Exposure to anthrax vaccination and pyridostigmine bromide (PB) tablets as associated with geographic location during the First Persian Gulf War

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Abstract

Data from over 600 Reserve Component Persian Gulf War veterans were analyzed to assess associations between anthrax vaccination, receipt of pyridostigmine bromide tablets, gender, ethnic minority status, ground force status, and rank with geographic location during the months of January and March 1991. Substantial associations were detected. Veterans who had deployed forward on land were more likely to report anthrax vaccination, use of pyridostigmine bromide tablets, to be ethnic minorities, to be females (in selected areas), and to be ground or land forces (Army or Marine Corps assets). Substantial associations were also found between anthrax vaccination and use of PB tablets with being a member of land/ground forces. Furthermore, anthrax vaccination was strongly associated with use of PB tablets. Use of PB tablets but not anthrax vaccination was associated with being near the suspected Khamisiyah nerve agent plume. Implications for future multivariate research into potential causes of Gulf War illnesses are discussed.

Keywords: Gulf War illnesses, Persian Gulf War, Anthrax Vaccination, Pyridostigmine Bromide, Gender, Geographic Location

1. Background

Despite the nearly universal admission that veterans of the first Persian Gulf war have reported higher levels of medical symptoms and poorer subjective health [1, 2, 3], it has proven difficult to pinpoint causal factors responsible for their conditions. For example, much debate has centered on the potential risks of anthrax vaccination [4, 5, 6] as well as the validity of past human trials with a previous version of the vaccine [7, 8]. Steele [9] found that geographic location was associated with classification of veterans with Gulf War illness. In her data, those who had served inside Iraq were more likely to have become ill than those who had served in Kuwait or Saudi Arabia or other areas to the south or west in the Persian Gulf region. Later, it was found that geographic location was significantly related to perceived exposure to nerve agents during or shortly after the war [10]. Thus, geographic location has the potential to become a confounding factor in any multivariate analysis of possible causes of Gulf War illnesses.

2. Methods

In 1996, the state of Ohio commissioned an independent study of the post-war health of Ohio's Gulf War veterans, through the Center for the Study of Veterans in Society (CSVS). The CSVS contracted with Kansas State University researchers to conduct the study among a random sample of veterans who had lived in Ohio as of August 1990 or as of March 1996, a study that came to be known as the Ohio Desert Storm Survey Project. The Defense Manpower Data Center provided a list of such veterans, along with current, accurate addresses for about a third of the veterans on the list. Obtaining accurate addresses for the remaining sample proved to be a major challenge, but surveys were initially mailed to veterans in late 1996, a process that continued through the spring of 1997. Details of the project methodology have been explained in several previous reports [11, 12, 13, 14].

3. Objectives of the Study

Our first goal was to assess possible associations between geographic location and exposure to anthrax vaccine and to pyridostigmine bromide anti-nerve agent tablets, two factors some believe to have been possible causes of Gulf War illnesses [15, 16, 17]. Our second objective was to determine if there was an association between location in or near the sarin nerve agent plume from the detonations at Khamisiyah shortly after the war and exposure to anthrax vaccine or pyridostigmine bromide tablets. A third objective was to investigate associations between geographic location and demographic factors that have been of interest in previous Gulf War health research [14].

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4. Analyses.

The Ohio Desert Storm Survey project began fielding surveys soon after the initial revelations that toxic nerve agents might have been released during the initial air war (January 16-23, 1991) or during the demolition of ammunition dumps during the first weeks after the ground war had concluded (March 4-10, 1991). That allowed time to revise the surveys to include information concerning each veteran's geographic location at those two critical times. With respect to the January locations, our initial plan had been to correlate ill health with location downwind from bombed ammunition sites that might have released toxic nerve agents or mustard gas. However, it is not yet clear if such toxic releases were accurately plotted or what damage they might have done to the health of veterans [1: 48-53]. Most of the unit logs or records that might have recorded exposures to chemical agents were, in violation of military regulations, destroyed after the war [1: 48]. Preliminary research on our part did not uncover substantial relationships between January locations and subsequent ill health. Therefore, we changed our focus from the possible January plumes to associations between geographic location in January and March with exposures to anthrax vaccine and PB tablets.

We asked veterans to identify which, if any, of five locations they had been in during January 1991, as shown in Table 1 and which, if any, of seven locations during March 1991, as shown in Table 2. Tapline Road was used to distinguish northern and southern locations in Saudi Arabia because it was a landmark familiar to most troops nearby, as it was the main road running just south of the Iraq-Kuwait border, the road that became the main supply route for soldiers, equipment, vehicles, and supplies involved in the grand flanking maneuver used for the invasion of Iraq.

The locations listed in the survey differed from January to March because we needed to account for troop movements inside Iraq, which had not occurred (other than for special forces and at least one errant junior officer known to the senior author who strayed into Iraq in front of the First Infantry Division a few days before the ground campaign began) in large numbers until after the ground war had started.

We also had also asked veterans if they had taken or received various vaccinations and/or PB tablets. Among those vaccinations was anthrax vaccine. Each veteran could respond "yes," "not sure," or "no" with respect to each exposure. A far higher percentage of "not sure" answers occurred for anthrax vaccine than for PB tablets.

As described previously [10], we had developed a low/medium/high risk model of geographic exposure to the plume from Khamisiyah in March 1991. The high risk locations for that plume were assumed to have been in the area of Iraq, northwest of Kuwait and the area of Iraq directly west of Kuwait. Veterans who had been in both areas in March were assumed to have been at high risk whereas those who had been in only one area were assigned a classification of moderate risk. All other veterans (among those in the Gulf region at that time) were classified at low risk from the Khamisiyah plume.

Using two-way cross-tabulations with chi-square tests for association, we compared each geographic location at each time with self-reported receipt of anthrax vaccine and/or PB tablets. We also compared plume risk based on geographic location with receipt of anthrax vaccine and PB tablets in the same way, using two-way cross-tabulations and chi-square tests.

5. Results

Results for both anthrax vaccine and for PB tablets for January 1991 are presented in Table 1 whereas results for both items for March 1991 are presented in Table 2. For example, in Table 1, 59.3% of veterans who reported being in northern Saudi Arabia but south of Tapline Road responded that they had received anthrax vaccine, with 19.6% responding that they had not received that vaccine. The others had not been sure about it. The chi-square results were significant, indicating that a higher percentage of veterans who had been at that location thought that that they had received vaccine than all those veterans who said they had never been at that location (the latter percentages are not shown but are a much more conservative test than if we had used the "none of the above" group for comparison purposes).

Table 3 presents results for the association between the plume risk locations and use of PB tablets; the association with anthrax vaccine proved to be non-significant. Table 4 presents data on the association observed between reports of anthrax vaccination and use of PB tablets. Tables 5 through 10 present data on the associations between demographic factors and geographic location during January and March 1991. Only one specific location was associated ($p < .01$) with military rank. There was a higher percentage of junior enlisted (14.9 versus 7.7) and a lower percentage of officers (14.0 versus 23.0) surveyed who reported having been in northern Saudi Arabia, west of Kuwait in January. Table 11 presents Pearson zero-order correlations among the same demographic factors and with both anthrax vaccination and use of PB tablets.

6. Discussion

It must be remembered that allied forces were stationed in a variety of locations not specifically mentioned in our survey. For example, there were military forces in western Saudi Arabia, in Qatar, in Bahrain, at sea in the Persian Gulf and in the Mediterranean Sea, and other sites. From an overall perspective, use of anthrax vaccine and PB tablets appears to have been (not so surprisingly) associated with forward, inland locations; veterans outside those forward locations reported very little use of either anthrax vaccine or PB tablets. Associations of geography with anthrax vaccination and use of PB tablets were stronger for January than for March locations, presumably because those preventive medical measures were rationed in favor of those areas presumed to be at higher risk of attack, based on *pre-war* intelligence estimates. PB tablets seemed to have been used nearly equally in January at most forward locations except for central Saudi Arabia. Anthrax vaccine seems to have been used most for veterans who, in January, had been forward in northern Saudi Arabia or near the eastern Saudi ports. Anthrax vaccine use was lower among veterans who reported having been in the area just south of Kuwait.

Use of PB tablets appears to have been slightly more common among those at highest risk of the Khamisiyah nerve agent

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plume, but whether that was mere coincidence or was a reflection of a deliberate response to nerve agent releases, we cannot determine.

Anthrax vaccination was moderately correlated with use of PB tablets, which might have occurred because of background factors such as willingness to comply with medical orders, nearness to high risk areas, or other correlated demographic factors.

Ethnic minority status did not appear to vary significantly within the forward areas though ethnic minorities seemed more likely to report having been located in forward as opposed to safer, rear areas. Women veterans appear to have been more likely to have reported locations in intermediate locations, neither front nor rear, but in support areas immediately behind the more forward areas of the combat zone. Army and Marine Corps veterans were more likely to report having been in forward locations than were Naval or Air Force personnel. At the same time, ground/land force personnel were more likely to report having received anthrax vaccinations and/or PB tablets.

While many of our observations make sense from a military perspective, they do not bode well for multivariate analyses designed to isolate causes of ill health among Gulf War veterans. High correlations among potential predictor variables have the potential to make identification of significant predictors more difficult, creating more challenging demands in terms of both theoretical and statistical considerations.

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Table 1. Percentages of Gulf War veterans reporting exposure to anthrax vaccination and/or pyridostigmine bromide (PB) tablets as a function of geographic location within the Persian Gulf region in January 1991, statistically tested in comparison to percentages for veterans at all other Persian Gulf locations combined.

Location within Persian Gulf Region January 16-23, 1991(first week of air war)	Anthrax Vacc. Exposure YES	NO	χ^2	PB Exposure YES	NO	χ^2
Northern Saudi Arabia, South of Tapline Road, within 100 miles of Iraqi or Kuwaiti Borders (King Khalid Military City)	59.3	19.6	18.92***	77.2	17.2	64.98***
Near Eastern Saudi Arabian Ports	56.1	20.3	18.50***	78.3	17.6	103.66***
Northern Saudi Arabia, West of Kuwait, North of Tapline Road (Hafir al Batin)	53.4	21.5	8.86*	82.7	11.8	106.28***
Central Saudi Arabia (Riyahd)	47.8	28.9	0.00	65.6	31.2	6.46*
Northern Saudi Arabia, South and East of Kuwait	43.8	22.3	9.14*	80.5	15.0	35.97***
None of the Above	10.4	59.3	109.89***	5.3	82.7	217.73***

Among veterans located in the Persian Gulf area in January 1991, the overall percentage of veterans who said "YES" to anthrax vaccination was 47.3%; the corresponding percentage for "NO" was 29.2%. The overall percentage of veterans who said "YES" to receiving/taking PB tablets was 59.5%; the corresponding percentage for "NO" was 33.6%.

* $p < .05$ ** $p < .01$ *** $p < .001$

Note: Chi-square tests are evaluated against percentages of exposures for all other subjects, with 2 degrees of freedom. Differences from 100% are associated with intermediate "not sure" category of response.

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Table 2. Percentages of Gulf War veterans reporting exposure to anthrax vaccination and/or pyridostigmine bromide (PB) tablets as a function of geographic location within the Persian Gulf region in March 1991, statistically tested in comparison to percentages for veterans at all other Persian Gulf locations combined

Location within Persian Gulf Region March 4-10, 1991 (first weeks after ground war was over)	Anthrax Vacc. Exposure YES	NO	χ^2	PB Exposure YES	NO	χ^2
Northern Saudi Arabia, within 100 miles of Iraqi or Kuwaiti Borders (King Khalid Military City and Hafir al Batin)	59.6	19.5	52.63***	74.7	19.3	136.89***
Iraq, Northwest of Kuwait	50.0	25.5	0.57	81.9	13.8	32.86***
Near Eastern Saudi Arabian Ports	48.2	25.7	3.06	61.6	30.8	9.19*
Southern Iraq, West of Kuwait	46.5	24.8	3.63	76.3	17.3	39.66***
Northern Kuwait, North of Kuwait City	37.9	31.7	8.23*	66.7	25.0	11.73**
Southern Kuwait, South of Kuwait City	36.2	32.3	10.14**	66.9	25.4	10.56**
Iraq, North of Kuwait	35.7	32.1	6.48*	73.5	0.5	13.62**
None of the Above	12.8	58.1	110.98***	9.6	79.5	170.77***

Among veterans located in the Persian Gulf area in March 1991, the overall percentage of veterans who said "YES" to anthrax vaccination was 48.2%; the corresponding percentage for "NO" was 28.8%. The overall percentage of veterans who said "YES" to receiving/taking PB tablets was 55.3%; the corresponding percentage for "NO" was 36.3%.

* p < .05 ** p < .01 *** p < .001

Note: Chi-square tests are evaluated against percentages of exposures for all other subjects, with two degrees of freedom. Differences from 100% are associated with intermediate "not sure" category of response.

Table 3. Percentages of Persian Gulf war veterans in various proximities to the suspected Khamisiyah nerve agent plume of March 1991 who reported different levels of exposure to pyridostigmine bromide tablets

Levels of PB Exposure	Location Relative to Khamisiyah: Low Risk	Moderate Risk	High Risk
None	44.6	17.8	15.0
Not Sure	9.2	6.7	5.0
Yes	46.2	75.6	80.0
N	478	90	80

Chi-square (df = 4) = 51.36 (p < .001), r = .27 (p < .001)

Note: Anthrax vaccine exposure was not significantly correlated with location relative to the Khamisiyah plume of March 1991 (r = .03, p < .46).

Table 4. Percentages of Persian Gulf war veterans reporting different levels of anthrax vaccination as a function of different levels of exposure to pyridostigmine bromide tablets

Anthrax Vaccination Status	Receipt of PB Tablets: No	Not Sure	Yes
No	51.5	20.8	15.3
Not Sure	24.7	37.7	19.3
Yes	23.8	41.5	65.3
N	239	53	352

Chi-square (df = 4) = 124.04 (p < .001), r = .42 (p < .001)

Table 5. Percentages of ethnic minority Persian Gulf war veterans reporting their presence in different Persian Gulf region locations as recalled for January, 1991

Location within Persian Gulf Region January 16-23, 1991 (first week of air war)	Ethnic Minority THERE	ELSEWHERE	χ^2
N. Saudi Arabia, S. of Tapline Road, within 100 miles of Iraqi or Kuwaiti Borders (King Khalid Military City)	10.3	7.3	1.60
Near Eastern Saudi Arabian Ports	9.5	7.4	0.89
Northern Saudi Arabia, West of Kuwait, North of Tapline Road (Hafir al Batin)	8.6	8.2	0.03
Central Saudi Arabia (Riyahd)	10.8	7.9	0.84
Northern Saudi Arabia, South and East of Kuwait	8.8	8.2	0.05
None of the Above	4.4	10.4	4.62*

* p < .05 ** p < .01 *** p < .001

Note: Chi-square tests are evaluated against percentages of exposures for all other subjects, with 2 degrees of freedom. Differences from 100% are associated with intermediate "not sure" category of response.

Table 6. Percentages of ethnic minority Persian Gulf war veterans reporting their presence in different Persian Gulf region locations as recalled for March, 1991

Location within Persian Gulf Region March 4-10, 1991 (first weeks after ground war was over)	Ethnic Minority THERE	ELSEWHERE	χ^2
Northern Saudi Arabia, within 100 miles of Iraqi or Kuwaiti Borders (King Khalid Military City and Hafir al Batin)	8.2	7.6	0.09
Iraq, Northwest of Kuwait	6.4	8.1	0.04
Near Eastern Saudi Arabian Ports	9.4	6.9	1.34
Southern Iraq, West of Kuwait	6.4	8.5	0.73
Northern Kuwait, North of Kuwait City	6.2	8.5	0.79
Southern Kuwait, South of Kuwait City	5.4	8.5	1.41
Iraq, North of Kuwait	9.5	7.7	0.32
None of the Above	4.0	9.3	4.30*

* p < .05 ** p < .01 *** p < .001

Note: Chi-square tests are evaluated against percentages of exposures for all other subjects, with 2 degrees of freedom. Differences from 100% are associated with intermediate "not sure" category of response.

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Table 7. Percentages of female Persian Gulf war veterans reporting their presence in different Persian Gulf region locations as recalled for Jan., 1991

Location within Persian Gulf Region January 16-23, 1991 (first week of air war)	Females THERE	NOT THERE	χ^2
Northern Saudi Arabia, South of Tapline Road, within 100 miles of Iraqi or Kuwaiti Borders (King Khalid Military City)	23.1	13.7	8.99**
Near Eastern Saudi Arabian Ports	20.1	14.6	3.38
Northern Saudi Arabia, West of Kuwait, North of Tapline Road (Hafir al Batin)	14.5	18.2	1.44
Central Saudi Arabia (Riyahd)	9.7	18.2	4.07*
Northern Saudi Arabia, South and East of Kuwait	7.1	19.0	9.47**
None of the Above	7.3	22.5	15.78***

* p < .05 ** p < .01 *** p < .001

Note: Chi-square tests are evaluated against percentages of exposures for all other subjects, with 2 degrees of freedom. Differences from 100% are associated with intermediate "not sure" category of response.

Table 8. Percentages of female Persian Gulf war veterans reporting their presence in different Persian Gulf region locations as recalled for January, 1991

Location within Persian Gulf Region March 4-10, 1991 (first weeks after ground war was over)	Females THERE	NOT THERE	χ^2
Northern Saudi Arabia, within 100 miles of Iraqi or Kuwaiti Borders (King Khalid Military City and Hafir al Batin)	20.8	13.0	6.51*
Iraq, Northwest of Kuwait	5.3	19.5	11.24**
Near Eastern Saudi Arabian Ports	15.5	19.0	1.33
Southern Iraq, West of Kuwait	7.6	20.6	
Northern Kuwait, North of Kuwait City	6.2	20.7	16.43***
Southern Kuwait, South of Kuwait City	5.4	20.3	16.11***
Iraq, North of Kuwait	7.1	19.0	7.12**
None of the Above	8.0	20.7	12.69***

* p < .05 ** p < .01 *** p < .001

Note: Chi-square tests are evaluated against percentages of exposures for all other subjects, with 2 degrees of freedom. Differences from 100% are associated with intermediate "not sure" category of response.

Table 9. Percentages of ground/land force (Army or Marine Corps) Persian Gulf war veterans reporting their presence in different Persian Gulf region locations as recalled for Jan. 1991

Location within Persian Gulf Region January 16-23, 1991 (first week of air war)	Ground/Land Component Forces THERE	NOT THERE	χ^2
Northern Saudi Arabia, South of Tapline Road, within 100 miles of Iraqi or Kuwaiti Borders (King Khalid Military City)	90.7	52.6	91.63***
Near Eastern Saudi Arabian Ports	84.3	51.4*	75.05**
Northern Saudi Arabia, West of Kuwait, North of Tapline Road (Hafir al Batin)	94.6	50.1	126.33***
Central Saudi Arabia (Riyahd)	67.7	65.1	0.24
Northern Saudi Arabia, South and East of Kuwait	90.3	60.2	37.23***
None of the Above	7.9	85.1	282.50***

* p < .05 ** p < .01 *** p < .001

Note: Chi-square tests are evaluated against percentages of exposures for all other subjects, with 2 degrees of freedom. Differences from 100% are associated with intermediate "not sure" category of response.

Table 10. Percentages of ground/land force (Army or Marine Corps) Persian Gulf war veterans reporting their presence in different Persian Gulf region locations as recalled for March, 1991

Location within Persian Gulf Region March 4-10, 1991 (first weeks after ground war was over)	Ground/Land Component Forces THERE	NOT THERE	χ^2
Northern Saudi Arabia, within 100 miles of Iraqi or Kuwaiti Borders (King Khalid Military City and Hafir al Batin)	89.9	32.6	227.74***
Iraq, Northwest of Kuwait	90.4	60.9	30.75***
Near Eastern Saudi Arabian Ports	71.9	60.2	9.64**
Southern Iraq, West of Kuwait	91.1	56.9	61.11***
Northern Kuwait, North of Kuwait City	81.4	60.6	21.46***
Southern Kuwait, South of Kuwait City	81.5	61.0	19.29***
Iraq, North of Kuwait	83.3	62.5	13.92***
None of the Above	12.0	82.4	252.63***

* p < .05 ** p < .01 *** p < .001

Note: Chi-square tests are evaluated against percentages of exposures for all other subjects, with 2 degrees of freedom. Differences from 100% are associated with intermediate "not sure" category of response.

Table 11. Pearson Zero-order correlations among demographic variables and exposures to anthrax vaccination and pyridostigmine tablets for Persian Gulf war veterans deployed in the Persian Gulf region

	Gender	Minority Status	Land Forces
Gender	---	0.16***	0.12***
Minority Status	---	---	0.09***
Anthrax Vacc.	0.15***	0.07+	0.45***
PB Tablets	0.14***	0.11**	0.60***

\+ p < .10 *** p < .001

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