

Waiving Informed Consent: Long-Term Consequences for the U.S. Military

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In December 1990, the Department of Defense (DoD), anticipating the invasion of Kuwait for Operation Desert Storm, petitioned the Federal Drug Administration (FDA) to waive the federally mandated informed-consent requirements in the case of two investigational drugs: pyridostigmine bromide (PB) and botulinum toxoid (BT). PB, administered orally, was thought to be an effective pre-treatment against the nerve agent soman. The BT vaccine was potentially effective against the bacterium causing botulism (1). Fearful of the possibility that Saddam Hussein would conduct chemical and biological warfare against American troops, the Joint Chiefs of Staff felt that these two investigational drugs could protect U.S. soldiers. The concerns of military leadership were well-founded. Saddam Hussein had used chemical nerve agents and mustard gas against his own people in the Iran-Iraq War (2). However, while military intelligence confirmed that Iraq had the capability to make biological and chemical (nerve agent) weapons, no evidence indicated Iraq had ever made a weapon with soman (3).

FDA did not approve PB and BT. They were considered experimental and fell under the category of investigational new drug (IND). Federal regulations stipulate that if any Federal agency, including the military, desires to use an unapproved drug, that agency must first fully brief the individuals receiving the IND. This briefing must include mention of associated drug use hazards, and the potential recipients' written consent must be obtained. Prior to the Gulf War, informed consent for INDs could only be waived in extreme emergencies, even for the military. However, the U.S. military determined that it was not feasible to seek the informed consent of 700,000 personnel deployed to the Middle East. In 1990, in the months preceding the Gulf War, the military petitioned the FDA to waive the informed consent regulations. The FDA, not wishing to intervene in national security policy and with the approval of an Institutional Review Board (IRB), issued the waiver in an interim ruling in December 1990 (4). However, as part of the approval for the waiver, the military was required to provide information sheets about PB and BT to the recipients detailing the possible side effects. In addition, the military was expected to carefully document the use of the INDs as well as any adverse reactions.

Approximately 300,000 military personnel received the PB pills and 8000 individuals received the BT vaccine during the Gulf War (5). Despite the specific requirement by the FDA that the military track data on both drugs, no procedure was ever established to document which personnel received the drugs and if any adverse side effects were noted (1). Many military personnel experienced systemic medical problems both during and after the Gulf War that were not combat related. Such problems have been termed as the Gulf War Syndrome (GWS). Most notably, over 100,000 Gulf War veterans complained of maladies ranging from chronic fatigue to paralysis in the

years immediately following the war (3), and of these, 20,000 reported debilitating symptoms (6). In preliminary studies, PB has now been implicated as the primary catalyst of the GWS, however the research is still in its early stages (3).

Waiving Informed Consent

The Federal regulations that govern informed consent for human subjects fall under the purview of the Department of Health and Human Services (DHHS). The regulations state that informed consent may be waived when using INDs, but a number of conditions must be met. No more than minimal risk can exist for the patient, and after the treatment is concluded, the participants must be notified of both the procedure and the possible risks (7). FDA, bound by the DHHS regulations, established their own framework of rules regarding INDs. Prior to the Gulf War waiver, FDA maintained that the informed consent process could be waived only in a life-threatening emergency with the patient unable to communicate and without time to obtain consent from patient's legal representative (7).

The Joint Chiefs of Staff decided it was not feasible to obtain the informed consent of 700,000 military personnel deployed to the Gulf War region and that the pending conflict was essentially an emergency situation by FDA standards. However, prior to granting the military informed consent waivers for the use of PB and BT, FDA required the military to convene an IRB (1). To meet this Federal requirement for the BT vaccine, the military actually convened two IRBs. The first IRB, the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) Human Use Committee, was the panel typically used by Army research personnel to consider protocols involving human subjects. The USAMRIID concluded that it was unethical to waive the informed consent of military personnel who would receive BT (8). They further recommended that oral, not written, consent be obtained because oral consent was feasible, and it also respected the rights of the soldiers. Six days later, for reasons not stated in any DoD documents or in any IRB minutes, the DoD then convened a second, entirely different IRB, the Surgeon General's Human Subjects Research Review Board (HSRRB). The HSRRB approved the BT protocol as submitted and recommended that informed consent be waived

(9).

Even though FDA waived the requirement for obtaining informed consent for the use of PB and BT in the Gulf War, the approval was contingent upon the military providing those service members who received the INDs with information sheets describing the PB and BT treatments in detail. The sheets were to explain the reasons for using the INDs, the symptoms of botulism and a nerve agent attack, and most importantly any potential side effects or reactions. In addition, the soldiers were also asked to report any of these side effects or reactions. Apparently, the information sheets never made it to the Gulf War theater, so the personnel who received the treatments did not receive any written information about the INDs. However, even a cursory glance at the information sheets that were approved by the Army for dissemination shows that they were at best superficial.

Ethical Issues

In 1978, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research issued the Belmont Report that identified three principles that are fundamental in determining whether a research protocol is ethical. They are: respect for persons, beneficence, and justice. These are the primary ethical considerations of an IRB when evaluating a research protocol (10). The crux of the respect-for-persons principle is the preservation of a person's autonomy when making decisions about his/her own medical care. It is this aspect of the Belmont Report that is at issue in waiving informed consent. By swearing an oath to the military and the nation, service members willingly sacrifice some autonomy concerning decisions about their own lives. Enlisting in the military is a supreme sacrifice and highly commendable, but should soldiers lose all rights to autonomy, especially when it comes to their health? The DoD defends its actions in waiving informed consent for INDs by stating, "Allowing a soldier to refuse treatment would endanger him/her as well as those who would try to save their lives and ruin mission success"(5). This paternalistic approach by the DoD overlooks one critical aspect: What exactly constitutes "treatment?"

There has been much debate as to whether the military's use of PB and BT constitutes research or treatment. In the clinical trials held

months before the Gulf War, only a select group of male human subjects were tested with PB and BT. There was no testing for interactions with other chemicals or drugs likely to be used with the INDs, and no long-term studies were conducted (5). Additionally, persons with health problems typical of military populations were never studied in conjunction with the drug testing, and women never participated in any trials (2). Is it ethical and reasonable to maintain that military members receiving drugs tested on a very small, isolated population were receiving “treatment?” Despite the fine line between treatment and research with investigational drugs, FDA’s own regulations clearly state that informed consent is required even when the unapproved drug is to be used in a therapeutic manner because the drug has not yet passed full FDA efficacy and safety trials (11).

The respect-for-persons principle was again violated when the information sheets for the INDs were “lost” (5, 12). These sheets should have been paramount in the minds of military medical professionals overseeing the PB & BT programs. The IRB approval and FDA authorization for PB and BT were contingent on the investigators adhering to the approved protocols, which included the distribution of the information sheets. The INDs found their way successfully to the Gulf War theater, and if DoD leadership had considered the sheets a similar priority, they would have been delivered also. Did the military view the information sheets as “not feasible” just as they did for informed consent? When FDA later evaluated the military’s use of INDs during the Gulf War, it identified “significant deviations from Federal regulations published in Title 21, Code of Federal Regulations (CFR), parts 50 and 312.” (1). FDA cited several areas in which the military was not in compliance. Most notably FDA admonished the military for not disseminating the information sheets prior to the use of INDs in the Gulf War. FDA also issued DoD a stern reprimand for not keeping detailed records on who received the drugs and, most importantly, any adverse reactions suffered by military personnel.

Lastly, the most glaring ethical issue was DoD’s use of two different IRBs. When the Army’s first IRB found that it was unethical to administer BT to military personnel without their informed consent, the DoD convened a second IRB that produced the desired result of recommending the waiver of informed consent

with no impediments. The military was clearly circumventing the system and in doing so trivialized the IRB process and violated Federal regulations. It appears the military was only seeking IRB approval as a formality in an administrative procedure and lost sight of the purpose of the review. FDA, very concerned about the military’s use of multiple IRBs when seeking informed consent waivers, censured the military in October of 1999 for this violation and changed the federal regulations regarding military IRBs (1). As a result, IRBs convened by the military to evaluate IND protocols are now required to include at least three members who are not employees or officers of the federal government and are not affiliated with the protocol in any way.

Long-Term Consequences

In December 1997, DoD announced plans to vaccinate all 2.4 million U.S. troops against the biological threat of anthrax. If not treated in its initial stages, anthrax is deadly (13). The current anthrax vaccine is approved by the FDA and was originally designed for agricultural workers and veterinarians. It is a six-shot protocol that is administered over a period of 18 months. Because of this extended treatment period, DoD decided that it must vaccinate all 2.4 million personnel in the unlikely event that all U.S. forces faced a biological threat.

Almost immediately after DoD made its announcement, military members began to protest, based in part on the revelation that service members were given experimental drugs without their knowledge in the Gulf War. Military, medical, and legal critics of the anthrax-vaccine decision were not satisfied that the vaccine was approved by the FDA (13 -15). The sole manufacturer of the anthrax vaccine, Michigan Biologic Products Institute (now Bio-Port) has failed numerous FDA inspections. Most recently, Bio-Port was cited for 23 violations, some of which included sterility and potency deviations, and some microbial contamination (14, 15). In fact, to date the Michigan plant still has not passed an FDA inspection (15, 16).

There have never been any published studies of human efficacy or long-term effects for the anthrax vaccine (15). Moreover, according to an April 1999 General Accounting Office (GAO) report, long-term effects of the anthrax vaccine have never been studied. To further add to the

debate over the efficacy of the anthrax vaccine, the Institute on Medicine has stated that the licensed anthrax vaccine is only effective against cutaneous anthrax and furthermore has never been tested for pulmonary anthrax, which would be the method of delivery in a combat arena (13). A chief Army biological researcher wrote in a 1994 textbook on vaccines that “the current vaccine against anthrax is unsatisfactory” (14). Despite the military’s assertions that it is only interested in protecting the welfare of its soldiers, GAO charges that DoD is extremely negligent in tracking adverse reactions to the anthrax vaccine, which was a significant problem with the INDs used in the Gulf War. In fact, many military personnel have reported adverse reactions to the anthrax vaccine. However, in the absence of any established tracking and monitoring system, there is no way to accurately identify any percentages.

With the data supporting the questionable status of the anthrax vaccine and considering DoD’s past history, it is not unreasonable to expect military personnel to have doubts about both the efficacy of the anthrax vaccine and the military’s plans for implementation. To combat potential insubordination, DoD court-martialed those personnel who refused the vaccine, stating that allowing soldiers to refuse the vaccine would undermine discipline and be prejudicial to good order. Many military members, outraged at DoD’s response and facing involuntary inoculation, chose to resign from the service rather than risk their health. The military is already facing serious retention and recruiting problems, and DoD’s refusal to make the anthrax vaccine voluntary is only adding to an already critical personnel shortage.

Prior to the mandated anthrax vaccination of all U.S. troops, the military’s policies against the threat of chemical and biological warfare were deterrence, containment of the enemy, and use of other defensive measures such as protective suits and warning devices (13). It was not until the Gulf War that troops were inoculated against the threat of possible biological warfare, and it was not until 1997 that troops were forcibly inoculated in peacetime. There has been much criticism directed toward DoD for implementing the anthrax vaccine in peacetime. DoD responded that even though there is no threat of war, the 18-month treatment period for the anthrax vaccine requires that it must prepare its forces for any future contingencies. However, GAO asserts that based on military intelligence

data, the biological warfare threat for U.S. troops has not changed since 1990 (14).

A Final Note on Accountability

Accountability is an imperative moral trait required of all military personnel and is considered the cornerstone for military command and leadership. By court-martialing military personnel who refuse the anthrax vaccine, DoD is holding these people accountable for their actions. For those court-martialed, this accountability will not cost them just their jobs within the military. In addition, they are dishonorably discharged and lose all their veterans’ benefits as well as their retirement benefits. The nation recognizes the right to make autonomous health-related decisions for all citizens, but it appears, not for military personnel who pay a high price for both autonomy and accountability.

This exacting level of military discipline and accountability is unfortunately glaringly absent from DoD’s use of INDs in the Gulf War. Especially troubling are the following:

- DoD convened a second IRB for an IND protocol when the first did not produce the desired recommendation to waive informed consent.
- No one was held accountable for the lost information sheets in the Gulf War. If military officers lost strategic documents protecting troops’ safety, they would most definitely face severe punishment.
- No one was held accountable for the incredible lack of record keeping including tracking adverse reactions during and after the Gulf War. Not only did military personnel suffer from a lack of treatment information, but also the entire medical field suffered from the loss of critical data.

This clear double standard in accountability will only continue to haunt the military. Public reports on the military’s use of experimental drugs on troops without their knowledge and the anthrax debacle will only continue to exacerbate personnel issues. FDA has recently issued more stringent rulings to prevent some of these ethical transgressions from occurring in the future and to compel the military to abide by the laws they are supposedly defending. However, not until DoD embraces the Federal policies designed to respect basic human rights and autonomy will the

military regain some of its medical credibility and confidence in leadership.

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