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Survey of fox trappers in northern Alaska for rabies antibody

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SUMMARY

The purpose of this research was to determine whether trappers in northern Alaska acquired immunity to rabies virus from non-bite exposures while trapping and skinning arctic foxes (*Alopex lagopus*). In coastal Alaska recurring epizootics presumably provide trappers ample opportunity for contact with rabid animals. Serum neutralization analyses of blood samples collected from 26 individuals were conducted. All but three had negative rabies neutralizing antibody levels (< 0·05 I.U./ml). Two of these had previously received rabies vaccine but one individual who had trapped for about 47 years with an estimated harvest of over 3000 foxes and who had never received pre- or post-exposure rabies vaccination had a rabies serum neutralizing antibody concentration of 2·30 I.U./ml. This represents the first report of an unvaccinated person acquiring rabies virus antibody with a titre above the 0·5 I.U./ml level considered acceptable by the World Health Organization.

Clinical rabies affects the central nervous system and, in humans, is nearly 100% fatal. Very few cases of human rabies have been reported in the Arctic: none in Canada [1]; one in Greenland since 1960 [2]; and only three in Alaska, the last in 1943 [3]. A Russian report of 30–50 rabies deaths per year [2] is believed to include all deaths nationwide from arctic and other strains of the rabies virus. One possible explanation for these observations is that because fox rabies occurs principally during the winter, people are protected from bites by heavy clothing. Even if a person's skin is punctured, much of a fox's saliva would be wiped from the animal's teeth as they penetrate the clothing. However, Alaska natives have lived for many generations by trapping, hunting and skinning animals and have multiple opportunities for exposure to rabid foxes, both arctic and red (*Vulpes vulpes*).

The traditional method of skinning, placing a bare hand in an animal's mouth or using one's mouth to grasp the carcass or hide, is still used. If exposures such as these result in acquired immunity to rabies, this could be part of the reason that human rabies is rare in the Arctic.

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Skinning and other handling of rabid animals has caused human rabies deaths [4–6], but this has not been reported from the Arctic. The rabies virus found in arctic populations of foxes differs from other rabies strains [7] although it shares some features with the virus present in southeastern Canada and northeastern US [8]. If the arctic strain has reduced human virulence, it may maintain sufficient antigenicity to elicit an immune response following a minor exposure. A study of Florida raccoon (*Procyon lotor*) hunters reported levels of rabies neutralizing antibody up to 0·11 I.U./ml [9]. A recent study in northern Canada [1] found rabies antibodies in the serum of Eskimo (Inuit) hunters and trappers at levels up to 0·09 I.U./ml. The low levels reported in these studies may have resulted from cross-reactions rather than from the presence of rabies antibody. A study in Nigeria to screen for rabies virus complement-fixing (CF) antibodies, which included 72 human subjects, reported that 2 had titres $\geqslant 64$ [10]. Although CF test results are virtually impossible to compare with serum neutralization test results, this study suggests that persons may develop some level of antibody to rabies virus. Cross-reaction with other antibodies is also possible [10, 11].

In consultation with staff of the North Slope Borough Departments of Wildlife Management and Health and Social Services in Barrow, Alaska, a list of 57 current or former fox trappers was compiled. Forty-two of these were contacted (all by E.F. and some by M.B.), and 27 agreed to participate. Each participant, after signing a consent form, had a 5 ml blood sample collected. One sample was damaged by the laboratory, leaving 26 for analysis. Blood samples were analysed for rabies antibody using the Rapid Fluorescent Focus Inhibition Test (RFFIT) at the Veterinary Medical Center at Kansas State University (Manhattan, KS, USA). All results were confirmed by RFFIT at a second laboratory (Serologicals, Inc., Clarkston, GA, USA) using similar methodology.

Twenty participants were Alaska Native, six were non-Native; the mean age was 48·4 years (range 26–77 years). All but three subjects had trapped and skinned foxes; these three, as well as two others, were known to have received either pre- or post-exposure rabies prophylaxis (Table 1). All but three subjects (subjects 4, 6 and 24; Table 1) had a rabies neutralizing antibody level of $< 0{\cdot}05$ I.U./ml (i.e., not detectable) and less than the World Health Organization standard of 0·5 I.U./ml for an acceptable response to rabies vaccination [12]. Subjects 4 and 6 had received post-exposure prophylaxis with duck embryo vaccine (DEV) and human diploid cell vaccine (HDCV), respectively (Table 1).

The third person with detectable rabies antibodies was a 68-year-old Native male with a rabies neutralizing antibody level of 2·30 I.U./ml (Subject 24; Table 1). This subject had trapped for about 47 years and estimated that he had trapped and skinned over 3000 foxes. He never wore gloves or other protection while skinning. His medical records at the U.S. Public Health Service Native Hospital and the health clinic in Barrow and at the Alaska Native Medical Center in Anchorage confirmed that he had not received pre- or post-exposure rabies prophylaxis. He could not recall ever being bitten by a fox.

Subjects 2, 11 and 16 were vaccinated but had no detectable rabies neutralizing antibody levels (i.e. $< 0{\cdot}05$ I.U./ml) (Table 1). Subjects 11 and 16 had received three pre-exposure doses of DEV 13 years previously while subject 2 received post-exposure prophylaxis 32 years earlier with an unknown vaccine.

Table 1. *Selected characteristics of subjects who had detectable antibodies, or had previously received rabies vaccine, Barrow, Alaska, U.S.A., 1991*

ID	Age	Sex	Race	Years trapped	Numbers of foxes trapped	Vaccine type*	Vaccine administration	Year given	Titre† (I.U./ml)	Comments
2	42	M	Native	None	None	?	Post-exposure	*c*. 1959	< 0·05	Treated after dog bite
4	39	F	Non-Native	None	None	DEV	Post-exposure	1976–77	1·80	Contact with rabid fox
6	43	M	Native	1977–86	> 100	HDCV	Post-exposure	1984–85	2·30	Bitten by red fox
11	39	M	Non-Native	1979–90	25	DEV	Pre-exposure	1978	< 0·05	Job requirement
16	41	M	Native	None	None	DEV	Pre-exposure	1978	< 0·05	Job requirement
24	68	M	Native	1944–90	> 3000	None	—	—	2·30	No vaccine administered

* DEV, Duck embryo vaccine; HDCV, Human diploid cell vaccine.
† < 0·05, Not detectable.

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We identified one subject with a high rabies antibody level who had no history of receiving rabies vaccine, either for pre- or post-exposure prophylaxis. The rabies neutralizing antibody level was 2·30 I.U./ml and it is unlikely to be due to a cross-reaction. Both laboratories we used have considerable experience with RFFIT for rabies antibodies and neither experienced any problems with serum toxicity or other complications which could cause false positive results. It is reassuring that the laboratories independently identified the same three individuals as having rabies antibodies present.

Given the length of time subject 24 trapped, the regular rabies epizootics in arctic Alaska, and the numbers of foxes he handled, it is likely that he encountered rabid foxes. Because of the episodic occurrence of fox rabies and the variable persistence of antibodies following vaccination that we found in our subjects, we cannot determine when exposure might have taken place.

Our results suggest that acquired immunity may partly explain the rarity of human rabies in the Arctic. Perhaps the arctic strain of rabies virus has less virulence for people than for wild animals yet retains sufficient immunogenicity to elicit an immune response in humans following a relatively minor exposure. In a case of human rabies following a bat bite, a possible lower virulence for humans was suggested as a reason for the person's survival [13].

This is the first report of probable exposure to wild rabies virus leading to a rabies neutralizing antibody titre above that considered acceptable by WHO [12]. Although the number of individuals we tested was relatively small, we included subjects with a good deal of diversity. Age varied considerably as did the number of years that individuals trapped or skinned, the number of foxes they had processed and how recently they were involved with these activities. We believe our findings warrant further study in a larger group of persons living in the Arctic.

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