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SEROLOGIC EVIDENCE OF ARBOVIRUS INFECTIONS IN HUMANS AND WILD ANIMALS IN ALASKA

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ABSTRACT: Blood samples were collected from humans and several species of free-ranging wild animals in Alaska. Sera were tested for antibody to Jamestown Canyon (JC), snowshoe hare (SSH), Northway (NOR), Klamath (KLA), Sakhalin (SAK), Great Island (GI), and Silverwater (SIL) virus. JC antibody was found in 54% of 121 human, 89% of 97 bison (*Bison bison*), 51% of 84 Dall sheep (*Ovis dalli*), 43% of 68 snowshoe hare (*Lepus americanus*), and 3% of 33 arctic fox (*Alopex lagopus*) sera. SSH antibody was found in 42% of 121 human, 89% of 97 bison, 41% of 84 Dall sheep, and 65% of 68 snowshoe hare sera. NOR antibody was found in 14% of 121 human, 94% of 97 bison, 84% of 84 Dall sheep, 43% of 69 caribou (*Rangifer tarandus*), 3% of 68 snowshoe hare, 48% of 64 grizzly bear (*Ursus arctos*), 3% of 33 arctic fox, and 78% of 27 moose (*Alces alces*) sera. KLA antibody was found in 5% of 121 human and 40% of 97 bison sera. SAK antibody was found in 2% of 97 bison and 3% of 33 arctic fox sera. GI antibody was found in 1% of 97 bison sera. No SIL antibody was found in any sera tested. Thus the natural host ranges of JC, SSH, NOR, and KLA viruses have been extended by inference from the occurrence of antibody.

INTRODUCTION

Virus isolations from selected hematophagous arthropods and selected mammals in Alaska have revealed the presence of eight distinct arbovirus serotypes. Northway virus (family Bunyaviridae) was isolated from a variety of species of *Aedes* and *Culiseta* mosquitoes and from tundra redback voles (*Clethrionomys rutilus*) (Calisher et al., 1974). Ritter and Feltz (1974) reported the occurrence of snowshoe hare virus (family Bunyaviridae) in snowshoe hares (*Lepus americanus*), varying lemmings (*Dicrostonyx rubricatus*), tundra redback voles, *Aedes* sp. mosquitoes, and blackflies (*Simulium* sp.). Other virus isolations include Silverwater virus (family Bunyaviridae) from hare ticks (*Haemaphysalis leporis-palustris*), and Great Island virus (family Reoviridae) and a virus of the Sakhalin serogroup (family Bunyaviridae) from bird ticks (*Ixodes signatus*) collected from the nests of common murres (*Uria aalge*) (Ritter et al., 1978). New Minto virus (family Rhabdoviridae) was recovered from hare ticks (*H. leporis-palustris*) (Ritter and Feltz, 1974), Jamestown Canyon virus (family Bunyaviridae) was isolated from mosquitoes of the *Aedes punctor* complex, and Klamath virus (family Rhabdoviridae) was isolated from tissues of both a tundra vole (*Microtus oeconomus*) and a tundra redback vole (Ritter and Calisher, unpubl. data).

Finding such a variety of viruses in mosquitoes, ticks, biting flies and small mammals prompted us to attempt a determination of the prevalence of antibodies to these viruses in humans and wildlife populations in Alaska in order to assess their potential significance. Results of a limited serologic survey for antibody to these viruses are reported in this paper, with discussion of the possible significance of the results.

MATERIALS AND METHODS

Serum collections: Blood samples from free-ranging arctic fox, moose, caribou, grizzly bear, and Dall sheep were collected during population studies (Fig. 1). Bison (*Bison bison*) samples were from animals harvested by hunters. Snowshoe hares, redback voles, red squirrels (*Tamiasciurus hudsonicus*), and common ravens (*Corvus corax*) were collected by live-trapping or shooting for the present study. Human sera were from Eskimo reindeer herders resident on Alaska's west coast. Moose sera were collected during 1968, bear sera from 1973–1978, bison sera from 1975–1979, caribou sera during 1978, and all others during 1979. Sera were separated from clots by aspiration and stored at −20 C or colder until tested.

Serologic tests: In a preliminary survey for antibody to NOR virus, sera from moose, caribou, bison, Dall sheep, and grizzly bear were tested by a constant virus-serum dilution neutralization test (Pantuwatana et al., 1972). Serum antibody titers of 1:16 or greater were considered indicative of past infection with the virus. All subsequent tests for antibody were performed by a serum dilution–plaque reduction neutralization (Lindsey et al., 1976). Sera causing 90% or greater plaque reduction were considered indicative of past infection and will hereafter be referred to as positive. Human sera were tested as above

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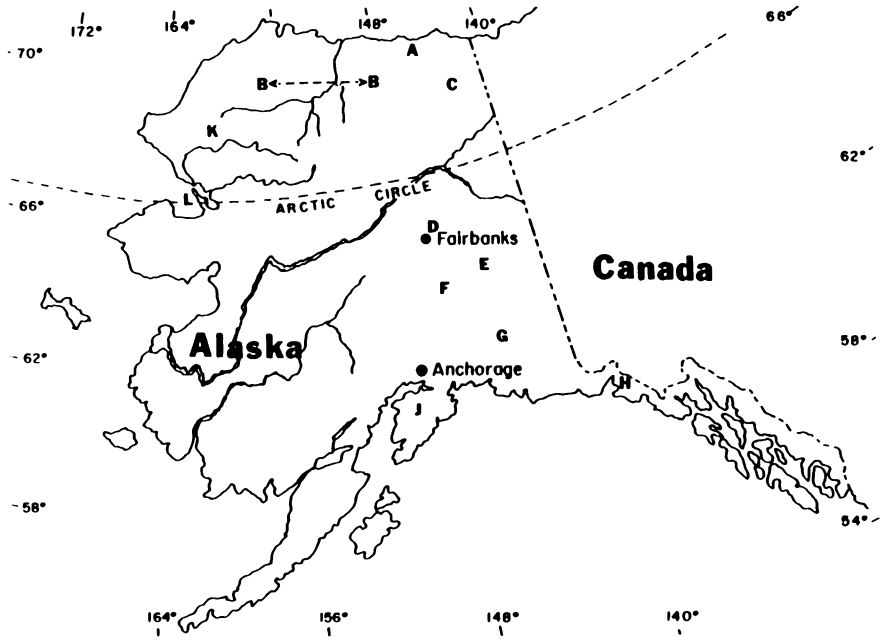

FIGURE 1. Locations at which blood samples were collected in Alaska. A. Arctic fox (n = 33). B. Grizzly bear (n = 64). C. Dall sheep (n = 7). D. Snowshoe hare (n = 68), red squirrel (n = 4), redback vole (n = 8), common raven (n = 15). E. Bison (n = 87). F. Dall sheep (n = 77). G. Bison (n = 10). H. Moose (n = 3). J. Moose (n = 24). K. Caribou (n = 69). L. Human (n = 121).

except that fresh human serum was used to dilute virus in order to enhance neutralization (Chappell et al., 1971).

Viruses: Viruses were obtained from the reference collection of the Vector-Borne Diseases Division, Centers for Disease Control, Ft. Collins, Colorado 80522, USA. The following viruses were used in these tests: Jamestown Canyon (JC) (61V-2235), snowshoe hare (SSH) (Burgdorfer), Northway (NOR) (0234), Klamath (KLA) (M-1056), Sakhalin (SAK) (LEIV-71C), Great Island (GI) (CanAr 41), and Silverwater (SIL) (131).

RESULTS

Results of preliminary tests with NOR virus are presented in Table 1. These results provided impetus for subsequent testing for antibodies to NOR virus and other arboviruses, the results of which are presented in Table 2. Humans, bison, snowshoe hares, and Dall sheep had the highest antibody prevalences for several viruses. None of the sera tested had antibody to SIL virus and sera from redback voles, red squirrels, and common ravens had no antibody to any of the viruses tested. Three arctic foxes had antibody, one each to JC, NOR, and SAK viruses.

TABLE 1. Prevalence of antibodies to Northway virus in sera of five species of wild mammals in Alaska.

Host	No. examined	Prevalence*
Bison	78	85
Caribou	69	43
Grizzly bear	64	48
Dall sheep	44	50
Moose	27	78

* Prevalence = Number positive/number tested (percent).

DISCUSSION

JC and SSH viruses are antigenically related members of the California serogroup. Various wildlife species serve as vertebrate hosts for these viruses, as determined by virus isolation (Hoff et al., 1969; Issel, 1973; Ritter et al., 1978) and/or serological surveys (Hoff et al., 1969; Feltz et al., 1972; Issel et al., 1972; Issel, 1973; Leduc, 1979; Zarnke and Yuill, 1981). The principal vectors for both viruses appear to be species of *Aedes* mosquitoes (Sudia et al., 1971) which are found in great abundance on the tundra and elsewhere, albeit for relatively brief periods during the year. Both SSH and JC viruses have

TABLE 2. Results of serum dilution–plaque reduction neutralization tests for six arboviruses in Alaska.

Species	No tested	Number with antibody to indicated virus (% prevalence)					
		JC[a]	SSH	NOR	KLA	SAK	GI
Human	121	65 (54)	51 (42)	17 (14)	6 (5)	0	0
Bison	97	86 (89)	86 (89)	91 (94)	4 (4)	2 (2)	1 (1)
Dall sheep	84	43 (51)	34 (41)	61 (84)	0[b]	0[b]	0[b]
Snowshoe hare	68	29 (43)	44 (65)	2 (3)	0	0	0
Arctic fox	33	1 (3)	0	1 (3)	0	1 (3)	0
Raven	15	0	0	0	0	0	0
Redback vole	8	0	0	0	0	0	0
Red squirrel	4	0	0	0	0	0	0

[a] JC = Jamestown Canyon; SSH = snowshoe hare; NOR = Northway; KLA = Klamath; SAK = Sakhalin; GI = Great Island
[b] Six tested

been implicated as causes of human encephalitis (Fauvel et al., 1980; Grimstad et al., 1982).

In North America, antibody to viruses of the California serogroup has been found in humans (Thompson and Evans, 1965; Sudia et al., 1971), snowshoe hares (Zarnke and Yuill, 1981; Grimstad et al., 1982), bighorn sheep (*Ovis canadensis*) (Trainer and Hanson, 1969; Zarnke and Yuill, 1981), white-tailed deer (*Odocoileus virginianus*) (Issel et al., 1972), eastern chipmunks (*Tamias striatus*) (Gauld et al., 1974), eastern gray squirrels (*Sciurus carolinensis*), eastern fox squirrels (*Sciurus niger*), eastern cottontails (*Sylvilagus floridanus*), southern flying squirrels (*Glaucomys volans*) (Moulton and Thompson, 1971), white-footed deer mice (*Peromyscus* spp.) (Srihongse et al., 1980; Calisher, unpubl. data), arctic ground squirrels (*Citellus undulatus*) (McLean et al., 1974), golden mantled ground squirrels (*Citellus lateralis*) (Newhouse et al., 1971), and hispid cotton rats (*Sigmodon hispidus*) (Calisher, unpubl. data). In the present study, high prevalences of antibody to JC and SSH viruses were comparable to those reported in earlier investigations. This is the first report, however, of antibody to California serogroup viruses in bison and arctic foxes. The red fox (*Vulpes fulva*) is apparently involved in the natural epizootiology of LaCrosse virus (Amundson and Yuill, 1981), which is another member of the California serogroup. The arctic fox may fill a comparable econiche for JC virus in the arctic.

The high prevalence of antibody to JC and SSH viruses in bison and Dall sheep suggests that these species may play an important role in the brief summer amplification of these viruses. Alternatively, they may be dead-end hosts for JC and SSH viruses but particularly attractive to mosquitoes which transmit them. One should not ignore the possibility that this was actually cross-reacting antibody which had been produced following infection by another California serogroup virus. Experimental studies of the duration and magnitude of viremia and virulence of JC, SSH, and NOR for bison and Dall sheep are warranted if we are to evaluate the roles that these mammals play in the epizootiology of these three viruses.

Since JC and SSH viruses are antigenically related to each other, the neutralizing antibody detected in these tests does not assist in making a clear assessment of the etiologic agent causing antibody production. Antibody could be a result of infection by JC, SSH, or both viruses. In fact, of 86 bison with antibody to JC virus, 17 had monotypic antibody to JC virus and 69 had antibody to both JC and SSH viruses. Alternatively, of 86 bison with antibody to SSH virus, 17 had monotypic antibody to SSH virus and 69 had antibody to both. The results with Dall sheep sera were not much different. Of 84 specimens, 21 had monotypic antibody to JC virus, 12 had monotypic antibody to SSH virus, and 22 had antibody to both. It is clear, however, that the high prevalences and broad range of species with antibody to California serogroup viruses reflect an abundance of vectors, intense virus transmission and a wide spectrum of vertebrate host species on which the arthropod vectors feed. These may be the most significant clues to the puzzle posed by obvious arbovirus maintenance in a brief amplification season. Higher antibody prevalence to SSH virus than to JC virus in hares (Table 2) was not in itself remarkable.

Antibody to California serogroup viruses in humans reflects both presence of the virus(es)

and exposure to the vector species. No clinically identified disease has been definitely attributed to JC or SSH virus in Alaskan residents.

NOR virus was first isolated from mosquitoes collected near Northway, Alaska and from sentinel rabbits located near Fairbanks (Calisher et al., 1974). Subsequent isolations have been from mosquitoes and tundra redback voles from Alaska's Interior (Ritter et al., 1978) and also mosquitoes from Northwest Territories, Canada (McLean et al., 1977). Serologic evidence for NOR virus infections in humans and five species of wild mammals in Alberta has been reported (Zarnke and Yuill, 1981). NOR virus belongs to the Bunyamwera serogroup. Members of this group have been isolated from equines and caribou and are known to cause fatal diseases in equines (Hoff et al., 1970; Hoff et al., 1971; Moulton and Thompson, 1971; Berge, 1975).

In this study, prevalences of antibody to NOR virus in humans and snowshoe hares are comparable to those reported previously (Zarnke and Yuill, 1981). The prevalences in large mammal species (Tables 1, 2) are remarkable and may reflect their attractiveness to species of *Aedes* and *Culiseta* mosquitoes, the presumed principal vectors of NOR virus. Discrepancies between prevalences for bison and Dall sheep as presented in Tables 1 and 2 may be attributed to different methods and personnel involved in the two surveys. Since the type of serologic survey reported here provides cumulative rather than point prevalence, longer lived mammals (i.e., human, bison, and Dall sheep) may inordinately influence the results.

KLA virus was first isolated from tissues of a mountain vole (*Microtus montanus*) in Oregon (Berge, 1975). It has also been isolated from two species of voles (*Clethrionomys rutilus* and *Microtus oeconomus*). However, little is known of the epizootiology of this virus in Alaska. The low antibody prevalences to KLA virus determined in the present study do not provide sufficient data to draw useful conclusions. Nevertheless, the absence of antibody in five species of wild mammals, some of which had high prevalences of antibodies to bunyaviruses, suggests that this may be a virus not associated with an arthropod vector.

SIL virus is an apparently nonpathogenic virus of snowshoe hares which is transmitted by ticks (Hoff et al., 1971; Ritter et al., 1978). The absence of antibody to this virus in snowshoe hares in the present study is somewhat surprising, since the virus was previously reported from Alaska (Ritter et al., 1978). Most previous serologic surveys of hares have found evidence of infection with this virus, albeit at varying prevalences (Hoff et al., 1969; Zarnke and Yuill, 1981). One study reported a low prevalence of antibody to SIL virus as the hare population neared the peak of its 10-yr population cycle (Hoff et al., 1969). Since the hares in the present study were from a population in a near-peak stage of its cycle, a parallel, although unexplained, situation might have been taking place.

In summary, this study has shown that humans and wild mammals in Alaska have been exposed to a number of arboviruses known to occur there and that high prevalences of antibody occur in certain species. Further, the known natural host range of JC, SSH, NOR, and KLA have been extended by inference from antibody determinations in a variety of wild animals.

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