

Chapter 18

MEDICAL ETHICS IN MILITARY BIOMEDICAL RESEARCH

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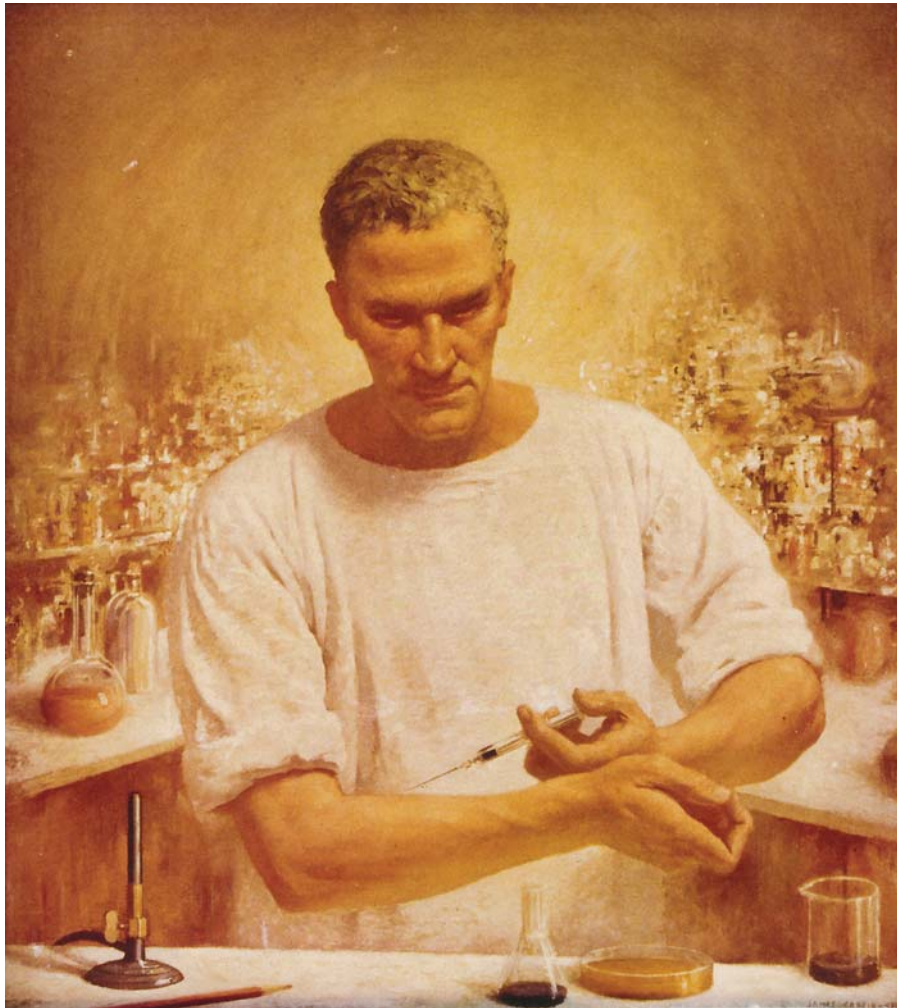
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J.O. Chapin

Research Heroic—The Self-Inoculation

1944

The sixth of seven images from the series *The Seven Ages of a Physician*. As the painting title implies, the physician-researcher, following the ethical guidelines of research, is willing to inoculate himself in the pursuit of scientific knowledge for the betterment of all patients.

Art: Courtesy of Novartis Pharmaceuticals.

INTRODUCTION

In his preface to *Principia Ethica*, Moore writes,

it appears to me that in ethics, as in all other philosophical studies, the difficulties and disagreements, of which history is full, are mainly due to a very simple cause: namely to attempt to answer questions without first discovering precisely what question it is which you desire to answer.^{1(pi)}

The “precise question” of this chapter has two parts: (1) is there an ethical justification for military biomedical research? and (2) if military biomedical research is an ethically legitimate enterprise, can military biomedical researchers conduct their work in an ethically responsible manner?

As Moore suggests, the question of whether military biomedical research is ethically legitimate has its own history of difficulties and disagreements. Although there is little challenge that an ethical basis for biomedical inquiry exists in general, the line of distinction is extremely thin between (a) legitimate and ethical biomedical military research and (b) nonmedical research activity causing some researchers extreme moral anxiety over what they call, “the militarization of the biomedical sciences.” Certain scientists see the need to protect the benevolent nature of biomedical science (reducing morbidity and mortality) by maintaining complete dissociation from military-sponsored biomedical research.² An argument for nonparticipation, based on various sources, is the focus of a main section of this chapter, as is a counterargument for participation that concentrates on the first part of the question—the moral legitimacy of military biomedical research.

By their very nature, military biomedical research programs appear to be ethically suspect.³ Even though military medicine enjoys a rich history of scientific advances in preventive medicine, the Society for Social Responsibility in Science, for example, advocates, “a tradition of personal moral responsibility for the consequences for humanity of professional activity...to ascertain the boundary between constructive and destructive work.”^{4(pp25–26)} The idea is that military biomedical research that is constructive, which I take to mean supports the goals and ideals of the healing tradition of medicine, is ethically legitimate. Military biomedical research that is destructive, contributing to harming or directly supporting the killing of human life, would be unethical. The ethical tension derives from trying to determine what biomedical research is constructive and what is destructive. One might

find, for example, no ethical objection to military biomedical researchers vaccinating soldiers to prevent them from dying of disease.⁵ Is it just as ethical for those same researchers to investigate the efficacy of chemical protective clothing, or combat helmets and body armor with the same end in mind, preventing harm to the soldier? This view begs a question of whether any military biomedical research can be constructive, even vaccine research dating to Walter Reed himself. Consequently, there are various groups who advocate that all military vaccine research and development be controlled by public health agencies to preserve the constructive nature of this research. The purpose would be to reduce the potential for ethical conflict among researchers and to limit destructive applications of the science.⁶ Arguments for distinguishing between offensive and defensive research will follow later in this text.

If there is an ethical distinction between constructive (defensive) and destructive (offensive) military biomedical research, there is a need to examine whether this research can be conducted in an ethically responsible manner. Protection of research subjects in military biomedical research is ethically essential. Currently, the Department of Defense (DoD) policy for the conduct and review of human subjects research, which applies to all elements of the DoD and to its contractors and grantees, upholds the protection of the fundamental rights, welfare, and dignity of human test subjects.^{5(p12)} Likewise, the DoD purports to adhere to the strictest guidelines regarding the use of animal models in its research and development programs.⁶ Animal protocols are subjected to layers of review at various command and service levels. While the entire subject of animal use remains under intense ethical scrutiny, the military seeks to be sensitive to the obligation of humane treatment of research animals and resolute in complying with all federal requirements for their care and use in biomedical research.

Finally, a discussion of the ethical conduct of military biomedical research needs to examine the efforts to expand scientific studies specific to the needs of military women. In the past, protocol designs have excluded military women for a variety of reasons. Now it is ethically essential to understand the reasons for the past exclusion of women and establish guidelines to alter the practices of the past. As the roles of military women expand, they will confront a host of new medical challenges. Re-

search efforts must look to address these new challenges to preserve and maintain the health and safety of military women.

In summary, this chapter will consider the ethical nature of military biomedical research to determine its moral legitimacy. If found to be an ethically legitimate enterprise, it then must consider the ethical obligations and responsibilities inherent to

conducting this research. The ethical tension in the first part of this question is profound. If there is no inherent moral legitimacy to conducting military biomedical research, that is to say, if all military biomedical research is destructive in nature, then no amount of ethical conduct, regulatory compliance, or open disclosure to the public can change the inherent immorality of the research.

THE NATURE OF MILITARY BIOMEDICAL RESEARCH

The nature of military biomedical research is linked to the objective of conducting research and development studies that address relevant and significant military-related problems.⁷ To be militarily significant, the research and development study must have immediate or long-range usefulness, as distinguished from the general advancement of knowledge of medicine. The requirement for the research to be militarily significant stems from the passage of the Mansfield Amendment in the 1970 military appropriations bill. The amendment required that the DoD only fund research that could solve military problems. The intent of this legislation has been stretched in recent years with the DoD budget containing funding for breast cancer research. Critics of the funding of military biomedical research point to this program as lacking a “direct and apparent relationship to a specific military function or operation.”^{7(p78)} Many scientists would prefer to be funded from sources other than the military and face personal ethical conflict about whether to apply for grant money from the military. This conflict aside for the moment, the Mansfield Amendment does place practical and ethical limitations on military biomedical research that opens the door to problematic, contentious, and serious ethical issues about its nature and conduct. Consequently, to better understand the ethical issues at stake, a brief description of the various military biomedical research programs is appropriate. Once the nature of these programs is understood, one can begin to determine the fundamental question of their moral legitimacy, clarify the constructive and destructive aspect of their applications, and develop an ethical construct for the conduct of this research.

Currently, military biomedical research comprises five major research areas: (1) military disease hazards research, (2) medical biological defense research, (3) combat casualty care research, (4) human systems technology research, and (5) medical chemical defense research. The military conducts biomedical research and development in its own

medical research laboratories, institutes, and non-governmental laboratories through contracts with universities and industry. The fundamental purpose of this research, as stated previously, is to solve military medical problems of importance to national defense. Each of these research areas pose a proverbial double-edged sword regarding their medical orientation thereby upholding principles of healing and preventing harm as opposed to the notion of destructive applications of the research that would then associate this research with nonmedical purposes. This tension is pervasive throughout the ethical analysis of military medical research and this discussion will return to it continually.

Military Disease Hazards Research

The major thrust of military disease hazards research includes basic and applied studies related to prevention, diagnosis, and treatment of infectious diseases that could threaten the success of military operations. Basic research in microbiology, immunology, pathogenesis, and vectors transmission of disease is designed to improve the technology base for development of disease prevention, war-fighting sustainment, and treatment measures. Applied research focuses on the development and testing of vaccines, prophylactic and therapeutic drugs, and rapid identification and diagnostic methods and equipment.

The military human immunodeficiency virus (HIV) research program is a component of the military disease hazards research program. The goals of this program are aimed at reducing the incidence of new HIV infection in military populations, reducing the rate of progression from asymptomatic to symptomatic disease, and reducing the HIV-attributable death rate. Research projects focus on evaluating the courses of infection in military populations, identifying risk factors related to transmission, testing and evaluating vaccines for prophylaxis, and testing and evaluating drugs and vaccines for early intervention.

Medical Biological Defense Research

The goal of medical biological defense research is to ensure the sustained effectiveness of US military forces in a biological warfare environment by providing medical countermeasures that deter, constrain, and defeat a biological warfare threat. Basic research concentrates in three areas of protecting the US military's war-fighting capability during a biological attack: (1) prevent casualties with medical countermeasures (vaccines, toxoids, drugs); (2) diagnose disease (forward deployable kits, confirmation assays); and (3) implement treatment methods (antitoxins and drugs) to prevent lethality and maximize return to duty rates.

An essential element of this program is publishing in scientific journals to maintain scientific credibility, demonstrating an open program in support of the Biological Weapons Convention (BWC) treaty, and developing an element of deterrence. The element of deterrence associated with a medical biological defense research program differs from the concept of nuclear deterrence. In nuclear deterrence potential adversaries basically play the old game of "chicken" with each party to a potential conflict threatening a retaliatory strike in the event the other side conducts a first strike. The possibility of either side launching an offensive strike with the opposing side capable of retaliating deters either side from using the weapon. This concept of retaliation does not apply to biological weapons.

The problems inherent with biological weapons include verification (what countries have them) and enforcing mechanisms against their development and use (ie, the BWC). Unlike a nuclear attack, biological agents for use as weapons are readily available. Another dissimilar factor is the capability of terrorists to acquire and use biological agents. Therefore, the element of deterrence in the biological arena is not one of retaliation but of defense—if it is possible to be protected from biological agents, then the use of those agents by an adversary has no tactical or strategic advantage from a military perspective. Defense against biological weapons includes the need for effective international measures of verification; international agreements against proliferation of offensive research programs; and a defensive research program for detection, identification, and treatment measures to decrease the military advantage and usefulness of biological warfare agents. Specific arguments regarding the deterrence effect of a medical biological research program will be developed in the following section of this chapter.

Combat Casualty Care Research

The mission of combat casualty care research is to provide integrated capabilities for medical care and treatment of injured soldiers at all levels of care, far forward on the battlefield, to reduce mortality and morbidity, and effect early return of soldiers to their military duties. Research and development are conducted in areas of wound healing, thermal burns, hemorrhagic shock, sepsis, organ system injury, blood preservation and blood substitutes, combat stress, and field medical materiel. Basic research in areas of wound healing and the pathophysiological response to trauma of cellular and organ metabolism attempt to minimize mortality, lost duty time, and unnecessary evacuation due to minor combat trauma. Enhanced readiness to treat combat casualties focuses on developmental efforts in surgical equipment, resuscitation fluid production systems, and computer-assisted diagnosis and life-support equipment.

The ethical tension created by combat casualty care research stems from the type of research necessary to solve the problems of the modern day battlefield. Projectile weapons with high muzzle velocities create different types of wounds than those normally seen in hospital emergency rooms. Thus, training combat surgeons on wounds created by weapons with low muzzle velocities does not prepare them for what they will see in combat. Simulation with gelatin molds is inadequate in wound healing experiments as well. Consequently, military medical researchers have sought for years to gain approval to study ballistic phenomena using animal models. However, to date, animal rights groups have prevented the establishment of any such facility. The prospect of military medical researchers shooting anesthetized, stray dogs to gain knowledge for improving the level of care of wounded soldiers on the battlefield was believed to be unethical by these groups. Further discussion of the issue of the use of animals in military medical research follows in a later section of this chapter.

Human Systems Technology Research

The purpose of human systems technology research is to enhance human capability to function safely and effectively in military systems and operations. This research attempts to identify and solve health problems posed by new combat materiel and new concepts for combat operations. The results of this research help health policy makers

and combat materiel developers keep the limits of human physiological and psychological endurance in mind when developing new doctrine and new military hardware. The major areas of this research include physiology in extreme environments, bio-mechanical stress, operational medicine and human performance, health effects of toxic hazards, and non-ionizing radiation bioeffects. Program goals seek to enhance soldiers' performance under all operational conditions; protect soldiers from hazards of military materiel and operations; develop human performance models; and improve military operations concepts, policies, and doctrine.

The central focus of human systems technology research, like the other research areas, is preventing injury to the combat soldier. Although the aim of this research is consistent with the goal of medicine—to sustain and enhance the quality of human life—the potential for ethical conflict is considerable when medical researchers conduct studies that do not focus solely on the welfare of a human being but focus also on maintaining and sustaining a person's physical and psychological efficiency as a soldier—a human weapon system.

One aspect of this potential conflict concerns the use of soldiers as human research subjects. To determine the possible deleterious effects of new military hardware on military personnel, human trials must eventually be conducted. Historically, military researchers have been negligent in protecting the rights of research subjects.⁸ The advent of institutional review boards (IRBs), other systematic review procedures, and federal regulations provide the means for protecting human subjects—even soldiers. Nonetheless, there is a tension, if not competition, between protecting the rights of research subjects on the one hand and conducting research that some view essential to national security interests on the other.

Medical Chemical Defense Research

The mission of medical chemical defense research is to preserve combat effectiveness by timely provision of medical countermeasures in response to chemical warfare defense needs. Research efforts in this area strive to maintain the technologic capability to meet present requirements and to counter

future threats, to provide the degree of individual-level protection and prevention to preserve the fighting strength of combat units, and to provide for the medical management of chemical casualties to enhance survival and to maximize and expedite returning soldiers to duty. Basic research includes investigation of pharmacology, pathophysiology, and toxicology of chemical warfare agents, pretreatment and antidote drugs, and skin decontamination compounds to determine both their mechanisms of action and their interaction with one another.

The ethical dilemma associated with medical chemical defense research is the inability to conduct human trials to demonstrate the efficacy of pretreatment or antidote drugs because to do so would mean having to expose research subjects to actual chemical agents. Consequently all current pretreatment and antidote drugs remain unlicensed by the US Food and Drug Administration (FDA). In a letter dated 30 October 1990, during Operation Desert Shield (ODS), the deployment phase of the Persian Gulf War, the Department of Defense applied for a waiver to use investigational pretreatment drugs under an investigational new drug application filed with the FDA.^{9(pp346–348)} Such use, intended for therapeutic use, not research, caused an acrimonious debate in the editorial pages of the country's leading newspapers. The charge against the DoD was that it was experimenting with these drugs on soldiers without their informed consent. References to the Nazi doctors' experiments during World War II were elicited in statements against the approval of the FDA waiver. Maintaining a distinction between research and accepted medical practice is a philosophical problem that has troubled medical ethics for a long time. The conclusion of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research holds two key factors in mapping this distinction: (1) the level of risk, and (2) the intent of the medical professional.⁸ The waiver issued by the FDA for the Persian Gulf War did not solve the ethical problem of the military in trying to balance the rights and welfare of its members against the military necessity of sustaining a combat ready force. Nor, for that matter, does the criteria of level of risk and intent settle the issue of whether a medical professional is doing research or providing accepted medical therapy.

THE ETHICAL LEGITIMACY FOR MILITARY BIOMEDICAL RESEARCH

[I]t is deemed unethical for physicians to...weaken the physical and mental strength of a human being

without therapeutic justification [and to] employ scientific knowledge to imperil health or destroy life.¹⁰

In examining the ethical justification for military biomedical research, one finds that the literature on this issue runs the gamut of political and sociological perspectives. Views tend to be polarized ranging from complete prohibition of any military-sponsored biomedical research on the one hand, to secret programs that would include testing on an unwitting and uninformed populace on the other. Both of these extreme views are unethical positions. Complete prohibition of military medical research cannot be morally acceptable because it results in moral evil, namely failing to preserve the health and welfare of soldiers deployed in combat. Secret programs also result in moral evil and consequently are unethical. If there is any possibility of bringing these diverging groups closer to some middle ground perhaps it is found in the quotation cited above from the World Health Association.

Implicit in this quotation is the “do no harm” principle. The many efforts by those opposed to biomedical research by the military stem from their attempt to preserve this principle—keep medical scientific knowledge from becoming “militarized” and used to harm rather than to heal. Ironically, those who support military biomedical research also base their arguments on a “firstly, do no harm” principle. The aim of military biomedical research is, in fact, to go beyond this principle of nonmaleficence (avoiding harm) by preserving and enhancing the lives of those who serve the military forces of the United States (the principle of beneficence).

The ethical tension that develops from the principle of nonmaleficence is whether the moral legitimacy of medical research, in general, applies to military medical research. The moral legitimacy of medical research is based on the good that results from the research enterprise. So too, the moral legitimacy of military biomedical research must stem from the good it produces mitigated against any harm that is likely to result as well. Because most medical researchers desire that their science alleviate human suffering, many are reluctant to participate in military medical research for fear that medical research is akin to weapons research in the physical sciences and engineering. The fear that military medical research aids in the development of biological and chemical weapons keeps many scientists from participating in military medical research and others calling for its complete prohibition. The major claim of this argument is that scientists who participate in military research fuel the arms race. Military sponsorship of scientific research determines and influences the type of research con-

ducted. Hence any scientist who accepts military sponsorship is *de facto* working for the military, its aims, goals, and objectives. Because military activity is antithetical to the principles of science, ethical problems exist for those scientists who participate in military-sponsored research—to include medical research. The question to ponder is whether those who support a military biomedical research program and those who oppose it can stand together on the same moral high ground.

As alluded to earlier, complete dissociation from military medical research, while eliminating any moral problems for scientists, also risks losing the benevolent gains in vaccines, drug therapies, and material preventive and protective measures relevant to military problems but also to direct civilian applications of this research. For example, the development of a number of investigational vaccines against diseases such as Venezuelan equine encephalomyelitis (VEE), tularemia, anthrax, Q fever, and botulism were safe and efficacious in reducing disease from accidental exposure to laboratory workers. The use of VEE vaccine proved useful in eradicating the disease in horses in the epizootic in Texas in 1971. The Rift Valley Fever vaccine was used successfully in high-risk personnel during an outbreak of the disease in Egypt in 1977 and 1978. In 1989 military investigators identified an Ebola-like virus in monkeys and in 1995 military investigators were part of the World Health Organization team to investigate the Ebola outbreak in Africa. Since the 1950s, military medical researchers have been investigating the Hantaan virus known to cause the disease called Hemorrhagic Fever with Renal Syndrome (HFRS) that has already killed more than 50 people in the United States.

Although these research advances have direct civilian application, the research has greatly reduced the morbidity and mortality of military personnel. Historically disease and nonbattle injuries have accounted for over two-thirds of the combat losses suffered by the United States in past military engagements. In Vietnam, although disease was the single greatest cause of morbidity, the admission rate was 40% less than the Korean War due largely, in part, to the efforts of military biomedical research and development.¹¹ This point alone should be sufficient to undermine the moral claim that complete dissociation from military medical research completely upholds the principle of “do no harm” or eliminates any ethical problems for medical scientists. Clearly the loss of medical advances stated previously would result in tremendous harm but the misuse

of this medical knowledge also presents the possibility of greater evil than the good that results from it.

Despite the possibility of consensus building upon the “do no harm” principle, military biomedical research does present a double-edge sword. Most often what is learned in the area of biomedical research has potential uses for both good and evil. Clearly, in some cases, there is a distinction between offensive (destructive) and defensive (constructive) research. Consistent with previous discussion of the just war doctrine, the distinction between offensive and defensive research (and medical research is defensive unless one views biological defense as offensive in bioweapons development) becomes morally important. Certainly scientists who view their work as consistent with this doctrine are no more unethical than soldiers who do the fighting. Likewise, scientists who choose not to participate are no more unethical than a pacifist or conscientious objector who would object to any participation in killing—even a just war. What is critical regardless of the path chosen by a scientist is that if military medical research is morally legitimate, areas of scientific inquiry remain open programs and the knowledge gained from this research cannot be subverted by weapons designers to defeat advances in reducing injury and disease.

Consequently, in reviewing the arguments on this issue, three major areas of dispute emerge. First, there is disagreement because funding is limited and continued financing of a military program compels university and industry to accept military projects to get much-needed research grants. As time goes on, so it is suggested, these researchers, having been coerced into accepting DoD money, are compelled to work solely on military goals that may detract, for example, from vaccine research in public health initiatives. Second, there is the argument that the defensive (constructive and benevolent) component of segments of the military biomedical research programs is ambiguous enough to cause other nations to believe that the United States is working on offensive developments. Hence, military biomedical research could lead to a proliferation of biological and chemical weapons. Third, there is, at a minimum, an implicit position that the production of vaccines and drugs against devastating disease, although a laudable goal, cannot be viewed in isolation solely for the protection of US military forces. The production and selective use of military biomedical advances can be viewed as a component of strategic offensive policy that would not benefit general populations, particularly those

of developing nations where the United States is most likely to engage in offensive operations.

Disagreements about the funding of the scientific enterprise in the United States and how to best achieve the goals associated with that enterprise extend beyond military biomedical research. Those opposed to military programs view the use of limited national resources for military purposes as immoral. They contend that shifting of military dollars to public health agencies, such as the National Institutes of Health, will provide the same benefits the military program currently produces. The difficulty with this position is that some military problems have no immediate direct impact on public health; thus research aimed specifically at military problems would be neglected. The economic burden, which has a moral component, is balancing the use of financial resources for social purposes mitigated against the needs to protect national security.

Considering the history of the development of the atomic bomb, many scientists have come to believe that they have no control over the results of their work when conducted under the auspices of military funding and oversight. Their argument is simple: The only way to control the results of one’s work is to control what one works on in the first place. The ambiguity related to biological defensive versus offensive research is such that many scientists claim the only way to control proliferation of biological weapons, for example, is to not participate in any military-sponsored biological research. Some contend there is no distinction at all between offensive and defensive biological research and contend the military simply mislabels offensive research as defensive to attract researchers. This argument is critical to the moral legitimacy claim of military biomedical research and will be developed further in this chapter.

Finally, is it possible that if the United States can protect its military from endemic diseases in a combat zone or use technology to advance healing of its wounded soldiers, that these medical interventions constitute contributing to the military aims of war fighting and hence lack the moral legitimacy of the healing arts in general? The question of the extent to which a member of the healing profession may participate in activities not strictly medical and still uphold the principle of “do no harm” is an interesting and debatable one. It is, however, to ask a different question (back to Moore again) than whether medical professionals directly engaged in preventing or relieving suffering of soldiers constitute direct contribution to offensive activity.

Should Military Biomedical Research Be Prohibited?

The question of specifically prohibiting military biomedical research is embedded in a larger argument regarding the ethics of prohibiting or limiting research.¹²⁻¹⁵ The ethical issues at stake in this debate are part of a spectrum of issues revolving around fundamental decisions of scientists to participate or refuse to participate in research based upon the perceived social consequences of their work. The dual nature of military biomedical research fundamentally establishes this ethical conflict for researchers pondering participation in military programs. The conflict stems from a genuine conviction that doing what can be done to enhance the lives and well-being of members of the US military is a moral obligation—what ethicists call a *prima facie* duty—one ought to do good when one is able to do it. When taken alone, this principle is unassailable. When juxtaposed to a competing claim, namely, “do no harm,” these ethical principles appear in conflict. The problem then becomes how to decide which principle carries greater weight in the ethical decision-making process. One method is to conduct a risk/benefit analysis to determine which action produces the greater benefits (good) while limiting harm (evil).

There are several versions of risk and benefit arguments used by those opposed to direct involvement of biomedical scientists in military biomedical research.^{3,16,17} The forms of the arguments tend to run from the general to the specific. One attempts to argue that there are good reasons to limit scientific inquiry in general and then demonstrate limiting or restricting specific inquiry. Such arguments are persuasive only to the extent that the general argument itself is sound in its reasoning—that the general premises are true and that the conclusion to limit or prohibit research follows from those premises.¹³

Usually these types of arguments are difficult to answer. In developing a risk/benefit ratio, the facts needed to evaluate a premise or calculate a risk or benefit are not known. This is not the case with military biomedical research. It is known with a great degree of certainty that medical research can produce a host of preventive and therapeutic treatments that will benefit the lives of military personnel with considerable applications to the general populace at large. The inherent risk, based on historical evidence, of the likely perversion of this research for nefarious purposes is also known.^{3,6,16} The difficulty faced in solving this problem is not a fac-

tual one but rather one of differing values and deciding how to proceed. There are honest disputes about whether the medical advances produced by military biomedical research are worth the possible risk of medical scientists being exploited and the proper end of the healing arts being perverted for evil purposes. Hence the fundamental question shifts from one of moral legitimacy of military medical research to one of whether the potential benefits of this research are such to pursue it, knowing the potential for harm. In other words, can this research be conducted in such a manner as to preserve the integrity of the research? Can a system of appropriate checks and balances be established that will allow the conduct of research when the probability of harm resulting from the research is unknown? A review of the basic arguments is appropriate at this time.

The Nonparticipation Point of View

Those who hold that physicians should not participate in any form in military research believe that there are three “steps” that occur in the corruption of military medical research. These are: (1) the militarization of medicine, (2) the inevitable escalation of biologic and chemical weaponry because of the products of military medical research both in US forces and the forces of any adversary, and (3) with this escalation a violation of law, morality, and ethics. I will discuss each in turn.

Militarization

Those opposed to military biomedical research argue against the possible offensive uses of this research. The most contentious and likely research program for possible offensive applications is the Medical Biological Defense Research Program. Critics contend that defensive research to protect military members from naturally occurring diseases and biological weapons is, “highly ambiguous, provocative, and strongly suggestive of offensive goals...it is urged that physicians refuse participation in such research.”^{18(pp25-26)}

Nonparticipationists document that overall funding for military programs increased by more than 400% in the late 1980s. Over the same period of time, federal support for research in basic science issues in the civilian sector sharply declined.¹⁸ From 1980 to 1984, total federal research support in the United States for life sciences decreased by 2% while DoD funding increased by 26%. With 100 university labo-

ratories participating in DoD programs with this increased funding, nonparticipationists perceive a trend that could alter research priorities in developing fields, such as genetic engineering.⁵

Nonparticipationists also argue that military operations can never be exclusively defensive, that biological research is fraught with ambiguity between offensive and defensive applications and, therefore, medical professionals who conduct research for the military are in "ethical peril." To strengthen this claim, critics of the military program contend that public funding supporting a military program does not serve the public interest, particularly in time of budget cutting. The nonparticipationist also claims that the threat of disease either endemic or as a biological weapon is overstated by the military. Further they suggest that the responsibility for governmentally sponsored medical research for prophylactic, protective, and other peaceful purposes in the United States belongs to the National Institutes of Health (NIH) and the Centers for Disease Control (CDC). Consequently, the NIH or CDC should have the responsibility and, more importantly, the resources for this type of medical research.^{3,16} Such a position is less likely to pervert nature of biomedical research and, most importantly, less likely to place medical professionals in ethical peril.

Escalation

Universal agreement exists by those opposed to military biomedical research (within the area of vaccine and drug development) that such research will lead to a biological arms race analogous to the development of nuclear weapons.¹⁶ Although the nonparticipationist will concede that the production of vaccines against devastating diseases is a laudable goal, such conduct cannot be ethically judged in isolation from the purposes of the agencies who directly supervise the research effort. It is possible that a medical scientist might consent to, or be misled into, work that has offensive applications under the guise of defensive work.

When the military supports large programs to develop vaccines against exotic diseases that pose no likely public health concern such as dengue fever, anthrax, VEE, and numerous pathogens, one can make informed speculations of the likely use of these pathogens as offensive weapons knowing one's own soldiers are protected against them. Consequently this research can be construed as a potential component of offensive strategy that would drive likely adversaries into similar research programs and hence the escalation of a biological arms race. Therefore,

medical scientists have the responsibility not only to avoid working directly in ways that support offensive development, but also to act in such a way as to avoid contributing to the arms race, even if engaged in clearly defined defensive research.

Violation

Following from the assertion that biological medical research by the military cannot be solely defensive in nature, medical scientists have an obligation to not participate in research. US government policy and international agreements forbid the development, production, and stockpiling of microbial or other biological agents, or toxins that have no justification for prophylactic, protective, or other peaceful purposes. Interpretation of Article I of the Biological Weapons Convention¹⁹ (BWC) is ambiguous in that it does not preclude research into offensive agents necessary to determine what means are required to defend against them.

Nonparticipationists contend that because the line of distinction between offensive and defensive research remains blurred, medical scientists violate the spirit if not direct intent of the various agreements to avoid work that would contribute to the development of offensive capabilities with biological agents. Opponents of military biomedical research argue that material developments in diagnostic equipment and sensor devices potentially could produce vector delivery systems and that antibiotic therapy could really produce means to defeat or inhibit diagnosis, defeat current vaccine use, or generate a novel agent.

The advocates of nonparticipation concede that the study and production of some biological agents (for example, toxin proteins) may have scientific merit, but such work raises questions regarding US compliance with the BWC. Consistent with the logic of having the NIH conduct disease-oriented research, moving control of this type of research to civilian agencies would dispel concern about the offensive intent of the work, uphold the deterrent effect of the BWC, and protect against the perversion of the healing arts in medical research.

The Participation Point of View

Those who hold that physicians should participate in military research answer the three "steps" by (1) exploring the complexities that the militarization argument overlooks, (2) maintaining that existing safeguards preclude inevitable escalation, and, thus, (3) there are no violations of law, morality, or ethics. Once again, I will discuss each in turn.

Militarization

Those who advocate participating in military biomedical research reject the militarization viewpoint as confusing the primary aims of public health research versus the national defense interests and the health of military personnel. If the NIH, for example, were directed to accept the mission requirements of a military-oriented medical research program, this realignment of mission would hinder NIH research in diseases of national interest. If NIH sought to contract this research, it would be no different from the current program with the exception of civilian control. Some scientists advocate civilian control because of a prevailing attitude of distrust of military-sponsored research. Some contend that it is ethical to participate with the military in times of national crisis but doubt that permanent association has any moral imperative. Advocates of a military program counter this claim with evidence of the proliferation of biological warfare capabilities even by some countries who signed the BWC. As long as activities of Third World countries remain unpredictable regarding their intentions in offensive biological capabilities, a credible biological defense research program is needed.

This point is particularly relevant given that the United Nations revealed in August of 1995 that Iraq had an active offensive biological and chemical weapons program.²⁰ For over 4 years, Iraq had hidden all information of a program to produce and deploy almost 200 biological warheads—in bombs, artillery shells, and missiles, all capable of reaching Saudi Arabia and Israel during the Persian Gulf War. The bacterium anthrax was loaded in at least 50 bombs, and botulin—the toxin causing botulism—had been loaded into approximately 100 bombs. Additionally, Iraqi scientists grew a poisonous fungus found on peanuts and corn to produce aflatoxin, to be used as a warfare agent.²⁰

Consequently, advocates of biomedical military research contend that given examples such as Iraq, participation by university and industry is consistent with an ethical imperative of developing the means by which the United States can protect and defend the lives of military personnel against a consistent threat of a potential adversary that threatens its national security.

Escalation

The participationists espouse the view that whatever potential may exist for creating offensive applications from defensive research (the escalation factor), the possibility is extremely minute because

military biomedical research is perhaps the most closely monitored, regulated, and inspected research that occurs within the United States. An exhaustive environmental impact review of the military program was conducted in 1989 culminating with the publication of a final programmatic environmental impact statement (PEIS).²¹ Congressional scrutiny is applied to this program in the annual budget review process. The military prepares resource requirements and program description and justification in the Congressional Descriptive Summary that becomes part of the President's budget. The House and Senate Armed Services Committees evaluate this program and authorize its funding. These committees perform their own evaluations and review of the military program prior to any final authorization and appropriation of funds. The General Accounting Office conducts periodic reviews and hearings on the appropriateness of the research and the use of resources consistent with the aims and intents of the program. Special interest groups, using the Freedom of Information Act, gain access to both research data and laboratories on a routine basis. The public and scientific community can and do act on their own initiative to review military research. Finally the military provides reports annually to the United Nations and to the Biological Weapons Convention. Consequently, rather than view this research as some secret, clandestine program that could mask offensive research or increase the paranoia of a potential adversary, participationists contend the opposite—that a completely open program, to include publishing in peer-reviewed journals, serves a function of deterrence (the use of an agent would have little or no strategic or tactical military advantage) and hence stability.

Violation

Advocates of military biomedical research demonstrate the legal aspect of their work based upon the research conforming to regulations and standards of the following agencies: the US Department of Agriculture, Department of Health and Human Services, Food and Drug Administration, National Institutes of Health, Public Health Service, Centers for Disease Control, Department of Labor, Department of Transportation, Environmental Protection Agency, Department of Energy, Department of Commerce, and the Nuclear Regulatory Commission. Proponents of military medical research contend that this research is consistent with the intent of the BWC, particularly Article X that gives States that are Parties to the Convention the right to par-

ticipate in the fullest possible exchange of information, equipment, and materials for peaceful purposes.

Finally, regarding the alleged ambiguity of offensive and defensive research, supporters of military biomedical research hold that there is an empirical distinction that separates offensive from defensive research.¹⁷ Citing the regulatory controls over this research, participationists contend that the likelihood of a rogue scientist developing an offensive capability under the guise of defensive research is highly suspect. Additionally, advocates of this research point to the historical record to substantiate the benevolent aspect of their work—the marked decrease in morbidity and mortality of soldiers deployed to combat zones. Participationists contend that those who doubt the defensive intent of their work can only talk of the potential to create offensive uses of biomedical advances or the possibility that military could develop offensive capabilities or future hypotheticals for offensive development. Meanwhile, countries like Iraq continue to demonstrate a resolve to blatantly ignore international agreement to limit the development and use of biological warfare agents, and worse, in doing so see themselves gaining a military equalizer to imbalances of their conventional military capability. Currently, there is little evidence to support the fears of the nonparticipationists regarding the legal aspects of military biomedical research. The ethical concerns remain in doubt, however, regarding the consistent application of law and ethics to military biomedical research in the future.

National Risk vs National Security

Whether the merits of the contrasting views of militarization, escalation, and violation are persuasive depends upon one's first principle—the ethical standard one holds as dominant over other principles. To date, there is little in the professional literature of ethics demonstrating how traditional ethical principles apply to the dual nature of military medical professionals. Although the literature does discuss the social responsibility of medical professionals to include medical scientists, there is, in fact, very little to clarify the competing duties of the uniformed medical professionals to the military, to society, and to their patients. Thus far this discussion has focused on the competing nature of the duty of military medical professionals between their patients and society but only from the standpoint of preserving the ethical integrity of the healing professions. Another aspect to consider is that mili-

tary biomedical research, as beneficial as it might be to military personnel with subsequent civilian applications, by its nature creates significant risks for local civilian populations and hence ought to be prohibited. The solution to this vexing problem again hinges upon some kind of risk and benefit analysis.

Dispute currently exists about what risks are worth taking when pursuing research. These risks include potential harm to research subjects, non-research subjects, and the researchers themselves. Identifying risks to research subjects (participants) requires formulating risk and benefit equations as discussed previously. These risks are different from the kind that populations at large face from potential accidents or sabotage. Furthermore, the public has demonstrated resolve to protect itself from such risks.²²⁻²⁵ Based on the principle of justice, current ethical practices in research require a fair and equitable distribution of burdens and benefits. When the issues of human subject research in the military are in question, if the risks are disproportionate to the benefits then there would be grounds to ethically suspect the conduct of the research.

Risks to nonresearch participants include the issue of public safety. Several aspects of military medical research, particularly in the area of infectious disease, pose at a minimum a potential public health threat in the event of a laboratory accident. The issue of public safety revolves around the idea of real versus perceived threat that the research poses to public health. Nonetheless, there have been several challenges to military medical research projects being conducted at university labs as well as government facilities. How much risk is ethically acceptable must be mitigated against the potential harm to an unsuspecting or, worse, uninformed local population. Finally, there is also the question of how much risk is acceptable for the researchers themselves. For example, should a lab worker working with virulent anthracis cells drop the flask containing the cells on the floor, the infected lab worker could be treated with penicillin. The spill would be treated with chlorine bleach that would kill the cells. Hence, the issue of public risk versus military benefit is mitigated by the ability to conduct risk and benefit analysis.

Having said all this, the general principle of prohibiting research that poses unacceptable risk (and the operative word is unacceptable) has merit. There is a trade-off regarding the perceived risks and the reasonable precautions or likelihood of there being a real threat to a community, particularly from military biomedical research. Currently, all biomedical

research protocols conducted by the military undergo intense scrutiny at all levels of institutional review for scientific merit, protection of research subjects, and safety. The application of the risk principle applies to the entire research community, not just the military.²⁶ Consequently, the question becomes one not about the moral legitimacy of military biomedical research but one of inherent risks, in magnitude far greater than civilian research so as to limit or prohibit its conduct.

Summary

There seems to be a prevailing attitude among certain scientific circles that if the military is funding research, there must inherently be something nefarious about its conduct. The military has contributed to this perception in the past by conducting unethical research. The lysergic acid diethylamide (LSD) studies (which were discussed in detail in Chapter 17, *The Cold War and Beyond: Covert and Deceptive American Medical Experimentation*) for example, are clearly unethical judged by the standards of the day regarding the lack of informed consent from research subjects. Even though these experiments were not medical protocols, military medical research tends to be painted with the same broad brush of suspicion based upon a lapse of ethical judgment from the past.

There is a line, be it distinct or vague, between justifiable and unjustifiable biomedical research and the use of these data for purposes that violate the integrity of the medical community. Such a possibility exists for all medical data, not just data from military medical research.^{27,28} More problematic are those protocols designed in other than biomedical programs that require the participation of medical personnel to validate the data. For example, while enhancing the lethality of a particular weapon, developers may request the participation of biomedical

personnel to verify the lethal or nonlethal aspects of the weapon. This is the case with recent studies in the development of nonlethal microwave weapon technology that has a lethal capability. Such an example poses a more vexing issue for the biomedical researcher who may be participating in research that has no benevolent goal, even if one argues that a nonlethal incapacitating weapon is benevolent versus a lethal weapon. Using medical knowledge for the purpose of causing harm, for instance to validate that a particular weapon has capacity to kill or maim in order to increase the capacity of that weapon to do so, is simply the wrong use of medicine and medical research, because it turns the medical researcher into a weapons developer. Furthermore, such an example clearly demonstrates the point regarding the issue of social responsibility and the consequences of research. No person, operating in any capacity, ought to be compelled to act in such a way as to violate personal conscience or moral obligations. Nor should medical professionals use medical knowledge for the expressed purpose of endangering or destroying life.

Indeed, there are two parallel issues that emerge regarding the ethical legitimacy of biomedical research. Returning to the principle of “do no harm,” there is a distinction to be made between research that has benevolent ends and research that has nonbenevolent ends. Medical professionals ought to stay in the business of healing and not hurting, which includes not participating in or contributing to weapons research and development. However, there is also a need to establish a clear distinction between offensive and defensive goals within the realm of biomedical military research. Even though this is not an ideal world, preserving the ethical integrity of biomedical research and providing for the welfare of military personnel ought not be competing or mutually exclusive goals. Both can be done and both should be done.

THE ETHICAL CONDUCT OF RESEARCH

“Research is a complicated activity in which it is easy for well-meaning investigators to overlook the interests of research participants—to the detriment of the participants, scientists, science, and society.”^{29(p1)} Upholding the ethical principles of biomedical research is part of the intricacies of the entire research enterprise. The breaches of ethical principles, be they intentional or unintentional, are replete in the historical literature.^{30–34} From the Nazi doctors (discussed in Chapters 14 and 15 in this volume) to the

infamous Tuskegee syphilis studies and the more recent revelations of radiation studies conducted by the US Department of Energy (discussed in Chapter 17 of this volume), breaches in conduct exist. Such conduct has led to the promulgation of the Nuremberg Code, The Declaration of Helsinki, the Belmont Report, and a host of federal regulations in an attempt to provide clear guidelines regarding the ethical conduct of biomedical research.

These efforts notwithstanding, while scientific

research continues to produce substantial social benefits, it continues to pose vexing ethical questions regarding the protection of human subjects, the use of nonhuman animals, and expanding study populations to include women and minority groups. Military biomedical research is not immune to these questions. Hence there is a need to consider how each of these issues impact, in an ethical sense, the conduct of biomedical research in the military.

Criteria for Conducting Ethically Responsible Research

The National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research conducted hearings on the ethical problems in human research from 1974 to 1977. The mission of this panel as outlined in its summary statement, was, in part, to

conduct a comprehensive investigation and study to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects.⁸

The recommendations of the panel were later codified into public law.³⁵ The fruit of the National Commission's labor appears in *The Belmont Report*.⁸ The three basic principles, intended as succinct guidelines to govern the use of human subjects in research, include^{8(PartB)}:

1. Beneficence: maximize the good outcomes while avoiding or minimizing unnecessary risk, harm, or wrong;
2. Respect: protect the autonomy of persons, with courtesy and respect for individuals as persons (as ends in themselves and not mere means); and
3. Justice: ensuring reasonable, nonexploitive, and carefully considered procedures and their fair administration—fair distribution of risks and benefits among persons and groups.

These three principles are the foundation for the following six norms that govern the ethical conduct of research^{29(p19)}:

1. Valid research design: valid design yields correct results taking into account relevant theory, methods, and prior studies;
2. Competence of the researcher: the investigator must be capable of conducting various procedures in a valid manner;

3. Identification of consequences: a risks and benefits analysis must be conducted. Ethical research adjusts procedures to ensure privacy, confidentiality, minimized risks, and maximized benefits;
4. Selection of subjects: the subjects must be appropriate for the purposes of the study, representative of those who will benefit from the research, and appropriate in number;
5. Voluntary informed consent: voluntary means freely, without threat or inducement. Informed means the subject knows what a reasonable person in the same situation would want to know prior to granting consent. Consent means an explicit agreement to participate; and
6. Compensation for injury: the researcher is responsible for what happens to a research subject. Federal law requires that subjects be informed regarding compensation for injury, but the law does not require compensation.

The application of the general principles and norms stated above often narrow specifically to three fundamental requirements: (1) informed consent, (2) risk and benefit assessment, and (3) the selection of subjects of research. Of these three areas, informed consent (deriving from the Nuremberg Code, 1947) is the most contentious regarding the use of soldiers as subjects in research. Why is informed consent important? What does it entail? Is consent different from mere approval? The answers to these questions are found in the federal regulations written to address these situations.

Informed Consent

Although the importance of informed consent is generally unquestioned,^{36,37} there is controversy over whether it is possible to actually obtain truly informed consent from a research participant. General agreement exists regarding the three basic elements in the consent process: (1) information, (2) understanding, and (3) voluntariness. The aspect of information requires full disclosure by the investigator including a statement of the purpose of the research, description of foreseeable risks and discomfort, description of benefits, a disclosure of alternative procedures, statement regarding confidentiality of the records, explanation of compensation and medical treatment for injuries resulting from participation, a point of contact regarding the rights of the research volunteer, a statement regarding the voluntary nature of the participant, and any addi-

tional information regarding the findings of the research, withdrawal criteria, or circumstances by which the investigator can terminate the participation of the research volunteer.

How well a research subject understands or comprehends information relevant to the research is dependent upon a number of factors. Because comprehension is often a matter of how the investigator conveys information to the research volunteer, the investigator needs to tailor the informed consent process to each individual based upon the subject's intelligence, maturity, language level, and other special aspects of the participant. If necessary, a third party is part of the process to assess the understanding of the research participant. Printing consent forms in the native language of the subject may be necessary as well as providing interpretation for those subjects who may not be able to read the consent form. On the face of it, using a subject who cannot read a consent form sounds, in and of itself, ethically suspect. Such practice is acceptable regarding children and may be acceptable in other instances as well. The key component is the aspect of comprehension. Regardless of how the information is conveyed and the level of comprehension obtained, investigators are responsible for ensuring that the subject comprehends all the information.

The aspect of voluntariness of consent that differs from mere approval is the element of rights conveyed upon the volunteer in the consent process. This element requires conditions free from coercion and undue influence.

Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance.^{8(PartC)}

Perhaps the least understood aspect of gaining informed consent is the communication process that takes place between the investigator and the research subject. Failing to understand the nuances of body language, general attitude and friendliness, or general empathy for the research subject are some factors that can contribute to the perception of coercion.

The aspect of voluntariness is absolute concerning informed consent in the same way that informed consent is absolute to the conduct of ethical research. Consequently it is reasonable to ask whether soldiers can ever provide true voluntary consent. The aspect of coercion is problematic in that an element of coercion tends to exist in research on a sliding scale. That is to say that some element of incen-

tive exists for subjects to participate in research. At some juncture the potential exists to cross the line from benefits and appropriate incentives to deception and coercion. If this aspect of "mitigated coercion" associated with medical research cannot be justified, then the use of soldiers in biomedical research is unethical.

Is It Ethical to Conduct Research on Soldiers?

There are several issues at stake in what amounts to the fundamental question of this section. First, and perhaps foremost, is the issue of the ethical status of soldiers. When a person joins the military, the individual incurs unique obligations to the country and to other service members. These obligations cause a shift in the ranking of usually applicable ethical priorities. By joining the military, individuals implicitly agree to subordinate their autonomy for the sake of accomplishing the military mission. Service members also agree, implicitly, to risk personal injury or loss of life if need be in compliance with lawful orders of their superiors. This implicit consent applies not only in direct warfare but in preparations for war as well. Nonetheless, even though service members voluntarily allow themselves to be treated as a means in some instances, the military has an obligation to protect the interests and welfare of soldiers consistent with accomplishing the military mission. The extent to which this reciprocal relationship functions varies in times of peace and war, and the willingness to protect the autonomy of soldiers is mitigated in direct proportion to the perceived threat to national interests.

Although service members subordinate autonomy relative to accomplishing a wartime mission, this does not mean that individual autonomy should be compromised regarding medical research—even medical research that has direct impact on soldiers and the military mission. With regard to medical research, soldiers are still entitled to full autonomy and due the requisite consideration regarding their use in research as that provided to civilians. Consequently, the DoD policy for the conduct and review of human subjects research, which applies to all elements of the DoD and its contractors and grantees, "requires that the fundamental rights, welfare, and dignity of human subjects in DoD-supported research be protected to the maximum extent possible, and establishes this as a responsibility of the military chain of command."^{38(p9)}

The Department of Defense adheres to all protections established by the federal government to

include: Department of Defense 32 CFR 219; Department of Health and Human Services 45 CFR 46; the Food and Drug Administration 21 CFR 50 and 56; and Department of Defense 10 USC 980, which requires: (a) the informed consent of the subject in advance; or (b) in the case of research intended to be beneficial to the subject, the informed consent of the subject or legal representative of the subject is obtained in advance. In essence, if an individual cannot give his or her own consent, investigators cannot enroll the person into a nontherapeutic (ie, of no benefit to the subject) study. Quite simply, the answer is “no” to the question “Are there ethical exceptions for military medical research?” concerning the corpus of historical and contemporary guidelines of medical research (levels of risk, voluntariness, informed consent).

As straightforward as this analysis seems to be, given the DoD’s own stated policy, there is still considerable concern over the application of these standards particularly in the area of informed consent. There are those who may argue that given the coercive nature of the military, soldiers are incapable of providing voluntary consent in the purest sense of the term. If this is the case, and unless there are justifiable exceptions to the ethical criteria for military medical research, then it would be unethical to use soldiers as research subjects. Is it necessarily true that simply because the military is inherently coercive that soldiers lose their autonomy and hence the ability to provide voluntary informed consent?

First, it is necessary to understand that soldiers have the desire to participate in military biomedical research. In fact, some soldiers volunteer to be part of a unique program designated specifically for use as research volunteers.³⁹ These soldiers are recruited directly from their advanced individual training programs for the sole purpose of volunteering for various biomedical research protocols. Even though these soldiers need never volunteer for a study during their tour of duty with the Military Research Volunteer Program, their mere participation makes them vulnerable to exploitation and the military needs to guard against the potential for abuse. Nonetheless, many soldiers do volunteer by choice for a variety of studies based on the written protocol that describes the research methodology and possible side effects of the study. More importantly, these soldiers may withdraw from any study, at any time, without fear of reprisal from their superiors or the investigators.

For many of these soldiers, participating in medical research is a matter of pride and the self-satis-

faction of knowing they are making a unique contribution to the welfare of other soldiers. Many see their efforts as a unique sacrifice and service to their country, and these soldiers view their participation as voluntary. The military maintains a database of the names of all its test subjects participating in greater-than-minimal-risk studies for 75 years. The requirements of the protocol approval process for DoD biomedical research preserves the key aspects of autonomy and informed consent in times of peace and war. Consequently it appears that these individuals voluntarily concede their autonomy by virtue of being in the military, that such concession of autonomy is justifiable, and the spirit as well as the intent of the informed consent process is not compromised.

Practicality and American Moral Ideals

The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise the free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision....The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.^{40(Art1)}

The Nuremberg Code makes no distinction between peacetime and the exigencies of war regarding the requirement for informed consent of an individual prior to participating in research. This point is particularly troubling given the findings of the Advisory Committee on Human Radiation Experiments,⁴¹ a panel created by the Clinton Administration to investigate reports of unethical and possibly life-threatening experimentation on human subjects. The Committee discovered that tens of thousands of service members were exposed to radiation in research without their consent.

The examples of the radiation research⁴² and the infamous LSD⁴³ studies occurred prior to the rigorous screening and protocol review process of today. Moral hindsight allows the privilege of criticizing and, when necessary, condemning immoral practices of the past. Nonetheless, the radiation experiments and LSD studies conducted on military personnel without their informed consent did occur

after the adoption of the Nuremberg Code of 1947 and the top-secret rules adopted by the DoD in 1953,⁴⁴ which required researchers to inform human subjects of health risks associated with radioactive, chemical, and biological warfare experiments.⁴⁵ There is no ambiguity in the requirements of the Nuremberg Code regarding voluntary consent. Consequently, the researchers involved in these protocols failed in their duties and responsibilities owed to the victims of their research.

As disturbing as these examples appear regarding the outright disregard for the rules and guidelines of human research, they are clearly distinguishable from the more perplexing problem of trying to draw distinctions between medical research and medical practice and the need to determine whether military personnel have been treated as uninformed research subjects. The advances in medical technology and therapeutic treatments have blurred the distinction between therapy and research. This fuzzy line of demarcation applies in the military and has potential for ethical conflict as one seeks to protect the rights of military personnel from unethical practices regarding their use as human subjects.

The Persian Gulf War Experience

The history of research with soldiers demonstrates a prevailing attitude that when a threat to the nation's security appears imminent (as was the case of nuclear war in the 1950s and the fear of lysergic acid diethylamide [LSD] use on American personnel in the 1960s), the requirements of informed consent and review approval represent impediments to national security—the urgency of the situation demands the conduct of these studies. Such a rationale has been used to justify egregious abuses of autonomy and respect for human welfare in clear cases of research when such a defense is unjustifiable.

The Persian Gulf War added a new dimension to the issue of protecting military members not only from abuses of research mentioned previously but from the imminent prospect of facing chemical and biological weapons. Chemical weapons comprise a broad spectrum of devices that include lethal agents (nerve, blood, blister, and phosgene), incapacitating agents (so-called tear gas agents), smoke, and herbicides. Nerve agents, a particular threat from the Iraqi arsenal, attack a person through the skin inhibiting the action of the enzyme cholinesterase. Inhibition of cholinesterase causes violent muscle contraction in the victim with death resulting from

asphyxiation. Additionally, Iraq was known to have an arsenal of biological weapons that work by spreading disease. Anthrax and botulism are typical biological agents that can be delivered on the battlefield by bombs, missiles, and rockets.

Prior to commencing Operation Desert Storm (ODS), the combat phase of the Persian Gulf War, the DoD sought and obtained a one-time waiver of informed consent requirements (known as Rule 23[d]) for the use of investigational drugs and vaccines on American forces serving in the Persian Gulf. The Food and Drug Administration (FDA) defines investigational drugs as those not approved for use by the general public. Until 1987, the use of investigational agents was permitted solely for research purposes. The FDA modified this rule approving the use of investigational agents to treat life-threatening conditions where no comparable drug or therapy is available. Changes notwithstanding, the FDA requires physicians to obtain a patient's informed consent before using an investigational drug for therapy.⁴⁶ In persuading the FDA to waive their requirements on the use of investigational agents, the DoD argued that in the exigencies of war obtaining soldiers' informed consent was "not feasible."⁴⁷ This case study highlights many issues, the least of which includes where to draw the line between medical practice and medical research. The FDA approval of the informed consent waiver rekindled discussion of how to make a distinction between therapy and research but also raised the specter of the Nazi doctors—namely, did the DoD make guinea pigs out of US military personnel serving in the Persian Gulf War?^{48–52}

There are two basic positions regarding the use of investigational drugs and the informed consent waiver approval as it applied to military members during the Persian Gulf War. The major point of contention hinges on whether the use of investigational agents by the military in this one-time occurrence constitutes medical research or medical treatment. Presumably if the intended use is for research, the waiver is unethical as opposed to medical treatment where the exigencies of war provide justification to waiving consent with the purpose of protecting soldiers from chemical and biological weapons.

The Research Point of View

The first position contends that the military intent for using investigational agents was to conduct medical research. Consequently, the Nuremberg Code would prohibit the use of these drugs on sol-

diers who did not provide informed consent. More recently, the Department of Defense Authorization Act (1985) also prohibits the military from conducting research on humans unless it has obtained the informed consent of the subject in advance. This prohibition even extends to research intended to be beneficial to the subject. Consequently, those who hold this position view the waiver of informed consent as patently unethical. A moderated position of this view concedes the intent of the military as one of medical practice but insists that in the use of investigational agents, even when there is evidence that a derived benefit from their use exists, such a benefit does not automatically transform what is experimental into therapy. If this were the case, then the informed consent process could simply be circumvented by redefining these activities. In either case, the argument upholds the absolute of informed consent in research activities. Advocates of this view believe the use of investigational agents constitutes research. Therefore, the use of these agents with a waiver of informed consent is unethical.

The Practice Point of View

Those who condone the waiver of informed consent articulate a position that argues the use of investigational agents as a preventive treatment against biological and chemical weapons is not medical research. The DoD was attempting to use these agents in what was considered an immediate “life-threatening” situation to protect the lives of military members from the effects of biological and chemical weapons. This use is within the scope of the US Food and Drug Administration’s (FDA) regulation on investigational drugs.⁵³ The principle of preventing unnecessary harm (nonmaleficence) to military members overrides all other principles in this view, even the prerogative of soldiers to make their own decisions regarding medical treatment (autonomy). Because the use of these agents was intended as a preventive therapy and not research, and because the military already has precedent to impose medical therapies on military members to ensure mission accomplishment, the action regarding the use of investigational agents in this context was not viewed as unethical by the FDA or DoD leadership.

The Distinction Between Research and Practice

The Persian Gulf War example provided the opportunity to examine the conceptual distinction between medical research and medical practice. *The Belmont Report* addresses this issue and is the start-

ing point for this discussion. According to the *Report*, the term practice refers

to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.^{8(PartA)}

The term research, by contrast,

designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships).^{8(PartA)}

The *Report* goes on to further clarify departures by physicians from standard or accepted practice, but such departures from standard practice do not, of themselves, constitute research.

The fact that a procedure is “experimental,” in the sense of new, untested or different, does not automatically place it in the category of research.^{8(PartA)}

The use of investigational agents by the DoD for preventive treatment against biological and chemical warfare agents was new and untested. One of the agents, pyridostigmine bromide (PB), is approved by the FDA for therapeutic use for a different purpose than as a pretreatment chemical agent antidote. Consequently, the DoD was compelled by law to file a new investigational drug application for an already approved FDA drug. FDA approval requires safety and efficacy testing in both animals and humans. Safety and efficacy data exist in animal studies for PB use as a chemical agent pretreatment. Only safety data exist for this use in humans because efficacy testing would require exposing human subjects to a nerve agent. This activity is unethical under existing human use review board standards. Therefore, the FDA cannot grant complete licensure for the use of this drug as a chemical nerve agent pretreatment.

At this juncture the issue becomes how to gain approval to use these investigational agents even though they lack full approval status. Having conducted risk-benefit analysis, given the best intelligence data regarding the Iraqi intent to use biological and chemical weapons, and lacking any current pretreatment standard of care for exposure to nerve agents, soldiers faced a greater risk from these weapons unprotected than they did from receiving

the investigational drugs. Now the issue shifts to the appropriateness of requiring soldiers to take drugs known to be safe without the option of informed consent. The military could have allowed soldiers to take these drugs voluntarily. The DoD argued, however, that to allow soldiers to refuse to take the drugs would needlessly risk their lives and the lives of their protected compatriots:

Our planning for Desert Shield contingencies has convinced us that another circumstance should be recognized in the FDA regulation in which it would be consistent with the statute and ethically appropriate for medical professionals to “deem it not feasible” to obtain informed consent of the patient—that circumstance being the existence of military combat exigencies, coupled with a determination that the use of the product is in the best interest of the individual. By the term “military combat exigencies,” we mean military combat (actual or threatened) circumstances in which the health of the individual, the safety of other personnel and the accomplishment of the military mission require that a particular treatment be provided to a specified group of military personnel, without regard to what might be any individual’s personal preference for no treatment or for some alternative treatment.⁴⁷

The Dilemma of Choice

Earlier in this discussion the conclusion was drawn that there are no exceptions to the right of informed consent to participate in research. One can argue that even the use of a new, unproved therapy should not be imposed on soldiers without their consent. Can the Persian Gulf War example—the use of unproved therapy (given it is consistent with the criteria of *The Belmont Report*)—provide a qualified exception in the context of actual or threatened combat?

The basic responsibility of the FDA is to protect the American public (to include military members) from unsafe and ineffective drugs. A problem arises when a drug passes safety testing but criteria for testing efficacy are beyond the bounds of ethical conduct. Which is more harmful: (a) to withhold the potential benefit or (b) risk facing the life-threatening situation without protection? One might readily answer that no protection produces a greater risk. Does that mean that the use of the drug is required or should soldiers be allowed to choose voluntarily? The answer to this question depends upon whether military members have a duty to subordinate individual self-interest for the good of the many. The success of a military mission depends upon unit cohesion, trust, and interdependence of unit members. Military units spend countless hours

training and preparing for their wartime missions. The success of small unit tactics depends upon unit members being able to perform their assigned tasks when called upon to do so. Unprotected soldiers suffering injury from chemical and biological agents become liabilities to the welfare of their unit members when they are unable to perform their assigned role. Ultimately, the success of the overall mission is potentially jeopardized. If there is a derived benefit from taking these investigational agents and some members fail to accept this benefit, the negative effects of biological and chemical weapons not only impacts on those members not protected but degrades the capability of the entire unit and ultimately the welfare of the other unit members. Although some may argue that requiring military personnel to sacrifice their autonomy is morally indefensible, such a sacrifice has justification based on the principle of duty.

Summary

The protection of military personnel from the inherent risks of medical research and from innovative, new, and unproved practice is of paramount importance. Those who serve in defense of their country have a heightened sense of duty to their comrades-in-arms and to the nation. Those who exercise command authority over military personnel have an obligation to protect the rights, dignity, and autonomy of their subordinates to the extent possible without jeopardizing the military mission or the welfare of military personnel as a whole.

There exists an ethical framework and criteria by which medical research can be conducted that preserves the ethical status of military members. Military personnel have the prerogative to volunteer for research and to deny them this privilege can potentially violate their personal autonomy. The experience in the Persian Gulf War and Rule 23(d) illustrates the difficulty of making choices that satisfy the demands of competing ethical principles and the potential for blurring the distinction between research and therapy. Significant to the Persian Gulf War is the need to acknowledge the risk associated with the use of unproved therapies. When the DoD finds it necessary to seek another waiver for the use of investigational agents in times of war, careful and comprehensive study of military members who take these agents is a moral imperative. The mysteries of Gulf War illnesses suggest that the military should do a better job of obtaining information regarding side effects and illness that may stem from the agents themselves or effects of the agents com-

bined with unique environmental exposures and stress of the battlefield. Simply stated, the military needs to devise a more effective method for recording and sorting medical information on the battlefield, particularly when it requires waivers from standard legal and ethical practices in medical research or therapy. This point suggests that if exceptions to es-

tablished practices to informed consent exist, and military personnel later suffer from medical conditions linked to the use of investigational agents administered without informed consent, then they ought to receive just compensation and the record trail to support such claims ought to be available, exigencies of combat notwithstanding.

ETHICS AND THE ISSUE OF ANIMAL EXPERIMENTATION

More than the other topics of this chapter, the use of animals in research is as much a social and political question as it is a philosophical one. With few exceptions the voices in this debate are volatile and intractable, expressing virtually no hope of reaching common ground or compromise. Consequently it is imperative to examine the arguments with the intent of gaining understanding of the ethical stakes from both sides of this debate.

There exists the presumption that most people want to “do the right thing” regarding actions to fellow humans and nonhuman animals. With this presumption comes the recognition of the value of biomedical research in advancing cures, treatments, and prophylaxis enhancing quality of life (even though some opposed to animal research deny such value). Value is ascribed to medical research because of the good that it adds to human life. Advocates of animal research support its practice because they view the value of human life greater than nonhuman animal life. One can hold this position without denying that nonhuman animal life has value, only that human life has greater value. As a society, however, the United States is becoming more ambivalent over the use of animals to gain medical advances at the expense of nonhuman animals, using lower animal life models or computer modeling as alternatives. The source of this ambivalence may stem from emotionally charged rhetoric, or the desire to be more sensitive to creatures who can experience pain, suffering, and lost preferences, or possibly a paradigm shift of viewing nature as a cosmic unity. This ambivalence might also stem from the realization that a concept of speciesism is valid in regard to the treatment of nonhuman animals, pricking moral consciousness beyond caring about the welfare of animals to affording them rights.

The Moral Status of Animals

The position one chooses to embrace regarding the use of animals in research derives from whether or not one has a fundamental belief in the moral

equality and rights of animals.^{54,55} The moral equality position advocates rights in the sense of human rights where it follows that the use of animals by humans constitutes a moral wrong. The logical starting point to determine whether it is ethical to use animals in research begins by determining whether it is ethical for humans to use animals for any purpose. Many critics of animal research assert the right of nonhuman animals to be treated as ends in themselves. If one holds the position that it is wrong for humans to use animals for any purpose then there is no moral distinction to make between justifiable and unjustifiable use of nonhuman animals in research. There is no middle ground, no basis for mediation, no common principle by which antagonists in this debate can reach consensus. Logical consistency demands that using animals for food, clothing, sport, entertainment, and education also violates the so-called rights of animals. If, however, one concedes that not all uses of animals for human needs are unethical, the debate narrows as to why using animals in research is morally wrong but other uses are morally permissible.

Animal Suffering vs the Primacy of Human Life

One might easily suggest, as many do, that the main problem with using animals in research is the suffering inflicted upon them.⁵⁶ Advocates for animal rights have framed the antivivisection debate as one depicting all animal research as cruel, unnecessary, and unscientific as opposed to distinguishing between the humane and inhumane use of animals. Hence the fundamental value argument in this context places the research community in a position of upholding the primacy of human life over animal life. If animals have moral equality with humans then one cannot help but question, as do many who favor vivisection, as to the matter of priority when defending the rights of animals on the issue of suffering. For example, the use of animals for food and clothing probably exceeds biomedical research by higher than a thousand-fold. Further-

more, the majority of animals used in research are mice and rats. This dichotomy or, less charitably, logical contradiction has led many people to conclude that animal research is merely a target of opportunity—an issue easily isolated from mainstream animal use, namely hunting, domestic pets, and the food and clothing industries.

It is not possible to conclude, however, from the preceding discussion that the use of animals in research and related suffering they might incur, is automatically justifiable simply because their use for other purposes is condoned. Many animals have “expressed preferences” and the ability to pursue those preferences. Consequently animals should not be treated as mere objects. Animal lives count for something as does their ability to feel pain and to suffer. On balance one has to consider whether the pain an animal might experience in research is justified given the magnitude of benefit derived. Hence one returns to the question at hand: Are humans ethically justified in the use of animals either in general or specific instances, and if so, what ethical obligations apply to researchers who use nonhuman animals in their research? Surprisingly, there appears to be no consensus among philosophers in applying ethical theories to answer these questions. There is indication, however, that even arguments for complete abolition of animal research do not completely exclude exceptions for valuing human life as greater than nonhuman animal life.⁵⁷

Application of Ethical Theory

The major ethical theories are versions of (a) teleological or consequentialist views—the basic theory of this type is generally known as classic utilitarianism or (b) deontological views focusing on the inherent rightness or wrongness of an action irrespective of the good (bad) consequences that result from doing an action. Closely akin to the deontological view is the rights-based account of moral obligation that emphasizes the notion of respect and justice that reflect upon a particular moral judgment as right or wrong. Finally the contractarian view espouses ethical obligations forged from mutual agreement of consenting parties who function as moral agents.

The animal rights’ proponent fundamentally opposes the use of animals by humans based on the belief that animals have inherent value. If animals have inherent value (moral equality), then regardless of the good humans can derive from their use, it is morally impermissible to violate the rights of

animals that derive from their inherent moral worth. This argument requires a conceptual definition of inherent value. Antivivisectionists conceive (in minimal properties) sentience, purposiveness, and the capacity to feel pain to be sufficient to afford animals moral status. One criticism of these criteria is that they are not sufficient. The necessary trait to confer moral status on a living entity is moral autonomy—the capacity to make moral choices. Because this trait is lacking in nonhuman animals they deserve less or no moral consideration. One attacks this criticism by pointing out that humans lack, at various times, the capacity to function as moral agents (ie, a baby; a senile, demented, or retarded person; a comatose patient) yet their moral value is still regarded. Likewise sentient animals should be afforded equal consideration and their well-being should not be disrupted.⁵⁸

If this argument is sound (if its premises are true and the conclusion follows from the premises), then humans incur fundamental duties regarding their actions toward animals. These duties derive from the respect or moral concern they are now obligated to afford to animals but are in conflict with the consequentialist (utilitarian) view. A consequentialist may well agree with the concept that animals have moral worth but reject the absolute view of violating that worth when doing so maximizes the greatest benefit balanced against the harm to an animal. Most researchers are likely to be utilitarian in their view of using animals in research. Even Peter Singer, viewed by many as the founder of the animal rights’ movement, concedes the use of animals as research subjects could be justified if it produced more utility than disutility.⁵⁴ His major claim is simply that it is wrong to give less consideration to the suffering of an animal than one would give to the similar suffering of a human being. This claim does not support the abolition of animal research. It only compels the researcher to demonstrate (from a utilitarian calculation) that the good to be derived from the animal’s suffering outweighs the evil of the suffering. If one accepts the aggregate benefit of using animals for medical cures, especially when a particular protocol involves no pain to the animals, there can be little left to worry about in the utilitarian calculation. One criticism of this view is that the perceived benefits of an experiment are in doubt until after the experiment has run its course. If there is no benefit, then only retrospectively can it be concluded that the animal’s loss produced no aggregate benefit. This view still grants some moral status to animals and places an obligation on researchers to develop

well-designed protocols using the lowest form of animal model suitable to validate the scientific hypothesis. Consequently one considers the welfare of animals without having to take the extreme position of an animal rights' advocate.

A Definitive Rights Position

Regan presents a clearly articulated position in *The Case for Animal Rights*.⁵⁹ Regan's position revolves around a fundamental right—the right not to be harmed on the grounds that doing so benefits others. This position is in distinct contrast to the classic utilitarian. Harm in Regan's view is the loss of the capacity to form and satisfy desires. For any living thing that can form and satisfy desires, the ultimate harm is death—the complete loss of one's ability to form and satisfy those desires. As to the issue of delineating a list of which animals are capable of forming desires, Regan is reluctant to "draw lines." He is quite satisfied that at least mammals and birds have this desire but will admit that humans have this capacity to a greater degree than other mammals and birds. Consequently, Regan postulates that if four humans and a dog are in a lifeboat that can support only four occupants, none of the humans should be harmed because each stands to lose more than the dog. Regan calls this scenario the application of the "worse-off" principle. Because a human being's capacity to form and satisfy desires is greater than that of any nonhuman animal, a human stands to lose more in death than the dog. Harming any of the humans is avoided because they stand to lose more than the dog. Peter Singer believes that this conclusion demonstrates an inconsistency in Regan's position.⁵⁴

Regan also formulates a rule of action called the "miniride" principle. In this view, there is an attempt to minimize the overriding of an individual's rights. In this way one is not using a utilitarian view of aggregate happiness but rather is focusing on the individual. Thus, in Regan's mind, utilitarian reasoning is avoided. The problem is that in applying the miniride principle the same conclusions are derived as when the principle of utility is applied. Regan simply wants to emphasize focusing on the individual and minimizing any overriding of the animal's rights as opposed to focusing the aggregate happiness produced by the principle of utility.

Critics suggest that Regan, in his formulation of these moral principles, fails to establish standards that support the total abolition of animal research.⁶⁰ Hypothetically, if it were known with certainty that an experiment could produce a vaccine that would

save human lives, then it would be justified in either of Regan's principles to harm the animal, even to the point of death, to produce the vaccine. Therefore, even someone like Regan, a complete abolitionist of animal research, who advocates a moral rights position, would have to concede that at least some medical research with animals is morally permissible (justified).

Summary

What is interesting about the preceding comparison of the utilitarian and rights positions is that in either case, whether one accepts the moral equality claim or subscribes to the view that humans have greater capacity to satisfy desires, both views justify at least some medical research. Consequently the question then becomes a matter of deciding which experiments are justifiable and which are not. This question becomes more a matter of oversight and regulation than the outright prohibition of animal research. This debate has increased the burden for scientists to justify their use of animals but in so doing has benefited the animals and contributed to better science.

In considering the proponent and opponent positions of animal research the views can be summarized in the context of competing ethical theories and interests. From both a teleological and deontological perspective there are reasonable arguments to justify the use of animals in research. Both perspectives provide ethical principles by which to consider any justification for animal research: comfort, well-being, pleasure, sentience, and purposiveness. Although researchers may be able to move away from animal use with emerging technology, at least for the present their use is still required. Hence the question is less about the ethics of animal research and more about the ethics in animal research. Researchers should use animals with good reason. Protocols must adhere to sound experimental design and subscribe to the ethical and legal codes of conduct relevant to the care and use of animals in research. Most significantly, researchers must take great strides to reduce the pain and suffering inflicted on animals in the conduct of research. Finally, as a society there ought to be a commitment to developing alternatives to animal use when such alternatives will produce credible scientific results.

Military research may present a problem regarding the development of alternatives to animal research. One example is the need to conduct physiologic studies regarding methods to combat biological and chemical weapons. Data obtained from ani-

mal studies indicated the safety and efficacy of the nerve agent antidote used by the US military during the Persian Gulf War. Given that the goals of military biomedical research are directly linked to enhancing the well-being and reducing the suffering of military personnel, most Americans would accept the use of animals in this research as ethically justifiable. Consequently, the issue narrows to defining how much animal use is justified in serving the aims of military biomedical research. To this end, military researchers face the same ethical concerns as civilian researchers in mitigating animal suffering for the benefits derived to improve the human condition. Ethical analysis provides guidelines to govern animal care committees for the humane care and use of laboratory animals. This same

analysis does not support a complete prohibition of animal research. Application of ethical parameters might well suggest that animal use in military biomedical research has greater justification than civilian research as military research consistently aims at reducing significant human suffering and death produced by the weapons of modern warfare. In many instances, animal studies are the only way to verify the harm that exists to military personnel from various weapons, but animal studies are also necessary to study the effects of American weapon systems and military material on American personnel. To this end, military biomedical research needs to consider the ethical requirements of conducting good science while considering the humane treatment and welfare of laboratory animals.

MILITARY WOMEN'S RESEARCH PROGRAM

A national agenda is forming on women's health that focuses on the previous lack of female subjects in research; the lack of funding for research of women-unique diseases; the need to improve access to healthcare for women; and the desire to improve preventive care for women. The problem of specific data gaps related to women's health issues has already received national attention. The General Accounting Office issued a report in June 1990 demonstrating that despite federal policy dating back to 1986, women continue to be excluded in biomedical research populations.⁶¹ As recently as June 1994, the National Institutes of Health (NIH) issued new guidelines to enhance medical research standards to include more women and minorities in research studies. Not only are women and minorities to be included but their subpopulations are to be noted and numbered.^{62,63}

The efforts to overcome data gaps created by previous policies have significant relevance for military women. The US military deployed nearly 40,000 women to Southwest Asia during the Persian Gulf War. Throughout this deployment significant female soldier health and performance issues surfaced in the areas of occupational and environmental health hazards, psychosocial and posttraumatic stress illness, clinical safety and efficacy of licensed and investigational pharmaceutical and biological products, and preventive health and sustained duty performance. Similar to the civilian medical community, there are scant research studies of military relevance that focus on women-unique health problems and military women are excluded disproportionately to their male counterparts as research subjects.

In the 1990s several programs were instituted to redress this problem.^{64,65} In 1994, the Congress established the Defense Women's Health Research Program (DWHRP) to "address the critical health and performance issues impacting women in the military."⁶⁵ There were two main components of the research programs: (1) those utilizing institutions that are part of an agency or activity of the DoD or other US military service department (the intramural program) or civilian institutions that would collaborate with military institutions; and (2) those utilizing agencies outside the government, both for profit and nonprofit, both public and private (the extramural program).

The intramural research program solicited research proposals in the following four areas: (1) major factors affecting the health and work performance of military women; (2) psychological and health issues resulting from the integration of women into a hierarchical male environment or related women and men living and working in close quarters; (3) health promotion and disease prevention; and (4) access to delivery of healthcare. The extramural program solicited research proposals in four areas related to the intramural research: (1) operational effectiveness for mission accomplishment; (2) health promotion and disease prevention; (3) psychological health and well-being; and (4) access to and delivery of healthcare. By fiscal year 1995 a total of 66 research programs had been funded for the intramural and extramural programs. Similar levels of research activity will likely continue well into the future to redress the prior lack of research into issues pertaining to the health of women serving in the military.

THE PROBLEM OF EXCLUSION

Various articles have been written exploring the problem of exclusion.^{66,67} The fundamental issue, having already identified probable causes for a gender bias in healthcare, is to recognize the ethical imperative for correcting recognized deficiencies. One aspect of ethical analysis is to determine whether there exists sufficient ethical justification for a particular practice, namely an exclusion policy toward women in medical research and treatment protocols.

Given the basis for biomedical research to obtain generalizable data for improving health and treatment, one must ask whether exclusion practices violate the principle of beneficence. The application of beneficence suggests that research practices should maximize benefit and minimize harm. To violate this principle the practice of exclusion must cause harm or diminish expected benefits. Applying this principle to the practice of excluding women from research protocols, several harms are evident. First, the physiological differences between men and women make it inappropriate to simply generalize findings from research conducted on male subjects. For instance, a variety of male-only studies for heart disease, cholesterol, and asthma medication led to treatment alternatives actually detrimental to women's health. Even though one can argue the need for uncomplicated data from a homogeneous test population, this scientific requirement (or expediency perhaps) does not justify conducting studies on all male groups. During the Persian Gulf War, female soldiers received the same dosage rates of pyridostigmine bromide, a nerve agent pretreatment antidote, as their male colleagues. Testimony during the Senate hearings on illnesses associated with service in the Persian Gulf suggested physiological differences in men and women could affect safe dosage levels for women causing various side-effects and a possible connection to unexplained illnesses in women who had served in the Persian Gulf War. Consequently, studies conducted without female test subjects may lack the very scientific merit the study was initially designed to support.

These obvious harms aside for the moment, one explanation offered in the past to defend exclusion practices is that such practices actually prevent harm to women and other minorities simply because they are minorities. The early history of biomedical research in this country is replete with the exploitation of disadvantaged groups as research participants. The infamous Tuskegee syphilis study stands as a permanent fixture to these unethical abuses. Consequently, exclusion practices might be

offered as a way of protecting minorities from these past practices of exploitation. Thus the principle of beneficence is upheld in the sense that excluding minorities from studies protects them from the possible harm of exploitation. This explanation fails to consider that the harm of exploitation is a product of failing to adequately inform the research subject of the inherent risks to research participation. Informed consent is supposed to mitigate against exploitation. The paternalism of "protecting" minorities is a subtle form of unjust discrimination and applies protectively only in the case of nonclinical investigations. In clinical investigations, exclusion and paternalism possibly deny minorities the benefits of the research. Hence, the real issue is not a matter of "protecting" minorities from harm but allowing them to participate as equals in the research enterprise with full knowledge of the risks so they may also derive the benefits of the research outcomes. Therefore, a practice of exclusion lacks ethical justification in relationship to the principle of beneficence.

One must not judge too harshly the failure of the position that exclusion protects minorities from exploitation in the research process. The backlash of Tuskegee and similar studies not only led to a paternalistic view of protecting minorities but also caused a reluctance on the part of minority groups to participate in the scientific enterprise. Both of these trends fail to uphold the principle of beneficence. Additionally, the exclusion practice in seeking to do good (granted a charitable interpretation) violates the principle of justice. Current ethical practices in research, based on the principle of justice, require a fair and equitable distribution of burdens and benefits—giving people what they deserve (benefits) mitigated against the amount of their involvement in the process (risk-taking). An exclusion practice cuts two ways in violating the principle of justice. First, medical research is subsidized with tax dollars. If a segment of the population financially supports the research enterprise and then cannot benefit from its outcomes, such a practice violates the justice principle. Likewise, if a segment of the population benefits from research but does not accept the associated risks, be they physical or financial, this practice also violates the principle of justice. Consequently the requirement to expand protocols to include women satisfies both aspects of the justice principle.

Another consideration used to justify exclusion of women from studies is the possibility of a woman

research participant getting pregnant during the study resulting in harm to the unborn child (commonly referred to as unforeseeable teratogenic risk). The principle of nonmaleficence (avoid causing harm) is the ethical principle oftentimes used in this defense. Military research protocols and the accompanying informed consent require special counseling for fertile women volunteers regarding the hazards of birth defects and miscarriage should pregnancy occur in the course of the study. Researchers funded on DoD dollars must inform women of the need to use birth control during the study. Pregnancy is often used as an exclusion criteria to withdraw women subjects from a study. Given these conditions, complete exclusion from the onset of a study may be too general and broad a practice. Even though precaution is clearly warranted to avoid potential harm to an unborn child (and one can debate whether enforced contraceptive use is too strong a precaution), a real harm is created by simply excluding women with the ability of conceiving children. The key to mitigating risk with fertile women subjects is to determine the degree of risk each protocol actually presents to a developing child—the greater the risk, the more exclusive the selection criteria could be for fertile women. Still this parameter need not mean total exclusion. Not all fertile women are sexually active nor would be necessarily so while participating in a study.

Past research practices of exclusion should not be construed as intentionally seeking to discriminate against women. The lack of enlightened sensitivity and thinking in this area is more likely attributed to convenience, saving money, simplifying the design of protocols, and simplifying logistical requirements to accommodate both sexes during the conduct of a study. The fact remains that there exists a gender bias in selecting research subjects and this bias is harmful to the welfare of women. Value judgments have been made in American society about practices that cause harm—they are unethical. Hence because exclusion practices cause harm, or at least have been demonstrated to cause harm, exclusion practices are unethical.

CONCLUSION

The ultimate mission of military medical research is to provide preventive and therapeutic products for the welfare of the soldier. To this end military medical research must remain committed both in a professional sense and an ethical one. Military medical research is a noble enterprise with a long history of significant contributions to healthcare,

Much is being done to correct the previous gender bias in research selection. The military medical research programs are expanding to cover women-unique problems associated with military duty and job performance. Most notably perhaps was the creation of a DoD breast cancer research program in 1993. Congress directed the Army to execute a breast cancer research program based upon a number of factors. The major effort came from a highly visible lobbying effort by the National Breast Cancer Coalition, a grass roots advocacy effort to eradicate breast cancer, seeking congressional funding for the breast cancer program at the National Cancer Institute (NCI). The US Congress responded by directing \$210 million to the US Army Medical Research and Development Command (which later became the US Army Medical Research and Materiel Command) to create a breast cancer program.⁶⁸ The overall objective of this funding is to promote research directed toward reducing the incidence of breast cancer, increasing survival rates, and improving the quality of life of those diagnosed with the disease. This program extends beyond the traditional military medical research mission and is indicative of the strides being taken to correct past practices. Still the lesson to learn is that it is necessary to stay vigilant to uncover other biases in medical research and healthcare as yet undetected.

Finally, now that the research community is expanding its horizon to include women-unique studies, women must be willing to become active participants in the research process. What must be guarded against in the developing process of a women's health agenda, however, is that whatever biological and physiological differences might be discovered do not become a means to perpetuate unjust discriminatory practices in employment and career paths. This is perhaps unlikely, but a word of caution is prudent when the study of environmental, physiological, and nutritional aspects of women's health specifically related to military duty is begun. Such differences, by themselves, ought not be used to exclude women from such service. Instead, ways to solve these various problems should be explored.

not only for soldiers but for the greater society as well. The US Army Medical Research and Materiel Command has been managing and administering targeted appropriations to the Department of Defense from Congressional direction since 1992. Appropriations totaling in excess of \$1.1 billion for breast cancer, women's health issues, and other

specified programs highlight key aspects of military medical research with a clear vision committed to ethical aims of improving quality of life. These programs are managed by skilled, multidisciplinary teams of military and civilian scientists and clinicians. The National Academy of Sciences and the Institute of Medicine have participated in program reviews and development seeking to substantiate the ethical and scientific credibility of these programs. These programs received strict review of Congressional oversight committees and are committed to public accountability in the investment of funds to address the research needs of targeted diseases.

Unlike the past, stakeholder participation is at the very heart of the implementation strategy of these research programs. Open communication

among research participants, scientists from various disciplines, consumer advocate groups, leading government, academic, and private organizations are all partnering to ensure unique issues and gaps in medical knowledge no longer exist. Expanding the opportunities for gender specific research is only one facet of the program that lends credence to the fact that times have changed and that program development and funding target these specific gaps and remedy the failures of the past. The growth of military medical research is not only a good thing for the military but for society as a whole. The growth of ethical awareness toward the use of medical research for the benefit of society and preserving the very core of the healing professions—caring, compassion, and the relief of suffering—continues as a necessary and essential component of these research programs.

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