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Protecting Soldiers from Friendly Fire: The Consent Requirement for Using Investigational Drugs and Vaccines in Combat†

George J. Annas‡

This could be the world's largest friendly fire incident.¹

I. INTRODUCTION

In his classic treatise On War, Karl von Clausewitz emphasizes that courage is the "first quality of a warrior." He defines two types of courage: "courage in the presence of danger to the person; next, moral courage, or courage in the presence of responsibility, whether before the judgment seat of an external authority or before that of the internal authority of conscience."² Both were involved in the U.S. military's decision to seek a waiver of informed consent requirements for the use of investigational drugs and vaccines on U.S. troops in the Persian Gulf War. The danger of chemical and biological attack was seen as demanding this waiver; while the Nuremberg Code, medical ethics, and respect for the human rights and dignity of American soldiers cautioned against it. The legal maneuvering to revise consent regulations for wartime conditions provides a case study illustrating how the boundary line between therapy and experimentation can become hopelessly blurred, the differences between law and ethics, and the ethical obligations of military physicians.

II. THE NUREMBERG CODE AND THE U.S. ARMY

The Nuremberg Code was promulgated by U.S. judges acting under the authority of the U.S. Army at the trial of Nazi doctors at Nuremberg in 1947.³ The defen-

† This article is adapted from George J. Annas, Changing the Consent Rules for Desert Storm, 326 NEW ENG. J. MED. 770 (1992).
‡ Edward Utley Professor and Chair, Health Law Department, Boston University School of Public Health; Professor, Boston University School of Medicine; Professor, Boston University School of Law; A.B., 1967 magna cum laude, Harvard College; J.D., 1970, Harvard Law School; M.P.H., 1972, Harvard School of Public Health.
¹ Paul Sullivan, founder of the National Gulf War Research Center.
³ See 2 U.S. GOV'T PRINTING OFFICE, TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY TRIBUNALS UNDER CONTROL COUNCIL LAW NO. 10, at 189–98 (1946–1949) [hereinafter TRIALS OF WAR CRIMINALS] (finding Karl Brandt guilty of "responsibility for, and participation in, Freezing, Malaria, Lost Gas, Sulfanilamide, Bone, Muscle and Nerve Regeneration and Bone Trans-
dants in the Doctors' Trial were charged with war crimes and crimes against humanity for performing both lethal and nonlethal experiments on concentration camp prisoners. Most were found guilty, and seven were hanged. The judges also enunciated the Nuremberg Code, a ten-point declaration governing human experimentation based on "principles of the law of nations as they result from the usages established among civilized peoples, from the laws of humanity, and from the dictates of public conscience." The first and central principle provides that the voluntary, competent, informed, and understanding consent of the subject is "absolutely essential." There are no exceptions for soldiers or for wartime, and until the Gulf War, the U.S. mili-


1. 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 free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, 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. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

   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.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve a subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probably [sic] cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

tary had accepted the Nuremberg Code as their guide. The military had never argued that there should be any exception to the Code’s informed consent requirement. Current U.S. statutory law also requires that informed consent be obtained for all “investigational purposes” of drugs, except where an investigator deems it “not feasible,” or in his professional judgment, “contrary to the best interests of [the subjects].”

In 1990, following Iraq’s invasion of Kuwait, the Department of Defense (DOD) sought a waiver of the informed consent requirements of existing human experimentation regulations from the Food and Drug Administration (FDA). With this waiver, DOD could authorize military use of investigational drugs and vaccines on soldiers involved in the Gulf War without their informed consent. The basis of the waiver request was military expediency. In DOD’s words: “In all peace time applications, we believe strongly in informed consent and ethical foundations . . . but military combat is different.” DOD’s rationale was that informed consent under combat conditions was “not feasible” because some troops might refuse to consent, and the military could not tolerate such refusals because of “military combat exigencies.”

FDA granted the request and issued a new general regulation, Rule 23(d), which permits drug-by-drug waiver approval on the basis that consent is “not feasible” in a “specific military operation involving combat or the immediate threat of combat.”

III. THE DISTRICT COURT

Shortly after the regulation was promulgated, and just prior to Operation Desert Storm, Sidney Wolfe’s Health Research Group (a part of Public Citizen Litigation Group) brought suit on behalf of an unnamed soldier (John Doe) and his wife to enjoin DOD from using Rule 23(d) drugs and vaccines on troops in the Gulf without consent. FDA had granted Rule 23(d) waivers for the use of two agents, pyridostigmine bromide thirty mg tablets (for use as a “pretreatment” prior to nerve gas attack) and pentavalent botulinum toxoid vaccine (to protect against botulism in biological warfare). These were the only waivers that have ever been granted under the rule.

U.S. District Judge Stanley Harris made it clear that he had no desire to get involved with military matters. In his words, “DOD’s decision to use unapproved drugs is precisely the type of military decision that courts have repeatedly refused to second-guess.” He characterized the decision as one to protect individual service-men and as “strategic” in nature, and thus not reviewable by a court. He went on to say, however, that if he thought he had the authority to review the military’s decision, he would uphold it.

6 Exceptions from General Requirements, 21 C.F.R. § 50.23(d) (1997).
9 See id. at 1374.
11 Id. at 15.
12 See id.
13 See id. at 18.
Consistent with the Nuremberg Code, the Defense Authorization Act prohibits DOD from using any of its funds "for any research involving a human being as an experimental subject" unless the subject’s informed consent has been obtained. This congressional restriction was in reaction to U.S. Army experiments using both radiation and LSD on servicemen at the beginning of the cold war. Judge Harris, however, found this statutory prohibition inapplicable because "the primary purpose of administering the drugs is military, not scientific."

The "not feasible" exception previously had applied only to subjects who were unable to communicate, unconscious, or incompetent. Nonetheless, Judge Harris decided that FDA could reinterpret the exception as long as its interpretation was not "arbitrary, capricious or manifestly contrary to the statute." Finally, Judge Harris rejected the claim that forced administration of unapproved drugs violates the Fifth Amendment liberty interest of servicemen. Instead, he found the military’s interests in trying to prevent injury to troops and “successfully accomplishing the military goals of Operation Desert Storm” sufficient to justify the exception to informed consent. The decision did not mention the Nuremberg Code.

IV. THE COURT OF APPEALS

John Doe appealed. At the hearing, held in March 1991 after the war was over, the Department of Justice (DOJ) introduced a letter into evidence from DOD to FDA which stated that the military requirements for use of the two agents without informed consent had ended. In the letter, DOD also informed FDA that “Central Command has recently reported that the military command in the theater of operations decided to administer the [botulinum] vaccine on a voluntary basis. The pyridostigmine tablets were used without prior informed consent.” On the basis of the end of the war and the DOD letter, DOJ argued that the case was moot and should be dismissed.

The majority of the court, in a 2-to-1 opinion written by Judge Ruth Bader Ginsburg (now Justice Ginsburg) in July 1991, disagreed. The court concluded that even though DOD had withdrawn its two specific waivers, Rule 23(d) remained in effect, and therefore the use of unapproved agents without consent was capable of

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19 See id. at 17.
20 See id. at 17–18.
22 See id. at 1375.
23 Annas, supra note †, at 771; see STAFF OF SENATE COMM. ON VETERANS’ AFFAIRS, 103D CONG., REPORT ON IS MILITARY RESEARCH HAZARDOUS TO VETERANS’ HEALTH? LESSONS SPANNING HALF A CENTURY 21 (1994) [hereinafter SENATE REPORT].
24 See Sullivan, 938 F.2d at 1375.
25 See id.
both repetition and evading review. The court of appeals relied heavily on government reports concerning the proliferation of nuclear, chemical, and biological weapons systems, especially among third world nations like Iraq. On the merits, the court disagreed with the lower court that the case was beyond court review because it was military in nature. Instead, the court of appeals defined the issue as a challenge to FDA’s authority to issue a waiver of its consent regulations to DOD, not as an action challenging military decisions. The court of appeals did agree, however, with all the other conclusions of the lower court. Again, no mention was made of the Nuremberg Code.

Judge Clarence Thomas (now Justice Thomas) dissented. He agreed with DOJ, arguing that, because the war was over and because it was virtually impossible for John Doe himself to be subjected to the rule again, the case should be dismissed as moot. He said that the majority “surely overstates” the risk of future chemical warfare, noting that “after all, American soldiers have not been the victims of organized chemical attack since the First World War.” He also stressed that there was no “reasonable likelihood that John Doe personally” will be involved in any future war using chemical weapons. Thomas stated, “The majority focuses on Rule 23(d) in the abstract—and in the process forgets about Doe, the plaintiff.”

V. THE COURTS AND WAR

Since the time of Cicero it has been said that *inter arma leges silentae sunt*—amid the clash of arms the laws are silent. This was certainly true of the forced internment of Japanese-Americans during World War II, and was true of the courts here as well. While troops are in the field, courts are unlikely to make any decisions that make them appear to be interfering with military decisionmaking. This realpolitik is disturbing because it undermines progress in human rights, but nonetheless remains consistent. The brief history of international human rights, after all, has been written primarily in the aftermath of war: the founding of the United Nations in 1946, the Universal Declaration of Human Rights in 1948, and current efforts to foster human rights in the wake of the cold war. Neither of these two courts could acknowledge (let alone discuss) the Nuremberg Code. Rule 23(d) permits direct violations of the Nuremberg Code, and acknowledging this could have embarrassed the United States by making us look hypocritical internationally. This is because members of the Bush administration were calling for a “Nuremberg-like” tribunal to try Saddam Hussein and his military leaders for violations of international

26 See id. at 1376.
27 See id. at 1377.
28 See id. at 1380.
29 See id. at 1381.
30 See id. at 1381, 1383.
31 See id. at 1383.
32 See id. at 1384–85 (Thomas, J., dissenting).
33 Id. at 1385.
34 Id. at 1386.
35 Id.
law at the time these cases were heard in our own courts. International human rights laws, of course, must apply to both victors and vanquished.

Even though Rule 23(d) authorizes violation of the consent requirements of the Nuremberg Code, it can reasonably be argued that the Code was not actually violated in the Gulf War. The argument is that the Code applies only to human experimentation or research on human beings and that DOD was not actually conducting research. What was at stake with the pyridostigmine bromide tablets was the use of an approved and licensed drug for an unapproved use. This can be justified if good scientific evidence supports its safety and it could even be considered treatment (or "pretreatment") if nerve agent attack appears imminent, as it did to the commander of the XVIII Airborne Corps whose 41,650 soldiers took the drug in tablet form for one to seven days at eight-hour intervals. Members of the military (unlike civilians) have no right to refuse any medical treatment that can make them fit for combat or return them to active duty. Thus, if pyridostigmine can reasonably be considered treatment, it needs no exception to Nuremberg: Nuremberg is simply inapplicable. I think this argument is correct. But this means that the military was simply wrong to ask for a waiver of the requirement of informed consent to administer this agent in a research trial. The court of appeals should have used this rationale for its decision. If the drug is really treatment, no waiver of consent is necessary; if it is experimental, no waiver of consent should be permitted. The Army, Navy, and Air

37 See Jill R. Keeler et al., Pyridostigmine Used as a Nerve Agent Pretreatment Under Wartime Conditions, 266 JAMA 693, 694 (1991). All organophosphorus (OP) nerve agents, which include tabun (GA), sarin (GB), soman (GD), and VX and its analogs:

operate on the same principle: they knock out the enzymes (ie acetylcholinesterase) that control the body's balance of acetylcholine—a critical neurotransmitter that determines proper electrical activity in the body. Overstimulated by a surplus of acetylcholine, pupils become constricted, one loses muscular control and normal breathing becomes impossible. The first defence, of course, is proper NBC [nuclear, biological, and chemical] clothing and masks . . . . The next step is to prepare soldiers for a possible chemical environment by the pre-emptory administration of pyridostigmine (bromide ionic form in the USA). The latter compound protects the body's aforementioned enzyme acetylcholinesterase by, ironically, inhibiting it to a level of about 40 per cent. During the 1990-91 Gulf War the US armed forces used 30 mg tablets of pyridostigmine bromide (PB), one tablet that should have been taken every eight hours. The idea is to allow a temporary inhibition of enzyme by PB so that if a nerve agent is encountered, enough enzyme will remain after exposure so that a crisis can be averted, especially with the subsequent use of an auto-injector and anti-convulsive medication (such as diazepam). The USA fielded a Mark I auto-injector that contains an oxime (2-PAM-Chloride) to help reverse enzymes blocked by the nerve agent, and atropine to counteract overstimulation by accumulated acetylcholine. The theory on reversing enzyme inhibition by oximes may be sound, but in fact there is some question as to the effectiveness of oximes in practice . . . .

. . . . [O]nce a soldier is exposed, soman is the most difficult to reverse and treat among the nerve agents known to be commonly deployed. The field injector used by the USA (PAM-Cl, atropine) is severely limited when it comes to soman. OP Nerve Agents: A Bibliography, 10 JANE'S INTELLIGENCE REV., Jan. 1, 1998, at 44, 44; see infra note 45 (describing the signs and symptoms of nerve agents sarin, soman, and VX).

38 See Edward G. Howe & Edward D. Martin, Treating the Troops (Symposium), HASTINGS CENTER REP., March 1991, at 21, 27-28; Pharmacy Ethics: Waivers for Military Use of Investigational Agents, 48 AM. J. HOSP. PHARM. 1525, 1527-28 (1991); Schuchardt, supra note 15, at 100-05 (stating that "it is reasonable to conclude that the Pentagon did not conduct 'research' on the soldiers in the Gulf.").
Force seem to have agreed with this, and were prepared to use pyridostigmine long before the waiver was even sought.\textsuperscript{39}

It is much more difficult, however, to make this argument regarding botulinum toxoid vaccine. This vaccine had been used by about 3000 laboratory workers in the past, but its use was discontinued briefly in the mid 1970s (before sufficient safety or efficacy data had been gathered to qualify it for licensure), and few laboratory workers have used it since. It remains an experimental agent. The Centers for Disease Control and Prevention (CDC) have an elaborate consent form which explains its experimental nature under their investigational new drug protocol.\textsuperscript{40} Its experimen-


\textsuperscript{40} The text of the consent form reads:

NOTE: It is desirable that individuals who will receive this toxoid read this consent form at least 24 hours before they are inoculated.

CONSENT FORM

TITLE: Inoculation with Pantavalent (ABCDE) Botulinum Toxoid

PURPOSE: Pantavalent (ABCDE) Botulinum Toxoid is a biological product which has been distributed by the Centers for Disease Control (CDC) since 1987. It has been granted an Investigational New Drug (IND) status by the Food and Drug Administration (FDA), Department of Health and Human Services. It is not commercially available in the United States. The toxoid itself is free of cost.

INOCULATION SCHEDULE: You will be given the toxoid in an initial series on three different dates. 0-2-12 weeks. Your arm will be examined by the investigator two days after each inoculation. You will receive an initial booster 12 months after the first injection of the initial series and, if you continue to work in a high risk laboratory, you will be given subsequent boosters at 2-year intervals. Before receiving a second or subsequent booster, you will be asked to have a 15-20 ml tube of blood taken from a vein in your arm. This is done to check your serum for antibody protection levels (immunity) by the CDC before administration of the booster. The booster will not be given for at least another two years if serum antitoxin levels are found to be satisfactory.

BENEFITS AND RISKS FROM PARTICIPATION: This is an investigational product which may protect you from contracting botulism after exposure. Botulism is a very serious intoxication characterized by weakness, extreme dryness of the mouth, and nerve paralysis. Even with modern treatment, about 8% of botulism patients die. Over 90% of individuals who had both the botulinum toxoid initial series and at least one booster will develop protective antitoxin levels. An unprotected individual involved in a serious exposure to botulism may require botulism horse-antitoxin after such an exposure. Your participation may also provide important public health information on the effectiveness of this toxoid.

The use of this toxoid during pregnancy has not been studied and the toxoid should not be given to pregnant women.

The investigator should be notified if you are enrolled in another medical study. If you ever contract a botulism-like intoxication, the investigator should be notified.

During the first 48 hours from 5 to 7% of individuals receiving this toxoid may experience certain minor side effects such as mild or moderate local reaction at the site of the inoculation. Usually this is redness only, but swelling and/or limitation of arm movement may occur. Rarely, in less than 1% of cases, more generalized reactions have
tual nature explains why a U.S. Army institutional review board at Fort Detrich voted in October 1990 to require consent to this vaccine if it was to be used in combat.\textsuperscript{41}

been reported. These may consist of one or more of the following: general malaise; fever and/or chills; headache, sore joints, and stiff neck; dizziness, nausea, or vomiting; double vision; prickling sensation on face and body. If you have any reactions that are suspected to have resulted from the toxoid, you should report them to the investigator listed on this consent form.

There is only negligible risk from having blood taken from your arm/vein.

In the event of physical injury resulting from the administration of botulinum toxoid, there is no provision for compensation on or medical treatment from the CDC.

GENERAL CONDITIONS OF CONSENT: I have read the above statement and I understand the benefits and risks involved. I have been given this opportunity to ask any questions at any time I might desire, and I understand that I have the right to withdraw at any time. I understand that I will not be identified by name in any published report. If, during the course of this study, important facts about my personal health should be discovered, I will be notified.

INFORMATION CONTROL: I understand that the CDC, an Agency of the Department of Health and Human Services, is required to solicit information under provisions of Section 505 (K) of the Federal Food, Drug and Cosmetic Act and cannot otherwise release the vaccine. I further understand that the physician(s) will, therefore, furnish CDC with a report of my response to this vaccine, but that I will not be identified by name in any published reports. Information from this report, together with data from all other patient reports received during the same calendar year, will be compiled and a cumulative report filed annually with FDA. Access to patient files kept by the CDC is granted to the FDA. The information requested is considered relevant and necessary to the investigation of the efficacy and safety of the vaccine and individually-identified data requested may be shared with health departments and other public health or cooperating medical authorities. I understand that an accounting of such disclosures will be made available to me upon request.

\textsuperscript{41} A record of the October 4, 1991 institutional review board meeting, dated October 5, 1991, reads in part:

The Committee is aware that this protocol depends upon an anticipated waiver of informed consent that is being negotiated with FDA and other agencies as a policy decision related to operation Desert Shield. The Committee has no direct knowledge of the stipulations of this policy nor is the Committee aware that it has been implemented. The 12 week period required for full primary vaccination affords some time for implementation of informed consent, at least within the spirit of the Declaration of Helsinki. Full compliance with written documentation of informed consent as described in Army Regulation 70-25 or 21 C.F.R. 50 may not be necessary, however. The ability to use investigational drugs, biological, and devices in human subjects is predicated on a subject's ability to trust that health care professionals are working in his best interest. Human use committees approve protocols because they trust that their judgment of the protocol and the integrity of the investigators will result in execution of a study exactly the way it is described in the protocol. Our regulations require written documentation of informed consent and documentation of the actions taken with subjects in research, but if our trust is not matched by the integrity and intention of the investigator/care giver, no paper documentation can assure compliance. In which case, there is no difference between oral and written informed consent. In the present scenario, the intent to use pentavalent botulinum toxoid is for the benefit of the soldiers at risk to exposure. The health care providers that will administer the vaccine in the field are there solely for the benefit of the soldiers. There is no reason to believe that those soldiers will refuse vaccination when told of the high risk of death due to botulinum toxin exposure, the low risk of mild reaction to vaccine and the benefit of possible protection if vaccinated. If a soldier does refuse vaccination, and he is one who would be at high risk, he may be required by his commander (AR 600-20, para 5-4) to be vaccinated for his own
The reason the military may not have violated the Nuremberg Code by using this vaccine on troops is not because the vaccine can legitimately be considered treatment or therapy, but because the military appears to have ultimately decided to give our troops in the Gulf information about the vaccine and the right to refuse to be vaccinated. We can be somewhat skeptical about the meaning of "voluntary" under imminent combat conditions. Nonetheless, this decision merits commendation, and one would like to know more about how and why military commanders in the field chose not to take advantage of the legal authority they had to use this vaccine on their troops without consent.\textsuperscript{42} No matter what their motivation, the field commanders did the right thing and took the principles of the Nuremberg Code more seriously than did DOD, FDA, or these two courts.

As the court of appeals noted, DOD had argued in court that these agents had not been tested previously in controlled clinical trials "because humans cannot intentionally be exposed to chemical or biological [warfare] agents in order to test the effectiveness of a drug." This is true, but only because it violates another dictate of the Nuremberg Code: "No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur." General Norman Schwarzkopf and his medical command seem to have understood that one cannot pick and choose which provisions of the Nuremberg Code to take seriously without being hypocritical.

Immediately after the war, I opined (wrongly, it turns out) that the risk of chemical and biological warfare in the Gulf had been overstated. Likewise, DOD assured the nation until 1996 that no troops had been exposed to Iraqi chemical weapons. In mid 1997, however, the Pentagon admitted that as many as 100,000 U.S. troops may have been exposed to low levels of the nerve agent sarin after the war when American combat engineers exploded the Kamisiyaw ammunition depot.\textsuperscript{43} There are at least two explanations for covering up these exposures. First, pyridostigmine bromide is designed as a pretreatment to a soman attack (followed by atropine and 2-PAM in the event of attack), but it may be contraindicated for sarin (another agent held by Iraq).\textsuperscript{44} Therefore, use of this drug may indicate either a protection and also for the protection of others if his loss would put others at risk. An alternative action a commander would make, would be to replace him with one who is vaccinated and reassign the soldier within the company where he could personally face the consequence of his decision without risk. No one need be evacuated because of refusal to be vaccinated. The protocol was unanimously approved by the Committee with the recommendation that requirement of full compliance with documented informed consent as defined in AR 70-25 and 21 C.F.R. 50 be waived and in its stead an abbreviated oral informed consent statement be substituted and administered as described above.

See also Keith Epstein & Bill Sloat, Objection to Gulf War Vaccine Was Overridden, CLEVELAND PLAIN DEALER, Dec. 21, 1997, at 16A (reporting that 8000 troops were given the botulinum toxoid vaccine without being told it was unlicensed).

\textsuperscript{42} This instruction, however, apparently did not always make its way to the war zone. In one survey of 150 Gulf War veterans, for example, of the 17 who reported getting the botulinum toxoid, 15 were told they could not refuse it. See SENATE REPORT, supra note 23, at 21.


\textsuperscript{44} See SENATE REPORT, supra note 23, at 11–13; Robert W. Haley & Thomas L. Kurt, Self-Reported Exposure to Neurotoxic Chemical Combinations in the Gulf War, 277 JAMA 231, 232 (1997); I. Koplovitz et al., Reduction by Pyridostigmine Pretreatment of the Efficacy of Atropine and 2-PAM Treatment of Sarin and VX Poisoning in Rodents, 18 FUNDAMENTAL & APPLIED TOXI-
Neither General Schwarzkopf nor General Powell seems to have understood how PB worked and its likely ineffectiveness against sarin. In questioning before the Senate Veterans Affairs Committee on January 29, 1997, for example, the following exchange occurred between General Schwarzkopf and Senator Jay Rockefeller on this issue of the effectiveness of PB, atropine, and 2-PAM against sarin:

SEN. ROCKEFELLER: ... Now if you took all three, PB, atropine, and 2-pam you were brilliantly prepared for the chemical weapon—type of chemical destructive weapon which we knew Iraq did not have. That is, somin [sic].

I don't even know how to deal with that in my mind, that tens and tens of thousands of soldiers were given the atropine/2-pam, I'm not quite sure, PB. Many, many soldiers weren't warned, weren't you know, under the Nurenburg [sic] trials investigational drugs, all the rest of it, but they didn't know about it. But even if they had, if it had all been done correctly, it would have been completely ineffective against what it was we know the Iraqis would put on us if they were going to do it.

I cannot fathom how DOD could allow something like that to happen. Do you have any thoughts?

GEN. SCHWARZKOPF: I can't—I don't know either. Obviously I didn't know about this.

SEN. ROCKEFELLER: How could they not know about it?

GEN. SCHWARZKOPF: It's a shock right now. We knew that they had—as far as I was concerned, atropine[,]...[which] is a treatment against nerve gas poisoning. . . . And I've had to inject myself, inject an orange. We had the troops inject oranges and all this other thing to learn how to administer the stuff. So that's where the atropine came from. As far as I was concerned, the other medications that were being sent over there that we'd been told about I thought were completely effective against a nerve agent. I know nothing's going to be effective against a mustard agent because of its burning capabilities, but I thought it was a nerve agent, or perhaps a blood agent.

I think that you're probably seeing, and I—it's fair to say this that we were preoccupied with the Iraqi chemical weapons. I mean, we were scared to death of the Iraqi chemical weapons because they're mass casualty producers and they're indiscriminate in who they kill. I mean, they don't just kill a soldier. They kill anybody who they come in contact with.

And what you are probably seeing, or what you are probably recounting, is a reaction, perhaps an over-reaction to coming up with any kind of antidote that they could come up with to prevent our troops from being killed by [] chemical weapons.

SEN. ROCKEFELLER: But they wouldn't have done it—they would have been totally ineffective.

GEN. SCHWARZKOPF: You're one up on me, Senator, because I don't know that.

SEN. ROCKEFELLER: That's my concern, that somebody like me could be one up on you, when you were theater commander out there.

GEN. SCHWARZKOPF: It concerns me a little bit, too.


General Powell later testified, on April 17, 1997, before the same committee that although he had no personal knowledge of the effectiveness of PB against sarin, he relied on FDA's approval of its use in the Gulf as complete justification:

The one issue that was especially difficult for us and for me personally was the use of PB, as Senator Rockefeller referred to it, and the other vaccines that were available to us, and prophylactics that were available to us, to protect our troops against nerve agents and against some of the biological agents. We knew that these were experimental drugs. We knew that they did not enjoy the level of approval that the FDA normally gives to such drugs for mass consumption.
breakdown of intelligence before the war or acknowledge an inability to protect troops against both sarin and soman at the same time. Second, even a small exposure to sarin could produce delayed nerve damage, especially in concert with other exposures. There is likely no single cause of Gulf War syndrome, but this could be one

But members of the committee, I must say to you, that we approved the administering of those drugs to our troops with the full assurance from the FDA that they were safe for human use and that they were effective. The suggestion that somehow I, as chairman of the Joint Chiefs of Staff, would sit in the Pentagon and approve the use of medicines for our troops that I knew at the time to be improper or injurious to our troops or put them at some risk—it's just not accurate, sir. It is not accurate. The FDA approved those medicines, those vaccines, those toxoids for use with our troops under investigational waiver authority. And that's the way in which we used them.

We knew there was a risk in doing this because it did not enjoy the highest level of general circulation FDA approval. And I still remember a meeting in the tank one day, our command center for the Joint Chiefs of Staff, where, after the chiefs had examined this with their own surgeon generals, we brought all the surgeons general together, with the assistant secretary of defense for health, and asked if we were absolutely sure that this was an effective prophylactic method and whether or not the FDA approved these items as being safe for use by our troops. And the answer was yes.

Holds Hearing on Gulf War Illness: Hearings Before the Senate Comm. on Veterans' Affairs, 105th Cong. (Apr. 17, 1997) [hereinafter Hearing on Gulf War Illness] (testimony of General Colin Powell, Former Chairman of the Joint Chiefs of Staff), available in LEXIS, Legis Library, Poltrn File.

45 See Hearing on Gulf War Illnesses, supra note 44; Robert W. Haley et al., Letter, 278 JAMA 385, 385–87 (1997) (listing useful sources); Robert M. Sapolsky, The Stresses of Gulf War Syndrome, 393 NATURE 308 (1998). The Medical NBC Officer Field Manual describes sarin, soman, and VX as follows:

Nerve agents are primarily organophosphorus esters similar to insecticides. Those of military importance are combined under this term. Although some have been given names, they are usually known by their code letters: GA (TABUN); GB (SARIN); GD (SOMAN); and VX.

Sarin (GB) Colorless liquid giving off colorless vapor with a faint fruity odor.

\[
\text{CH}_3 \quad \text{H} - \text{C} - \text{O} - \text{O} \\
\downarrow \quad \downarrow \quad \downarrow \\
\text{CH}_3 \quad \text{P} \\
\downarrow \\
\text{CH}_3 \quad \text{F}
\]

Soman (GD) Colorless liquid giving off a colorless vapor with odor of fruit (camphor when impure). Permanently binds to receptors in two minutes. After that 2 Pam Chorilide is not useful.

\[
\text{CH}_3 \quad \text{H} \\
\downarrow \\
\text{CH}_3 \quad \text{C} - \text{C} - \text{O} - \text{O} \\
\downarrow \quad \downarrow \quad \downarrow \\
\text{CH}_3 \quad \text{CH}_3 \quad \text{P} \\
\downarrow \\
\text{CH}_3 \quad \text{F}
\]

VX—in some countries the “V” agents are known as “A” agents. Colorless to amber oily liquid with faint odor of rotten flesh.

\[
\text{C}_2\text{H}_2\text{O} \quad \text{O} \\
\downarrow \quad \downarrow \\
\text{P} \quad \text{CH(CH}_3)_2 \\
\downarrow \quad \downarrow \\
\text{CH}_3 \quad \text{SCH}_2\text{CH}_3\text{N} \\
\downarrow \\
\text{CH(CH}_3)_2
\]
The Characteristic Signs and Symptoms of Nerve Agent Poisoning are:

<table>
<thead>
<tr>
<th>Severity</th>
<th>Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>MODERATE Symptoms (buddy aid)</td>
<td>Casualties with MODERATE poisoning will experience an increase in the severity of most or all of the MILD symptoms. Especially prominent will be an increase in fatigue, weakness and muscle fasciculations. The progress of symptoms from mild to moderate indicates either inadequate treatment or continuing exposure to agent.</td>
</tr>
<tr>
<td>SEVERE symptoms (buddy aid)</td>
<td>Casualties with SEVERE symptoms may experience most or all of the MILD symptoms, plus most or all of the following: Strange or confused behavior. Wheezing, dyspnea (severe difficulty in breathing), and coughing. Severely pinpointed pupils. Red eyes with tearing. Vomiting. Severe muscular twitching and general weakness. Involuntary urination and defecation. Convulsions. Unconsciousness. Respiratory failure</td>
</tr>
</tbody>
</table>

46 See The Iowa Persian Gulf Research Project: Hearings Before the Subcomm. on Human Resources and Intergovernmental Relations of the House Comm. on Government Reform and Oversight, 105th Cong. (Jan. 21, 1997) (statement of David A. Schwartz, M.D., M.P.H.), available in LEXIS, Legis Library, Fednew File [hereinafter Iowa Persian Gulf Hearings]; Haley et al., supra note 45, at 385-86; see also Iowa Persian Gulf Hearings, supra (statement of Robert W. Haley, M.D.) (describing symptoms of Gulf War syndrome and possible sources of exposure). It has been persuasively suggested that the institutional inability of the Department of Defense to investigate the possible link of PB and low level nerve gas exposure to Gulf War syndrome is based on a desire to continue to present the Gulf War as a “clean” war with few casualties:

If there is such a thing as institutional stubbornness, the Pentagon has it. All bureaucracies react to something that could cost them face much the way a sea anemone touched by a finger does—they close up and seal off. But DOD is particularly prone to such reactions, which makes the science worth studying in the story of Gulf War syndrome behavioral as much as biological.

More than most bureaucracies, the military faces very public tests of its effectiveness. Since it failed one of those tests in Vietnam, exposing itself to years of abuse, humiliation, and low public esteem, the Pentagon has been especially defensive, and eager for redemption—which the Persian Gulf War provided. It dispatched the military’s Vietnam complex, sending institutional pride to new heights. It was the mythical “perfect war.” Then along comes not only a nasty set of illnesses, but a plethora of investigators muddying the myth by churning up questionable decisions, vulnerabilities, and just plain mistakes on the military’s part.

The apparent stonewalling seems to have been an attempt to paper over bungling or negligence that would tarnish the Gulf victory, as well as the careers and reputations of those associated with it. This same phenomenon surfaced in the investigation of the terrorist bombing at Khobar Towers in Saudi Arabia. . . . The inclination was to priori-
VI. ROLE OF MILITARY PHYSICIANS

What should physicians in the military do when asked to administer investigational agents without the informed consent of the soldiers? Even if such administration is legal (as the courts have ruled), it is unethical and following orders is no excuse for unethical conduct, even in combat. It would seem that the only justification a physician could have for participating in the administration of experimental or investigational agents without consent is that the physician sincerely believes that the agents are therapeutic under combat conditions. This is a difficult position to defend, because war does not change the investigational nature of a drug or vaccine. Such a decision would also be contrary to military regulations, which state that although a serviceperson must accept standard medical treatment, or face court-martial, soldiers have no obligation to accept interventions that are not generally recognized by the medical profession as standard procedures.47

A related question is whether the military physician is primarily responsible for the health and well-being of the soldiers under the physician’s care (as in civilian life) or must subordinate the medical interests of the soldier-patients to the military mission. Remarkably there is no written policy or standard view on this question in the military. This issue deserves critical attention in peacetime, because it is not susceptible to rational thought during wartime. An unequivocal policy upholding traditional patient-centered ethics, although not legally required, seems the most responsible position for U.S. military physicians to take.

VII. SHOULD THE NUREMBERG CODE APPLY TO THE MILITARY?

The United States is and should remain at the forefront of the worldwide human rights movement. In crafting exceptions for the military, even in wartime, we do more damage to ourselves than to our enemies because any major retreat from supporting human rights is destructive both to our credibility and to the cause of human rights. Also, it is simply not true that members of the U.S. military cannot understand or appreciate military missions to such an extent that informed consent is “not feasible” in combat situations. According to DOD itself, this was not true in Desert Storm (nor in Korea or Vietnam). Although the U.S. Supreme Court has ruled that U.S. soldiers cannot sue the military for money damages for violation of the Nuremberg-Code, all of the Justices have said that an injunction against such violations can be sought in a civilian court (as did the plaintiff in the Desert Storm case).48 Unfortunately, during war courts ignore human rights and thus our soldiers are left without a remedy as a practical matter. Our military must have the courage to continue to take the Nuremberg Code seriously in its own ranks, because no court will second-guess last-minute rule rewriting or impose Nuremberg’s legal and ethical dictates on the military in wartime.

47 See W.H. Johnson, Civil Rights of Military Personnel Regarding Medical Care and Experimental Procedures, 117 SCIENCE 212, 213 (1953).
The U.S. military is interested in the possible combat-related use of approximately twenty vaccines which are currently investigational. There is a clear need for a policy on their use. The Gulf War experience should reinforce the lessons of the Nuremberg Code: except where the agent has had enough extensive human testing to have been proven safe, no agent should be used on American troops without their informed consent. Investigational agents can be used in combat, but soldiers must make the decision based on what is known about their risks and benefits. The pyridostigmine experience provides a useful example. Although soldiers were ordered to take pyridostigmine tablets, there was no effective way to monitor their use, and as the military investigators noted, “full compliance with an every-eight-hour regimen would be unlikely when soldiers themselves believed the nerve agent threat was low.” Nonetheless, at the beginning of hostilities in January, compliance seems to have been “well over 99%.” In short, it is not only ethically wrong to force compliance on soldiers, it is also militarily unnecessary.

In December 1995, I was invited to participate in a meeting on Rule 23(d) sponsored by the Presidential Advisory Committee on Gulf War Veterans’ Illnesses. During the meeting, DOD representative continually referred to American soldiers as “the kids” and the responsibility of DOD to protect “the kids.” I probably waited too long to tell him that I found this offensive, but he apologized for his choice of words. Nonetheless, the words are telling. Rule 23(d) treats American soldiers like kids and applies the basic rules for research on children to them with regard to consent—someone else makes the decision for them because they are seen as too immature to make it for themselves. For an adult this is always an affront to human dignity and disrespectful of personhood. In this regard, Rule 23(d) is a mistake and an aberration. As General Dennis Reimer, the Army’s Chief of Staff, has emphasized, the Army is (and should be) committed to treating all its troops “with dignity and respect.”

Soldiers are not pieces of equipment. They have numbers, but they retain their humanity and basic human rights. DOD should have exercised a third kind of courage—the courage to admit its mistake—and asked FDA to rescind Rule 23(d) and removed this pointless blot on our military laws. Instead, when Public Citizen petitioned FDA to revoke the rule in 1996, DOD supported continuing the waiver of consent rule as “fully consistent with law and ethics.” In mid 1997, FDA asked for public comments on what should become of the rule. The answer remains simple:

49 For current DOD biological warfare research proposals, see Joint Program Office for Biological Defense, U.S. Dep’t of Army, Joint Vaccine Acquisition Program: Final Programmatic Environmental Assessment (June 1997).
50 See supra note 37; see also Senate Report, supra note 23.
52 Accessibility to New Drugs for Use in Military and Civilian Exigencies When Traditional Human Efficacy Studies Are Not Feasible; Determination Under the Interim Rule that Informed Consent is Not Feasible for Military Exigencies; Request for Comments, 62 Fed. Reg. 40,996, 40,996 (1997). The three major reasons DOD presents to retain the current waiver rule all confuse and conflate research with treatment:

1. When the President commits U.S. military forces to a combat, peacekeeping, or humanitarian deployment, the U.S. Government has a duty to take all reasonable precautions to bring about a successful completion of the mission and a safe return of the deployed forces.

2. The Government’s duty to take all reasonable precautions to preserve the fighting force must include recognition of the startling proliferation of chemical and biological weapons among potential adversaries and terrorist organizations and an obligation to
it should be rescinded because it violates every code and ethical principle developed
since World War II to regulate research with human subjects, and it is unacceptable
to permit commanders to turn soldiers into research subjects.53 The field command-

implement the best possible medical countermeasures.

3. Implementation of the best possible medical countermeasures may require the
standardized treatment use of an investigational new drug or vaccine for all personnel
at risk in a military combat exigency, including those personnel who, for whatever rea-
son or no reason at all, would prefer an alternate treatment or no treatment.

Id. at 41,000.

It should also be noted that even though DOD continues to support the rule, it apparently does
not follow it. In Bosnia, for example "nearly 4,000 soldiers were told during military briefings that
the vaccine, called TBE, was 'already known to be very safe and extremely effective'" although it
was a research vaccine designed to protect against tick-borne encephalitis and not approved by FDA.
Bill Sloat & Keith Epstein, Army Misled Troops Who Got Vaccine in Bosnia, CLEVELAND PLAIN
DEALER, Jan. 25, 1998, at 1A.

53 On October 24, 1997, Leonard Glantz, Michael Grodin, and I wrote the following response
to FDA's request:

We strongly urge the FDA to revoke the interim final rule that is described in the re-
quest for comments as permitting "the Commissioner . . . to determine that obtaining
informed consent from military personnel for the use of an investigational drug or bio-
logic is not feasible in certain situations related to military combat." The central issue
the proposed rule raises is "Can military personnel, all of whom are competent adults,
be used as subjects of medical research without obtaining their informed consent?" Because
the answer to this question is so clearly "No" we will only respond to the first
question: "Should the FDA revoke the interim rule? If so, why?"

The answer is that the FDA must revoke the interim rule because it violates every
code and ethical principle developed since World War II to regulate research with hu-
man subjects. The Nuremberg Code that states, "The informed consent of the human
subject is absolutely essential." While there are exceptions to this blanket statement for
young children and other incompetent subjects, we know of no exception to this rule
for competent adults until the

The interim rule amended 21 C.F.R. 50.23. Prior to this amendment, this section
dealt entirely with a class of subjects who were "confronted by a life-threatening situa-
tion necessitating the use of a test article," and "informed consent cannot be obtained
from the subject because of an inability to communicate with, or obtain legally effec-
tive consent from, the subject." 21 C.F.R. 50.23 (1) and (2). This entirely reasonable
rule permitted the use of an investigational substances [sic] in currently life-threatening
situations for people who were not able to speak for themselves, but for whom we could
reasonably surmise would want the use of a substance that could well save their lives.
But it would be scandalous if this rule permitted the use of lifesaving investigational
substances on competent adults without their consent. It is the subject's very incom-
petence that makes this rule ethically acceptable.

It is simply wrong to place a rule that enables soldiers to be used as human subjects
without their consent in the section of the regulations that deals with exceptions to the
informed consent requirement based on lack of feasibility of obtaining consent. Every
soldier on active duty is capable of giving consent. It might be burdensome or difficult
for the military to obtain consent from these soldiers, but it is certainly "feasible." Since
every soldier must be given the investigational substance, every soldier could, at
that point in time, be given information that would enable him or her to determine
whether to become a research subject. Military personnel would, of course, also have
to be told that they were not required to participate in such research. The military's po-

1. It is not acceptable to defer to a soldier's personal preference
concerning a preventive or therapeutic treatment that "might" save his
life, or avoid endangering other military personnel.

2. It is not defensible militarily or ethically, to send a soldier un-
protected into danger.

3. Special military exigencies sometimes must supersede normal
rights and procedures that apply to civilians and, thus, military regula-
ers in Desert Storm seem to have realized this instinctively. Soldiers who fight to protect basic human rights must be protected by them.

All of this might be true. But it is unrelated to the question of whether it is acceptable for the military to require soldiers to become human subjects. If the military has a substance that it believes will keep soldiers healthy in battle, it should use it. Soldiers in battle are subject to all types of risks not incurred by civilians. The risks that soldiers are exposed to is a command decision, subject to review through military and international codes. What is clearly unacceptable is to turn soldiers into human subjects.

A whole body of international rules has been developed along with federal and state rules that are designed to protect human subjects. The cornerstone of all these rules is the necessity of the consent of competent subjects. Indeed, protecting human subjects and treating them with respect has been the consistent policy of the Department of Defense since 1953 when the Secretaries of the Army, Navy and Air Force adopted a memorandum entitled “Use of Human Volunteers in Experimental Research.” That memorandum authorized the use of Armed Services personnel for human volunteers subject to certain conditions. The first condition was “The voluntary consent of the human subject is absolutely essential.” This adoption of the Nuremberg Code’s ethical requirement as a precondition to the use of military personnel as human subjects has been the policy of the military until it asked the FDA to excuse it from this vital ethical norm.

The exception to the requirement of informed consent for competent adults who are in the military is the only exception we know of based on employment or status. The Office of Protection from Research Risks has particular rules for research performed on fetuses, prisoners and children. But each one of these rules is designed to give those classes of subjects more protection than they might receive under the general rules. The interim rule is the only one that provides a class of people with less protection because of the class to which they belong.

Because the interim rule deviates so substantially from national and international rules and norms that protect human subjects and require their respectful treatment, and because they are so inconsistent with the rest of FDA policy protecting human subjects, we urge you to revoke the interim rule.
The importance of establishing rights in a dead body has been, and will continue to be, magnified by scientific advancements. The recent explosion of research and information concerning biotechnology has created a market place in which human tissues are routinely sold to and by scientists, physicians and others. The human body is a valuable resource.\(^1\)

I. INTRODUCTION

The body of the nineteenth century philosopher Jeremy Bentham is on display in a glass cage at University College, London.\(^2\) Bentham applied his utilitarian perspectives to the body by suggesting that corpses, including his own, would be of greater use to society stuffed and displayed as an “auto-icon” rather than simply buried away.\(^3\) Preserved, exhibited and studied, the corpse, he said, could serve “moral, political, honorific, dehonorific, money-saving, money getting, commemorative, genealogical, architectural, theatrical, and phrenological” ends.\(^4\)

But the corpse is more than a utilitarian object; it is an ambiguous entity—subject to conflicting beliefs and contradictory representations.\(^5\) It has sacred meaning. We maintain burial grounds as sacred places and celebrate national holidays to commemorate the dead. And every religious faith has beliefs pertaining to

\(\)\(^1\) Brotherton v. Cleveland, 923 F.2d 477, 481 (4th Cir. 1991) (citation omitted).
\(\)\(^3\) See id. at 203–04.
\(\)\(^4\) Id. at 205 (quoting Jeremy Bentham).