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Prevalence of serum antibodies to *Coxiella burnetii* in Alaska Native Persons from the Pribilof Islands

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Abstract

Background: Q fever is a febrile illness caused by infection with the bacterium *Coxiella burnetii*. It is most often transmitted by inhalation of the bacteria after it is shed by infected livestock. Recent studies have found very high *C. burnetii* infection rates among marine mammals, but it is not known if shedding by marine mammals creates a risk of Q fever among humans. To better understand infection of humans with exposure to marine mammals, the prevalence of antibodies against *C. burnetii* in serum samples taken from Alaskan Native persons residing on the Pribilof Islands was evaluated. The Pribilof Islands support large populations of northern fur seals infected with *C. burnetii* that may increase the risk of exposure for island residents.

Methods: Serum testing for IgG antibodies against *C. burnetii* (phase I and phase II) was performed and demographic data was analyzed utilizing banked serum specimens drawn from island residents from 1980-2000.

Results: The overall seroprevalence rate was 11.6% (95% CI = 9.3-14.4%; 72/621). This is higher than the previously reported 3.1% (95% CI = 2.1-4.3%) seroprevalence for the U.S. population.

Conclusions: These results suggest that Alaskan Native persons may be at higher risk for exposure to *C. burnetii* than the general U.S. population, possibly due to proximity to large populations of infected marine mammals.

Keywords

Q fever; *Coxiella burnetii*; Alaska Native persons; serosurvey; marine mammals

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Introduction

Q fever is a zoonotic disease caused by the globally distributed bacterium *Coxiella burnetii* (Maurin & Raoult, 1999). Elevated antibody titers against Phase I and Phase II antigenic phases correspond to chronic and acute forms of disease, respectively, as well as provide evidence of past infection (Fournier et al., 1998). Approximately half of infected persons develop clinical symptoms; the most commonly recognized forms of acute disease are a nonspecific flu-like illness, pneumonia and hepatitis (Anderson et al., 2013). Chronic Q fever is rare and most commonly presents as endocarditis in those with pre-existing valvular disease. Fatality rates in untreated chronic Q fever may exceed 65% and may occur years after the initial infection (Anderson et al., 2013, Maurin & Raoult, 1999).

Ruminants are considered the primary *C. burnetii* reservoir, with the most common impact on ruminant health being loss of pregnancy due to high levels of infection in the placenta (Angelakis & Raoult, 2010). Humans are typically infected by *C. burnetii* after inhalation of the bacteria in aerosolized secretions from ruminants. It is estimated that inhalation of <10 organisms can initiate an infection (Tigertt et al., 1956). Other species, including wildlife, have also been associated with human infections (Fournier et al., 1998). Human exposure to marine mammals is emerging as a potential risk factor for Q fever infection. A case of Q fever endocarditis was reported in 2010 in a lifelong resident of Greenland with harbor or hooded seals implicated as a possible source of infection (Koch et al., 2010). *Coxiella* placental infection has been confirmed in a Pacific harbor seal in California by immunohistochemistry (Lapointe et al., 1999), a Steller sea lion in Washington by PCR (Kersh et al., 2010), and 109 (74.7%) of 146 placental tissue samples collected from a Northern fur seal rookery on St. Paul Island, Alaska by PCR (Duncan et al., 2012). In addition, of 218 Pacific harbor seals sampled in Washington, 50 (22.9%) tested positive for antibodies against *C. burnetii* (Kersh et al., 2012). The significance of these new findings and the relationship to human infection is poorly understood.

Canadian serosurveys have found 15% of trappers and 18% of Cree hunters to be positive for Q fever antibodies against *C. burnetii* (Levesque et al., 1995, Levesque et al., 2007). Because Q fever is often underdiagnosed due to its nonspecific clinical presentation and lack of readily available testing in some areas, the public health implications of this disease is unknown in the Bering Sea region. Persons residing on St. Paul and St. George, part of the Pribilof Islands in Alaska, may be particularly at risk for exposure to the pathogen based on proximity to seals and their rookeries and a high prevalence of *C. burnetii* found among animals at the seal breeding site on St. Paul. It is not known if the *C. burnetii* strains that infect marine mammals can be transmitted to humans and cause Q fever. The purpose of this investigation was to test stored serum samples from St. Paul and St. George residents for IgG antibodies to *C. burnetii* and examine Q fever seroprevalence related to demographics in this population.

Materials and Methods

The Alaska Area Specimen Bank (AASB) is a repository of more than 400,000 human samples stored from past research and investigations for use in studies to advance

understanding of Alaska Native people's health (Parkinson et al., 2013). The AASB Oversight Committee manages the specimen bank. This group is made up of representatives from the Alaska Native Tribal Health Consortium (ANTHC), the Centers for Disease Control and Prevention (CDC) and Alaska Native Tribal Health Organizations (THO). We analyzed 621 serum samples collected from 621 individual St. George and St. Paul residents from 1980–2000 and stored at −20 to −30°C in the AASB. The AASB also provided demographic information including age, community, and gender. The study protocol was approved by the CDC and Alaska Area institutional review boards in compliance with all applicable Federal regulations governing the protection of human subjects.

An enzyme-linked immunosorbent assay (ELISA) was used to initially screen serum specimens for IgG Phase II antibody seropositivity (Verion-Serion, Wuerzburg, Germany) according to the manufacturer's instructions with the exception that samples were diluted 1:100. Any serum samples positive or equivocal by ELISA were then tested by immunofluorescence antibody assay (IFA) in order to obtain end point titers for IgG to both phase I and phase II *C. burnetii* antigens. Q fever seropositivity was defined as a phase I or phase II IgG titer ≥ 1:64 by IFA. The IFA test was performed by the method of Philip et al. (Philip et al., 1976) and adapted to *C. burnetii* using Nine Mile phase I and II antigens as described elsewhere (Peter et al., 1985).

Statistical analysis was performed using Epi Info version 3.3.2 (CDC, Atlanta, GA). The χ^2 test was used to compare the statistical significance of Q fever seroprevalence among groups. Age group differences were evaluated by the χ^2 test for trend. Values of $P < 0.05$ were considered significant in all statistical tests.

Results

The Pribilof Islands of St. Paul and St. George are located off the coast of Alaska in the Bering Sea (Figure 1). Stored serum samples previously collected from island residents were analyzed for this study. Among the 621 study participants, the male to female ratio was 1.15:1 and the majority were residents of St. Paul (76%). The median age of the study population was 27 years (range, <1 year – 91 years). The largest age group was 21–40 years (43%; 266/621), while the 70+ year group included the lowest number of individuals (4%; 26/621) (Table 1).

Out of the 621 study participants on St. Paul and St. George, 72 had a positive antibody titer to *C. burnetii* resulting in an overall seroprevalence of 11.6% (95% CI = 9.3–14.4%). Seventy-two persons aged 4–81 years had a positive Phase II IgG antibody titer to *C. burnetii* antigen of 1:64 or greater indicating past infection. Forty-nine of the 72 positive samples had a Phase II IgG titer of 1:64, but Phase II IgG titers of 1:1024 and 1:2048 were observed. Of the 72 seropositive persons, the majority (78%) were residents of St. Paul. Of 151 St. George residents tested, 16 (10.6%; 95% CI 6.5–16.6%) had positive samples. Of 470 St. Paul residents tested, 56 (11.9%; 95% CI 9.3–15.2%) had positive samples. There was no statistically significant difference in seropositivity between island residence or gender of participants. Seroprevalence for the total population increased with age and was highest among persons 60–69 years of age (22.9%) (Table 1). A linear t-test for trend for the

relationship between age and Q fever seropositivity was statistically significant (P =0.008). The majority of the samples were taken during the 1980's with 148 samples from 1980–1984, 420 samples from 1985–1989, 51 samples from 1990–1994, and 2 samples from 1995–2000. However, there was no statistically significant relationship between year of specimen draw and seropositivity, analyzed either by individual year or by the 5-year groups described above.

Discussion

The Q fever seroprevalence among the residents of St. Paul and St. George during the years specimens were drawn (1980–2000) is higher than that of the general adult U.S. population, which was approximately 3% in samples taken during 2003–2004 (Anderson et al., 2009). However, the seroprevalence of Alaskan residents is unknown and may be higher than the general U.S. population and more closely approximate the findings from our study. A study that evaluated the seroprevalence among Alaska residents participating in outdoor activities that may increase the risk of exposure to zoonotic pathogens found that 8.3% of participants were positive for Phase II IgG antibodies (Miernyk et al., 2019). That study also found a seroprevalence of 11.7% among Alaska Native persons that participated in the study, similar to Pribilof Islands residents. These results suggest that Alaska Native persons have a greater risk of exposure to *C. burnetii* than non-native persons. The contribution of infected marine mammals to that increased risk remains to be determined. Also, the current serologic status of St. Paul and St. George residents is unknown as the most recent serum specimen tested in this study was ≥10 years old.

Although there is evidence that *C. burnetii* is present in the environment and wildlife of St. Paul (Duncan et al., 2012), it is unclear whether Q fever is a public health threat for current Pribilof Islands residents as we have no evidence of current symptomatic illness. At the time of the serosurvey, the St. Paul Health Center had not requested any diagnostic testing for Q fever for ill island residents. Due to the nonspecific presentation of Q fever disease, it has long been underreported and underdiagnosed. The results presented here support efforts by local health departments and Alaska Native tribal leaders to educate health care workers of the potential risk for Q fever infection and use of appropriate diagnostic testing and treatment methods for patients that present with compatible symptoms. The greatest risk of *C. burnetii* infection for Pribilof Island residents is likely to come from inhalation of dried and airborne *C. burnetii* derived from newborn Northern Fur Seals or placenta. Efforts to more clearly define the burden of *C. burnetii* infection and determine if there is a current health risk among St. Paul and St. George residents should be considered for future surveillance activities.

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Impacts:

- Q fever is a zoonotic disease caused by inhalation of the bacterium *Coxiella burnetii*
- Some Alaska Native persons live in close proximity to large populations of marine mammals that are infected with *Coxiella burnetii*, but it is not known if this creates a greater risk of Q fever among these populations
- The results of this study show that antibodies against *Coxiella burnetii* are more common among Alaska Native persons living near marine mammals than in the general population, suggesting that living near marine mammals exposes people to the bacteria

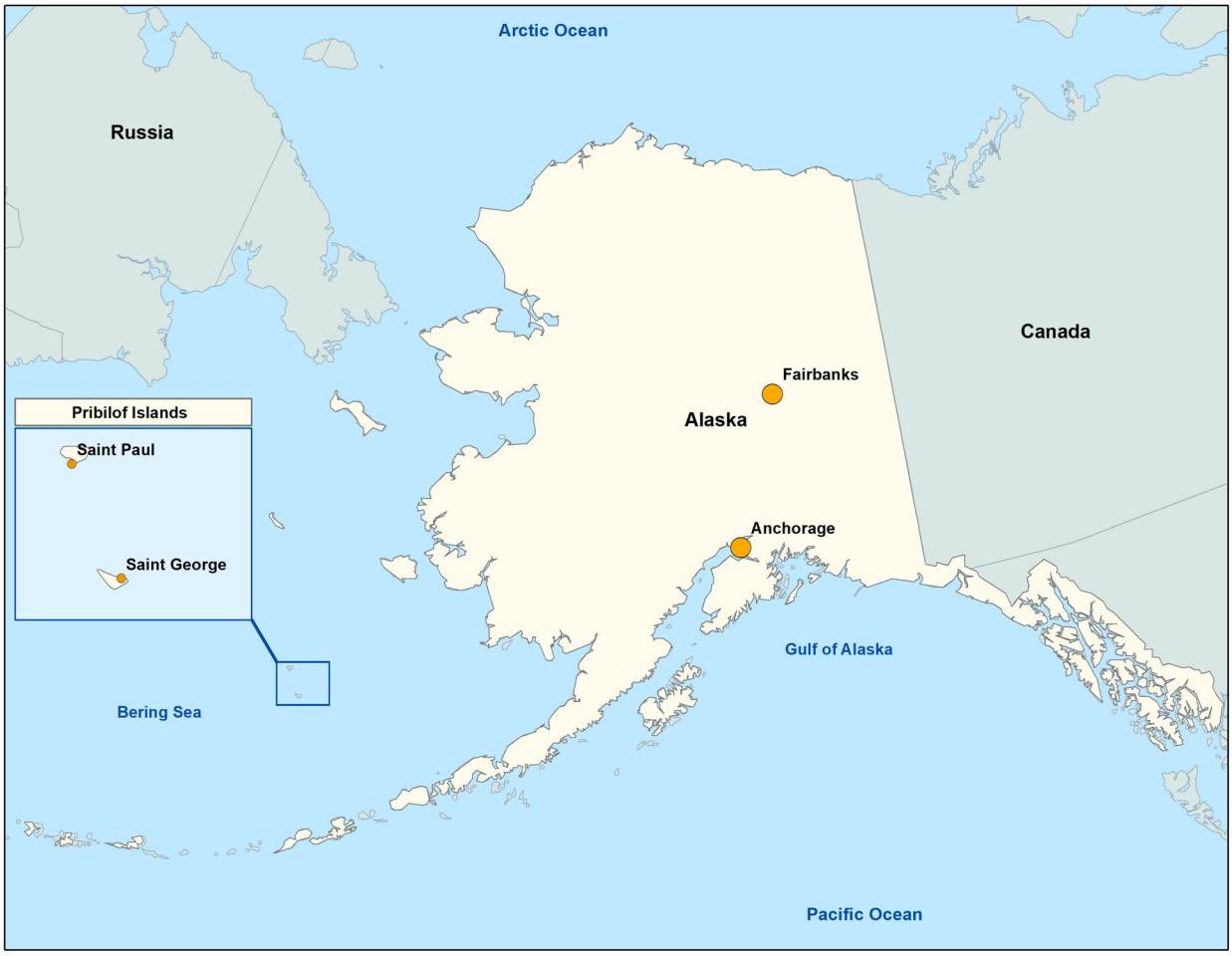

Figure 1:
Map of Alaska showing the location of the Pribilof Islands.

TABLE 1.

Characteristics of St. Paul and St. George study participants

Characteristics	Category	Number of participants (%)	Seroprevalence (%; 95% CI)
Age (years)	0-9	83 (13)	9/83 (10.8; 5.6-19.6)
	10-19	105 (17)	5/105 (4.8; 1.8-10.9)
	20-29	145 (23)	15/145 (10.3; 6.3-16.5)
	30-39	121 (19)	13/121 (10.7; 6.3-17.6)
	40-49	62 (10)	12/62 (19.4; 11.3-31.0)
	50-59	46 (7)	8/46 (17.4; 8.8-31.0)
	60-69	35 (6)	8/35 (22.9; 11.8-39.3)
	70-79	19 (3)	1/19 (5.3; <0.0001-26.5)
	≥80	5 (<1)	1/5 (20.0; 2.0-64.0)
Gender	Male	332 (54)	38/332 (11.5; 8.4-15.4)
	Female	289 (46)	34/289 (11.8; 8.5-16.0)
Residence	St. Paul	470 (76)	56/470 (11.9; 9.3-15.2)
	St. George	151 (24)	16/151 (10.6; 6.5-16.6)