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**The Occurrence of *Echinococcus multilocularis*
Leuckart, 1863, in Japan**

ROBERT RAUSCH* AND JIRO YAMASHITA**

Since 1937, when alveolar hydatid disease was first recognized on the Japanese island of Rebun, 25 cases have been investigated clinically. About one per cent of the population of the island is believed to be infected (Yamashita *et al.*, 1955). Five cases also have been reported from other islands, some of these involving emigrants from Rebun (Inukai *et al.*, 1955; Yamashita, 1956).

The causative organism of this disease on Rebun has been termed *Echinococcus granulosus* (Batsch, 1786) by the Japanese workers. However, after a study of the cestode involved and a consideration of its ecology, the writers have concluded that the etiologic agent undoubtedly is *E. multilocularis* Leuckart, 1863. Evidence for this conclusion and a discussion of the problem are presented in this paper.

THE ADULT CESTODE. Few specimens of *Echinococcus* have been procured from carnivorous mammals on Rebun. Only two adult cestodes, from a dog, have been preserved. The terminal segments of these strobilae contained immature eggs. In this limited material, however, characters of diagnostic value were discernible. These cestodes have been compared by the writers with specimens of *E. multilocularis* from naturally and experimentally infected canine animals from Alaska and South Germany. The latter, provided by Dr. Hans Vogel, Institut für Schiffs- und Tropenkrankheiten, Hamburg, were reared in dogs fed larval cestodes of human origin.

The cestodes from Rebun measured 2.0 and 2.7 mm. in length. Each had three segments. The genital pore, in the mature and gravid segments, was in a relatively anterior position. The uterus was well developed in the terminal segment of each cestode, and was clearly of sacculate form. The number and distribution of the testes could not be determined.

Vogel (1955) and Rausch (1956) observed that position of the genital pore provides a reliable character for differentiating *E. multilocularis* from *E. granulosus*. The combination of characters seen in the cestodes from Rebun (genital pore in anterior position, sacculate uterus, and small size of strobila) is compatible only with *E. multilocularis*.

THE LARVAL CESTODE. Of 25 cases of alveolar hydatid disease confirmed from Rebun, 15 have terminated fatally. The alveolar structure of the larval cestode has been determined histopathologically by Japanese workers in 16 cases following surgery or autopsy (Ambo *et al.*, 1956).

For our use, Professor H. Ambo, Faculty of Medicine, Hokkaido University, kindly provided two blocks of tissue taken at the autopsy of a male patient whose death was caused by alveolar hydatid disease. The patient had lived on Rebun to the age of 16 years, and had then moved to Hokkaido. Death occurred at the age of 21 years. One of the blocks contained large numbers of larval vesicles. The second had been cut at the periphery of the zone of larval invasion, so that some uninvaded hepatic tissue was included.

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The latter was more useful, enabling comparisons to be made with sections of infected hepatic tissue from patients in South Germany and St. Lawrence Island, Alaska. The specimens from Germany were provided by Dr. Hans Vogel.

Sections stained with hematoxylin-eosin were prepared. Microscopically, the remaining hepatic tissue showed generalized cirrhosis. Hepatic cells regarded as normal were grouped mainly about the portal triads, but clusters of cells were scattered elsewhere. Degenerating hepatic cells, taking a strong eosinophilic stain, were abundant. The structural organization of the tissue had been disrupted to the extent that the hepatic lobules were no longer distinguishable. Hyperplasia of the bile ducts was not observed. Fibrous tissue was most dense in the vicinity of the larval vesicles. Here also were focal areas of leukocytic infiltration, involving lymphocytes and macrophages. Polymorphonuclear leukocytes were not numerous, and few giant cells were seen.

The area of tissue containing the larval vesicles had the aveolar appearance such as is seen in typical *E. multilocularis* infections in man (Fig. 1). The cysts were varied in size and shape, generally in close apposition. The growth of isolated, small vesicles well away from the more severely affected areas indicated an active invasion of the adjacent hepatic tissue, and the dense fibrous tissue surrounding the vesicles suggested an infection of long duration. Islets of hepatic cells "entrapped" among the cysts were undergoing degeneration. The subgerminal (laminated) membrane varied greatly in form, and in some areas its proliferation had given rise to very thick-walled alveoli lacking the germinal layer. This latter layer was usually well developed and cellular. A few scattered scolices were observed.

These sections were identical with those from patients from Germany and Alaska in important details. Expected differences in the degree and extent of the tissue reaction were noted, but the structure and characteristics of the larval vesicles corresponded exactly, and all demonstrated the extreme degree of proliferation of the subgerminal layer which appears to be peculiar to the growth of the larval *E. multilocularis* in man. Workers in Europe have had the impression that this larval cestode perhaps rarely produces scolices in man; however, scolices may occur much more frequently than realized, since they may be so few as to be overlooked unless many sections are examined. Scolices were also present in one of the sections from a patient from Germany.

The investigations on Rebun have so far not disclosed the larval cestode in mammals other than man. However, Ishino (1941) collected an infected vole, *Microtus oeconomus* Pallas, in 1935 on the island of Simushir, in the Middle Kuriles. A photograph of this vole, which is preserved in the collections of the Laboratory of Parasitology, Hokkaido University, was published by Yamashita (1956). For reasons brought out below, the finding of this animal is significant, and a brief description of it is presented below.

In this vole the liver, the primary locus of infection, was almost totally involved and macroscopically was identical with *E. multilocularis* infections seen in the same species of vole on St. Lawrence Island, Alaska. The liver contained many small vesicles, in all of which there were many scolices and great numbers of calcareous corpuscles. There was little evidence of a severe tissue reaction, and hepatic cells were lacking in the totally involved areas. The sections did not differ in any recognizable way from sections of *E. multilocularis* larvae in naturally infected voles from St. Lawrence Island.

DISCUSSION

Rebun lies about 30 miles west of the northern tip of Hokkaido Island, Japan. It is a mountainous island, with an area of about 80 square kilometers. Most of its population of about 10,000 people live in coastal villages, and gain their livelihood through fishing.

The indigenous mammals* are: two species of shrews, *Sorex unguiculatus* Dobson and *S. minutus* Linnaeus; a red-backed vole, *Clethrionomys rufocanus smithii* Thomas; and a chipmunk, *Tamias sibiricus lineatus* Siebold. Also present are rats, *Rattus rattus* Linnaeus and *R. norvegicus* Berkenhout, but the house mouse, *Mus musculus* Linnaeus, has not been introduced. A red fox, *Vulpes vulpes japonica* Gray, became established after its introduction from the Middle Kuriles in the period 1924-26 (Inukai *et al.*, 1955). The Japanese mink, *Mustela sibirica itatsi* Temminck, was introduced in 1940-44 from the island of Hokkaido.

Few domesticated animals, other than dogs, are kept on the island. In 1954, there were 20 horses, 13 swine, 3 cattle, 4 goats, and 28 sheep. In 1956, there were 8 horses, 20 swine, 3 cattle, 1 or 2 goats, and only 5 sheep, the most of the latter having been killed by dogs. Many dogs are kept as pets and are not restrained. In addition to these, about 100 feral dogs live in the more inaccessible parts of the island, but often enter the villages at night. The people also have house cats.

Of these mammals, it appears that only dogs, foxes, or cats could serve as the final host of *Echinococcus multilocularis* on Rebun. Ambo *et al.* (1954) autopsied 70 dogs on Rebun during 1953, but found none infected. In 1954, Yamashita and his co-workers made a survey of the parasites of dogs here. Of 154 autopsied, including 13 feral dogs, only two contained the adult cestodes. A higher proportion of feral animals might be infected, since they would be expected to eat any small mammals that they could capture. Dogs naturally infected with *E. multilocularis* have been found on St. Lawrence Island, Alaska, and are easily infected experimentally (Rausch and Schiller, 1956).

Foxes are much fewer in number than formerly, and none have been found infected. However, it is probable that *E. multilocularis* was introduced on Rebun through foxes brought from the Kurile Islands. The sequence of events leading to the introduction of the foxes has been reviewed by Inukai *et al.* (1955), but a brief recapitulation would seem appropriate here.

In 1916 the Russian government sent 10 arctic foxes, *Alopex lagopus* Linnaeus (also sometimes called "blue fox") to Ushishir Island, in the Kuriles, and a second lot of 20 animals was released there in 1917. The animals increased rapidly in numbers, and were soon distributed to other islands in the Kurile chain.

The foxes originated in the Komandorskii Islands, off the coast of Kamchatka. *E. multilocularis* is a common cestode on Bering Island, in the Komandorskii Islands, but it is not found on the nearby Mednyi Island (Barabash-Nikiforov, 1938; Afanas'ev, 1941). Since the previous absence of any microtine rodent or other amenable intermediate host precluded comple-

*For convenience, names of mammals are given here according to Ellerman and Morrison-Scott, *Checklist of Palaearctic and Indian Mammals*, Brit. Mus. (Nat. Hist.), London, 1951. Since Japanese mammalogists disagree with some of the opinions expressed by these workers, attention is called to Tokuda, *A Revised Monograph of the Japanese and Manchukorean Muridae*, Trans. Biograph. Soc. Japan, 4:1-127, 1941.

tion of its life cycle, the cestode was apparently introduced on Bering Island in about 1870, when a red-backed vole, *Clethrionomys rutilus* Pallas, was established there to provide food for the foxes (Rausch, 1952; Rausch and Schiller, 1956). We do not know if *E. multilocularis* existed in the Kuriles before introduction of the arctic foxes. Since the necessary host mammals already were present (vole and red fox), it is possible that the cestode was also there. The finding of the infected vole mentioned above confirms the presence of the cestode in the region in recent times.

Red foxes were brought from the Kuriles to Rebun Island during 1925-26, to establish a harvestable fur crop and to aid in the control of voles. The foxes multiplied rapidly, becoming abundant in the first years. After about 10 years, however, they were reduced in numbers by poaching, and possibly by disease and other factors. At the present time they are few. It appears certain that the cestode whose larva causes alveolar hydatid disease was introduced on Rebun through these foxes.

The house cat might be of importance in the epidemiology of alveolar hydatid disease on Rebun, but this has not been determined. Ambo *et al.* (1954) found one infected cat among 57 autopsied during 1953. Cats have been experimentally infected with *E. multilocularis* by Vogel (1955), and Rausch (unpublished data) infected voles with eggs obtained from experimentally infected cats. It is evident that *E. multilocularis* is capable of de-

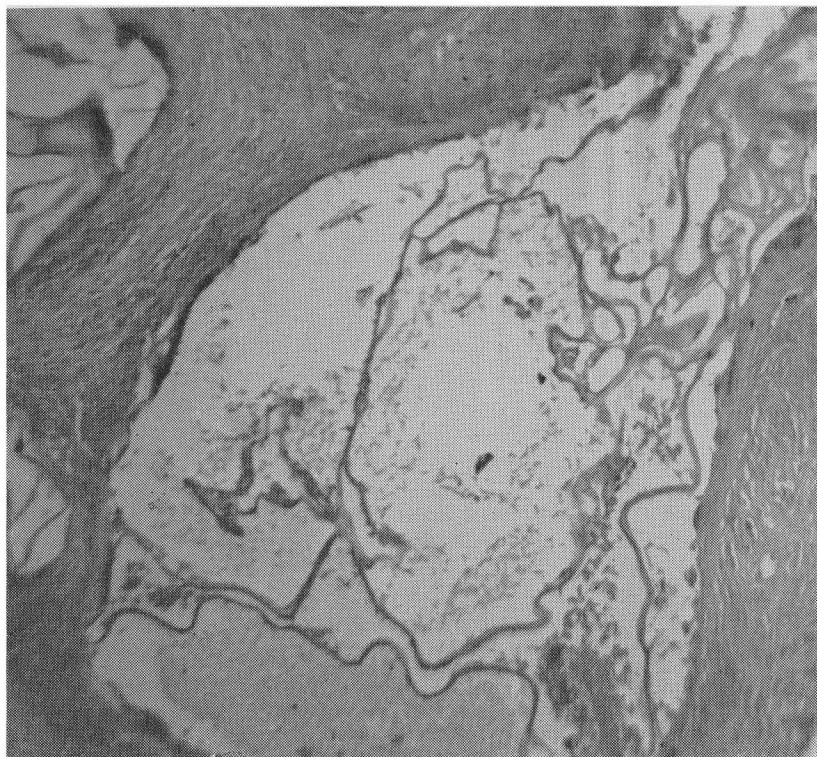


Figure 1. *Echinococcus multilocularis* infection of human liver (Rebun Island). 240 X.

velopment and production of eggs in cats, and the close association of these animals with man could have considerable epidemiological significance.

The red-backed vole is probably the intermediate host for *E. multilocularis* on Rebun. Although the species found here, *Clethrionomys rufocanus*, has not been infected experimentally, it is known that the related *C. rutilus* is an important intermediate host on Bering and St. Lawrence Islands. On Rebun, the red-backed vole is found in non-forested regions, particularly in grassy and marshy places. Here they would be especially susceptible to predation by cats.

The other small mammals on the island appear to have little or no importance. The shrews are probably susceptible to infection, as is *Sorex tundrensis* Merriam on St. Lawrence Island, but shrews are not often eaten by other mammals. Rats have been found resistant to experimental infection. We do not know if the chipmunk, a sciurid, can serve as a host to this cestode. Experimental work in Alaska suggests that sciurids are not suitable hosts (Rausch and Schiller, 1956).

In our opinion, the larger domesticated animals are not involved in the life cycle of *E. multilocularis*. They apparently are not susceptible to infection, or at best larval growth in them is not normal (Rausch and Schiller, 1956). On Rebun, the few animals examined by Yamashita have been negative. Most of the animals to be slaughtered are sent to the abattoir at Wakkanai City, on Hokkaido, and no infected animal has been observed here.

The Japanese workers maintain that human infections originate from eggs transmitted through water (Yamashita, 1956). Although the eggs of *Echinococcus* have not been identified in water tanks placed along the small streams, Ambo *et al.* (1954) recovered eggs of other species of helminths from them. It is believed that such waters might be contaminated by the feces of dogs.

The danger exists that *E. multilocularis* might also become established on Hokkaido and other islands if infected dogs are introduced from Rebun. Since it appears that potentially suitable intermediate hosts are widely distributed in the Japanese islands, the movement of dogs from Rebun should be carefully controlled. Because of the differences in ecological and faunal relationships in the three regions where *E. multilocularis* is presently being studied (Japan, Alaska, South Germany), the comparative epidemiology of this cestode should prove to be of unusual interest.

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