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STUDIES ON ECHINOCOCCOSIS

II. ECHINOCOCCOSIS IN JAPAN

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Though the hydatid cysts of this parasite have been found sporadically among domestic animals and human beings, in Japan until recently there has for many years been no adequate explanation of their occurrence. The question of autochthonous human hydatid infections in this country has been brought into sharp focus since the pathologists and surgeons of the Hokkaido University have discovered that hydatid infections show up with relatively high frequency among the residents of Rebun Island. This is a small island about 30 miles off the northwest coast of the Hokkaido main island, with an area of 80 km² and 10,000 inhabitants. At the request of the Hokkaido Health Department the first survey of the island was planned in the summer of 1948. Since that time more than 10 surveys of the infection have been carried out among the native residents of that island for the purpose of finding a method of control if possible. Recently, on the other hand, all the members of the author's laboratory having cooperated in a survey of the hydatid cyst infections of this parasite have carried out the experimental studies.

Here the author proposes to present an epidemiologic outline of this disease in Japan using both the results of his investigations and the reports of other investigators.

Animal Cases of Hydatid Cyst Infections

The occurrence of hydatid cyst infection of domestic animals has been thought to be rare in Japan and the infection, of any, has been usually considered to be of foreign origin. Nevertheless, some cases of infection have been recorded that could not be attributed to a source outside of this country yet there seemed no adequate explanation for their occurrence.

JANSON (1893) stated that there were some cases of echinococcosis of cattle which might have been brought into Kyushu from China. According to the late KOIZUMI, 0.5% of the cattle, 0.5% of the horses and less than 0.5% of the pigs in Tokyo have harboured the hydatid cysts. EGUCHI and IWATA (1949), in their

text book, stated that 5% of the cattle in Matsuyama district were found by TANIGUCHI to be infected with the hydatid cyst.

The hydatid cyst infection of domestic animals has been found sporadically at the slaughter houses in various districts of our country; some of them are preserved in this laboratory. However, there has been established no evidence of the source of the infection of these animals.

Recently the unilocular hydatid cyst infection in the lung of a sheep, a Corriedale ram, raised in Yuni district in the neighbourhood of Sapporo, has been found by the author and his co-workers (Fig. 1) and another case of infection has been reported in Horokura from a sheep imported from Australia in 1954 (Fig. 3).

It is known with certainty that in the Kuril Islands the foxes which had been presented by the Russian Government were infested with the adult tapeworm of this parasite. ISHINO (1941) discovered hydatid cyst infections in the lung and liver from 2 blue foxes collected in Simushir Island of the Middle Kurils in 1935, and he added that the fox is also an intermediate host of this parasite. It is interesting that at the same time he collected a vole which had been infested with the hydatid cyst. His specimen of the vole, *Microtus oeconomus* PALLAS, is now reserved in this laboratory (PLATE II). In this case the hydatid cyst has characteristic alveolar structure, demonstrating an aggregation of small cysts including many scolices.

Dog and Cat Infections with *Echinococcus granulosus*

As is generally known the adult tapeworm harbours in the small intestines of mammals covering 11 species including dog, fox, wolf, etc., and the eggs delivered are evacuated in the faeces of the host animals. The egg upon being swallowed by the intermediate hosts as a contamination passes into the small intestine and the embryo emerges to penetrate the intestinal wall until it reaches the circulatory system. This has been ascertained in 45 species including cattle, sheep, horse, pig, man, etc. The embryos grow slowly and in due course develop into a hydatid in the liver, lung or other organs.

In Japan, no adult worm infection of this parasite had ever been found in the animal until recently. Since the discovery of the disease in Hirosaki and in Rebun Island, a close relationship between the incidence in man and dog has established. A report of a woman contracting this disease in Oura Village near Hirosaki City, Aomori Prefecture was published by SATO and KITABATAKE in 1954. A number of dogs were collected with the purpose of autopsy examination for the presence of *Echinococcus granulosus*, the adult worm of the hydatid cyst, in order to discover a possible source of the human infection in this village. One specimen of this tapeworm was found from 1 of dogs kept by the patient. It

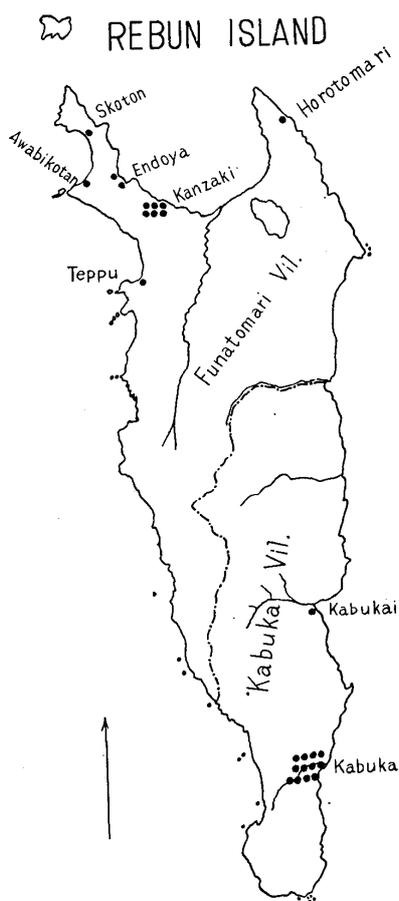
has thus become clear that there is a relationship of the infection in the case of this woman and the dog.

AMPO et al. (1954) have revealed that in Rebun Island the cat is a host animal of this parasite. Out of 57 cats collected in the island they recovered an adult worm from a cat raised by a fisherman. In 1954 the author and his co-workers made a careful survey of the host animals in that island and discovered that the dog is also a host animal of the parasite. Among 154 autopsied which included 13 stray dogs, 2, that is 1.3% of the total, were proved positive for *Echinococcus* tapeworm.

Human Cases of Hydatid Cyst Infections

Up to the present, in Japan, about 70 human cases of the hydatid cyst infection have been found from different prefectures: Kumamoto, Oita, Nagasaki, Fukuoka,

MAP 1. Sketch Map Showing the Distribution of 25 Patients of *Echinococcus* in Rebun Island



Miyazaki, Yamaguchi, Osaka, Hyogo, Aichi, Ehime, Gifu, Toyama, Kanagawa, Niigata (Niigata City and Naoetsu City), Miyagi (Sendai City), Aomori (Hirosaki City) and Hokkaido (Rebun Island). Of these cases 2 in Sendai, 1 in Niigata, 1 in Naoetsu, 1 in Hirosaki and 25 on Rebun Island were of the type of multilocular or alveolar hydatid cyst, while the others were unilocular hydatid cyst. Moreover, some patients found in the Hokkaido main island are known to have formerly lived in the Kuril Islands or on Rebun Island. The hydatid cysts of these patients also belonged to the multilocular or alveolar type.

In December of last year, the present author received a letter from Professor M. NAGAHANA, Tottori University, informing the occurrence of 1 patient of unilocular echinococcosis in Yonago City; the author had also a chance of observing a lung and liver infected multilocular hydatid cyst obtained from a woman by Professor K. SHIMPO of the Sapporo Medical College. This patient had formerly been employed in the Kuril Islands during some months every year. Very recently the author has heard particulars of a case of echino-

coccosis of the liver of a man who had lived in the neighbourhood of a fox breeding farm in the Middle Kurils and was operated by a surgeon of the Sapporo Medical College. At the Meeting of the Japanese Parasitological Society on April 6, 1956 in Tokyo, H. UNO, E. KUBOTA and M. MIKAMI of Hirosaki University have reported cases of the alveolar hydatid diseases of a man and a woman found separately in Kuroishi and another place near Hirosaki City.

Of the patients found in Japan about 60% are men and about 40% are women. The highest percentage of infection is seen in the age group of the thirties and forties.

Relationship of Infection Between Animals and Human Beings in Echinococcosis in Japan

As above mentioned, up to the present there have been found about 70 cases of human echinococcosis in Japan. The relationship between animals and human beings in echinococcosis has been made clear by 2 surveys, of which 1 is the case of Oura Village near Hirosaki City, Aomori Pref. and the other is that of Rebun Island. SATO and KITABATAKE (1954) recovered an adult worm, *Echinococcus granulosus*, from 1 of 2 dogs raised by the patient of echinococcosis among 7 dogs surveyed in Oura Village. It thus became clear that there was a relationship regarding the infection between that woman patient and the dog.

Here the author wishes to report the results of epidemiological surveys which have been carried out for the past 7 years in Rebun Island by himself and other investigators. Twenty-five cases of the hydatid disease have been found in Rebun Island. The first patient of this disease was found in 1937. The settlement of the island was commenced in relatively old days, and the inhabitants have been there since 1786 engaging in fishing. At that time, if there had already occurred such a fatal disease, some facts would have been left in the written records or in the memory of the people. It is highly probable that this disease was not endemic in the island. The tapeworm might have been transmitted by some animals which were in close contact with man.

From the historical evidence the endemic animals are not responsible for the disease. Since the early settlement cattle, horse, pig, sheep, goat, cat and dog have been brought in mostly from Hokkaido main island as domestic animals. Cattle, horses, pigs, sheep and goats among these are very few in number and accordingly are out of the question.

Adult worms of the parasite have been obtained recently from 1 cat and 2 dogs in the island. There has been no evidence of any epidemic of the echinococcosis in the dog and cat in Hokkaido. Therefore, the above mentioned host animals might have been infected by other sources within the island possibly by

some wild animals which have been transferred from other places.

The wild mammals which are new to the island are Japanese mink and red fox according to record. The Japanese mink of the island was introduced from Hokkaido during 1940~1944 in order to control the voles and rats. The mink of the island could not be a transmitter of the tapeworm. This statement is based upon the fact that mink were transferred successfully to the nearby Rishiri Island from Hokkaido prior to the introduction in Rebun Island. However the disease has never been reported from Rishiri. Before the introduction of the Japanese mink, during the years from 1924 to 1926 12 pairs of red fox from the Middle Kurils were sent to the island and were released there. The red fox and blue fox have lived in close association in the islands of the Kuril Chain. The blue fox was not a native of the Kurils but was transferred from the Commander Islands off Kamchatka. The foxes feed mostly on wild mice in the islands.

In the year 1935 ISHINO discovered *Echinococcus* from the blue foxes in Simushir Island of the Kurils. At the same time he collected a vole which had been infected with the parasite, as noted above. BARABASH-NIKIFOROV (1938) proved that about 50% of the field mice in Bering Island of the Commander Islands are infested with an intermediate stage of *Taenia echinococcus*. AFANÁSEV (1941) has observed that *Evotomys rutilus* (= *Clethrionomys rutilus*) is the only intermediate host of *Echinococcus granulosus* (BATSCH) in the same island. It is highly probable that the infested blue foxes were transferred into the Middle Kurils and the parasite spread among the field mice upon which the native red foxes fed. It then infested the foxes. Indeed some patients among those discovered in Japan to be suffering from this disease originally lived in the Middle Kurils.

There remains some doubt that the red foxes which were sent from the Middle Kurils to Rebun Island were infested by *Echinococcus granulosus* and played a role in transmitting of the parasite to that island. By about 10 years after the original introduction from the Kurils, the red fox had increased greatly in Rebun Island. Since that time on account of the killing the decline in number of the foxes has become very apparent. In addition to this, dogs have increased in number in the island. They attack the foxes. The fox has bequeathed to the inhabitants of the island not a fur but a fatal disease. The symptoms of echinococcosis, in general, appear clearly about 10 years after the infection as seen in the fact that there have been approximately 10 years from about 1924 or 1926 and the appearance of the hydatid disease among inhabitants in 1937.

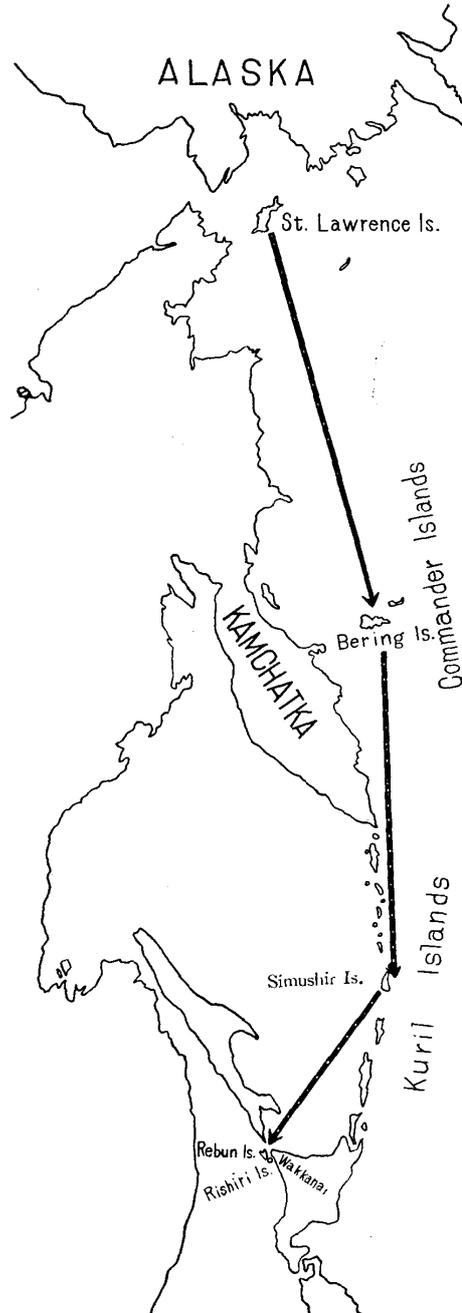
After that time, there is no doubt but that dogs and cats came to harbour this tapeworm by eating certain intermediate hosts infested with the hydatid cyst or by swallowing the eggs of this tapeworm of foxes. However, no inter-

mediate host of this tapeworm, excepting man, has yet been found in this island. The above mentioned BARABASH-NIKIFOROV (1938), ISHINO (1941) and RAUSCH and SCHILLER (1951) have already established that the wild mice had been naturally infected with hydatid cyst in Bering Island of the Commander Islands, in Simushir Island of the Middle Kurils and in St. Lawrence Island of Alaska respectively.

RAUSCH (1952) states "There is considerable evidence that the species of *Echinococcus* found in St. Lawrence Island is of Asiatic origin. This hypothesis is particularly tenable when one considers that the *Echinococcus* situation on Bering Island, in the Kommandorskii group, appears to be epizootiologically identical with that on St. Lawrence Island." Moreover, he says "Bering Sea currents unquestionably are such that mammals are transported on floating ice from Siberia to St. Lawrence Island." He has reported that the voles, *Microtus*, *Clethrionomys*, *Ondatra*, *Peromyscus*, have been successfully infected by using the St. Lawrence Island form.

Recently the author and his co-workers have proved that white mice come to harbour hydatid cyst in the lung and liver by taking the eggs in the faeces of the dog which had been infected artificially by giving the scolices of the sheep strain of Australia. From these facts, the possibility that mice and voles may play a part in sylvatic echinococcosis should be taken into consideration and appropriate studies must be made to investigate this matter also in Rebus Island or the other endemic areas. Perhaps

MAP 2. Sketch Map Showing the Most Probable Route of Infection of *Echinococcosis* of Rebus Island



echinococcosis in St. Lawrence Island, Bering Island, Simushir Island and Rebun Island are of Asiatic origin as suggested by RAUSCH. RAUSCH and SCHILLER (1954) reported the tapeworm of St. Lawrence strain as *Echinococcus sibiricensis* n. sp. The author's tapeworm collected from the dogs in Rebun Island was not a gravid form and the eggs were not completed, so the differences between his material and their tapeworm cannot be ascertained.

CONCLUSIONS

A main preventive measure of hydatid cyst infection consists in eliminating the dogs and wild Canidae which harbour adult tapeworm. The presence of the infected dogs which seed their environment with many eggs of *Echinococcus granulosus* leaves no doubt as to the source of hydatid disease in human beings and also in domestic animals in Japan. While the number of dogs does not have a direct bearing on the incidence of hydatid disease there is no doubt that a reduction in the dog population by destroying ownerless and useless ones would be of some value. Ownerless dogs must live as vagrants and would be the first to feed on viscera of dead animals. In Rebun Island, there are about 100 stray dogs. They conceal themselves in the mountain in the daytime and come out at night to the neighbourhood of the human homes or streets. The most important source of hydatid infection is surely the dog infested with *E. granulosus*. Effective control measures consist in 3 items, namely, (1) protecting dogs against acquiring infection, (2) eradicating infection already present in dogs, and (3) destroying the stray dogs and the wild foxes. No dogs should ever be allowed in abattoirs. Any control of this disease in native inhabitants and domestic animals will depend on the people who are aware of the danger of feeding uncooked domesticated herbivore's viscera to their dogs. On the other hand all cysts must be destroyed not only in abattoirs but on farms where private slaughtering is carried out. The greatest factor in prevention is efficient systems of meat inspection and of educating the public. Acceptance of these necessary measures of inspection and education is also in general the most important factor in a control program. The residents must be educated and informed in a simple yet effective manner; the best propagating measure is probably a visual one such as a cinema, or if this is not available, film strips. For such purposes lecture-meetings using film strips are nowadays being often held in Rebun.

Exterminating the infections in dogs at once using taeniocidal drugs should be considered. The simultaneous treatment must be given by the staff members of Health Centers or veterinarians in the same manner as rabies vaccine is being administered to all dogs. If this procedure proves practicable and effective, it may be advisable to treat all dogs annually.

The washing of the hands before eating would materially reduce the infection in human beings. Special attention in endemic areas should be paid to teaching habits of cleanliness to all. This precaution would reduce the infection during childhood which is the most susceptible period.

In general, it is well ascertained that water is not a common source of infection to man. Fecal contamination of food or of the hands from actual contact with dogs or other animals such as sheep which may collect dried dog's faeces on the skin is the most frequent source of the disease. However, in so far as Rebus Island is concerned, it is presumed that the human infection of this disease, as a special case, is mainly transmitted by water. In this island the natives use stream water for drinking and washing purposes without any treatment. There are small wooden tanks installed for storing the mountain streams in various places. Having examined the water of these tanks, AMBO, ICHIKAWA, IIDA and ABE (1954) found the eggs of the parasites, *Ascaris lumbricoides* and *Taenia taeniaeformis*. Although the egg of *Echinococcus granulosus* has not actually been found, the present author strongly suspects that the eggs of the tapeworm of dogs and cats, especially stray dogs in the mountain, might be introduced. Therefore, it is insisted that the building of adequate water-works by the local authorities is urgently required.

Recently SCHILLER (1954) reported that he had succeeded experimentally in making the infection of microtine rodents with hydatid cysts through transmission of *Echinococcus* eggs by the blowfly. Accordingly, the significance of flies as vectors of hydatid disease relating to human and domestic animal must be taken into consideration.

It being held by some investigators that in Rebus there may be a carnivore-rodent cycle in existence, in which the rodent replaces the herbivore as a host for the hydatid cyst, the extermination of the wild mice and rats was carried out on a large scale over the island last year. The capture of stray dogs is very difficult. They live in deep mountains in the day time and there still remain many of them.

What is the most important problem in respect to domestic animals lies (1) in the condemnation of edible offal and (2) in the proper diagnosis which is almost always made by post mortem despite the fact that the infection sometimes is so serious that the destruction of the liver tissue is sufficient to cause the death of the animals.

In human echinococcosis, X-ray and various serological tests are employed. The most frequent of these are complement fixation using hydatid fluid from sheep, horses or pigs as test antigen, precipitin reaction and intradermal reaction. Recently the complement fixation (using an alcohol extract of the diseased part

of the human liver including multilocular hydatid cysts) has been tried by ICHIKAWA and IIDA (1955) on the patients of Rebun proved echinococcosis by operation, and they say that this test obtained satisfactory results. MIKAMI, FURUKAWA and KATAYA (1951) have carried out the precipitin test using the serum and urine of the patient diagnosed echinococcosis clinically, but they have not obtained satisfactory results. Now the present author and co-workers are planning the study of the method of diagnosis on the hydatid disease in domestic animals.

Some reports have states that an antimony preparation was effective in human echinococcosis. Also in Japan, there are 2 cases where good results were obtained by using "Nesbosan". However, the actual treatment of the hydatid disease at present is purely surgical. In this regard, studies on the resection of a large part of the liver are carried out by MIKAMI and his co-workers.

Here the author would state his belief that the finding of some experimental small animals which are susceptible to the hydatid disease is a matter of first consideration for the purpose of discovering the most effective drug for this disease. So the infection of small animals, including white mice, white rats, Asiatic chipmunk (*Eutamias asiaticus*), voles, etc. is being studied by the author and co-workers. They are hoping to be able to provide many small animals which harbour the hydatid cyst, for the study of treatment of the hydatid disease.

With regard to the investigation of the disease itself, further information on hydatid infections in domestic herbivores and hydatid tapeworm infections in carnivores, especially dogs and foxes is much needed, especially in Japan. In Hokkaido the Committee on Echinococcosis of Rebun Island was established in 1954, and surveys of this disease have been carried out as noted above. Several investigators have participated including parasitologists, zoologists and members of the medical staffs of the Hokkaido University, Sapporo Medical College, Hokkaido Institute of Public Health and Hokkaido Health Department. The full reports of the results obtained by these many investigators are expected to be published in Japanese in one volume by the Hokkaido Health Department in the near future.

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EXPLANATION OF PLATES

PLATE I.

- Fig. 1. Hydatid cyst of the lung of Corriedale ram raised near Sapporo.
- Fig. 2. Showing the scolices within the alveolar hydatid cyst of a man who had lived in Rebun Island until the age of 16 years and died at 21 in Asahikawa, Hokkaido, in 1952. This case is the first one in which the scolices from hydatid cyst as related to Rebun Island were discovered by Professor H. AMBO, Faculty of Medicine, Hokkaido University, 1952.
- Fig. 3. Hydatid cyst of the liver of a sheep imported from Australia.
- Fig. 4. Hydatid cyst of a cattle lung found in the Shibaura Slaughter House of Tokyo.

PLATE II.

- Fig. 5. Alveolar hydatid cyst found in the liver of a vole, *Microtus oeconomus* PALLAS, collected 1935 in Simushir, Middle Kurils.
- Fig. 6. Alveolar type of hydatid cyst of the same vole, showing many scolices.
- Fig. 7. A portion of the same material, enlarged.

