environmental Protection Agency. Fort Detrick and other installations involved in the biological warfare program took on new identities, and their missions were changed to biological defense and the development of medical countermeasures. The necessary containment capability, Biosafety Levels 3 and 4 (BL-3 and BL-4, which are discussed below) continued to be maintained at USAMRIID.

In 1984, the Department of Defense requested funds for the construction of another biological aerosol test facility in Utah. The proposal submitted by the army called for BL-4 containment, although maintaining that the BL-4 inclusion was based on a possible need in the future and not on a current research effort. The proposal was not well received in Utah, where many citizens and government officials still recalled the secretive projects of the military: the areas on Dugway Proving Ground still contaminated with anthrax spores, and the well-publicized accidental chemical poisoning of a flock of sheep in Skull Valley, Utah, in March 1968.<sup>10</sup> Questions arose over the safety of the employees and the surrounding communities, and a suggestion was even made to shift all biological defense research to a civilian agency, such as the National Institutes of Health. The plan for a new facility was revised to utilize a Biosafety Level 3 (BL-3) facility, but not before congress had instituted more surveillance, reporting, and control measures on the army to ensure compliance with the Biological Weapons Convention of 1972.

### Safety in Research and Patient Care

Currently, the medical biological defense research effort (part of the U.S. Army's Biological Defense Research Program [BDRP]) is concentrated at USAMRIID at Fort Detrick. The army maintains state-of-the-art containment laboratory facilities at USAMRIID, with more than 10,000 ft<sup>2</sup> of BL-4 and 50,000 ft<sup>2</sup> of BL-3 laboratory space. BL-4, the highest containment level, includes laboratory suites that are isolated by internal walls and protected by rigorous entry restrictions, air-locks, negative-pressure air-handling systems, and filtration of all out-flow air through high-efficiency particulate air (HEPA) filters. Workers in BL-4 laboratories also

wear filtered positive-pressure total body suits, which isolate the worker from the internal air of the laboratory. BL-3 laboratories have a similar design, but do not require that personnel wear positive-pressure suits. Workers in BL-3 suites are protected immunologically by vaccines. U.S. governmental standards provide guidance as to which organisms may be handled under various containment levels in laboratories such as USAMRIID.<sup>17</sup>

The unique facilities available at USAMRIID also include a 16-bed clinical research ward capable of BL-3 containment, and a 2-bed patient care isolation suite where ICU-level care can be provided under BL-4 containment. Here, healthcare personnel wear the same positive-pressure suits as are worn in BL-4 research laboratories. The level of patient isolation required depends on the infecting organism and the risk to healthcare providers. Patient care can be provided at BL-4. There is no patient-care category analogous to BL-3; humans who are ill as a result of exposure to BL-3 agents are cared for in an ordinary hospital room with barrier nursing procedures.

USAMRIID guidelines have been prepared to determine which level of containment should be employed for individual patients who require BL-4 isolation or barrier nursing care (Exhibit 19-1). Staff augmentation for BL-4 critical care expertise comes from Walter Reed Army Medical Center, Washington, D.C., under an existing Memorandum of Agreement. Patients can be brought directly into the BL-4 suite from the outside through specialized ports with unique patient-isolation equipment.

Finally, USAMRIID maintains a unique evacuation capability called the Aeromedical Isolation Team (AIT). Led by a physician and a registered nurse, each of the two teams consists of eight volunteers who train intensively to provide an evacuation capability for casualties suspected of being infected with highly transmissible, life-threatening BL-4 infectious diseases (eg, hemorrhagic fever viruses). The unit uses special adult-sized Vickers isolation units (Vickers Medical Containment Stretcher Transit Isolator, manufactured by Isolators Ltd., Shropshire, U.K.) (Figure 19-3). These units are aircraft transportable and isolate a patient placed inside from the external environment. The AIT can transport two patients simultaneously; obviously, it is not designed for a mass casualty situation. During the 1995 outbreak of Ebola fever in Zaire, the AIT remained on alert to evacuate any Americans who might have become ill while working to control the disease in that country.

**EXHIBIT 19-1**

**ISOLATION PROCEDURES FOR PATIENT CARE AT USAMRIID, BY DISEASE AGENT OR TYPE OF EXPOSURE**

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Biosafety Level 4 (BL-4) isolation suite admission; care providers in positive-pressure protective suits

Ebola virus

Marburg virus

Crimean-Congo hemorrhagic fever virus

Variola (smallpox) and monkeypox viruses

**A patient presumed to be a victim of biological agent attack until definitive diagnosis is made**

Biosafety Level 4 (BL-4) isolation suite admission; barrier nursing procedures\*

*Yersinia pestis* (pneumonic form)<sup>†</sup>

Lassa fever virus

Argentine hemorrhagic fever (Junin) virus

Bolivian hemorrhagic fever (Machupo) virus

Venezuelan hemorrhagic fever (Guanarito) virus

Normal hospital room; barrier nursing procedures\* or secretion precautions,<sup>‡</sup> depending on the agent

Tick-borne encephalitis complex

Yellow fever virus<sup>§</sup>

Venezuelan equine encephalitis virus<sup>§</sup>

Rift Valley fever virus<sup>§</sup>

Chikungunya virus<sup>§</sup>

Dengue virus<sup>§</sup>

*Brucella* species

*Vibrio cholerae*

*Bacillus anthracis* (pulmonary or cutaneous forms)

*Francisella tularensis* (pulmonary form)

*Yersinia pestis* (bubonic or septicemic form)

Normal hospital room; no special precautions

Eastern equine encephalitis virus

Western equine encephalitis virus

Hemorrhagic fever with renal syndrome (Hantaan, Seoul, Puumala viruses)

Japanese encephalitis virus

Sandfly fever viruses

*Coxiella burnetii* (Q fever)

*Chlamydia psittaci*

Botulinum toxin

Staphylococcal enterotoxin B

Ricin toxin

Saxitoxin

Trichothecene mycotoxins

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\*Barrier nursing procedures: wearing gown, gloves, and surgical mask, but caring for patients in isolation suites.

<sup>†</sup>Pneumonic plague initially requires respiratory protection: full-face respirator or Racal hood (manufactured by Racal Health and Safety, Inc, Frederick, Md).

<sup>‡</sup>Secretion precautions: wearing gown and gloves; special handling of potentially infectious dressings, drainage, and/or excreta.

<sup>§</sup>The patient must be protected from potential arthropod vectors: windows should be screened and/or closed.

USAMRIID: U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Md.



**Fig. 19-3.** Members of the Aeromedical Isolation Team (AIT) prepare to transfer a patient from a stretcher isolator into the Biosafety Level 4 (BL-4) isolation suite at the U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland. The interior of the isolator is maintained at a pressure negative to the external environment by a high-efficiency particulate air (HEPA) filtered blower. The isolator can be attached directly to a transfer port, visible on the external wall of the building, to allow movement of the patient into the suite without exposing the environment to the patient. Team members are seen wearing protective suits and positive-pressure, HEPA-filtered Racal hoods (manufactured by Racal Health & Safety, Inc, Frederick, Md). Photograph: Public Affairs Office, Fort Detrick, Frederick, Md.

Some biological defense research also continues at the U.S. Army Medical Research Institute of Chemical Defense, Edgewood Arsenal, Maryland, and the Walter Reed Army Institute of Research, Washington, D. C. USAMRIID and these laboratories conduct basic research in support of the medical component of the Biological Defense Research Program, which develops strategies, products, information, procedures, and training for medical defense against biological warfare agents. The products include diagnostic reagents and procedures, drugs, vaccines, toxoids, and antitoxins. Emphasis is placed on protecting personnel *before* any potential exposure to the biological agent occurs.<sup>18</sup>

#### A National Resource

Since biological warfare agents are often etiologic agents for naturally occurring diseases, the military research effort provides substantive benefits for civilian populations also. Products produced or being developed through military research include

- vaccines to prevent tularemia, Q fever, Rift Valley fever, Venezuelan equine encephalitis, Eastern and Western equine encephalitis, chikungunya fever, Argentine hemorrhagic fever, the botulinum toxicoses, and anthrax;<sup>18,19</sup>
- antitoxins for diseases such as botulism;
- human immune globulin preparations (passive antibody protection) against various bacteria and viruses; and

- antiviral drugs against multiple viral agents.

Some vaccines also have applicability for diseases of domestic animals (eg, Rift Valley fever and Venezuelan equine encephalitis). In addition, vaccines are provided to persons who may be occupationally exposed to such agents (eg, laboratory workers, entomologists, and veterinary personnel) throughout government, industry, and academe.

USAMRIID also provides diagnostic and epidemiological support to federal, state, and local agencies and foreign governments. Examples of assistance rendered to civilian health efforts by the former U.S. Army Medical Research and Development Command (renamed the U.S. Army Medical Research and Materiel Command in October 1994) include

- the massive immunization program instituted during the Venezuelan equine encephalitis outbreak in the Americas in 1971;
- the laboratory support provided to the U.S. Public Health Service during the outbreak of Legionnaire's disease in Philadelphia, Pennsylvania, in 1976;
- the management of patients suspected of having African viral hemorrhagic fever in Sweden during the 1980s;
- international support during the outbreak of Rift Valley fever in Mauritania in 1989;
- assistance with the outbreak of Ebola infections among monkeys imported to Reston, Virginia, in 1990; and

- epidemiological and diagnostic support to the World Health Organization–Centers for Disease Control and Prevention field team that studied the Ebola outbreak in Zaire in 1995.

The current research effort combines new technological advances, such as genetic engineering and molecular modeling, applying them toward development of prevention and treatment of diseases of military significance. The program is conducted in full compliance with requirements set forth by the U.S. Food and Drug Administration, U.S. Public Health Service, Nuclear Regulatory Commission, U.S. Department of Agriculture, Occupational Safety and Health Administration, and Biological Weapons Convention.<sup>18</sup>

Even though the United States stopped all offensive biological warfare research in 1969, the Biological Defense Research Program must remain strong

in view of

- evidence that some countries are not complying with the Biological Weapons Convention;
- the difficulty of verifying compliance with the Convention;
- the potential use of biological warfare by terrorists;
- the increased possibility of new threat agents based on advances in biotechnology; and
- the belief that a strong defense serves as a deterrent.

While some of the military's biological defense programs remain classified, based on worldwide threats and uncertainties, the medical Biological Defense Research Program is unclassified and continues to be an invaluable resource for the nation.

## SUMMARY

Although biological agents have been used in warfare for centuries to produce death or disease in humans, animals, or plants, the United States did not begin a biological warfare offensive program until 1941. It was concern about the Japanese biological warfare threat that motivated the United States to begin to develop biological weapons. During the next 28 years, the United States initiative evolved into an effective, military-driven research and acquisition program, shrouded in controversy and secrecy. Most research and development was done at Fort Detrick, Maryland, while production and testing occurred at Pine Bluff, Arkansas, and Dugway Proving Ground, Utah. Field testing was done secretly and successfully with simulants and

actual agents disseminated over wide areas. A small defensive effort paralleled the weapons development and production program.

With the presidential decision in 1969 to halt offensive biological weapons production, and the agreement in 1972 at the international Biological Weapons Convention never to develop, produce, stockpile, or retain biological agents or toxins, the program became entirely defensive, with medical and nonmedical components. The U.S. Biological Defense Research Program exists today, conducting research to develop physical and medical countermeasures to protect service members and civilians from the threat of modern biological warfare.

## REFERENCES

1. Fox LA. Bacterial warfare: The use of biologic agents in warfare. *Milit Surg.* 1933;72(3):189–207.
2. Bernstein BJ. The birth of the US biological-warfare program. *Sci Am.* 1987;256:116–121.
3. Department of the Army. Special Report to Congress. *US Army Activity in the US Biological Warfare Programs, 1942–1977.* Vols 1 and 2. Washington, DC: DA. 24 Feb 1977. Unclassified.
4. Cole LA. *Clouds of Secrecy: The Army's Germ Warfare Tests Over Populated Areas.* Totowa, NJ: Rowman and Littlefield; 1988.
5. Williams P, Wallace D. *Unit 731: Japan's Secret Biological Warfare in World War II.* New York, NY: Free Press; 1989.

6. Report to the Secretary of War by Mr. George W. Merck, Special Consultant for Biological Warfare, 3 Jan 1946. Cited in: Department of the Army. Special Report to Congress. *US Army Activity in the US Biological Warfare Programs, 1942–1977*. Vol 2, annex 1. Washington, DC: DA. 24 Feb 1977. Unclassified.
7. Baldwin IL. *Special BW Operations*. Washington, DC: The National Military Establishment Research and Development Board; 5 Oct 1948. Memorandum for Executive Secretary, Research and Development Board. Unclassified.
8. Hersh SM. *Chemical and Biological Warfare: America's Hidden Arsenal*. Indianapolis, Ind: Bobbs-Merrill; 1968.
9. Geissler E, ed. *Biological and Toxin Weapons Today* (Stockholm International Peace Research Institute). Oxford, England: Oxford University Press; 1986.
10. Harris R, Paxman J. *A Higher Form of Killing: The Secret of Chemical and Biological Warfare*. New York, NY: Hill and Wang; 1982.
11. Cowdrey AE. *The Medics' War*. Washington DC: Center of Military History, US Army; 1987.
12. Stockholm International Peace Research Institute (SIPRI). *The Rise of CB Weapons*. Vol 1. In: *The Problem of Chemical and Biological Warfare*. New York, NY: Humanities Press; 1971.
13. Foster JS, Director of Defense Research and Engineering, US Department of Defense. Letter dated 15 April 1965 to Honorable Richard D. McCarthy, US House of Representatives. Cited in: McCarthy RD. *The Ultimate Folly: War by Pestilence, Asphyxiation, and Defoliation*. New York, NY: Alfred A. Knopf; 1969: 153–154.
14. Kissinger HA. N.S. Decision Memorandum 35. 25 November 1969.
15. Kissinger HA. N.S. Decision Memorandum 44. 20 February 1970.
16. Department of the Army. General Order 137. Washington, DC: Headquarters, DA; 10 November 1971.
17. Centers for Disease Control and Prevention. *Biosafety in Microbiological and Biomedical Laboratories*. 3rd ed. Washington, DC: US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. May 1993. HHS Publication (CDC) 93-8395.
18. Huxsoll DL, Parrott CD, Patrick WC III. Medicine in defense against biological warfare. *JAMA*. 1989;265:677–679.
19. Takafuji ET, Russell PK. Military immunizations: Past, present and future prospects. *Infect Dis Clin North Am*. 1990;4:143–157.