Growing importance of prevention and control of alveolar echinococcosis

This article reviews progress in the fight against *Echinococcus multilocularis*, the tapeworm responsible for alveolar echinococcosis, which is usually fatal if not diagnosed and treated at an early stage.

The major species of *Echinococcus* infecting humans are *E. granulosus*, which causes unilocular echinococcosis, and *E. multilocularis*, causing alveolar echinococcosis. Larval cysts of varying size are produced in the liver and other organs. The adult tapeworms are found in dogs, foxes and other carnivores. Alveolar echinococcosis is considered a very serious illness, and most patients die if the disease is not diagnosed at an early stage so that surgery and/or chemotherapy can be employed \(1, 2\).

Research on alveolar echinococcosis has been promoted through WHO-coordinated working groups, special attention having been given to epidemiology, modern diagnostic methods, chemotherapy, and prevention and control based on the eco-epidemiology of final hosts. Information support for hygienic practice in populations at risk has been provided \(3\).

**Epidemiology**

People can be infected only if they enter the transmission cycle of *E. multilocularis*; intermediate and final hosts are responsible for transmission to humans, as shown in the figure.

Alveolar echinococcosis occurs in roughly the same areas as the final hosts: the arctic fox in Canada and the USA, the red fox in central Europe, some other fox species in Japan and the USSR, and the coyote in China. The intermediate hosts, among them the fieldmouse, meadow vole and several other small mammals, play an important role in transmission. Cats and dogs are significant in the domestic transmission of the parasite to humans and house rats.

People are at risk if directly exposed to *E. multilocularis* eggs in food, water, soil, dust and almost any other material. Individuals become infected without any remarkable clinical manifestations. Environmental contamination may occur directly from infective fecal materials or indirectly from...
intermediate or final host animals. Flies, beetles, cockroaches and sand slugs carry and disperse the eggs.

In areas of endemicity, therefore, precautions should be taken in respect of food that may be contaminated by *E. multilocularis* eggs. Human infection mostly occurs at some distance from the site of egg deposition. The geographical distribution and population density of the intermediate and final hosts often correspond with the occurrence of human infection. This can be seen in Alaska, where the arctic fox lives along the coast near the mouth of the Kuskokwim river, eastward towards Canada, and southward along the western shore of Hudson Bay. Human populations in these areas are at high risk of infection. The incidence of the disease in recent years has been 33 per 100 000 inhabitants on the western coast of Alaska, and 67 per 100 000 on St Lawrence Island.

In Western Europe, foci of alveolar echinococcosis were first reported in the middle of the nineteenth century, and there have recently been local endemics in Austria, France, Germany and Switzerland. In Austria there are some foci of endemicity in both relatively low-lying and Alpine regions. In Germany, 20 to 30 human cases are reported annually, although it seems that there is some underreporting and underestimating. In France, there are endemic foci in the southeast adjacent to the Swiss border; a third of patients who have the disease are engaged in agricultural work but specific risk factors have not been clearly identified. In Switzerland there were 0.18 cases per 100 000 inhabitants in 1980; in the canton of Jura an incidence of 0.74 per 100 000 was recorded in 1988, one of the highest in recent years.

In the USSR, endemics are extending to both European and Asian areas. Substantial morbidity, disability and mortality rates occur in northern Siberia, the Yakut ASSR, the Chukotsk Autonomous Territory, and the Yamal Peninsula. The incidence is as high as 1.7–10.0 per 100 000 inhabitants, and a monitoring programme based on serological diagnosis has been initiated in these areas in order to assess the magnitude of the problem and to identify priority areas for intervention.

In Asia, both Japan and China have been developing control programmes at national level. In Japan the endemic originated during the 1950s on Rebun Island, northwest of Hokkaido. After successful containment through the elimination of dogs and foxes the country remained free of echinococcosis for more than 20 years. In 1982, however, endemics started in the eastern part of Hokkaido and subsequently spread, the area of endemicity eventually covering the whole island and extending towards the north of Honshu Island. It was found that 14% of 1244 red foxes and 3% of 98 domestic dogs were infected. In this area, 3–17 cases of alveolar echinococcosis in humans have been recorded annually. Screening tests have been initiated in the population at risk, and the immunoblot method is used for confirmation.

In western China, where about 30 million people live, the disease is reportedly widespread. A National Echinococcosis/Hydatidosis Control and Training Centre opened in Urumqi in Xinjiang Autonomous Region in 1989, and WHO has been incorporating the regions of endemicity into projects for training technical personnel and for technology transfer.

Control strategies should be developed as a matter of urgency. Teams coordinated by WHO are investigating:

- key epidemiological factors, including the population densities and dynamics of the intermediate and final host species;
Transmission of alveolar echinococcosis in the life-cycle of *Echinococcus multilocularis*

1. *E. multilocularis* mainly parasitizes the small intestine of red or arctic foxes;
2. domestic dogs and cats may also enter the cycle when they eat infected rodents;
3. proglottids with eggs excreted in faeces;
4. egg;
5. intermediate hosts are rodents, mainly of the family Cricetidae, natural infections in soricid insectivores have also been reported;
6. accidental infection of man may result in metacestode development in the liver and other sites by extension or formation of metastases;
7. infected rodent liver;
8. metacestode consisting of conglomerates of small vesicles;
9. single vesicle with protoscoleces.

— interaction between intermediate and final hosts.

Very high incidences of *E. multilocularis* infection have been found among young foxes as well as young voles, which are intermediate hosts. This is of particular interest in the development of strategies for the interruption of transmission. Mathematically formulated eco-epidemiological models have been used in New Zealand to devise meaningful approaches for preventing *E. multilocularis* transmission to human populations, and for analysing the cost-effectiveness of control measures (4).

Collaborative studies on the physical properties of *E. multilocularis*, the conditions affecting survival of the eggs in nature, and the mechanisms of their dispersal are in progress. The inactivation of *E. multilocularis* eggs can be brought about if contaminated material is kept at −80°C for more than 48 hours.

**Diagnosis**

A serological method of diagnosis involving an enzyme-linked immunosorbent assay has been developed at the WHO Collaborating Centre for Research and Training in Parasitic Zoonoses at Zurich University, Switzerland, and has been widely applied in human and animal populations. The sensitivity and specificity of the test exceed 94%. It is also used to monitor the post-surgical condition of patients, in most of whom negative seroconversion occurs following successful resection of the lesion (5). The test also has a high predictive value in epidemiological surveys, even where the prevalence of alveolar echinococcosis is extremely low. In Japan, 150 000 serum samples were tested in areas of endemicity and positive samples were subjected to immunoblot analysis, resulting in the detection of 57 new cases. Serological techniques have been developed in Austria, Germany, the USSR, and elsewhere for early diagnosis, which permits treatment of *E. multilocularis* infection. Recombinant technology has been employed in Switzerland and the United Kingdom to develop highly specific antigens for this purpose. Progress is also being made in early diagnosis through computer-assisted tomography, ultrasound examination, and other methods.

*In vitro* culturing of *E. multilocularis* protoscolices and germinal cells has been achieved in Austria, Germany, Japan, and Switzerland. *E. multilocularis* cell lines were reproduced continuously over more than 50 passages. Such stability has encouraged the initiation of studies on immunology, growth promotion, cell-differentiating factors and drug screening. This technology replaces and/or reduces experimentation with laboratory and host animals and reduces the risk of laboratory infection.

**Treatment**

The survival rate after 10 years of infection has risen to 50.5%, thanks to improved diagnosis, chemotherapy and surgery. Progress in hepatectomy, reconstruction of the bile duct with an intestinal loop, biliary drainage, and liver transplantation have greatly contributed to this success. Treatment with benzimidazole and carbamates has prolonged survival, although these drugs and others, including mebendazole and albendazole, are parasitostatic rather than curative. Nevertheless, a regression of lesions has been reported in some patients. Adverse effects of chemotherapy, such as neutropenia and abnormal liver function, have been observed. Research continues, therefore, for still more effective and safer drugs.
Prevention and control

The key to prevention is the elimination of infective eggs from contaminated berries, vegetables and other foodstuffs. In Germany, procedures have been developed which do not affect the taste or nutritive value of produce. Heating at 45°C for three hours is considered an effective way of killing the eggs. The boiling and cooking of foodstuffs renders them safe. Freezing at −18°C does not destroy the eggs, even if they are kept for 240 days at this temperature, and consequently storage in household deep freezers is ineffective. However, at −80°C the eggs lose some infectivity and food becomes relatively safe.

Only in a small isolated area can one hope to eradicate _E. multilocularis_ infection through the elimination of foxes, as happened in Rebun Island in northeast Japan. However, a new approach is under investigation in Germany, where baits containing praziquantel were distributed at six-month intervals. The use of 20 baits per square kilometre resulted in uptake by 70–90% of foxes and a drastic reduction in the prevalence of _E. multilocularis_ in these hosts. It is intended to combine the use of praziquantel in baits with the established practice of administering oral rabies vaccine in the same way.

In Alaska, the administration of praziquantel to dogs at monthly intervals for five years interrupted dog/comensal rodent transmission. It has been suggested that a slow-release form of praziquantel might be useful for the treatment of foxes and that a combination of dog population management, dog movement control, and health education might significantly reduce human infection.

Since there is concern that the distribution of praziquantel in baits for foxes may lead to a transient increase in environmental contamination by infectious _E. multilocularis_ eggs that are passed out in the animals' faeces, field trials are only being conducted on a limited scale to investigate the efficacy and side-effects of the procedure.

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It is recommended that general hygienic measures should be applied in areas of endemicity to protect high-risk groups and prevent contact with foxes and other final hosts and their faeces. Vegetable gardens should be fenced to exclude foxes. Hunters should wear plastic gloves when handling foxes. Fruit and vegetables should be carefully washed and cooked, or industrially frozen at −80°C for at least three days before consumption. Immediate priority should be given to the development of reporting and surveillance systems to identify risk areas, risk groups, and the mode of transmission to humans (6).

References


