600 SPECIAL ARTICLE: ECHINOCOCCOSIS

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SPECIAL ARTICLE

Epidemiology and Diagnosis of Echinococcosis in Canada

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Two species of Echinococcus occur in Canada: (1) *E. multilocularis* and (2) *E. granulosus*. *E. multilocularis*, originating in the Arctic, is spreading southwards and has reached Saskatchewan and the Dakotas. The original hosts are foxes but dogs and cats are alternatives. The larvae occur in field mice as multilocular microcysts containing numerous protoscolices, but in man the cysts are alveolar and sterile and resemble both in histology and growth a cholangiocellular carcinoma of the liver with metastases. Signs and symptoms are chronic and poorly defined. Diagnosis is difficult. Test antigens are not yet satisfactory. *E. granulosus* has a sylvatic cycle, the adult tapeworms living in wolves and dogs, while the larvae occur only in Cervidae and man. The cysts occur almost exclusively in the lungs as unilocular, macrocystic, relatively benign tumours, although abnormal complications can occur. The Casoni intradermal sensitivity test, its technique and interpretation are discussed.

Deux espèces d'Echinococcus existent au Canada: 1) *E. multilocularis* qui a son origine dans l'Arctique et qui s'étend vers le Sud et a atteint la Saskatchewan et les deux Dakotas. Les hôtes originels sont les renards mais chiens et chats peuvent abriter également le cestode. Les larves s'observent chex des souris de champ, sous forme de microkystes multiloculaires contenant de nombreux protoscolex, mais chez l'homme, le kyste est alvéolaire et stérile et ressemble, au double point de vue histologique et du développement, à un cancer colloïdal avec métastases dans la foie. La symptômatologie est floue, mais de caractère chronique. Le diagnostic est malaisé. 2) *E. granulosus* suit un cycle sylvestre, les ténias adultes vivant sur le loup et le chien, alors que les larves ne se rencontrent que chez les cervidés et chez l'homme. Les kystes siègent presqu'exclusivement dans les poumons sous forme d'une tumeur uniloculaire, macrokystique, relativement bénigne, mais qui peut entraîner des complications anormales. Le test de sensibilité intradermique de Casoni, sa technique et son interprétation sont exposés par l'auteur.

ECHINOCOCCOSIS is a parasitic disease caused by the cystic larval stage of the tapeworms, *Echinococcus granulosus* and *E. multilocularis*. Classical hydatid disease is associated with *E. granulosus* in which the cyst is typically spherical and benign, whereas *E. multilocularis* produces alveolar hydatid cysts, with malignant and metastasizing microvesicles. Both species occur naturally in Canada.

Sir William Osler reported the presence of *E. granulosus* in Canada in 1883, but apart from Manitoba, where the disease was frequently encountered in immigrants from Iceland, the disease was rarely encountered here until 1950. At that time, the Indian Health Services, Department of National Health and Welfare, found, during routine chest radiographs for tuberculosis, that many Indians had pulmonary hydatid infections. It has since been established that the disease is endemic in the Northwest Territories, over 40% of some Indian and Eskimo tribes being infected. As a result of this endemicity and the influx of immigrants from the Mediterranean area where echinococcosis

is very common, the frequency of this disease is increasing as observed in Canadian hospitals.

While *E. granulosus* has a world-wide distribution, *E. multilocularis* is much more limited geographically. It is found in the U.S.S.R., both in Asia and Europe, on certain islands in the Bering Sea, in the Kurils in the northwest Pacific, and in the Bavaria-Tyrol region of Germany. There is evidence that the parasite is spreading in Europe, where the fox population is steadily increasing and moving westward from Poland.

Until recently, it was thought that *E. multilocularis* was confined to the Arctic archipelago in Canada, but in 1962 it was found on the mainland near Churchill, Manitoba.[1] In 1964 *E. multilocularis* was reported from North Dakota.[2, 3] This led to speculation that the parasite was probably also present in the Prairie Provinces, and this suspicion was confirmed in 1965 by Hnatiuk[4] who collected a field mouse two miles south of Saskatoon which was infected with the larval stage of *E. multilocularis*.

To date, only a few autochthonous cases of alveolar hydatid disease have been reported from North America, but now that the parasite is spreading to more heavily populated areas, there is little doubt that more cases will be seen within

Canad. Med. Ass. J.
Mar. 11, 1967, vol. 96

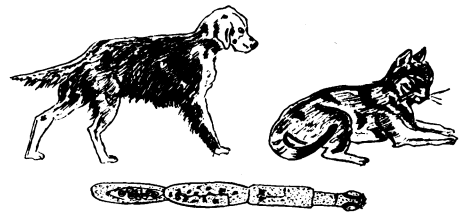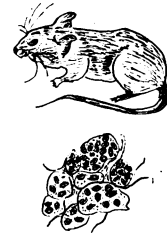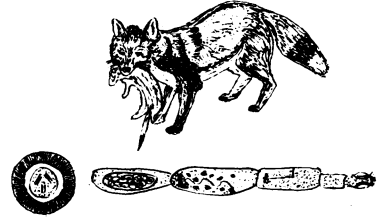SPECIAL ARTICLE: ECHINOCOCCOSIS 601
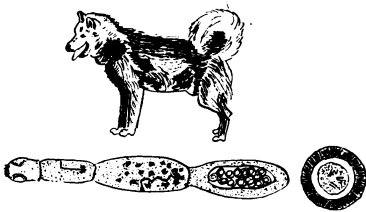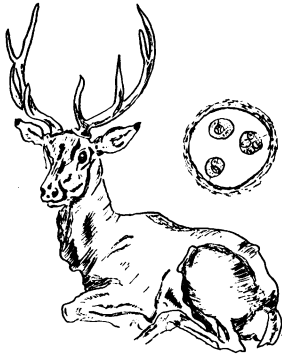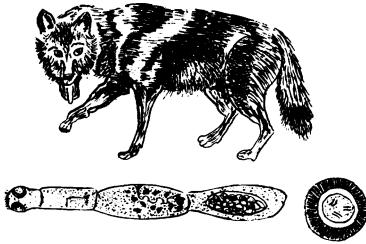
E.GRANULOSUS

E.MULTILOCULARIS

Fig. 1.—Life history of Echinococcus in Canada.

the next few years. *E. multilocularis* causes a very grave condition in man, and because of its epidemiology, it could become a serious threat.

Echinococcus granulosus and *E. multilocularis* have similar basic life-history patterns even though each species has specific definitive and intermediate host requirements.

The tapeworms, which have from three to five segments and measure about ¼ in. in length, are very host-specific and develop into sexual maturity only in the intestinal tract of carnivores, usually canines. In contrast, the cystic larval stage develops in a wide variety of mammals (*E. granulosus* in herbivores and *E. multilocularis*
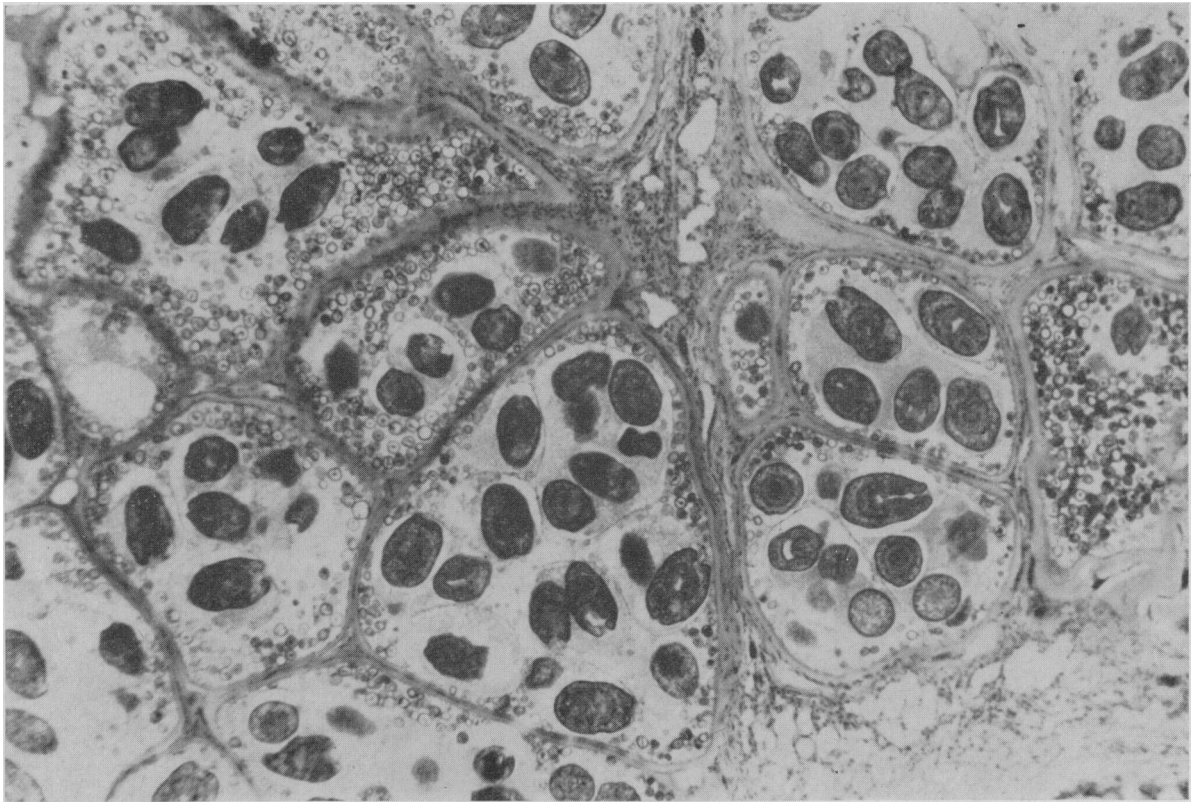
Fig. 2.—*Echinococcus multilocularis* cyst. In a normal rodent host the larva is a multilocular, microvesicular cyst containing a large number of protoscolices. (× 48.)

in rodents). These intermediate hosts, including man, can only become infected by ingesting eggs of the tapeworm which have been deposited by carnivores during defecation.

When Echinococcus eggs are swallowed by an intermediate host, the outer shell is digested away and the hexacanth embryos are liberated in the intestine; here, by means of their hooklets, they penetrate the intestinal wall and gain access to the blood vessels by means of which they are distributed to various parts of the body. Wherever they finally settle, they develop into the larval stage which is characterized by the formation of a cyst, the hydatid. Under ideal conditions, tapeworm heads or protoscolices eventually develop within the cyst. The cycle is completed when fertile cysts (those containing protoscolices) are eaten by an appropriate species of carnivore. Man can become infected only by the ingestion of ova, not by ingesting cysts.

ECHINOCOCCUS MULTILOCULARIS

Echinococcus multilocularis has received considerably less attention than *E. granulosus* because it was not reported from North America until 1954[5] and because of its more restricted geographical distribution. However, the parasite is spreading, and as it becomes established it will achieve greater notoriety because it produces one of the most insidious helminthic diseases of man.

The tapeworm stage develops in both white and red foxes, while the larval stage occurs in rodents of the genus Microtus, such as field mice and voles. This "sylvatic cycle", in itself, is only of minor importance in relation to human disease, for only hunters or trappers handling fox pelts would be likely to come in contact with the infective eggs. However, the tapeworms also develop in domestic dogs and cats (Fig. 1). Rodents, not normally a constituent of most dogs' diets, may be eaten by dogs which are underfed or receiving improper nourishment. In certain northern areas of this country where food is at a premium, it is highly probable that many dogs occasionally feed on rodents and may therefore become infected and consequently deposit eggs in the vicinity of human habitations. Rural dogs may also become involved in the same manner. Although dogs certainly represent a potential source of infection, their role will undoubtedly be of minor importance in regard to an increase in human cases.

The domestic cat, on the other hand, no matter how well nourished, will kill and eat rodents.

Canad. Med. Ass. J.
Mar. 11, 1967, vol. 96

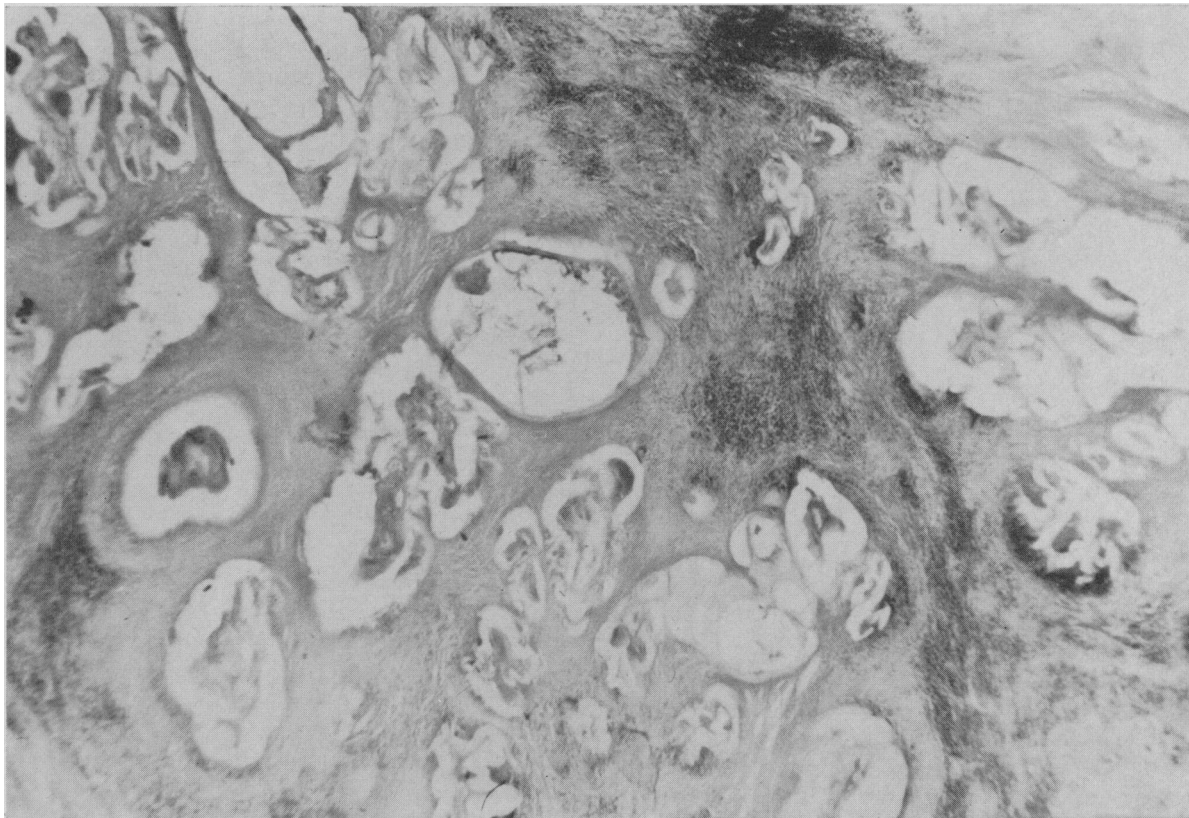SPECIAL ARTICLE: ECHINOCOCCOSIS   603

Fig. 3.—Human alveolar hydatid caused by *E. multilocularis*. The cyst is multilocular and microvesicular, but degenerate and sterile. The cyst mass was found in the liver of a 70-year-old Eskimo at autopsy. (× 40.)

The larval stage of the parasite, as previously noted, is known to be present in the prairies in field mice. It is anticipated therefore that a domestic cat–mouse cycle will soon become established. When this occurs, cats, especially those on farms and those which are semi-wild, will become a major source of infective material. It is this cycle which will be most important in causing an increase in the number of human cases of alveolar hydatid disease.

Alveolar hydatid is the larval stage of *E. multilocularis* as it occurs in man. In the normal rodent intermediate hosts the larva develops as a luxuriant multilocular, microvesicular, fertile cyst containing a very large number of protoscolices (Fig. 2). The cyst in man, on the other hand, is sterile or nearly so and while multilocular and microvesicular, it is obviously degenerate but still alive (Fig. 3). Alveolar hydatid disease has been present in southern Germany, northern Switzerland and France for years and until 1856 when Virchow showed its parasitic nature, it was regarded as an alveolar or mucoid carcinoma of the liver. In fact, histologically, it superficially resembles a cholangiocellular carcinoma of the liver with numerous small vesicles—usually well under 1/5 in.

in diameter, filled with a mucoid jelly-like content. It provokes a severe host reaction and becomes surrounded by dense fibrous tissue. The tumour usually becomes necrotic and caseated in the centre, probably because of the density of the host reaction. The periphery of the parasite is still alive and spreads by budding throughout the liver which it can completely infiltrate. Fragments can metastasize to the lungs, brain and elsewhere. Unlike that caused by the relatively benign *E. granulosus*, the disease terminates fatally, unless early surgical interference can remove the parasitic cyst. West, Hillman and Rausch[6] have reported on eight patients in Alaska who underwent radical liver resections in cases of alveolar hydatid disease.

Early diagnosis is of fundamental importance in order to permit a resection of liver tissue before infiltration involves too much of this organ.

A history of possible exposure to echinococcosis is important. Subjective symptoms are vague and ill-defined, and the signs may be confusing. An unusually long history of malaise but without anorexia or weight loss is common. The first sign is often a mild progressive jaundice and a history suggestive of epidemic hepatitis or

cholecystitis. An enlarged liver or a palpable liver tumour without any evidence of a primary tumour elsewhere, along with the vague symptoms outlined above, may be the presenting features. Eosinophilia may be absent, or if present is usually slight. Radiographic examination may show fine points representing areas of calcification, and while abdominal radiographs may also show a characteristic pattern, neither is diagnostic nor indicative of the extent of the infection.

There is no doubt that the disease is often overlooked or misdiagnosed, and statistics as to its incidence are quite misleading. In 67 autopsies in Switzerland in which alveolar hydatid occurred, only 18 had been diagnosed correctly, 16 had been diagnosed as jaundice or hepatitis, 18 as cancer, cirrhosis or tuberculosis, and in 15 no diagnosis had been made. All had liver involvement, but in some the lungs, spleen, brain and peritoneum were also infected.

Antibodies are present in the serum and the skin, but no thoroughly reliable test antigen is yet available. Those in use are prepared from other tapeworms or from fluid and membranes of cysts taken from infected animals. All of these contain antigens to host substances—often to liver substance—and consequently false positives occur. At present, hemagglutination and bentonite flocculation tests are undoubtedly the most reliable and useful means of detecting *E. multilocularis*, but it is hoped that a satisfactory antigen for an intradermal test will soon be available.

ECHINOCOCCUS GRANULOSUS

In countries other than North America, the human incidence of *E. granulosus* coincides to a great extent with the distribution of sheep, the intensity of the infection being greatest in areas where sheep are kept in close association with canines, particularly dogs. The use of dogs in tending flocks and the indiscriminate feeding of offal to these animals have resulted in an appalling situation because a large percentage of the population is thus exposed to infection.

Pigs, horses, goats, cattle and camels also serve as intermediate hosts, but their role in human infection is contingent upon local customs relating to the feeding and handling of canines.

In addition to the "domestic cycle" there are other "sylvatic cycles" in which one or both hosts are wild animals; for instance, in Australia there is a wallaby-dingo cycle, whereas in the Middle East a sheep-jackal cycle persists.

E. granulosus in Canada has a sylvatic cycle, the chief intermediate hosts being the larger cervidae: elk, moose, reindeer and caribou. The definitive hosts are wolves, coyotes and domestic dogs. It is extremely fortunate that the Canadian strain of the parasite will not develop in domestic herbivores and consequently it is restricted to areas where wolves, dogs and cervidae co-exist. The disease is thus endemic in the Northwest Territories, the Yukon, northern parts of British Columbia, Alberta, Saskatchewan, Ontario and Quebec.

The cervidae-wolf cycle is, again, only of minor importance in relation to human echinococcosis, for only hunters handling the pelts of infected wolves or coyotes will come into contact with the infective eggs. However, when the sylvatic cycle is interrupted and the domestic dog becomes the definitive host, the situation is quite different.

In northern Canada, the problem is a socioeconomic one. Game animals are still an important source of food, and portions of animals not suitable for human consumption are fed to dogs. This invariably includes the lungs, which are the organs that are most frequently infected with hydatid cysts. Ultimately dogs fed on this material become heavily infected with tapeworms. As these sledge dogs are considered valuable possessions, each family keep their animals tethered close to their dwelling where the soil eventually becomes grossly contaminated with dried feces and echinococcus eggs.

The rate of infection varies from tribe to tribe according to their food requirements and local customs. Coastal tribes subsisting primarily on a fish diet have little or no hydatid disease. During a survey of the MacKenzie Valley area, Dr. Robert W. Wolfgang[7] noted that one tribe which hung the lungs of their "kill" in trees as a type of pagan offering were also free of the disease. The incidence is highest, as one would expect, in hunting tribes.

Echinococcus eggs are extremely resistant to climatic conditions and in northern regions will survive for at least two years. Most infections are contracted at an early age because children play in contaminated soil around the home and put their contaminated fingers in their mouths. The incidence is also slightly higher in women than in men, and this is attributed to the fact that they pick up the eggs directly from the dogs' coats while caring for them. Eggs may stick to vegetation, and the eating of raw unwashed vegetables can result in infection. In a dry dusty season, eggs can also be inhaled.

In Canada, *E. granulosus* cysts occur almost exclusively in the lungs, whereas in other areas (particularly where the sheep-dog cycle exists) the liver is a more frequent site of infection.

However, the larvae may settle anywhere and cases are not uncommonly recorded in the long bones, spleen and uterus.

Wherever the larva settles, it slowly develops into a cyst receiving its nourishment from the host's plasma. As it grows, the parasite exerts an increasing pressure on the cells of the adjacent tissue, which it eventually kills. The host attempts to surround this foreign body with a fibrous tissue capsule. Typically, the cysts are spherical, but if they encounter mechanical obstructions such as the bile duct or a bronchus, the cyst may become lobed.

Several years may be required for the cyst to become fertile. A fully developed cyst ranges in size from a hen's egg to a melon and contains numerous brood capsules and protoscolices which actually are small tapeworm heads. No further development takes place unless the cyst becomes old or there is some environmental change which affects its metabolism; then, endogenous daughter cysts develop within the mother cyst. In this process, an individual protoscolex becomes rounded off and vacuolated, the hooks and suckers degenerate and, in time, it becomes a complete cyst containing brood capsules and protoscolices. This vesicular evolution of protoscolices can also take place outside the confines of the primary cyst, and when this occurs, the resulting condition is known as *secondary echinococcosis*. Protoscolices may be liberated from the parent cyst as a result of rupture, leakage or surgical intervention, and although many protoscolices die, some will find a suitable habitat in the body cavity and develop into new hydatids. Secondary echinococcosis is a very grave condition with a poor prognosis.

Symptoms are the direct result of mechanical pressure by the cyst on the surrounding tissue and thus vary both with the size and location of the cyst.

Small and moderate-sized liver cysts may be asymptomatic, the only complaint from the patient being a feeling of distension. As a rule, pain is absent, but on rare occasions it may be present, and it has been suggested that this is due to pressure on a nerve. If suppuration occurs, severe local pain is usually present. In advanced cases where the cyst is large there may be evidence of cholecystitis and biliary cirrhosis. Physical signs in smaller liver cysts are absent, but large cysts alter the shape of the organ and can be felt as a smooth, elastic, elevated mass. Small multiple cysts often simulate cancer and present an uneven contour on the surface of the enlarged liver.

Pulmonary cysts occur most frequently in the right lung and when small and centrally located are asymptomatic. The character and severity of symptoms will again depend on the size and location of the cyst. Because the parasite grows so slowly, it is possible for a large portion of the lung to be invaded without discomfort to the patient. Symptoms are similar to those found in other chronic chest diseases, namely, cough, hemoptysis, dyspnea and pain. Physical signs include enlargement of the chest, impairment of chest movement, areas of dullness on percussion, loss of respiratory murmur and displacement of liver or heart.

Although *E. granulosus* cysts behave essentially as benign tumours, several complications may occur which alter the course of the disease. Rupture is very common and may be spontaneous, although rupture of liver cysts is often the result of a blow or injury to the abdomen. About one-quarter of all liver cysts rupture. Any rupture which releases a large amount of hydatid fluid is rapidly fatal, the patient succumbing to anaphylactic shock. Small amounts of fluid leaking from a cyst will be tolerated, but when protoscolices are distributed, secondary echinococcosis will be a subsequent complication.

Lung cysts also frequently rupture into a bronchus, and if small, the membrane, fluid and protoscolices may be coughed up and a self-cure effected. Unfortunately, this is not always the case, and when a large amount of fluid is released, the patient is in danger of drowning, or the larynx may become blocked by a piece of cyst wall, in which case the patient suffocates.

Ruptured cysts may also discharge their contents, including brood capsules, protoscolices and detached hooks, into the blood stream and produce multiple emboli. Suppuration and septicemia of the cyst cavity (both in unruptured and ruptured cysts) are also fairly common.

Early diagnosis and surgical removal of the cyst is desirable, but as the patient is often unaware of the presence of a cyst until it has reached considerable size or some complication has developed, this is not always possible.

No single sign or symptom is pathognomonic of hydatid disease. An accurate diagnosis can only be reached when physical signs are considered in conjunction with other factors. A detailed history indicating possible contact with infected dogs is of primary importance.

Lung cysts are clearly visible in radiographs, and this technique is also useful for liver cysts which are located close to the surface. Cysts which are embedded deep in the liver require the use of radiological studies such as tomograms

using conventional radiographs with focal points at different planes or scintiscan methods using radioactive material such as the isotope of gold (^{198}Au) or rose bengal tagged with radioactive iodine (^{131}I).

An eosinophilia of over 5% is present in at least 50% of *E. granulosus* infections. However, it is not always present, but may occur in the marrow even when absent from the peripheral blood.

Although a considerable variety of test antigens for hydatid disease have been used, including extracts of other tapeworms, such as Taenia and Dipylidium, the usual source is hydatid fluid from fertile cysts of animal (less frequently, human) origin. This fluid probably represents molecules of host origin which have passed through the semi-permeable laminated membrane from the host animal. Accordingly, the fluid not only is of inconsistent composition but contains a great variety of potential or actual antigens. While numerous attempts have been made to fractionate the fluid to obtain a more specific test-antigen, none have been more than partially successful.

The antigens are used partly for sensitivity tests and partly for serological tests, and there is evidence that the latter react to a variety of but not all the antigenic components in the whole fluid.

The sensitivity test—called the Casoni reaction after its discoverer—is not only the most widely used, but is still the most reliable. It can, however, produce both false positives and false negatives, and as it is essentially a clinical test it must be interpreted by the clinician in relation to the other signs and symptoms.

The technique is simple; about 0.25 c.c. of the antigen is injected intradermally (with the bevel of the needle uppermost). It is wise to control this with a similar injection of sterile saline in the opposite arm as well as a stroke test with a blunt needle to exclude local sensitivities. A local passive sensitivity of the skin persists for some time at the site of inoculation, and consequently the injection must not be repeated near the original site of inoculation. There is often an immediate fall of 50% in eosinophilia if present—in 30 minutes to three hours—but this may be succeeded by a rise in 24-48 hours.

An *immediate* reaction is the appearance in 10-30 minutes of a raised wheal with a surrounding area of erythema. The wheal is sometimes quite irregular, but in a positive reaction it is at least an inch in its smallest diameter. A negative reaction is under ¾ in. in its maximum diameter, while a doubtful one lies between these measurements.

The control injection may produce a transitory wheal which disappears in a few minutes. If it persists and reaches the size of a doubtful reaction or if the stroke test is positive, the *immediate* reaction is without significance.

There may be a *delayed* reaction which appears in 10-24 hours. This consists of an area of erythema nearly 2 in. in diameter, with underlying induration. There is no reaction in the controls unless the patient suffers from allergic conditions or skin diseases. The *delayed* reaction may persist for a week.

Provided the controls are negative, an immediate positive test is strong presumptive evidence of a hydatid cyst, although not completely conclusive. A negative test, however, is valuable in excluding hydatid. A delayed positive is valuable evidence of the presence of a cyst and is especially valuable if the *immediate* test was doubtful. The absence of a *delayed* reaction has no significance.

A false negative is not uncommon, especially in children with lung cysts, and should not be regarded as excluding hydatid when a shadow appears on the radiographs.

The skin sensitivity persists for long periods—perhaps for life—after the removal or death of the cyst, and so false positives may result as they can do from the presence of tuberculosis, jaundice and other pathological or degenerative conditions of the liver. Because of this, a positive sensitivity test should be succeeded by a serological test.

The earliest serological test employed was complement fixation and the most potent antigen used appeared to be an alcoholic extraction of protoscolices. Even in the hands of experts, this test did not have a high degree of reliability and it was complicated and technically difficult.

Attempts were made to find less complicated tests and the first employed was a precipitin test, of which there were several variations. It apparently did not react to the same fraction of fluid as did the complement fixation test but it was not particularly delicate and was unreliable if the amount of antibody in the serum was small.

In recent years, the introduction of hemagglutination tests has promised more reliable results—especially the indirect hemagglutination test. This test is relatively simple and will detect a small amount of antibodies. Other testing procedures are under active study in various laboratories. These include a variety of flocculation tests (including bentonite, polystyrene), fluorescent antigen, gel diffusions and electrophoresis. None are as yet in general use.

Canad. Med. Ass. J.
Mar. 11, 1967, vol. 96

SPECIAL ARTICLE: ECHINOCOCCOSIS 607

If the Casoni and serological tests are positive and if there is a significant eosinophilia, it is highly probable that a hydatid cyst is present.

Exploratory puncture of the cyst in order to find the diagnostic hydatid elements is an extremely dangerous procedure because of the possibility of anaphylaxis or secondary echinococcosis due to leakage of fluid or protoscolices.

Surgical removal of the intact cyst is the only method of treatment. Rupture of the cyst during surgery may cause a fatal anaphylactic shock which may be hidden under anesthesia but supervenes after the operation. If the erythematous stage of the Casoni reaction is very evident, the risk of anaphylaxis is increased.

SUMMARY

Echinococcosis is diagnosed with increasing frequency in North America and it is therefore important that Canadian doctors be aware of its presence. Echinococcus granulosus infections are likely to be seen in immigrants, in armed forces personnel who have been stationed in endemic areas such as Cyprus, and in Canadians who have travelled abroad. The disease is also endemic in northern areas of this country, where 40% of some Indian tribes are infected. Hydatid disease should also be considered in patients with vague symptoms who have travelled or worked in the Arctic. Diagnosis is established by a consideration of symptoms, physical signs, radiographs, a positive Casoni intradermal test and a positive serological test.

Alveolar hydatid, caused by E. multilocularis, is still a rare disease in Canada. Once confined to the Arctic archipelago, the parasite has now spread into the Prairie Provinces and an increase in the number of human cases can be expected within the next decade. The parasite infiltrates the liver, ultimately destroying it. Metastases to the lungs and brain are not uncommon. Early diagnosis is of fundamental importance. There are, as yet, no reliable antigenic or serological tests and thus diagnosis is very difficult, but alveolar hydatid should be suspected in cases of unexplained liver disease.

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