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SELF-REPORTED CHANGES IN SUBJECTIVE HEALTH AND ANTHRAX VACCINATION AS REPORTED BY OVER 900 PERSIAN GULF WAR ERA VETERANS[1]

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Summary.—A 1999 study of United Kingdom servicemembers by Unwin, *et al.* recently found significant relationships between anthrax and other vaccinations, reactions to those vaccines, and later health problems for male current or former active military Gulf War veterans. Likewise, in 2000 Steele and in 1998 Gilroy found possible adverse effects of vaccinations on Gulf War veterans. However, the role of such vaccinations remains controversial; more recent government reports continue to dispute the existence of any data that might reflect adversely on the role of vaccinations on the health of Gulf War veterans. To address this controversy, the current study assessed similar relationships for over 900 Reserve Component Gulf War Era veterans from Ohio and nearby states. Gulf War veterans were more likely to report poorer health than non-Gulf veterans. Female veterans were more likely to report mild or severe reactions to vaccines than male veterans. Those veterans who received anthrax vaccine reported more reactions to vaccines than those who did not receive anthrax vaccine. Declines in long-term subjective health were associated with receipt of an-

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thrax vaccine by Gulf War veterans but not for those who did not deploy to the Gulf, although few of the latter received anthrax vaccine. Regardless of deployment status, veterans who reported more severe reactions to vaccines were more likely to report declines in subjective health. Female veterans reported poorer health during the Gulf War than did male veterans, but sex was not related to veterans' reports of subjective health at subsequent times. It is recommended that servicemembers who experience severe reactions to anthrax vaccine be medically reevaluated before receiving further anthrax vaccine and that careful follow-ups be conducted of those receiving the vaccine currently, in accordance with Nass's 1999 recommendations. We also recommend that safer alternatives to thimerosal (a mercury sodium salt, 50% mercury) be used to preserve all vaccines.

Controversy continues to surround the reported illnesses of allied Gulf War veterans (31). Some believe that most of the health symptoms of Gulf War veterans are merely products of hysteria (28) or somatization disorder (12), while others attribute much of their symptomatology to the long-term effects of wartime stress (1, 2, 12, 32, 33) common to all conflicts or extraordinarily stressful disasters (5, 12). The Iowa study group (13) found higher elevations of health problems among reservists than among active military veterans, among Gulf War veterans. The large Veterans Administration survey of 30,000 veterans (16) found better health reported among veterans who had not deployed to the Gulf compared to those who had deployed there (Table 1) and found that Reserve Component veterans reported greater health problems than active component veterans. However, Steele (30) did not find health differences among veterans as a function of reserve versus active component. A large survey of Canadian military servicemembers (8) indicated more health problems among those who deployed to the Gulf War than among nondeployers or controls. In summary, the best research to date appears to confirm the hypothesis that many Gulf War veterans have been reporting higher rates of medical symptoms than relevant control groups [8, Available at http://www.dnd.ca/menu/press/reports/health/health_study_eng_1.htm (cf. also, 13, 30, 36)].

However, persistent concerns have been expressed about factors other than stress that might be contributing to Gulf War illnesses. Such factors have included smoke from oil well fires, radiation from depleted uranium ammunition, exposure to chemical or biological warfare agents, as well as vaccinations and insect sprays and repellants (5). One particular area of concern has been the vaccinations (9) given to counter biological agents, such as anthrax or plague. Rook and Zumla (23) thought that vaccinations might interact with other factors, such as stress, to weaken the human immune system, making veterans more susceptible to illnesses. Steele (30) found that 34% of Gulf War veterans and 11.5% of non-Gulf War veterans who had vaccinations reported a complex of symptoms she defined as Gulf War illness compared to only 3.7% of veterans who received no vaccines and did

not deploy to the Gulf. Anthrax vaccine can cause mild reactions (12, 15), including localized pain and swelling, and, rarely, more severe reactions (34). Hersack (11), Deimel (4), and Swanson-Biearman & Krenzelok (34) admitted that 30% of anthrax vaccine recipients experienced mild reactions, with 4% having moderate reactions, and another 1% or less having severe local or systemic reactions. Rodriquez (22) and Matsumoto (17), in popular rather than scientific venues, recently have reported evidence that might link squalene antibodies in sick veterans to their ill health and, perhaps, to vaccinations received during Desert Storm. A recent GAO report (3) recognizes the assertion of the U.S. Department of Defense (DoD) that squalene was never used in its vaccines but prefers to leave the question open for further investigation rather than accepting DoD's assertion at face value. Squalene is apparently being used currently as an experimental adjuvant with anthrax vaccine (15).

In their study of male Gulf War veterans from Britain, Unwin, *et al.* (36) found that those who reported vaccination with anthrax and plague were more likely to have negative health outcomes but that relationship was substantially reduced, although not eliminated, when controlling for recalled initial reaction to the shots. However, Unwin, *et al.* (36) did not report results for female veterans (19) and apparently did not collect data on male or female reservists (24). Furthermore, as noted by Hersack (11, p. 32), there are substantial differences between the anthrax vaccine used by the British during the Gulf War and the vaccine used by the U.S. military. The two types of anthrax vaccine were made differently and regulated by different agencies. One report has indicated that no patterns of unexpected local or systemic adverse events have yet been identified among anthrax vaccine recipients in surveys of military personnel participating in the U.S. Anthrax Vaccine Immunization Program (AVIP) (37). However, the large Canadian military survey (8, p. 64) found higher cognitive dysfunction, chronic fatigue, posttraumatic stress disorder symptoms, and minor depression among those who had received either the plague or anthrax vaccinations.

In spite of claims by the U.S. military that the anthrax vaccine is completely safe and effective (7, 10, 11), some U.S. military servicemembers have refused anthrax vaccinations, resulting in disciplinary action and dismissal from the military (18, 38). Some professionals have continued to challenge the safety and efficacy of current anthrax vaccine (20) while others are working toward an improved vaccine (14, 29, 35, 38).[2]

The goal of this study was to assess the apparent effects of anthrax vaccination on the long-term health of U.S. male and female Reserve Compo-

[2]Trachtman (35) presented an interesting report on the challenging work being done by Colonel Arthur Friedlander and others at Fort Detrick to develop a better anthrax vaccine.

nent Gulf War veterans, with controls for vaccination reactivity and other key variables. As Hersack (11, p. 33) has noted in a report dated April 2001, no previous research has shown a causal relationship between anthrax vaccination and Gulf War illness, that any such claim is only an "allegation" (p. 4). As recently as February 2002, Hasenauer (10)—in a publication intended for worldwide reading by soldiers of all ranks—cited unnamed Department of Defense officials as indicating that there has never been any research anywhere showing even so much as a small "correlation" between anthrax vaccination and Gulf War illness. If one accepts the arguments of Hersack (11) and Hasenauer (10), one would expect acceptance of a null hypothesis of no correlation of any sort between anthrax vaccination and subsequent declines in health. In contrast, based on our own concerns about vaccinations, the concerns expressed by Rook and Zumla (23), and the results reported by others (8, 36), we expected negative relationships for changes in long-term subjective health with (a) reactivity to vaccinations and (b) having had an anthrax vaccination, when controlling for a number of relevant variables, including sex, age, educational attainment, military rank, and ethnic minority status. While only a controlled clinical study might provide the absolute best in "causal" data, until such a time as that study is reported, the best that can be done is to predict changes in health as a function of anthrax vaccination and relevant control variables that would diminish the chances of spurious or noncausal results.

Method

Sample

Population studies of Desert Storm veterans have been rare. Unwin, *et al.* (36) cited their own study in the United Kingdom and the Iowa study (13) in the United States as the only ones using random samples, serious follow-up attempts, and attempts to find personnel already discharged from the military. However, Steele (30) and the U.S. Veterans Administration (16) have also conducted population-based surveys of Gulf War veterans, in addition to the Canadian government (8). In addition, the Ohio Desert Storm Study (25, 26, 27) has the same characteristics although it focused on sampling Reserve Component personnel.

The sample design and descriptive data for our male and female veterans have been reported in detail previously (25, 26). In our study, 43.4% of veterans who deployed to the Gulf reported having received an anthrax vaccination, compared to the 40.6% reported by Kang, *et al.* (16) in their much larger VA study. Among those who did not deploy, 4.6% reported having had an anthrax vaccination, compared to 4.6% in the VA study.

Unfortunately, finding accurate addresses for Gulf War veterans has been a major problem for researchers (8, 13, 21, 30, 36). Kang, *et al.* (16),

the Iowa Persian Study Group (13), Gilroy Management Consultants (8), and Steele (30) overcame such difficulties by using multiple databases, including tax files, state drivers' license records, veterans records, national telephone directories, and credit bureau files, attaining a final response rate of 70–80%. Lacking such resources, the response rates achieved in the Ohio Desert Storm project were lower, as described elsewhere (25, 26, 27).

Measures

Primary variables.—Respondents were asked if they had received the anthrax vaccination, with responses of no, not sure, and yes. In our later regression analyses, the responses were recoded into dummy variables for not sure and for yes to control for the possibility that not sure responses were induced by uncertainty and anxiety associated with poor current health, i.e., I am not feeling healthy, maybe I did get that anthrax vaccine that has been discussed in the media as a possible problem. Of course, it is possible that some veterans confused another vaccination for an anthrax vaccination, especially those who were not sure if they had received an anthrax vaccination. Since many veterans were not told what vaccines they were receiving nor were their vaccinations recorded in their shot records, some confusion was probably unavoidable.

Respondents were asked if "For any of the above vaccinations or injections, did you have an adverse reaction (unusual inflammation, swelling, redness, tenderness, etc.)?" Responses included "no," "yes, but only a mild reaction," "yes, a severe reaction but was not hospitalized," and "yes, you had to be hospitalized for your reaction." For purposes of analysis and because very few respondents reported the most severe reactions, the severe categories were combined. Health status was measured by questions concerning "your general health" before Desert Storm (before August 1990), during Desert Storm (August 1990 to June 1991), after Desert Storm (July 1991 to June 1995), and during the past year. Responses included, "poor," "fair," "good," "very good," and "excellent," coded from 1 to 5 points, respectively.

Control variables.—Age of veterans was taken from the original database information provided by the Defense Management Data Center (DMDC). Ethnic minority status was created by recoding all minority categories into one category, with Caucasian as the other category, using data from the DMDC database. Ground force status was obtained by combining Army and Marine Corps into one category and Navy/Air Force into another category. Current education was taken from survey responses while sex was taken, with the exception of two erroneous cases, from the DMDC database. Military rank was categorized as officer, noncommissioned officer, and junior enlisted. Number of days in theater was taken from the DMDC database.

Analysis.—To present the clearest bivariate analysis of the relationship between anthrax vaccination status and subsequent subjective health, controlling for subjective health before the Gulf War, only subjects reporting excellent health in 1990 were used. For those subjects who had been in excellent health before the war, crosstabulations were performed, with chi-square tests, of vaccination status against subsequent subjective health (during the war 1991–1995, and 1996/1997) for three groups of veterans—those not mobilized, those mobilized but outside the Persian Gulf area, and those deployed to the Persian Gulf. For the two groups who did not deploy to the Gulf, the not sure and yes responses on anthrax vaccination status were combined because the sample sizes were extremely small (between 8 and 13 subjects), a situation also found by Kang, *et al.* (16), that few non-Gulf veterans received an anthrax vaccination. Therefore, results obtained for anthrax vaccination as it applied to *nondeployed* veterans will have quite limited value.

The second stage of the analysis plan was to compare reaction rates to vaccines by sex and to compare reaction rates with anthrax vaccination status, using crosstabulations.

The third stage of the analysis plan was to use ordinary least squares regression analysis to predict subsequent subjective health, controlling for prewar subjective health for those who deployed to the Gulf and for those who did not deploy there. The independent variables in each analysis included subjects' age, military rank, current educational attainment, minority status, sex, land force component, severity of reactions to vaccines or medications, and dummy variables for the responses of 'not sure' and 'yes' to anthrax vaccination. For those who deployed to the Gulf, an additional independent variable of number of days in theater was added to the model. The goal of the analysis was to assess whether any bivariate relationships found in the initial crosstabulation analysis would be sustained when controlling for the several independent variables used.

Results

Table 1 presents a comparison of subjective health (1996/1997) as a function of Gulf versus non-Gulf deployment, showing that subjective health appeared to be lower among Gulf War veterans., with percentages not too different from Kang, *et al.*'s much larger Veterans' Administration survey (16) and Steele's larger survey of Kansas veterans (30). Table 2 shows the percentages of veterans remaining in excellent health after the war for each time frame as a function of deployment status and anthrax vaccination status. Table 3 shows the same results in terms of the percentage of the same groups whose veterans reporting a decline from excellent health before the war to only fair to poor health at each time frame. The chi-square tests show whether the relationship between subjective health and anthrax vaccination status is significant for each combination of mobilization status and time frame.

TABLE 1
VETERANS' SUBJECTIVE HEALTH ($N = 969$) DURING PAST YEAR AS A FUNCTION OF GULF WAR DEPLOYMENT STATUS COMPARED WITH RESULTS FROM VETERANS ADMINISTRATION STUDY ($N = 20,917$)

Health Status	Gulf Veterans			Non-Gulf Veterans		
	Ohio	Kansas	VA Study	Ohio	Kansas	VA Study
n	649	1,545	11,441	320	435	9,476
Excellent	13	25	16	37	45	30
Very Good	23	na	28	30	na	37
Good	31	51	33	23	47	23
Fair	26	21	20	7	7	9
Poor	7	3	4	3	1	1

Note.—Chi-square test ($df = 4$) comparing Ohio Gulf and Non-Gulf veterans' subjective health was 115.4, $p < .001$; Kang, *et al.* (16) reported a chi-square of 13.1 ($p < .03$). Steele (30), in her 1998 survey of Kansas veterans, found a significant difference but did not present the precise statistical results. Her report did not include the response category "very good" health, as her survey used only four response categories.

For all groups, subjective health appears to worsen with age, although that trend was not tested statistically. The most consistent pattern was observed for Gulf War veterans, for whom anthrax vaccination appeared to have adverse effects at all three time frames. The 36% of veterans reporting only poor or fair health in the past year (1996/1997) corresponds closely to the 34% of veterans in Steele's study of Kansas veterans (30), who appeared to have a complex of health conditions related to having had vaccinations

TABLE 2
PERCENT VETERANS OF FORMERLY EXCELLENT HEALTH (AS OF 1990) REPORTING SUBSEQUENT SUBJECTIVE HEALTH STATUS OF EXCELLENT AS A FUNCTION OF ANTHRAX VACCINATION STATUS

Mobilization Status/Anthrax Status	Retrospective Time Frame		
	Gulf War	1991–1995	1996–1997
Not Mobilized			
No Anthrax Vaccination	94	87	76
Anthrax Vaccination (yes or not sure)	92	77	62
χ^2	1.6	20.9‡	26.8‡
Mobilized/Not to Gulf			
No Anthrax Vaccination	89	82	71
Anthrax Vaccination (yes or not sure)	67	33	33
χ^2	3.1	12.1*	5.7
Deployed to the Gulf			
No Anthrax Vaccination	55	40	37
Not Sure	57	28	23
Anthrax Vaccination	35	20	14
χ^2	14.1†	17.7†	22.0‡

Note.—Degrees of freedom for all chi-square tests are 4. Given the small number of cases ($7 < n < 14$) for nondeployed subjects who said 'not sure' or 'yes' to having had an anthrax vaccination, those two groups are combined for presentation in Tables 1 and 2.
*$p < .05$. †$p < .01$. ‡$p < .001$.

and having been deployed to the Gulf. Among those who did not deploy to the Gulf, the relationships between anthrax vaccination and subsequent health were less consistent, often not significant.

TABLE 3
PERCENT VETERANS OF FORMERLY EXCELLENT HEALTH (AS OF 1990) REPORTING SUBSEQUENT SUBJECTIVE HEALTH STATUS OF POOR/FAIR AS A FUNCTION OF ANTHRAX VACCINATION STATUS

Mobilization Status/Anthrax Status	Retrospective Time Frame		
	Gulf War	1991–1995	1996–1997
Not Mobilized			
No Anthrax Vaccination	1	1	2
Anthrax Vaccination (yes or not sure)	0	15	23
Mobilized/Not to Gulf			
No Anthrax Vaccination	11	7	7
Anthrax Vaccination (yes or not sure)	33	0	22
Deployed to the Gulf			
No Anthrax Vaccination	5	14	18
Not Sure	5	33	36
Anthrax Vaccination	10	30	36

We found that female veterans were more likely to report severe reactions to vaccines (10.6%) than male veterans (3.6%), as well as mild reactions (40.2% versus 31.6%), a difference significant ($p < .001$) by $\chi_2^2 = 23.1$. Among those females who said they received anthrax vaccine, 14.1% reported severe reactions and 51.3% reported mild reactions to all of their vaccines compared to 5.8% and 44.8%, respectively, for the male veterans. When we tested the relationship between reactions to vaccines and anthrax vaccination for all subjects, 46.4% of those who said they had received the vaccination reported mild reactions with 7.8% reporting severe reactions compared to 32.8% and 8.5% (respectively) for those not sure and 24.7% and 1.7% for those not receiving the vaccine, a significant difference ($\chi_4^2 = 69.5$; $r = .26$, $p < .001$).

Table 4 presents the results of the regression analyses. The strongest predictor of subsequent health is prior health. The second strongest predictor was reactions to (all) vaccines. The results indicate that higher rank and being Caucasian are associated with better subjective health at all three time frames. While not significant during the war, the apparent effect of anthrax vaccine at both time periods after the war remains statistically significant, even after controlling for 10 other variables, of which all but one are significant for at least one of the three time frames. However, the magnitude of the apparent effect of anthrax vaccination is small (beta $< .20$), explaining less than 3% of the variance in subjective health.

When the same regression model was tested for nondeployed veterans

TABLE 4

ORDINARY LEAST SQUARES REGRESSION MODELS PREDICTING SUBJECTIVE HEALTH STATUS FROM ANTHRAX VACCINATION STATUS FOR GULF WAR VETERANS, AGE, RANK, CURRENT EDUCATION, AND MINORITY STATUS, CONTROLLING FOR HEALTH STATUS PRIOR TO THE GULF WAR

Independent Variable	Subjective Health Status During		
	Gulf War	1991–1995	1996–1997
Health Before the Gulf War	.43‡	.22‡	.17‡
Subject's Age	–.02	–.04	–.10*
Military Rank	.12*	.13†	.15†
Current Education	–.03	.04	.12†
Minority Status	–.14‡	–.09*	–.09*
Sex	–.11†	–.07	–.05
Land Forces	–.09*	–.08	–.07
Reactions to Vaccines/Medications	–.19‡	–.23‡	–.17‡
Number of Days in Theater	–.02	–.06	–.03
Anthrax Vaccination (yes)	.01	–.10*	–.17†
Anthrax Vaccination (not sure)	–.01	–.10*	–.14†
Adjusted R^2	.293	.198	.187
F	23.84	14.60	13.62
df	11,595	11,594	11,594
p	<.001	<.001	<.001

Note.—Coefficients reported are standardized regression coefficients (betas).
*$p<.05$. †$p<.01$. ‡$p<.001$.

(minus the number of days in theater variable), anthrax vaccination status (yes) was not significant, with betas between .00 and –.05 for the three time frames. Anthrax vaccination status (not sure) was significant for 1991–1995 (b = –.15, $p<.001$) and for 1996/1997 (b = –.17, $p<.001$). Prior health was much more strongly related to subsequent health for the nondeployed veterans, with b = .89 (during the war), .67 (1991–1995), and .54 (1996/1997). Reactions to vaccines were significant for 1991–1995 (b = –.16, $p<.001$) and 1996/1997 (b = –.12, $p<.02$). The only other significant variables in the three time frames occurred for health in the past year (1996/1997), with education (b = .14, $p<.01$), ground forces (–.10, $p<.05$), and age (b = –.10, $p<.05$) being significant.

DISCUSSION

Lack of Medical Records

One of the major limitations of this research is that actual vaccination records were not used. In contrast, Unwin, *et al.* (36) asked veterans to review their shot records before responding to a mail survey. Surprisingly, Unwin, *et al.* (36) found relatively little evidence of methods effects, comparing veterans who used versus those who did not use their shot records. However, in our study, several veterans indicated that their vaccinations were not recorded. One said, "We all got numerous shots before and in Saudi Arabia not entered in our medical records." Another noted that she "received vac-

cinations in Saudi that we were told not to record in our shot record"; this nurse went on to say that she knew the vaccinations included anthrax vaccine but she was under orders to not record the shots in the servicemembers' medical records. Another veteran said, "I don't know what they shot us up with! They said it was to protect us from enemy contaminants and they didn't keep any records of who did or did not actually get the shots (no medical record entries!). Besides, they can always say they're giving you THIS when you're really getting shot up with THAT [emphasis by veteran]. All we know is what they tell us. I think Vietnam is proof it's often not the truth." Another subject said that she was given approximately three to five shots and that "we weren't given any record of types of shots being given." One noncommissioned officer who met with the senior author some years after Desert Storm indicated that he had been asked to take vaccines without any records being kept. The veteran said he had told the medical specialist that "If it isn't going in my shot record, it's not going in my body!" And he refused the vaccines, without penalty. Presumably the medical officer in charge knew it was medically improper, if not even ethically wrong, to fill out the soldier's shot record inaccurately, by omission.

Such comments were reiterated in Matsumoto (17, p. 96) who reported that, "Dr. Gregory Dubay, who commanded the 129th Medical Company, a former Alabama National Guard unit out of Mobile, gave thousands of anthrax vaccinations to troops" and that "Dubay—who both administered and took the vaccinations—says that he was under orders not to record the inoculations in the soldiers' medical records," for reasons of operational security.

It may never be possible to correlate "hard" evidence—medical records—with health outcomes for Desert Storm veterans because of the inadequacy of the medical records.[3] Therefore, self-reported data, despite its limitations, may be the best most researchers will be able to obtain, when surveying U.S. veterans, unless antibodies produced by the vaccine were still present in vaccinated veterans years later, in which case the absence of medical records might be moot.

Reactions to Vaccines

Regardless of how our results might have turned out, some veterans blamed anthrax vaccine for their health problems. One said, "I had a severe systemic reaction to anthrax vaccination with both injections—did not stay in hospital, but stayed in 'quarters' for two days each time." Overall, two specifically blamed anthrax for bad reactions, while one blamed the typhoid

[3]Notably, even one veteran who was not deployed to the Gulf region, only mobilized within the United States, said that, "I was given approximately three to five shots (can't remember) and we weren't given any record of types of shots being given." The poor record keeping apparently was not confined to those veterans sent to the Gulf.

vaccine. Another female veteran said, "Our problems are the result of the shots we were given. I believe whatever they gave us hadn't been properly tested and we're all suffering."

Our results paralleled those of Unwin, *et al.* (36) inasmuch as both our study and theirs indicated significant reactivity to anthrax vaccine. However, even the U.S. military has admitted recently that at least 30% of subjects vaccinated with anthrax vaccine will have noticeable reactions, with a few having more severe reactions (4). Both our study and that of Unwin, *et al.* (36) found that reactivity was associated with subsequent health problems. Finding similar results for these two studies is noteworthy because the two studies were somewhat dissimilar methodologically, as well as referring to two different types of anthrax vaccine. The Ohio study was conducted in the United States, while the Unwin, *et al.* research (36) was conducted in the United Kingdom. The response rates and sample sizes were much higher for the British study than for the Ohio study. The fact that similar findings were obtained in spite of these vast differences strengthens the argument, we think, that something about anthrax as administered during the Gulf War was problematic. Furthermore, since concurrent analyses (25, 26, 27) suggest our responses rates were higher for officers and nonminority personnel—the same personnel least likely to have adverse health outcomes—we think our results may be conservative.

Alternative Explanations

While our results seem to indicate adverse long-term health outcomes as a result of anthrax vaccination or reactions to vaccines administered under wartime conditions, there are at least three main alternative interpretations of our results. First, it may be that veterans are responding to some of the ingredients of the vaccine, such as mercury, which was used as a preservative, or alum or other ingredients used as adjuvants—rather than to the PA antigen, the primary component of the vaccine.

Secondly, it is possible that some veterans are more sensitive in general to their health problems so an underlying issue of somatic sensitivity caused the apparent relationships between reactivity and health. In other words, the more sensitive veterans were more likely to recognize that they had experienced adverse reactions to their vaccines, and they were more likely to notice negative downtrends in their subsequent health.

A third interpretation is that anthrax vaccine in combination with other factors had adverse effects but that the vaccine by itself was harmless. It is possible that other factors combined with the anthrax vaccine to make it problematic. Perhaps some veterans have genetic susceptibilities to certain chemicals or toxins. A cocktail effect of other vaccines administered concurrently with anthrax, insecticides used in the field, insect repellants used, pos-

sible exposure to chemical agents, stress experienced during the war, other components of the anthrax vaccine, oil-fire smoke, and many other things might have contributed to the apparent health outcomes of Gulf War veterans or to the possible relationship between anthrax vaccinations and negative health outcomes.[4] It is possible that only under the circumstances of the Gulf War, did anthrax vaccine present problems. One possibility is that some shipments of the vaccine were not stored properly at all points along the distant path from the United States to the Persian Gulf War zone (6). Perhaps some were not injected properly under the field conditions of the time.

Implications

Finding support for such alternative interpretations might mean that it would be reasonable to continue use of the anthrax vaccine today in spite of our negative results. Since Kang, *et al.* (16) have data on subjective health and anthrax vaccination, they could easily replicate our research with a much larger and more representative sample, confirming or rejecting our results, especially for those inevitable critics who may question the value of our research, given its limitations. At the least we would hope that our research would receive a fair hearing, unlike the comments of one reviewer to a previous draft, in which that reviewer said research that contradicted government policy should not be published lest it cause "confusion" in the field. However, in spite of these alternatives, our research may well be the first to show a systematic relationship between anthrax vaccination during the Gulf War and subsequent reactions and later declines in subjective health, controlling for a number of relevant variables. Accordingly, in contrast to comments reported by Hasenauer (10), it is no longer accurate to state that no study by anyone anywhere has ever found even a small correlation between anthrax vaccination and perceived long-term health effects. However, given the results from British (36) and Canadian (8) research, which suggest some involvement of vaccination with a related type of anthrax vaccine with adverse health outcomes among Gulf War veterans—not to mention Steele's findings (30) of the effects of vaccinations on health among Kansas veterans, our findings should not be discounted as an isolated, anomalous result. In fact, we wonder why RAND's third volume (9) of immunizations and Gulf War illnesses has yet to be published, even though a draft was reviewed as early as 1998 or 1999.[5] We recommend that mercury-based preservatives be

[4]One alternative that was ruled out was influence of pyridostigmine bromide pills, consumption of which was independently related to declines in subjective health, without altering the apparent impact of anthrax vaccination or reactions to vaccines.

[5]A call placed to RAND (310) 451-7002 on February 20, 2002, found that Volume 3 might be released (finally) in April or May 2002. While we do not yet know the conclusions of that report, we probably would have expected a much more expedited report had absolutely no

removed from all military and civilian vaccines as soon as possible and be replaced with safer alternatives.

At the very least, we agree with Nass (20) that accurate medical records should be maintained for those servicemembers who are vaccinated. Furthermore, those records should contain detailed information on any adverse reactions to vaccinations. Research should track relationships between vaccinations, reactions, and health outcomes to detect problems *before* they spin out of control. Most vaccinations can cause adverse reactions in a small minority of patients. The benefits of the vaccination must be weighed against the risks. One aspect of the potential benefits that should be considered is whether current vaccinations, designed to protect farm workers against cutaneous anthrax infection, will adequately protect servicemembers against the high dosage of anthrax that might be received if the anthrax spores were delivered in the air and inhaled in substantial quantities by servicemembers. In other words, suppose a soldier was near ground zero for an anthrax-filled bomb, and he inhaled millions of anthrax spores. Would such a victim survive, even if fully vaccinated and given subsequent antibiotic treatment? Or does vaccination best protect those on the fringes of an attack, just as a flak jacket protects against some projectiles but not against all direct hits?

Ideally, research should pinpoint those at the greatest risk from adverse reactions and any long-term adverse outcomes from military vaccination programs. We believe that those who have severe reactions to anthrax vaccine should be medically reevaluated prior to resuming the vaccination regime. Of course, the benefits may well outweigh the risks, even if a few patients experience adverse side effects or reactions, given their particular situation. Along these lines, Lieutenant General Ronald R. Blanck, Surgeon General of the U.S. Army has said, "It would be irresponsible to jeopardize soldiers' lives when we know there is a real threat and we have a safe vaccine" (4, p. 6). While the U.S. military maintains that "There have been no long-term side effects from the vaccine" (4, p. 8), our research and Unwin, *et al*'s (36) suggest to the contrary that anthrax vaccination might have direct and indirect long-term side effects on health, most notably for those individuals who have the most severe reactions to their vaccinations initially. Armed with such research data today and pending better information on the long-term safety of the current vaccine, we cannot but recommend that extreme caution be used with respect to the severe punishment of those servicemembers who have reservations about the safety of the anthrax vaccination for their long-term health.

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evidence linking vaccinations with any possible role in Gulf War illnesses been found. If we had to guess, we would suspect that there was probably some disagreement among Clinton administration officials about releasing the report at all, if its conclusions were not entirely favorable toward the roles of vaccines.

REFERENCES

1. Baker, D. G., Mendenhall, C. L., Simbartl, L. A., Magan, L. K., & Steinberg, J. L. (1997) Relationships between posttraumatic stress disorder and self-reported physical symptoms in Persian Gulf War veterans. *Archives of Internal Medicine*, 157, 2076-2079.
2. Bower, G. (1998) Gulf War syndrome may signal mental ills. *Science News*, 154, 23(December 5), 357.
3. Chan, K. (1999) *Gulf War illnesses: questions about the presence of squalene antibodies in veterans can be resolved.* (GAO/NSIAD-99-5, B-278779, March 29) Washington, DC: United States General Accounting Office.
4. Deimel, G. (1999) Anthrax vaccine—safe, effective. *Army Reserve Magazine*, 44(3), 6, 8.
5. Enserink, M. (2001) Gulf War illness: the battle continues. *Science*, 291(5505, February 2), 812-817.
6. Frank, K. J. (1999) Monitoring temperature-sensitive vaccines and immunologic drugs, including anthrax vaccine. *American Journal of Health System Pharmacy*, 56, 2052-2055.
7. Friedlander, A. M., Pittman, P. R., & Parker, G. W. (1999) Anthrax vaccine: evidence for safety and efficacy against inhalational anthrax. *The Journal of the American Medical Association*, 282, 2104-2106.
8. Gilroy, G., Inc. (1998) *Health study of Canadian forces personnel involved in the 1991 conflict in the Persian Gulf.* Vol. 1. (Prepared for the Gulf War Illness Advisory Committee, Department of National Defence) Ottawa, Ontario: Department of National Defense.
9. Golomb, B. A. (in press) *Immunizations: a review of the scientific literature as it pertains to Gulf War Illnesses.* Santa Monica, CA: RAND Corp.
10. Hasenauer, H. (2002) The anthrax threat. *Soldiers: The Official U.S. Army Magazine*, 57, 2(February), 4-7.
11. Hersack, R. A. (2001) *The anthrax vaccine debate: a clinical review for commanders.* Maxwell Air Force Base, AL: Air Univer.
12. Hyams, K. C., Wignall, F. S., & Roswell, R. (1996) War syndromes and their evaluation: from the U.S. Civil War to the Persian Gulf War. *Annals of Internal Medicine*, 125, 398-405.
13. Iowa Persian Gulf Study Group. (1997) Self-reported illness and health status among Gulf War veterans: a population-based study. *The Journal of the American Medical Association*, 277, 28-245.
14. Ivins, B. E., Pitt, M. L., Fellows, P. F., Farchaus, J. W., Benner, G. E., Waag, D. M., Little, S. F., Anderson, G. W., Gibbs, P. H., & Friedlander, A. M. (1998) Comparative efficacy of experimental anthrax vaccination candidates against inhalational anthrax in rhesus macaques. *Vaccine*, 16, 1141-1148.
15. Ivins, B. E., & Welkos, S. L. (1988) Recent advances in the development of an improved, human anthrax vaccine. *European Journal of Epidemiology*, 4(1), 12-19.
16. Kang, H. K., Mahan, C. M., Lee, K. Y., Magee, C. A., & Murphy, F. M. (2000) Illnesses among United States veterans of the Gulf War: a population-based survey of 30,000 veterans. *Journal of Occupational and Environmental Medicine*, 42, 491-501.
17. Matsumoto, G. (1999) The Pentagon's toxic secret. *Vanity Fair*, 435(May), 82-98.
18. Morris, K. (1999) U.S. military face punishment for refusing anthrax vaccine. *Lancet*, 353(9147), 130.
19. Murphy, F., Browne, D., Mather, S., Scheele, H., & Hyams, K. C. (1997) Women in the Persian Gulf War: health care implications for active duty troops and veterans. *Military Medicine*, 162, 656-660.
20. Nass, M. (1999) Anthrax vaccine: model of a response to the biologic warfare threat. *Infectious Disease Clinics of North America*, 13, 187-208.
21. The National Survey Research Team. (1998) National Health Survey of Gulf War Era veterans and their families. Conference on the Federally Sponsored Gulf War Veterans' Illness Research, Washington, DC, June 17-19.
22. Rodriquez, P. M. (1999) Breakthrough on Gulf War illness. *Insight*, 15(14, April 19), 10-11, 31-33.
23. Rook, G. A. W., & Zumla, A. (1997) Gulf War syndrome: is it due to a systemic shift in cykokine balance towards a Th2 profile? *Lancet*, 347(9068), 1831-1834.

24. SCHUMM, W. R., BELL, D. B., PALMER-JOHNSON, C. E., & TRAN, G. (1994) Gender trends in the U.S. Army and a discussion of implications for readiness and retention. *Psychological Reports*, 74, 499-511.
25. SCHUMM, W. R., BOLLMAN, S. R., JURICH, A. P., CASTELO, C., SANDERS, D., & WEBB, F. J. (2000) Understanding mail survey response rates among male Reserve Component Gulf War era veterans. *Psychological Reports*, 87, 859-880.
26. SCHUMM, W. R., JURICH, A. P., BOLLMAN, S. R., SANDERS, D., CASTELO, C., & WEBB, F. J. (1999) Understanding mail survey response rates among female Reserve Component veterans serving during the Persian Gulf War. *Psychological Reports*, 85, 653-664.
27. SCHUMM, W. R., JURICH, A. P., STEVER, J. A., SANDERS, D., CASTELO, C., & BOLLMAN, S. R. (1998) Attitudes of Reserve Component servicemembers regarding the consequences of frequent overseas deployments. *Psychological Reports*, 83, 983-989.
28. SHOWALTER, E. (1997) *Hystories: hysterical epidemics and modern media*. New York: Columbia Univer. Press.
29. SINGH, Y., IVINS, B. E., & LEPPLA, S. H. (1998) Study of immunization against anthrax with the purified recombinant protective antigen of Bacillus anthracis. *Infectious Immunology*, 66, 3447-3448.
30. STEELE, L. (2000) Prevalence and patterns of Gulf War illness in Kansas veterans: association of symptoms with characteristics of person, place, and time of military service. *American Journal of Epidemiology*, 152, 992-1002.
31. STEELE, L. (2001) Invited commentary: unexplained health problems after Gulf War service—finding answers to complex questions. *American Journal of Epidemiology*, 154, 406-409.
32. STRETCH, R. H., BLIESE, P. D., MARLOWE, D. H., WRIGHT, K. M., KNUDSON, K. H., & HOOVER, C. H. (1996) Psychological health of Gulf-era military personnel. *Military Medicine*, 161, 257-261.
33. STRETCH, R. H., MARLOWE, D. H., WRIGHT, K. M., BLIESE, P. D., KNUDSON, K. H., & HOOVER, C. H. (1996) Post-traumatic stress disorder symptoms among Gulf War veterans. *Military Medicine*, 161, 407-410.
34. SWANSON-BIEARMAN, B., & KRENZELOK, E. P. (2001) Delayed life-threatening reaction to anthrax vaccine. *Journal of Toxicology—Clinical Toxicology*, 39(1), 81-84.
35. TRACHTMAN, P. (2002) Hero for our time. *Smithsonian*, 32(10), 34-41.
36. UNWIN, C., BLATCHLEY, N., COKER, W., FERRY, S., HOTOPF, M., HULL, L., ISMAIL, K., PALMER, I., DAVID, A., & WESSELY, S. (1999) Health of United Kingdom servicemen who served in the Gulf War. *Lancet*, 353(9148), 169-178.
37. U.S. DEPARTMENT OF DEFENSE. (2000) Surveillance for adverse events associated with anthrax vaccination—U.S. Department of Defense, 1998-2000. *Morbidity and Mortality Weekly Report*, 49(16), 341-345.
38. ZEGERS, N. D., KLUTER, E., VAN DER STAP, H., VAN DURA, E., VAN DALEN, P., SHAW, M., & BAILLIE, L. (1999) Expression of the protective antigen of Bacillus anthracis by Lactobacillus casei: towards the development of an oral vaccine against anthrax. *Journal of Applied Microbiology*, 87, 309-314.

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