THE SEROLOGIC PREVALENCE OF Q FEVER (COXIELLA BURNETII) COMPLEMENT-FIXING ANTIBODIES IN THE PENINSULAR BIGHORN SHEEP OF SOUTHERN CALIFORNIA

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Abstract. Q fever is a rare illness in the Southern California desert. During the past 34 years only 6 patients have been diagnosed with the disease at the Eisenhower Medical Center, a referral center for much of the desert and surrounding mountains. In all but 2 instances, Q fever was identified in patients who have been in contact with imported domestic sheep who are brought to the desert to graze and lamb in the fall and winter. The sheep are sent back to Idaho, Wyoming, and Montana in the spring. With frequent infection by Coxella burnetii established in domestic sheep, we elected to study the prevalence of complement fixing antibodies to Coxella burnetii in native bighorn sheep that reside in the lower levels of the mountains surrounding the desert. From 1992 to 1999, of 268 serum samples drawn from male and female lambs and adult sheep, 27 tested positive (10%), which is strikingly low when compared with Dall sheep in Alaska (12 of 15), kangaroos, wild rabbits, and brown rats. Because changes have been made in Peninsular bighorn sheep habitat since the animals were listed as endangered in 1998, further follow-up in Q fever serology testing will be of interest.

INTRODUCTION

Q (query) fever was initially described by Derrick1 in Brisbane, Australia in 1937 after investigating an influenza-like illness in abattoir workers, and later Burnet and Freeman recovered a rickettsial-like organism from infected mice,2 and named it Rickettsia burnetii, then subsequently Coxella burnetii.3

Coxiella burnetii exists globally except for Antarctica and probably New Zealand.4 It infects arthropods of the class Arachnida including primarily ticks, and also reptiles and other vertebrates including humans, but causes natural disease predominantly only in humans. Domestic sheep, cattle, and goats are most commonly infected and often transmit the disease to humans by excretory products, milk, and hide but most effectively by parturient products. In 1949, an epidemiologic survey among domestic sheep in California indicated that 24% had microagglutinating antibodies to C. burnetii.5 More recent studies6-7 suggest that seroprevalence in these domestic ruminants is currently higher than it was 20 to 30 years ago. In most instances the diagnosis of Q fever is established serologically in humans as well as exposure in animals.3 There are several serologic methods that are used including complement fixation (CF), indirect immunofluorescence assay (IFA), and enzyme-linked immunosorbent fluorescence assay (ELISA). CF is quite specific but less sensitive than IFA and ELISA.4 C. burnetii exhibits an host-dependent antigenic variation termed phase variation 1 and 2 due to mutational changes in lipopolysaccharide profiles, which results in small-cell and large-cell variants; the former survives in the environment whereas the latter multiplies in the host monocyte or macrophage. Bacteria isolated directly from patients or laboratory animals are in phase 1 whereas those isolated after repeated passage through embryonated hens’ eggs are in phase 2. In an apparent paradox, antibodies to phase 2 antigen is associated with an acute illness and an antibody rise to phase 1 antigen occurs in chronic disease. In particular, the IgM antibody response to phase 2 antigen indicates an acute reaction, whereas repetitive replication in cell cultures results in poor antigenic stimulation and a less virulent organism resulting in a type 1 antibody of IgG and IgA subclasses and indicative of chronic infection.8 Impaired maturation of phagosomes and defective killing of C. burnetii appear to be responsible for the development of chronic Q fever9 and perhaps carriage of the organism and the absence of disease in ungulates.

Native American bighorn sheep (Ovis canadensis) have inhabited the United States for more than 25,000 years. Originally described by Lewis and Clark in 1804 the bighorn population was estimated to constitute more than 1 million animals ranging from the Prairies in the mid-west to the mountains near the Pacific Ocean. Currently less than 75,000 bighorn inhabit the continental United States. Two subspecies currently exist in Southern California, Ovis canadensis cremnobates and O. canadensis nelsoni. The former were listed as an endangered species in 1998 and inhabit the San Jacinto and Santa Rosa mountains extending from eastern Riverside county in California to the Mexican border.

Peninsular bighorn sheep are unique in that they are low level sheep. Typically, other subspecies of bighorn range from 4,000–10,000 feet elevation when given the choice, whereas peninsular bighorn access habitat from 400–4,000 feet despite having access to mountains as high as 10,000 feet. Peninsular bighorn sheep are gregarious and usually spend time in groups of 2–10 bighorn, but may form larger groups, especially during the lambing season when ewes and lambs often congregate. There are 8 subgroups of Peninsular bighorn in the Peninsular ranges that are connected by ram movement. It is important to have connectivity to maintain herd health.

The Peninsular mountains surround the western limits of the Coachella and Imperial Valleys of the Colorado desert of Southern California, which has virtually no large scale animal husbandry in the area. However, for nearly 4 decades ranchers from Idaho, Wyoming, and Montana have imported their sheep to areas near Palm Springs and Blythe, California to graze and lamb during the fall and winter months. Occasional cases of Q fever have been seen at the Eisenhower Medical Center, Probst Professional Building, Suite 308, 39000 Bob Hope Drive, Rancho Mirage, CA 92270. E-mail: laconemedico@aol.com
Center, a 265-bed general hospital that has also served as a referral facility to the area over the past 34 years. Most infections have been attributed to contact with these sheep often indirectly by living near or intruding into these sheep areas. Since the habitats of domestic and bighorn sheep are so strikingly different, we were interested in evaluating *C. burnetii* serologies of Peninsular bighorn sheep.

MATERIALS AND METHODS

From 1992–2004 blood was drawn from 268 Peninsular bighorn sheep and the serum separated and frozen. An aliquot of serum was sent to National Veterinary Services Laboratories (Ames, Iowa) for *C. burnetii* complement fixing antibodies. Phase 2 antibody was assayed. Both male and female bighorn were included as well as lambs and adult animals. A total of 64 male and 118 female adult bighorn were tested as well as 86 lambs (45M,41F). On average, 21 bighorn sheep were sampled each year of the study. Animals were tested from the northern Santa Rosa Mountains, San Jacinto Mountains, and Bighorn Institute’s captive herd. Lambs were sampled between day 1 and 3 months of age. Ewes and rams were primarily sampled during October, approximately 6 months after the peak of lambing season. Birth was not often observed in the wild, but with those bighorn ewes that gave birth to lambs at Bighorn Institute no evidence of parturition problems were noted.

RESULTS

Of the 268 bighorn sheep tested 109 were male and 159 female. Twenty-seven bighorn tested positive (11 male and 16 female), 25 having titers of 1:20, 1 each had titers of 1:40 and 1:80. None of the animals appeared ill.

Positive results were obtained in the years 1992–1999, and are divided as follows: 1992, 2/18 positive, 1:20(1), 1:80(1); 1993, 1/19 positive, 1:20(1); 1994, 2/20 positive, 1:20(2); 1995, 2/21 positive, 1:20(2); 1996, 9/28 positive, 1:20(9); 1997, 5/7 positive, 1:20(5); 1998, 4/30 positive, 1:40(1), 1:20(3); 1999, 2/30 positive, 1:20(2).

Since the Peninsular bighorn were listed as endangered in 1998, the Recovery Plan established guidelines and recommendations limiting livestock operations in the Peninsular ranges. These livestock restrictions may give us some understanding of the change of Q fever antibody testing in Peninsular bighorn since 1999.

DISCUSSION

Q fever is a disease of humans characterized by an influenza-like disease with pneumonia or hepatitis. In about 3% of individuals with symptomatic infection, a chronic infection of the liver (granulomatous hepatitis) or in individuals with valvular heart disease or prosthetic valves endocarditis ensues. Domestic ruminants are by far the major reservoir of animals that lead to human disease. Sheep, cattle, and goats in the United States who are most often infected by ticks (over 40 species are known), and then transfer *C. burnetii* in their excretions, hides, milk, and particularly byproducts of parturition by aerosolization and consequent inhalation by humans. In sheep, infection can cause an influenza-like syndrome and rarely abortion. Additionally in Nova Scotia and Maine outbreaks have been noted to be caused by parturient cats.

The existence of *C. burnetii* infection in feral animals has been documented in kangaroos, wallabies, and wallaroos in Australia as well as deer in central Europe and Alaska and marsupials and rodents in French Guiana. In Alaska complement fixing antibodies > 1:10 to *C. burnetii* are found in the sera of 12 of 18 Dall sheep suggesting that infection is widespread in Dall sheep of the Central Alaska Range. In California the seroprevalence in wildlife animals includes coyotes, gray foxes, skunks, raccoons, deer, mice, birds, and bears. In Idaho 6% of bears, and in Florida 10% of bears have Q-fever antibody whereas in Arkansas 80% of wild sheep possess antibodies to Coxiella burnetii.

We have not found any previous reports detailing exposure of bighorn sheep to *C. burnetii* in the United States. Our current serologic study of 268 peninsular sheep from Southern California indicates antibody to *C. burnetii* occurs in about 10% of animals. This prevalence is far less than has been reported from elsewhere where the infection exists in feral animals.

Implicit in this observation is that Q fever has not been a major factor in the decline in population of the Peninsular bighorn sheep. Indeed, pneumonia has been a prominent and major cause of lamb mortality but has been shown to be secondary to viral infection (usually parainfluenza) complicated by *Pasteurella hemolytica* superinfection. Our opinion is that the decline of peninsular bighorn sheep in Southern California results from loss of habitat due to human intrusion into bighorn habitat and not to infection. Supporting this conclusion is the recent observation that the number of bighorn sheep has increased by 100% since measures have been initiated to protect their habitat from human intrusion.

The absence of exposure to *C. burnetii* in Peninsular bighorn sheep but its high prevalence in imported domestic sheep into the Southern California desert certainly implies that their distant habitats exert a major influence on this observation. Furthermore it would also imply the natural absence of *C. burnetii*-infected arachnids in the remote areas of Southern California deserts and mountains appears to be due to the absence of animal husbandry in the area. When this does occur as with the importation of infected domestic sheep, human Q fever serves to identify habitat contamination.

In our study the CF test was used and although it is not as sensitive as the IFA and ELISA the blood was drawn within 3 months of lambing. In primary Q fever in humans, phase 2 antibody ordinarily persists at moderate titers for 3 months to 1 year. Thus, assuming a similar quantitative serologic response in mammals, it would appear that the interval of up to 3 months would accurately detect exposure to *C. burnetii*.

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REFERENCES