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Serosurvey and Observational Study of US Army Veterinary Corps Officers for Q Fever Antibodies from 1989 to 2008

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Impacts

- Military veterinarians are at risk prior to service, with moderate numbers of new cases developing during service and most maintaining titres for long periods of time.
- Women consistently demonstrated higher seroprevalence and incidence levels; as increasing numbers of women enter the veterinary profession and subsequently the US Army, this may warrant close monitoring.
- This study likely underestimates exposure and risk and does not address chronic health effects, which may be valuable to explore in future health studies.

Keywords:
Q fever; *Coxiella burnetii*; military; veterinarian; zoonoses; serosurvey

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Summary

Since World War II, the military has experienced outbreaks of Q fever among deploying units including recent case reports of Q fever in US military personnel returning from serving in the Middle East during Operation Iraqi Freedom and Operation Enduring Freedom. Occupational exposure and prevalence of Q fever among US Army Veterinary Corps officers have not been examined. A retrospective serosurvey and observational study of 500 military veterinarians were conducted using archived serum specimens from military veterinarians who entered and served between 1989 and 2008 and were tested for exposure to *Coxiella burnetii*. Corresponding longitudinal health-related, demographic, medical and deployment data were examined. A total of 69 (13.8%) individuals at military entry and 85 (17%) had late career positive titres. A total of 18 (3.6%) individuals showed seroconversion. Women were more likely to be seropositive after military service [prevalence ratio (PR) 1.96; 95% confidence interval (CI) 1.15–3.35] and were also more likely to seroconvert (incidence rate ratio 3.55; 95% CI 1.19–12.7). Women who deployed to Operation Iraqi Freedom were more likely to be seropositive (PR 3.17; 95% CI 1.03–9.71). Veterinarians with field service and pathology specialties had the highest incidence rates (7.0/1000 PY; 95% CI 4–12 and 3–19, respectively). This is the first report documenting US military veterinarians' exposure to *C. burnetii*. Military veterinarians are at risk prior to service, with moderate number of new cases developing during service and most maintaining titres for long periods of time. Women consistently demonstrated higher seroprevalence and incidence levels. As increasing numbers of women enter the veterinary profession and subsequently the US Army, this may warrant close monitoring. This study likely underestimates exposure and risk and does not address chronic health effects, which may be valuable to explore in future health studies.

Introduction

Q fever or 'query fever' is a zoonotic rickettsial disease caused by *Coxiella burnetii*. The Q fever organism is very stable in most environments, can withstand drying and is resistant to many disinfectants. It is transmitted to humans primarily by inhalation of aerosolized organisms that have been excreted by infected animals (usually livestock) or

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direct contact with contaminated animal tissues or objects (Reimer, 1993; McQuiston and Childs, 2002; Guatteo et al., 2006; Cutler et al., 2007; Rodolakis et al., 2007; Cooper et al., 2011). Both consumption of raw milk and transfusion of infected blood have been known to serve as a source of infection in humans (Acha et al., 2003), and as the organism can be transmitted by ticks between animals, they are suspected to be a source of infection for humans (Eklund et al., 1947; McQuiston and Childs, 2002; Cutler et al., 2007).

In humans, infections may be subclinical or disease may present itself as an acute febrile illness most commonly with a flu-like illness, pneumonia or hepatitis (Peacock et al., 1983; Brooks et al., 1986). Atypical manifestations may include acute cholecystitis, aseptic meningitis and acute respiratory distress syndrome (Brooks et al., 1986; Hartzell et al., 2007). Chronic Q fever appears to be uncommon and may not develop until years after initial infection. Chronic infection commonly manifests as endocarditis and among patients with pre-existing valvular heart disease (Kimbrough et al., 1979; Peacock et al., 1983; Brooks et al., 1986; Dupuis et al., 1986; Fenollar et al., 2001, 2004, 2006; Botelho-Nevers et al., 2007; Landais et al., 2007; Hartzell et al., 2008).

Q fever is recognized to be enzootic in the United States. A 2006 study reported the average annual incidence between 2000 and 2004 to be 0.28 cases per million persons in the United States (McQuiston et al., 2006). A Center for Disease Control and Prevention and prevention study reported the seroprevalence level of Q fever antibodies among stored sera of US individuals >20 years old from the National Health and Nutrition Examination Survey (NHANES) 2003–2004 at 3.1% (CDC, 2008; Anderson et al., 2009).

At-risk human populations include veterinarians, abattoir workers, sheep and goat herders, dairy farmers and individuals associated with similar occupations or exposures. Although a zoonotic and occupationally associated disease, Q fever has not been studied in depth specifically in military veterinarians; however, a recently published serosurvey conducted among 508 US veterinarians detected a 22% seroprevalence during 2006 (Whitney et al., 2009). This study provided evidence that routine contact with farm ponds, livestock (cattle and swine) and wildlife increases the risk of seropositivity in US veterinarians.

Since World War II, the military has experienced outbreaks of Q fever among deploying units (Spicer, 1978; Ferrante and Dolan, 1993; Aronson et al., 2006; Waag, 2007). Several articles and case reports have been published on the diagnosis of Q fever in military personnel returning from service in the Middle East during Operation Iraqi Freedom and Operation Enduring Freedom (Anderson et al., 2005; Leung-Shea and Danaher, 2006; Gleeson et al., 2007; Hartzell et al., 2007, 2008; Faix et al., 2008). The US Army Public Health Command initiated a Q fever registry programme in early 2007 and at least 135 diagnosed US military cases have been clinically reported between January 2007 and January 2011 (S. Scoville, personal communication). Exposures have occurred among personnel in various occupational specialties to include administrative, aviation and infantry personnel.

Military veterinarians deploy to many locations that are enzootic for Q fever to work with host country populations and are involved in humanitarian and civic action programmes and projects that provide direct care to local livestock. In addition, while military veterinarians deployed during war time are exposed to similar military environments as other soldiers, they may be at greater risk of exposure due to having closer contact with animals and working within pastoral locations in the region.

A substantial proportion (~40%) of US military service members have been or will deploy to southern and Southwestern Asia. As part of the stability operations performed by the US Armed Forces, US Army veterinarians are used extensively in nation building, training and humanitarian and civic action project efforts. Additionally, many US Army veterinarians are engaged in force health protection activities for US military members, thus living in the same environment as other military members but may not be in contact with animals. Understanding the burden of disease among military veterinarians is necessary to gauge what preventive measures may need to be taken to reduce occupational risk of exposure and infection, and consequently impact the development of long-term sequelae of infection.

We performed a retrospective serosurvey and observational study to better determine the importance and prevalence of *C. burnetii* IgG antibody among US Army Veterinary Corps officers using serum specimens contributed to the Department of Defense Serum Repository (DoDSR) at entry to military service and specimens obtained at the most recent career serum specimen submission (Rubertone and Brundage, 2002). Other demographic, service and medical risk factors were compared with Q fever IgG seroconversion among US Army Veterinary Corps officers to evaluate indications for risk factors and preventive measures.

Materials and Methods

Study design and population

This study used demographic, medical and deployment data routinely archived in the Defense Medical Surveillance System and previously collected serum specimens archived at the DoDSR. The Headquarters, US Army Medical Research and Materiel Command Institution Review Board approved this protocol. Informed consent was not obtained as all testing and individual information was de-identified.

The study was conducted and funded by the Armed Forces Health Surveillance Center (AFHSC) in Silver Spring, Maryland. The study population consisted of all US Army Veterinary Corps officers identified by military occupational code (64A, 64B, 64C, 64D, 64E and 64F) who served between 1989 and 2008. Individual serum contributions in the DoDSR were reviewed to determine the availability of serum specimens from each individual at the time of entry to military service. Each individual was required to have at least two serum samples archived at the DoDSR with the first specimen within ±1 year of entering the military. A random sample of 500 individuals was identified, and the population was further subdivided into two subcohorts consisting of officers whose earliest specimen was submitted between 1989 through 1999 or between 2000 through 2008.

All longitudinal health-related, demographic and deployment data were obtained from the Defense Medical Surveillance System including deployment survey forms, maintained and managed by the AFHSC (Rubertone and Brundage, 2002). Additional data elements extracted include the following: year of birth, gender, race, birth location, entry location, home of record state, home of record country, rank, unit assignment history and location, military deployment history, military occupational history and post-deployment health survey responses regarding joint and chest pain, fever, environmental exposures (i.e. animals and animal bites/exposures, sand and dust) and the prophylactic use of doxycycline. The ICD-9 codes extracted from health inpatient and outpatient records for possible diagnoses related to Q fever infections were as follows: fever (780.6), anorexia (783.0), malaise/fatigue (780.7), acute respiratory distress (518.82), acute cholecystitis (575.12), acute meningitis (047), endocarditis (421.1) and Q fever (083.0).

Laboratory testing

Identified specimens were retrieved, thawed and split into multiple 0.5-ml aliquots. Only one 0.5-ml aliquot was required for testing. Aliquots were refrozen at −30°C. Each specimen was labelled with a randomly generated, unique specimen identification number. No personal identifiers were used. Specimen linkage to personal identifiers was used only to link the specimens to individual demographic, medical and deployment information. Once the information was matched, it was de-identified and a file was provided to the testing laboratory to identify serum pairs representing the earliest and the most recent specimens. This file was blinded as to Q fever seropositivity status.

Specimen aliquots were batched and shipped in insulated shipping containers to the laboratory at US Army Public Health Command Region – South, Fort Sam Houston, TX, for serologic testing. The most recent serum specimen for each individual was screened using indirect immunofluorescent antibody testing (positive reaction at a ≥1 : 16 serial dilution) for both *C. burnetii* IgG phase I and phase II antigens (Focus_Diagnostics, 2007). Positive- and negative-control samples were used for each microtitre plate. If the positive or negative control fails on a plate, the assay was repeated. All the remaining sera were destroyed at the end of the study.

Any sample with immunofluorescent IgG antibody titres of ≥1 : 16 to either phase I or phase II antigens is considered a positive screening result. Positive-screened samples were then further tested with serial dilutions up to ≥1 : 512, and the corresponding earliest samples for these positive individuals were also tested with serial dilutions up to ≥1 : 512. The corresponding specimens were tested at the same time.

The screened positive specimens and the corresponding early specimens were re-evaluated after serial dilutions were performed. A positive specimen was redefined as having a titre ≥1 : 16 for both phase I and phase II antigens or a titre of ≥1 : 256 for phase II antigen only. Seroconversion was measured by titre changes between the early serum titre and most recent titres when there was a 4-fold increase in either phase I or phase II antigens for the most recent titres beginning at ≥1 : 32.

Statistical analysis

Statistical analysis was performed using statistical software (SAS Institute Inc., 2004; StataCorp., 2009). Summary statistics for exposures and outcomes were calculated; 95% confidence intervals (CI) were calculated using the exact binomial method. Incidence rate ratios (IRR) and prevalence ratios (PR) between levels of each independent variable were estimated in univariate analysis using Poisson regression. Incidence rates were calculated using person-time as the denominator. Demographic records from DMSS allow calculation of person-time since the date of entry into service, and any given serum draw was used to determine seropositivity. Person-time was also calculated for each demographic subgroup of interest. Annual prevalence was calculated using the cumulative total of individuals who entered each year and subtracting those that left the cohort from the previous year. The population total at the end of each year was used as the denominator. The assumptions used were as follows: (i) When an individual was tested seropositive at entry, they became a seroprevalent individual in the cohort. (ii) Seropositive individuals remained seropositive until they left the service or tested seronegative. (iii) Individuals who tested positive with their most recent specimen and not on entry were counted for only that year. The reference stratum of evaluated characteristics was reassigned when the value was zero. A *P*-value <0.05 was considered significant on all statistical tests.

Results

A total of 820 US Army Veterinary Corps officers who had served between 1989 and 2008 were eligible for the study. Those individuals who had at least two archived serum samples in the DoDSR with the first specimen within ±1 year of entering the military were 681 persons. Specimen access and availability were considered, and a random sample of 500 individuals was identified from this group (Fig. 1).

Out of the 500 individuals in the cohort, a total of 88 most recent specimens screened positive at ≥1 : 16 to phase I or phase II antigens. Corresponding early specimens were titred at the same time with the positive most recent screened specimens. Three specimens were determined to be false positives and were removed as positives. Upon further testing, a final total of 85 (17%) individuals had phase I or phase II titres (median = 1 : 32 and 1 : 64, respectively) on the most recent specimen, and 69 (13.8%) individuals had phase I or phase II titres (median = 1 : 32 and 1 : 128, respectively) on their earliest specimen. Applying a more conservative definition, further evaluation found 56 (11.2%) individuals had titres positive to both phase I and phase II antibodies on their more recent specimens, and 43 (8.6%) individuals were similarly seropositive with their early specimens. Five individuals who were seropositive with their early specimens were considered to have seroreverted in their later specimen. A total of 18 (3.6%) individuals demonstrated seroconversion.

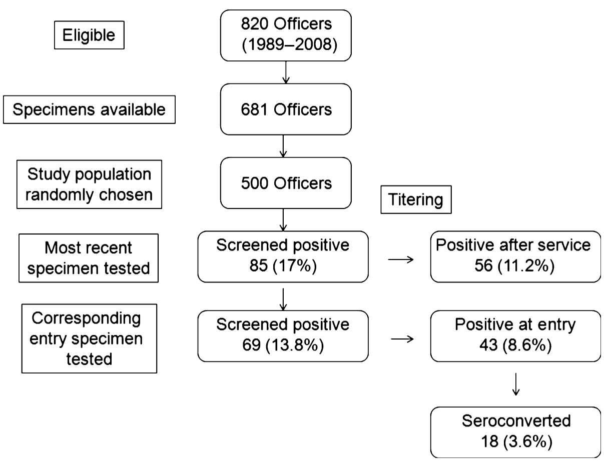

Fig. 1. Total military veterinarians represented between 1989 and 2008 in the Department of Defense Serum Repository (*n* = 820) identified along with those that had representative specimens (*n* = 681) from which a random sample was determined (*n* = 500). The latest, most recent serum specimens from military veterinarians (*n* = 500) were screened for IgG phase I and phase II antibodies to Q fever. Earlier entry specimens corresponding to the most recent positive specimens (*n* = 85) were tested and further titred jointly to identify seroconversion (*n* = 18).

The veterinary cohort was similarly distributed between male (48.2%) and female (51.8%; Table 1). At entry to the military, 6.6% of men and 10.4% of women were seropositive, but not significantly different from one another (PR 1.57; 95% CI 0.87–2.84; Table 2). However, women were more seropositive after service (PR 1.96; 95% CI 1.15–3.35; Table 3) than men. Seroconversions occurred among women at 3.55 (95% CI 1.19–12.7; Table 4) times higher incidence rate [7.1/1000 person-years (PY); 95% CI 4.1–12.2] than men (2.0/1000 PY; 95% CI 0.8–4.8).

The overall cohort consisted of 82.8% White people, 4.2% Black people, 4.6% others and 8.4% unknown. Seroprevalence at entry was similarly distributed within the cohort at 90.7%, 2.3%, 2.3% and 4.7%, as was seroconversion at 83.3%, 5.5%, 0% and 11.1%, respectively. Proportionally, twice as many White people were seroprevalent at entry (9.4%) as compared to other race ethnicities (4.3–4.8%); however, proportionately, White people were less likely to seroconvert.

When considering the factor of home of record at entry, regions with the highest seroprevalent individuals were from the Southwest (14.1%), the mountain (13.5%) and the Northeast (10.9%) states. Prevalence levels from the other regions ranged from 4.5% to 7.7% with the Midwest region having the lowest (Table 2).

Seroprevalent individuals tended to be older at entry (8.4 months), after service (10.8 months) and older among seroconverters (22.8 months) compared with the average age of the cohort. Individuals who entered in the 30–39 age group were 48% more prevalent than younger accessions, and similarly after service, the 40–49 age group was 2.16 (95% CI 0.91–5.1) times more seroprevalent than the youngest age group (Table 3). Conversely, among the seroconverters, the incidence rate was highest among the 20–29 age group (10/1000 PY; 95% CI 2–39; Table 4). Overall, seroprevalent individuals maintained a titre for 8.16 ± 5.4 years.

Among the different veterinary occupation specialties, seroprevalence ranged from 0.0% (comparative medicine veterinarians) to 60.7% (Field service veterinarians). Overall, the seropositive levels among each specialty were not statistically different from field service veterinarians. Incidence rates among the specialties ranged from 0 to 7.0/1000 PY. The highest incidence was shared among the field service and pathology specialties (7.0; 95% CI 4–12 and 3–19, respectively; Table 4).

Table 1. Q fever prevalence among a cohort (n = 500) of US Army veterinarians who served on active duty between 1989 and 2008

Characteristics	Study population n (%)	Positives n (%)	Prevalence ratios (95% CI)	P
Total	500 (100)	85 (17)		
Gender				
Male	241 (48.2)	33 (38.8)	Reference	
Female	259 (51.8)	52 (61.2)	1.47 (0.98–2.19)	0.074
Race				
White people	414 (82.8)	72 (84.7)	Reference	
Black people	21 (4.2)	3 (3.5)	0.82 (0.28–2.39)	0.78
Other	23 (4.6)	4 (4.7)	1.0 (0.4–2.5)	1
Unknown	42 (8.4)	6 (7.1)	0.82 (0.38–1.77)	0.7
Average service time (years)	8.7 ± 5.8	8.7 ± 5.7		1
Age at sampling (years)				
20–29	77 (15.4)	9 (10.6)	Reference	
30–39	270 (54.0)	42 (49.4)	1.33 (0.68–2.61)	0.51
40–49	125 (25.0)	28 (32.9)	1.92 (0.96–3.84)	0.063
50–59	28 (5.6)	6 (7.1)	1.83 (0.72–4.68)	0.34
Average age at sampling (years)	37.4 ± 7.0	38.3 ± 7.0		0.18
Occupational specialty				
Field service (64A)	283 (56.6)	53 (62.4)	Reference	
Preventive medicine (64B)	75 (15)	10 (11.8)	0.71 (0.38–1.33)	0.31
Laboratory animal (64C)	55 (11)	10 (11.8)	0.97 (0.53–1.79)	1
Pathologist (64D)	48 (9.6)	7 (8.2)	0.78 (0.38–1.61)	0.55
Comparative medicine (64E)	20 (4)	1 (1.2)	0.26 (0.04–1.83)	0.14
Clinical medicine (64F)	19 (3.8)	4 (4.7)	1.12 (0.46–2.77)	1
Ever deployed	152 (30.4)	22 (25.9)	0.8 (0.51–1.25)	0.37
OIF	118 (23.6)	17 (20.0)	0.81 (0.5–1.32)	0.41
OEF	32 (6.4)	5 (5.9)	0.91 (0.4–2.1)	1
Bosnia/Kosovo	6 (1.2)	0 (1.2)	0.98 (0.16–5.93)	1

OEF, operation enduring freedom; OIF, operation iraqi freedom.

The seroprevalence of those veterinarians who ever deployed was 11.2% (PR 0.998; 95% CI 0.58–1.71; Table 3), and the incidence rate was 4/1000 PY (IRR 1.03; 95% CI 0.39–2.75; Table 4). Similar prevalence levels were found among those who deployed to Operation Iraqi Freedom (11%; PR 0.98; 95% CI 0.55–1.76) and Operation Enduring Freedom (12.5%; PR 1.13; 95% CI 0.43–2.91). Incidence levels were 4/1000 PY (95% CI 1–10) and 6/1000 PY (95% CI 1–22), respectively. Women who deployed to any operation (18.6%) or deployed to Operation Iraqi Freedom (18.4%) exhibited higher seroprevalences at 2.89 (95% CI 1.13–7.4) and 3.17 (95% CI 1.03–9.71) times the level of men, respectively, whereas men who went to Operation Enduring Freedom had a relatively higher seroprevalence (14.3% versus 9.1%; PR 1.59, 95% CI 0.18–12.5), yet were not statistically different.

Further dividing the cohort into two cohorts based on the time of entry year (1989–1999 versus 2000–2008; Table 5), the earlier, 1989 cohort, has a greater number and higher percentage of men (58.2%) compared with the 2000 cohort where women are in greater number and percentage (62.8%). Interestingly, the seroprevalence among women in each cohort is practically the same (14.8% and 14.7%, respectively; Table 6). Incidence rates were the highest in women in both cohorts; however, women in the 2000 cohort were more likely to become an incident case (4.0/1000 PY; 95% CI 1.7–9.7 and 13.7/1000 PY; 95% CI 6.8–27.4, respectively; Table 7). Of the seroconverters in the 2000 cohort, 100% were women.

Seroprevalence levels for the 1989 and 2000 cohorts at entry were 8.0% and 9.2%, respectively, whereas seropositive levels after service had increased to similar levels (11.1% and 11.3%, respectively). Incidence rates were 2.74 (95% CI 1.09–6.93) times higher in the 2000 cohort (8.2/1000 PY; 95% CI 4.1–16.4; Table 7). Unique to the 2000 cohort, with increasing age groups (20–29, 30–39, 40–49 and 50–59), there is an increasing trend of seroprevalence (8.1%, 9.6%, 24% and 50%, respectively). Compared with the 1989 cohort, incidence rates for the 2000 cohort are higher for all age categories. Home regions with the highest seroprevalences for the 1989 cohort were from the mountain (18.2%) and Southwest (16.1%) states compared with the 2000 cohort were from Northeast (14.8%) and Southwest (12.1%) states.

Field service veterinarians had the highest seroprevalence levels in the 1989 cohort, whereas the preventive medicine

Table 2. Q fever prevalence (n = 43) among US Army veterinarians at entry to the US military (1989–2008)

Characteristics	Positive at ratios entry *n* (%)	Prevalence ratios (95% CI)	*P*
	n = 43 (8.6%)		
Gender			
Male	16 (37.2)	Reference	
Female	27 (62.8)	1.57 (0.87–2.84)	0.15
Race			
White people	39 (90.7)	Reference	
Black people	1 (2.3)	0.51 (0.073–3.5)	0.71
Other	1 (2.3)	0.46 (0.066–3.21)	0.51
Unknown	2 (4.7)	0.51 (0.13–2.02)	0.41
Age at entry (years)			
17–29	26 (60.5)	Reference	
30–39	16 (37.2)	1.48 (0.82–2.68)	0.21
40–49	1 (2.3)	0.496 (0.07–3.51)	0.71
Average age at entry (years)	29.3 ± 4.8		
Home of record region			
Midwest	3 (7.0)	0.79 (0.17–3.76)	1
Mountain	5 (11.6)	2.39 (0.61–9.38)	0.27
North	4 (9.3)	1.36 (0.32–5.78)	0.72
Northeast	11 (25.6)	1.92 (0.56–6.6)	0.38
Pacific	3 (7.0)	Reference	1
Southeast	7 (16.3)	1.11 (0.30–4.14)	1
Southwest	9 (20.9)	2.48 (0.71–8.71)	0.22
Unknown	1 (2.3)	1.18 (0.13–10.52)	1

Table 3. Q fever prevalence (n = 56) among US Army veterinarians after serving in the US military (1989–2008)

Characteristics	Positive after ratios service *n* (%)	Prevalence ratios ratios (95% CI)	*P*
	n = 56 (11.2)		
Gender			
Male	18 (32.1)	Reference	
Female	38 (67.9)	1.96 (1.15–3.35)	0.015
Average service time (years)	8.7 ± 5.64		
Average age at sampling (years)	38.5 ± 7.1		
Age at recent sampling (years)			
20–29	6 (10.7)	Reference	
30–39	25 (44.6)	1.19 (0.51–2.79)	0.82
40–49	21 (37.5)	2.16 (0.91–5.1)	0.09
50–59	4 (7.1)	1.83 (0.56–6.02)	0.45
Occupational specialty			
Field service (64A)	34 (60.7)	Reference	
Preventive medicine (64B)	8 (14.3)	0.89 (0.43–1.84)	0.84
Laboratory animal (64C)	7 (12.5)	1.06 (0.5–2.27)	1
Pathologist (64D)	6 (10.7)	1.04 (0.46–2.34)	1
Comparative medicine (64E)	0	0	
Clinical medicine (64F)	1 (1.8)	0.44 (0.06–3.03)	0.49
Ever deployed	17 (30.4)	0.998 (0.58–1.71)	1
Female	11 (64.7)	2.89 (1.13–7.4)	0.032
Deploy OIF	13 (23.2)	0.98 (0.55–1.76)	1
Female	9 (69.2)	3.17 (1.03–9.71)	0.0396
Deploy OEF	4 (7.1)	1.13 (0.43–2.91)	1
Female	1 (25)	0.63 (0.08–5.42)	1
Bosnia/Kosovo	0	0	

OEF, operation enduring freedom; OIF, operation iraqi freedom.

veterinarians were highest in the 2000 cohort (13.4% and 16.7%, respectively).

Discussion

This study is the first to examine seroprevalence and seroconversion to Q fever antibodies among US military veterinarians and demonstrates that military veterinarians are at risk for exposure to the *C. burnetii* organism. This cohort of US military veterinarians demonstrated a 17% overall seroprevalence to phase I or phase II antigens, which is similar to, although slightly less than, the 22% seroprevalence reported in a study of US veterinarians (Whitney et al., 2009). Additionally, use of a more conservative definition of seroconversion requiring antibodies to both phase antigens resulted in a prevalence that was half (11.2%) of that published by Whitney et al. The prevalence of phase I or phase II titres at the time of entry into the military was approximately 14%, indicating that many military veterinarians had exposure to *C. burnetii* prior to entering the military service.

Our study results differ from those of Whitney et al. or Anderson et al.; we report higher seroprevalence among female military veterinarians compared with their male counterpart. Similarly, other studies recently reported higher seroprevalence in male veterinarians in Germany (Bernard et al., 2012) and among veterinary students in the Netherlands (de Rooij et al., 2012).

Due to the increasing numbers of women entering the veterinary profession and corresponding increases in women in the US Army Veterinary Corps, the reported higher seroprevalence and incidence in females is a concern (Brown and Silverman, 1999; AVMA, 2008). Q fever is associated with increased adverse human pregnancy outcomes to include spontaneous abortion, intra-uterine growth retardation, oligoamnios, intra-uterine foetal death and premature delivery particularly when the infection occurs during early pregnancy (Jover-Diaz et al., 2001; Carcopino et al., 2009). Furthermore, additional evidence suggests that individuals showing acute or chronic infections may have a reactivation of the infection during subsequent pregnancies, although a retrospective serostudy among pregnant women performed in the Netherlands following a large national outbreak of Q fever during 2007–2008 reported no adverse pregnancy outcomes among women who had antibodies during early pregnancy (Van der Hoek et al., 2011).

Table 4. Q fever incidence among US Army veterinarians (1989–2008)

Factors	Seroconversion *n* (%)	Incidence rate per 1000 person-years (95% CI)	Incidence rate ratio (95% CI)	*P*
	n = 18 (3.6)	4.16 (2.6–6.6)		
Gender				
Male	5 (27.8)	2.0 (0.8–4.8)	Reference	
Female	13 (72.2)	7.1 (4.1–12.2)	3.55 (1.19–12.7)	0.012
Race				
White people	15 (83.3)	4.0 (2–7)	Reference	
Black people	1 (5.5)	6.0 (1–43)	1.49 (0.2–11.3)	0.7
Other	0 (0)	0	0	
Unknown	2 (11.1)	9.0 (2–36)	2.23 (0.51–9.8)	0.28
Average service time (years)	9.71 ± 6.8			
Average age at sampling (years)	39.3 ± 7.3			
Age at recent sampling (years)				
20–29	2 (11.1)	10.0 (2–39)	Reference	
30–39	7 (38.9)	3.0 (2–7)	0.35 (0.07–1.68)	0.19
40–49	8 (44.4)	5.0 (2–10)	0.5 (0.11–2.34)	0.38
50–59	1 (5.6)	3.0 (0.0–19)	0.27 (0.02–2.98)	0.29
Occupational specialty				
Field service (64A)	11 (61.1)	7.0 (4–12)	Reference	
Preventive medicine (64B)	2 (11.1)	2.0 (1–9)	0.33 (0.07–1.47)	0.15
Laboratory animal (64C)	1 (5.6)	1.0 (0.0–10)	0.2 (0.03–1.54)	0.12
Pathologist (64D)	4 (22.2)	7.0 (3–19)	1.03 (0.33–3.24)	0.96
Comparative medicine (64E)	0	0	0	
Clinical medicine (64F)	0	0	0	
Ever deployed	6 (38.9)	4.0 (2–9)	1.03 (0.39–2.75)	0.95
OIF	4 (16.7)	4.0 (1–10)	0.87 (0.29–2.66)	0.81
OEF	2 (11.1)	6.0 (1–22)	1.38 (0.32–6.02)	0.67
Bosnia/Kosovo	0 (0.0)	0	0	

OEF, operation enduring freedom; OIF, operation iraqi freedom.

Needless to say, the demographics of the veterinary profession have changed, which also has changed the demographics of the US Army Veterinary Corps. The primary source of veterinarians for the US Army historically was divided between veterinarians entering the military from practice and those entering the military directly after graduating from veterinary school. Around the year 2000, the military began providing veterinary scholarships under the Health Professions Scholarship Program where Veterinary Corps accessions almost exclusively come from now. With this in mind, knowing that seropositivity indicates evidence of exposure and immune response, it would be expected that a higher exposure would occur while in practice compared with during school. Yet in our 1989 subcohort, which likely had higher practice exposures showed a lower seroprevalence rate (8.0%) at entry to the military than those coming directly out of school (9.2%) in the 2000 subcohort yet similar.

Anderson et al.'s NHANES serosurvey study of a US representative population reported 3.1% seroprevalence, in our study, the military veterinarians showed nearly three times higher prevalence levels coming into the military, and the estimated annual average seroprevalence in this study cohort was 8.7% (6.6–14.95%; Fig. 2) Exposures may have been higher associated with prior exposures at home if coming from rural or agrarian backgrounds, exposures from taking jobs with veterinarians, exposures while in veterinary school, or other prior practice experiences. The attributable portion that these exposures contribute to the Q fever seroprevalence is between 4.9% and 6.1% at the time that they join the military (Anderson et al., 2009). Additionally, among these veterinarians, 3.6% were seroconverted which nearly parallels the seroprevalence levels reported in the NHANES study.

It is feasible to consider that many veterinarians will have some Q fever exposure while in veterinary school as evidenced from McQuiston's study of 24 veterinary school dairy herds reporting 92% of the herds having evidence of Q fever phase I antibodies or supported by de Rooij's 2012 study of veterinary students in the Netherlands with associated exposure risk while attending veterinary school. This later study reported high seroprevalence in veterinary students not from farming backgrounds whose veterinary school studies were focused on farm animal medicine and care. In our study, military veterinarians are assigned to many locations throughout the US and the world, it was

Table 5. Q fever prevalence among US Army veterinarians of the 1989–1999 and the 2000–2008 subcohorts at the time of entry to US military

Characteristics	1989–1999 Cohort *n* (%)	Positive at entry *n* (%)	Prevalence ratios (95% CI)	*P*	2000–2008 Cohort *n* (%)	Positive at entry *n* (%)	Prevalence ratios (95% CI)	*P*
	n = 261	21 (8.0%)			*n* = 239	22 (9.2%)		
Gender								
Male	152 (58.2)	11 (52.4)	Reference		89 (37.2)	5 (22.7)	Reference	
Female	109 (41.8)	10 (47.6)	1.27 (0.56–2.9)	0.65	150 (62.8)	17 (77.3)	2.02 (0.77–5.28)	0.17
Race								
White people	223 (85.4)	20 (95.2)	Reference		191 (79.9)	19 (86.4)	Reference	
Black people	14 (5.4)	1 (4.8)	0.80 (0.12–5.51)	1	7 (2.9)	0	0	
Other	13 (5.0)	0	0		10 (4.2)	1 (4.6)	1.01 (0.15–6.77)	1
Unknown	11 (4.2)	0	0		31 (13)	2 (9.1)	0.65 (0.16–2.65)	0.75
Age at entry (years)								
17–29	175 (67.1)	13 (61.9)	Reference		160 (67.0)	13 (59.1)	Reference	
30–39	75 (28.8)	8 (38.1)	1.44 (0.62–3.32)	0.46	64 (26.8)	8 (36.4)	1.68 (0.73–3.87)	0.3
40–49	11 (4.2)	0	0		15 (6.28)	1 (4.6)	0.9 (0.13–6.4)	1
Average age at entry (years)	28.1 ± 5.6	28.6 ± 4.6			29.4 ± 4.8	30.0 ± 5.0		
Home of record region								
Midwest	38 (14.6)	3 (14.3)	2.13 (0.23–19.41)	0.64	29 (12.1)	0	0	
Mountain	22 (8.4)	4 (19.1)	4.91 (0.59–40.81)	0.16	15 (6.3)	1 (4.6)	0.87 (0.09–8.77)	1
North	25 (9.6)	1 (4.8)	1.08 (0.07–16.36)	1	27 (11.3)	3 (13.6)	1.44 (0.26–7.96)	1
Northeast	40 (15.3)	2 (9.5)	1.35 (0.13–14.16)	1	61 (25.5)	9 (40.9)	1.92 (0.44–8.27)	0.49
Pacific	27 (10.3)	1 (4.8)	Reference	0.64	26 (10.9)	2 (9.1)	Reference	
Southeast	64 (24.5)	4 (19.1)	1.69 (0.20–14.41)	1	47 (19.7)	3 (13.6)	1.72 (0.19–15.76)	1
Southwest	31 (11.9)	5 (23.8)	4.35 (0.54–35.0)	0.2	33 (13.8)	4 (18.2)	1.58 (0.31–7.94)	0.69
Unknown	14 (5.4)	1 (4.8)	1.93 (0.13–28.57)	1	1 (0.42)	0	0	

Table 6. Q fever prevalence among US Army veterinarians of the 1989–1999 and 2000–2008 subcohorts after serving in the US military

	1989–1999 Cohort			2000–2008 Cohort		
Characteristics	Positive after service *n* (%)	Prevalence ratios (95% CI)	*P*	Positive after service *n* (%)	Prevalence ratios (95% CI)	*P*
	29 (11.1)			27 (11.3)		
Gender						
Male	13 (44.8)	Reference		5 (18.5)	Reference	
Female	16 (55.2)	1.72 (0.86–3.42)	0.16	22 (81.5)	2.61 (1.02–6.65)	0.035
Average service time (years)	12.5 ± 5.1			4.6 ± 2.4		
Average age at sampling (years)	41 ± 5.8			35.7 ± 7.3		
Age at sampling (years)						
20–29	0 (0.0)	0		6 (22.2)	Reference	
30–39	12 (41.4)	Reference		13 (48.1)	1.17 (0.47–2.97)	0.81
40–49	15 (51.7)	1.68 (0.82–3.42)	0.21	6 (22.2)	2.96 (1.05–8.35)	0.07
50–59	2 (6.9)	0.93 (0.22–3.4)	1	2 (7.4)	6.17 (1.78–21.4)	0.05
Occupational specialty						
Field service (64A)	13 (44.8)	Reference		21 (77.8)	Reference	
Preventive medicine (64B)	5 (17.2)	0.65 (0.25–1.74)	0.45	3 (11.1)	1.48 (0.49–4.47)	0.7
Laboratory animal (64C)	6 (20.7)	0.95 (0.39–2.35)	1	1 (3.7)	1.11 (0.17–7.24)	1
Pathologist (64D)	4 (13.8)	0.90 (0.32–2.58)	1	2 (7.4)	1.18 (0.31–4.56)	1
Comparative medicine (64E)	0	0		0	0	
Clinical medicine (64F)	1 (3.5)	0.53 (0.08–3.77)	0.69	0	0	
Ever deployed	9 (31.0)	1.14 (0.54–2.38)	0.83	8 (29.6)	0.87 (0.4–1.9)	0.83
OIF	5 (17.2)	0.88 (0.35–2.19)	1	8 (29.6)	1.06 (0.49–2.3)	0.63
OEF	4 (13.8)	1.93 (0.74–4.99)	0.25	0	0	
Bosnia/Kosovo	0	0		0	0	

OEF, operation enduring freedom; OIF, operation iraqi freedom.

Table 7. Q fever incidence among US Army veterinarians of the 1989–1999 and 2000–2008 subcohorts

Factors	1989–1999 Cohort Seroconversion n (%)	1989–1999 Cohort Incidence rate per 1000 person-years (95% CI)	1989–1999 Cohort Incidence rate ratio (95% CI)	1989–1999 Cohort P	2000–2008 Cohort Seroconversion n (%)	2000–2008 Cohort Incidence rate per 1000 person-years (95% CI)	2000–2008 Cohort Incidence rate ratio (95% CI)	2000–2008 Cohort P
	10 (3.8)	2.99 (1.6–5.6)			8 (3.3)	8.2 (4.1–16.4)		
Gender								
Male	5 (50.0)	2.38 (0.99–5.7)	Reference		0	0	Reference	
Female	5 (50.0)	4.02 (1.7–9.7)	1.69 (0.39–7.35)	0.42	8 (100.0)	13.7 (6.8–27.4)	0	0.016
Race								
White people	10 (100.0)	3.5 (1.9–6.5)	Reference		5 (62.5)	6.2 (2.6–15)	Reference	
Black people	0	0	0		1 (12.5)	45.2 (6.4–321)	7.29 (0.89–59.8)	0.15
Other	0	0	0		0	0	0	
Unknown	0	0	0		2 (25.0)	22.1 (5.5–88.5)	3.56 (0.7–18.1)	0.15
Average service time (years)	14.3 ± 5.5				3.9 ± 2.4			
Average age at sampling (years)	42.1 ± 4.5				35.8 ± 8.7			
Age at sampling (years)								
20–29	0 (0.0)	0	0		2 (25.0)	11.1 (2.8–44.4)	Reference	
30–39	3 (30.0)	2.1 (0.68–6.51)	Reference		4 (50.0)	6.2 (2.3–16.6)	0.56 (0.1–3.04)	0.62
40–49	7 (70.0)	4.5 (2.2–9.5)	2.16 (0.56–8.34)	0.27	1 (12.5)	8.2 (1.2–58.4)	0.74 (0.07–8.11)	1
50–59	0 (0.0)	0	0		1 (12.5)	29.7 (4.2–211.2)	2.65 (0.25–28.4)	0.41
Occupational specialty								
Field service (64A)	5 (50.0)	5.0 (2.1–11.9)	Reference		6 (75.0)	9.6 (4.3–21.4)	Reference	
Preventive medicine (64B)	2 (20.0)	2.5 (0.6–10.1)	0.51 (0.1–2.63)	0.42	0	0	0	
Laboratory animal (64C)	1 (10.0)	1.4 (0.2–10.3)	0.29 (0.03–2.49)	0.26	0	0	0	
Pathologist (64D)	2 (20.0)	4.3 (1.1–17.1)	0.86 (0.17–4.45)	0.86	2 (25.0)	18.6 (4.7–74.5)	1.94 (0.4–9.49)	0.61
Comparative medicine (64E)	0	0	0		0	0	0	
Clinical medicine (64F)	0	0	0		0	0	0	
Ever deployed	3 (30.0)	2.9 (0.94–9.1)	0.97 (0.16–4.25)	1	3 (37.5)	7.8 (2.5–24.1)	0.92 (0.14–4.74)	0.93
OIF	1 (10.0)	1.3 (0.19–9.7)	0.4 (0.009–2.9)	0.41	3 (37.5)	8.9 (2.9–27.6)	1.14 (0.18–5.87)	0.84
OEF	2 (20.0)	6.7 (1.7–26.9)	2.57 (0.26–12.9)	0.27	0	0	0	
Bosnia/Kosovo	0	0	0		0	0	0	

OEF, operation enduring freedom; OIF, operation iraqi freedom.

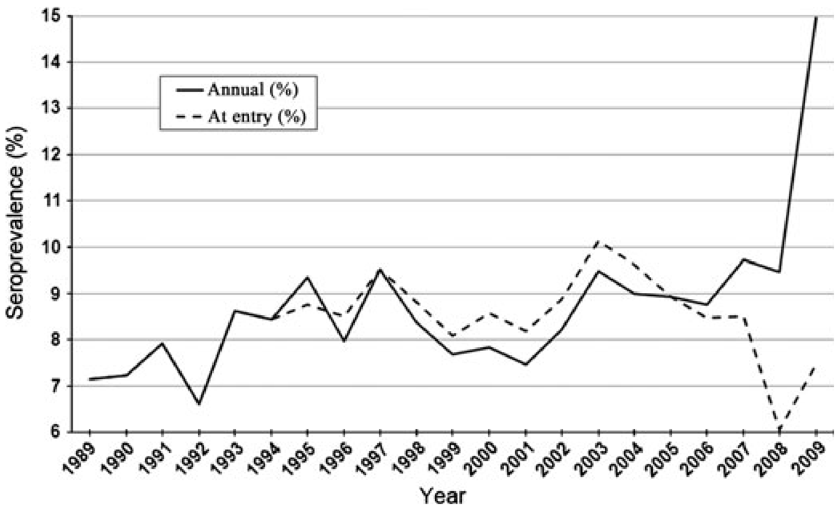

Fig. 2. Estimated annual Q fever seroprevalence (%) among US Army veterinarians while on active duty and at entry (1989–2009).

thought that higher seroprevalence and seroconversion levels would be found, yet the incidence only reached 4.2 per 1000 PY (95% CI 2.6–6.6) overall (Table 4). Interestingly, seroconversions were similar between the subcohorts (3.8% versus 3.3%, respectively), yet the 1989 cohort had a smaller incidence at 3.0 per 1000 PY (95% CI 1.6–5.6) compared with the 2000 cohort incidence of 8.2 per 1000 PY (95% CI 4.2–16.4; Table 7).

At any one time, there are nearly 450 active duty veterinarians in the US Army Veterinary Corps. Using the incidence and seroprevalence levels from this study means that every year there will be at least two new Q fever cases and if the incidence for the 2000 cohort is used, it will nearly double to 3.7 new cases every year. Knowing that approximately 45 new accessions are added to the Veterinary Corps every year, of these, four will be seropositive for Q fever when they enter the military. Additionally, assuming that the proportion of men and women are the same, women will have 3.1 new cases every year based on the 2000 cohort levels. This is an underestimate as the proportion of females is much higher.

Although all longitudinal health-related, demographic and deployment data available in the Defense Medical Surveillance System were retrieved for each member of the study cohort, this study has many limitations and many questions that still remain unanswered concerning how and what exposure variables relate to the risk of Q fever among US Army veterinarians. The most influential weakness is the ‘retrospectiveness’ of this study and the inability to gather information directly from the veterinarians represented, thereby limiting the key occupational-related exposure variables that would be useful and comparable found in other prospective cohort studies.

Using the archived deployment forms was not as helpful as anticipated. There were very few responses by deployed veterinarians that provided useful and comparable information. Additionally, this population appears to be very healthy and few military veterinarians had health events as captured by an ICD-9 code in their medical record corresponding to potential symptoms or sequelae of Q fever. This may be partly due to US Army veterinarians’ role as health professionals and military officers, which may predispose them to ‘soldier’ through illnesses or to self-treat without seeking formal health care that would result in provider-assigned diagnostic codes captured in the electronic health record. This may be an even more likely scenario when Q fever manifests itself as a ‘flu-like’ illness that may resolve itself within a few days or as a mild subclinical ‘not doing right’ syndrome.

An additional issue and limitation with this data set is associated with the occupational roles and the inability to capture or differentiate the involvement of veterinarians in this cohort who are assigned to special operations and civil affairs units compared with staff and force health protection–related roles. It would be expected that individuals who serve in special operations or civil affairs units would demonstrate higher prevalence associated with frequent exposures to higher-risk environments than those veterinarians who are primarily working on military installations or in office settings.

Due to the nature of this study (which utilized administrative medical records and post-deployment forms as the source of potential covariates), we were unable to control for potential confounders to the extent we would have liked. We did not anticipate the magnitude of missing data for several covariates of interest or the lack of distribution in values for other covariates. In addition, the original sample size and power calculations performed to determine how many subjects we would need relied on estimates of seroprevalence and seroconversion that were higher than those seen in our study. Therefore, our study was likely underpowered.

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If our sample size were larger, it is possible that several of our comparisons with P-values slightly above 0.05 (e.g. females with a higher PR at baseline than males: 1.47 (0.98–1.77; $P = 0.074$ or individuals 40–49 years of age with a higher PR than the youngest age category: 1.92 (0.96–3.84); $P = 0.063$; Table 1) might have attained statistical significance. However, as in any case where results do not meet pre-specified significance criterion (i.e. $P < 0.05$), another possible explanation is that there is no real association.

As with many seroepidemiologic studies, there are difficulties in interpreting laboratory test results and determining and measuring the longevity of antibody immune responses associated with Q fever. Over time, antibody levels are known to decrease or disappear, thus serorevert, and therefore, it is difficult to measure immune memory using present methods in this study that may assist in identifying a true exposure or infection of Q fever. There were five individuals who were positive for both antibody phases and later became negative on one or both antibody phases. It is likely that the numbers reported in this study are an underestimate of the full exposure and risk of Q fever among US military veterinarians.

It is understood that individuals who expose themselves to animals through occupation or hobby will be at higher risk for zoonotic diseases like Q fever. Few studies have examined the risks of Q fever infection and occupational exposures among veterinarians. This is the first study examining the evidence of Q fever seroprevalence and incidence among US Army veterinarians. The benefit of this study is that it is a descriptive report identifying new health information about an important US military population. Our findings indicate that veterinarians who come into the military have a likelihood of having been exposed to Q fever prior to service, with a moderate number of new cases developing while serving in the military, and most individuals in this study maintained a titre for long periods of time (mean = 8.16 ± 5.4 years). Although what is not known is the possible multiple exposures over time that may promote a constant titre from occupational re-exposure and immune stimulation.

This study shows that US military veterinarians are susceptible to zoonotic pathogens and may have other exposures that could cause undesirable health consequences. Studies considering other zoonotic pathogens may be militarily relevant. What is unknown about Q fever and US military veterinarians is the day-to-day lifestyle and other occupation exposures that predispose US Army veterinarians to Q fever as well as the implications of chronic health effects due to exposure, which was not part of this study and may be valuable to explore in future health studies.

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