GERM WARS

Beset by controversy, the U.S. military is using genetic engineering to design defenses against biological weapons

By MELISSA HENDRICKS

In 17 years as an Army virologist at Fort Detrick in Frederick, Md., Neil Levitt found his work a risky business. On several occasions, he says, his supervisors issued him a gas mask to screen out toxic fumes emitted by a faulty ventilation system. In another incident, he recalls, a malfunctioning exhaust hood blew radioactive iodine onto his face. And once he discovered that several liters of a debilitating virus had inexplicably disappeared from a lab freezer.

Levitt, who worked for the Department of Defense's Biological Defense Research Program (BDRP), says he repeatedly asked officials overseeing his work to investigate the safety violations. But the Army denied some of his requests and ignored others, he says, leading him to resign in 1986. With the Foundation on Economic Trends, a Washington, D.C.-based environmental action organization, Levitt sued the Department of Defense (DOD) for violating national environmental law. In an out-of-court settlement of that suit, the DOD agreed to conduct environmental impact studies of its biological warfare research facilities (SN: 2/28/87, p.132).

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— 1987 report to Army by scientific advisers assessing BDRP

Levitt's lawsuit helped spotlight and expand a long-running but largely low-key controversy among some biological scientists over military germ research. While the upfront issues center on safety, larger questions of national defense and international relations are so intertwined in the dispute they seem almost inseparable.

Critics of the BDRP contend that "accidents waiting to happen" at DOD-funded laboratories require a revamping of the nation's biological warfare program. Inadequate safety enforcement risks the well-being of scientists in the labs and of residents living nearby, they argue. But behind the immediate personal fears and concerns for public health, they acknowledge, lie more complex issues of national security and international treaty.

In the preliminary draft of its environmental impact statement on the overall BDRP, forced by Levitt's suit and released in January 1988, the DOD says the program poses no significant risks to researchers or the public; falls within the allowances of the 1972 Biological Weapons Convention treaty; and represents a vital defense against potential biological warfare threats. While information concerning those threats is classified, Army science advisers stated in a report issued last year that "there is reason to believe that at least one nation, USSR, continued the development of an offensive biological weapons capability after signing the treaty."

The Biological Weapons Convention treaty, signed by 111 nations including the United States and the Soviet Union, prohibits the development, production and stockpiling of biological weapons except for defensive purposes. However, it "does not preclude research into those offensive aspects of biological agents necessary to determine what defensive measures are required," according to a 1969 statement issued by then-National Security Adviser Henry Kissinger.

This exception troubles Levitt and others, who view offensive and defensive research as indistinguishable, says Jay Jacobson, an infectious-disease specialist and epidemiologist at the University of Utah School of Medicine in Salt Lake City: "It's like testing a vest against bullets. You first need to have the bullets." Intensifying complaints by critics in recent years has been the BDRP's use of genetic engineering—a technology unanticipated by the drafters of the treaty. Molecular biologist Keith Yamamoto of the University of California, San Francisco, notes that scientists can now create microorganisms that can cause deadly diseases for which no cures exist. "Using gene cloning destroys the distinction between offense and defense, and gives a loophole in the 1972 treaty," Yamamoto says.

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— epidemiologist and BDRP critic Jay Jacobson

Senate subcommittee hearings this past summer evaluated the safety of biological and chemical warfare research facilities. Testimony included Levitt's and that of Jeremy Rifkin, director of the Foundation on Economic Trends. Rifkin, best known for his outspoken opposition to genetic engineering, accused the DOD of failing to update safety policies as it expanded its budget for research on disease-causing organisms from about $16 million in 1980 to about $90 million in 1986.

The biological weapons issue has sparked debate in other political, scien-

tific and public circles. During the past few years, the Army has sought to scale up its biological warfare research facility at the Dugway (Utah) Proving Grounds. But nearby residents have protested the facility ever since the Army accidentally released nerve chemicals there in 1968, killing thousands of sheep. Following a lawsuit filed against the DOD by Rifkin, the Army agreed earlier this year to back down on its plans for expanding the facility. Moreover, more than 600 biological researchers have signed pledges to refuse DOD funds for their work, and a bill is pending in Congress to implement the Biological Weapons Convention treaty as U.S. law. Supporters contend a domestic law would be more effective at deterring violators than the existing treaty.

Biological weapons existed for centuries prior to the 1972 treaty. The Greeks and Romans poisoned drinking water with decaying corpses 2,000 years ago. During World War II, the Japanese experimented on prisoners of war with plague, anthrax, smallpox and other diseases. But not until this decade have scientists gained the capacity to design novel biological weapons surreptitiously and with ease. The nature of

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— molecular biologist and BDRP opponent Keith Yamamoto

genetic engineering makes it almost impossible for one nation to verify whether another is complying with the treaty, says Col. David Huxsoll, Commander of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick, the BDRP's leading medical research facility. He and other military planners say the United States must defend against the possibility of terrorists or hostile nations manipulating genes to build weapons.

The military says its strategy is to defend against as many perceived threats as possible. For example, DOD-sponsored scientists are seeking defenses against viruses that cause yellow fever, Rift Valley fever, Korean hemorrhagic fever and dengue fever; bacteria causing botulism, anthrax and plague; various snake-venom and animal toxins; and several parasitic organisms. The plans call for the development of drugs and vaccines capable of deterring several related biological weapons rather than only a single agent. One way to do this, says Leonard Smith of USAMRIID, is to find a common means of attack shared by a group of agents and to learn which proteins participate in the attack. Then, the theory goes, scientists could create a vaccine designed to make the body produce antibodies against those common proteins. Investigating a dozen toxins from several snake species, Smith has found several that appear to target a single protein at the junction where nerve signals are transmitted between cells. "This provides hope for finding a single vaccine against several different toxins," he says.

In similar work, John Middlebrook of USAMRIID has examined several related bacterial and snake-venom toxins to find a common "neutralizing epitope," a section of a toxin protein at which an antibody can block the toxin's activity. Among 14 or 15 different toxins studied so far, he has identified one antibody that neutralizes as many as four different toxins.

Parallel efforts in virology seek to create vaccines against several different genetic varieties of one virus. Joel Dalrymple of USAMRIID is attempting to improve the existing vaccine against the virus causing Rift Valley fever, a disease common in sub-Saharan Africa and spread to humans by mosquitoes. The vaccine now routinely given to U.S. military personnel has drawbacks: It is expensive, requires three injections and may not work against all 33 to 38 varieties of the virus. Dalrymple and his co-workers have identified two proteins in the virus' outer coat, one of which, G2, appears to induce immunity in mice. They are now producing antibodies to various pieces of G2 to see which best protect the mice against Rift Valley fever. The researchers hope that cloning the genes coding for those protein segments will lead to a more effective vaccine.

Still another technique uses a harmless "carrier" virus to transport into the human body immunity-inducing pieces from the protein coats of several different viruses. As a first step in building such a "polyvalent" vaccine, Dalrymple is examining the alphaviruses, which can cause fever, arthritis and death, and are found mostly outside of the United States. He is focusing on three different species of alphavirus to determine which genes to include in the polyvalent vaccine.

If successful, such efforts could benefit civilians as well as the Armed Forces. But skeptics contend the military's research goals are unrealistic. Even if BDRP scientists produced a vaccine effective against many different viruses, they say, enemy scientists could mutate an agent's genes to create an entirely new organism against which the drug or vaccine would not work. "Nature does this herself: A virus changes its clothes and comes back wearing a different coat," notes Yamamoto. "The military cannot make an infinite number of vaccines to an infinite number of agents."

BDRP scientists maintain that their goals, though far off, are attainable. "I won't accept the criticism that the number of viruses out there is overwhelming and too numerous to make a vaccine," Dalrymple says. "It is possible to make a vaccine against all alphaviruses causing human disease." He won't stop making vaccines against single strains of alphavirus while waiting for this to happen, he adds.

In more basic research, DOD-supported scientists seek to identify which proteins and genes of various biological agents are responsible for causing disease symptoms, and which might be prime targets for drugs and vaccines. Lt. Col. Martin Crumrine of

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— BDRP biochemist Donald Robertson

USAMRIID, Donald Robertson of Brigham Young University in Provo, Utah, and their collaborators are studying *Bacillus anthracis,* the bacterium that causes anthrax. Anthrax is endemic in parts of Africa and elsewhere, but only a few cases of the disease occur each year in the United States, usually in workers who contract it from woolly animals such as sheep or goats. Anthrax symptoms include skin ulcers, gastrointestinal pains and severe and sometimes fatal pneumonia.

Bacillus anthracis produces three toxin proteins. The existing vaccine contains one of the proteins, called protective antigen, which induces antibody production in the immunized host but is slow to take effect and requires repeated immunizations. Crumrine has cloned the protective antigen gene into *Escherichia coli* and *Bacillus subtilus* bacteria. If all goes well, he says, the bacteria will produce large quantities of protective antigen in a form suitable for use as a vaccine, which should be easier to produce and should work better than the existing vaccine. His

preliminary experiments indicate that the protective antigen produced by *B. subtilus* protects guinea pigs against anthrax without harming the animals.

Using a different strategy, Robertson is selectively mutating *B. anthracis* genes. He hopes to destroy the toxicity but not the overall chemical structure of the proteins for which the genes code. The resulting mutated and harmless bacteria, when used as a vaccine, would "fool" the human immune system into beefing up its defenses against *B. anthracis*. "Compare the recombinant anthrax protein to a car with its motor removed," Robertson explains. "The car lacking a motor looks identical to a car with a motor, but it does not run."

Although Robertson's and Crumrine's methods are essentially those used by molecular biologists to create vaccines against influenza, the AIDS virus, hepatitis B and other infectious agents, there are those who oppose military sponsorship of such studies. Critics say the knowledge acquired through such research – better understanding of a bacterium's genetic makeup, the function of each piece of each gene, its preferred growing conditions and ways to clone and produce its toxins – could be used to produce toxic proteins of a more dangerous nature.

"By separating and distinguishing parts of the molecule that make it infectious from the antibody-causing parts, scientists could make toxins that would have no antibody-eliciting section," Yamamoto says. Agents altered in this way could be used only offensively, he contends.

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Another factor troubling some people is that the basic research often involves the transfer of hazardous genes into genetically altered varieties of bacteria that live naturally in humans. Microbiologist Richard Novick, director of the Public Health Research Institute in New York City, says he "could see how this research could easily be perverted to build incapacitating agents." Novick, a civilian scientist, in the 1960s refused a DOD proposal that he introduce penicillin-resistance genes into a pneumonia-causing bacterium. "This would have been a disservice to the human population," says Novick. In the early 1980s, he again turned down DOD funds, this time for his studies of *Staphylococcus* bacteria, whose toxins attack the human gut and are a leading cause of food poisoning.

Novick and Yamamoto describe scenarios in which recombinant DNA techniques could lead to the creation of more dangerous toxins. By linking one toxin gene onto another toxin gene, they say, scientists could form "double-edged toxins" that could injure a cell in two ways. For example, one toxin could poison a cell while a second toxin inactivates the cell's enzyme normally responsible for degrading the first toxin. They also envision scientists attaching a toxin to another protein whose job is penetrating certain cells, as a means of selectively poisoning those cells. Such "coupled toxins" already are being studied as a means of fighting cancer and AIDS (SN: 12/3/88, p.358).

Military scientists argue that their biological warfare research will not result in such frightening scenarios. They say they work at incapacitating potentially haz-

Activists target chemical weapons

Flushed with the success of its lawsuits against the Army's biological weapons programs, the Washington, D.C.-based Foundation on Economic Trends last week sued U.S. Department of Defense (DOD) officials in an effort to shut down the nation's chemical weapons program. The suit contends the DOD has failed to document the safety of its chemical warfare program as required by the National Environmental Policy Act. DOD's program includes basic research, production of new chemical weapons and dismantling of older ones.

Under the act's regulations, organizations performing activities that may significantly affect the environment must first prepare environmental impact statements. According to the Foundation's lawsuit, the military has failed to prepare such statements for its chemical warfare program.

This year marks the first since 1969 that the DOD has produced any new chemical weapons. But the budget for chemical warfare research has grown steadily in the past decade, and there is evidence that safety precautions have not kept pace. This past June, for example, an in-house assessment of chemical safety released by the Army's Inspector General found that "chemical safety has slipped through a crack." It says the Army "suffers from a lack of published policy guidelines, inadequate staffing, no systematic program of oversight, and a less than clear statement of chemical safety responsibilities."

A July 1988 report by the U.S. General Accounting Office further criticized the nation's chemical warfare program for its failure to take into consideration, when choosing research locations, such factors as environmental conditions at laboratory sites and proximity to residential areas or public facilities. It also noted "numerous deficiencies" in emergency plans for chemical accidents.

Many of the deficiencies noted in the Inspector General's report have been rectified, and others are being resolved, according to Army spokesman Maj. Richard Bridges. "We are going to do everything in our power to make sure our installations and the communities surrounding them are afforded the safest possible practices," Bridges says. "And we have no intention whatsoever of injuring the public or our soldiers, our most precious commodity."

He notes that staff positions have been filled and safety regulations are being drafted, adding that budget restrictions and attention to details have slowed implementation of some government recommendations. He declines to comment on specifics of the Foundation's lawsuit. However, he says, "I cannot say with 100 percent certainty that every single environmental impact statement that is required for every installation that the Army owns is complete, is current, is on file."

The Foundation's suit asks the U.S. District Court for the District of Columbia to halt all chemical weapons research and production pending completion of appropriate environmental statements. The suit also seeks to halt the dismantling of older, obsolete weapons – an ongoing process the Army plans to complete by 1994. Millions of pounds of nerve gas are stored near major airports, schools and shopping malls, according to legal documents the Foundation filed. The suit contends that without proper environmental assessments, the scheduled disposal may create an even greater hazard than does storage.

The DOD sponsors chemical weapons research at dozens of government and private institutions across the country. A total of 11 sites in Alabama, California, Illinois, Maryland, Missouri, New York, Ohio and Pennsylvania handle "neat," or full-strength, chemical warfare agents. Dozens of other facilities conduct research on dilute versions. – *R. Weiss*

ardous agents, rather than turning them into weapons. In defensive research, USAMRIID's Huxsoll explains, scientists look at a virus' chemical nature, its size and structure. They learn what it infects, how to cripple it and how to grow it in limited, laboratory quantities. On the other hand, he says, scientists making a weapon would look at how to stabilize the virus, make it more potent and disseminate it, and how to grow it in large quantities.

Military scientists add that biological defense research often ends up benefiting public health efforts in areas neglected by other research efforts. Michael Buchmeier of Scripps Clinic in La Jolla, Calif., a recipient of both DOD and National Institutes of Health funds for his research on the often deadly Lassa virus, says: "It is difficult to get money to study diseases such as Lassa fever. We've gone to major companies and been refused funds. One agency with a good track record is the Army." Buchmeier says Lassa fever is a substantial public health problem in African countries, such as Sierra Leone, where it accounts for approximately 30 percent of the hospital deaths and a substantial number of miscarriages.

Critics counter that such militarily supported research has other international consequences. Growing and working with biological agents within an Army-supported research facility not only draws the nation closer to using those agents as weapons, but also leads other countries to suspect the United States is performing offensive research, they argue.

"If the United States makes a vaccine against a biological warfare agent, it provokes other countries to make other biological weapons," Jacobson says. "This leads to an escalation of weapons, as is occurring in the nuclear arms race." Shifting the DOD's biomedical research to civilian agencies, such as the National Institutes of Health and the Centers for Disease Control, critics contend, would reduce what Rifkin terms a microbiological version of "missile-gap paranoia."

With such a dichotomy of opinions, a modified biological defense effort acceptable to both sides seems unlikely. However, at this summer's Senate hearings, subcommittee chairman Carl Levin and Army representatives agreed that DOD-sponsored laboratories should abide by the same safety guidelines as the National Institutes of Health and the Centers for Disease Control. Both critics and some biological warfare researchers are increasingly discussing the necessity of an open research program, a sort of "global defense," as Jacobson calls it.

Dalrymple explains why the military may support such a defense: "If I could build a vaccine and put it in the literature, it would be a deterrent to any evil person thinking to put out these agents as weapons."

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— BDRP virologist Joel Dalrymple

Biomedical ethicist Thomas Murray, of Case Western University School of Medicine in Cleveland, cites another reason for openness. He believes people are afraid of biotechnology because they are aware that groups or individuals with mixed motives might create dangerous organisms, or that well-meaning researchers might do so unintentionally. "Fears," he says, "are seriously exacerbated by secrecy." □

Letters

Fetal fracas

The use of fetal tissue ("Fetal Cells Enter the Fray," SN: 11/5/88, p.296) cannot be separated from the abortion, since without the abortion, the tissue and organs of that fetus would not be available to anyone else.

Using the sacrificed life of one human individual for the purpose of prolonging the life or treating an ailment of another has never been an accepted practice in medical science. This research lowers the dignity and standards of research.

Monte Harris Liebman, M.D.
Milwaukee, Wis.

Rick Weiss' report that researchers see no reason to waste a potentially beneficial resource (fetal tissue) that is obtained from a perfectly legal procedure (abortion) reminds me of German efficiency during the Second World War when they tried to alleviate a soap shortage by making soap from the bodies of victims of the Holocaust.

To carry the concept a little further, with the way meat prices are rising, why do we dispose of the bodies of accident victims? We are wasting human protein that could be put to a better use in feeding the hungry.

Julius Nadas
Chicago, Ill.

Perhaps women *should* be remunerated for the fetal tissue from their induced abortions. This would subsidize the often prohibitive cost of the procedure while abetting research promising to soothe the physical woes of the flesh — positive consequences that may ease the trauma women associate with such a volatile issue.

John Colwell
Seattle, Wash.

The moral response to abortion is not to salvage cells but to save the lives of one truly precious natural resource, one truly oppressed minority group. Researchers can make do with spontaneous abortions and those necessary to save the mother's life; patience; and a generous conviction that another generation of biochemists and taxpayers must follow and sustain them.

David M. Williams
Ann Arbor, Mich.

The Bible, interesting sociomythological document that it is, has been construed by at least one sect to forbid blood transfusions. Arguments against fetal-tissue use based on the morality of abortion are on a par with such nonsense. In a nation that supposedly separates the religious establishment from the political process, the truly unethical element of the issue is the government's pandering to illogical minority pressure groups, thereby denying a possible medical treatment of great value to society as a whole.

Godfrey A. Sundmark
Bronx, N.Y.

Why did you turn an ethical debate centering on women over to men? Of a total 21 quotes, the speaker's gender was apparent in 18 cases. Of these, 14 were from men and only four were from women. The author of the piece was also male.

Barbara Mann
Toledo, Ohio

Your question might best be put to the National Institutes of Health, which included on its 21-member advisory panel only four women. As for my being male, I have no defense. — R. Weiss

Forgotten fossils

It seems the Society of Vertebrate Paleontology wishes to impose its own idea of fossil preservation ("NAS fossil report: Lacking backbone?" SN: 10/22/88, p.262). Probably the best way for a fossil specimen to disappear is for it to be collected by the paleontology lab of a large museum. Though excavated with the best of intentions, it is almost certain to be squirreled away with tens of thousands of other specimens. There, in the vast catacombs, it will rest in perpetual anonymity — undisturbed, unstudied, undisplayed and unremembered.

Jon M. Kramer
Director, Potomac Museum Group
Golden Valley, Minn.

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