REVIEW

Echinococcosis: a review

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Summary Echinococcosis in humans occurs as a result of infection by the larval stages of taeniid cestodes of the genus *Echinococcus*. In this review we discuss aspects of the biology, life cycle, etiology, distribution, and transmission of the Echinococcus organisms, and the epidemiology, clinical features, treatment, and effect of improved diagnosis of the diseases they cause. New sensitive and specific diagnostic methods and effective therapeutic approaches against echinococcosis have been developed in the last 10 years. Despite some progress in the control of echinococcosis, this zoonosis continues to be a major public health problem in several countries, and in several others it constitutes an emerging and re-emerging disease.
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Introduction

Echinococcosis in humans occurs as a result of infection by the larval stages of taeniid cestodes of the genus *Echinococcus*. Six species have been recognized, but four are of public health concern: *Echinococcus granulosus* (which causes cystic echinococcosis), *Echinococcus multilocularis* (which causes alveolar echinococcosis), and *Echinococcus vogeli* and *Echinococcus oligarthrus* (which cause polycystic echinococcosis). Two new species have recently been identified: *Echinococcus shiquicus* in small mammals from the Tibetan plateau and *Echinococcus felidis* in African lions, but their zoonotic transmission potential is unknown. Several studies have shown that these diseases are an increasing public health concern and that they can be regarded as emerging or re-emerging diseases.

In this review we discuss aspects of the biology, life cycle, etiology, distribution, and transmission of the Echinococcus organisms, and the epidemiology, clinical features, treatment, and effect of improved diagnosis of the diseases they cause. New sensitive and specific diagnostic methods and effective therapeutic approaches against echinococcosis have been developed in the last 10 years. Despite some progress in the control of echinococcosis, this zoonosis continues to be a major public health problem in several countries, and in several others it constitutes an emerging and re-emerging disease.

Echinococcus granulosus (cystic echinococcosis)

Description of the pathogen

Echinococcus granulosus is a cestode whose life cycle involves dogs and other canids as definitive hosts for the

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intestinal tapeworm (Figure 1), as well as domestic and wild ungulates as intermediate hosts for the tissue-invading metacestode (larval) stage. The metacestode (echinococcal cyst) is a fluid-filled, spherical, unilocular cyst that consists of an inner germinal layer of cells supported by a characteristic acidophilic-staining, acellular, laminated membrane of variable thickness.[1] Each cyst is surrounded by a host-produced layer of granulomatous adventitial reaction. Small vesicles called brood capsules bud internally from the germinal layer and produce multiple protoscolices by asexual division. In humans, the slowly growing hydatid cysts can attain a volume of several liters and contain many thousands of protoscolices. With time, internal septations and daughter cysts can form, disrupting the unilocular pattern typical of the young echinococcal cysts.

Epidemiology

Geographically distinct strains of *E. granulosus* exist with different host affinities. Molecular studies using mitochondrial DNA sequences have identified 10 distinct genetic types (G1—10) within *E. granulosus*.[2,3] These include two sheep strains (G1 and G2), two bovid strains (G3 and G5), a horse strain (G4), a camelid strain (G6), a pig strain (G7), and a cervid strain (G8). A ninth genotype (G9) has been described in swine in Poland[2] and a tenth strain (G10) in reindeer in Eurasia. The sheep strain (G1) is the most cosmopolitan form and is that most commonly associated with human infections. The other strains appear to be genetically distinct, suggesting that the taxon *E. granulosus* is paraphyletic and may require taxonomic revision.[2,3] The 'cervid', or northern syl-
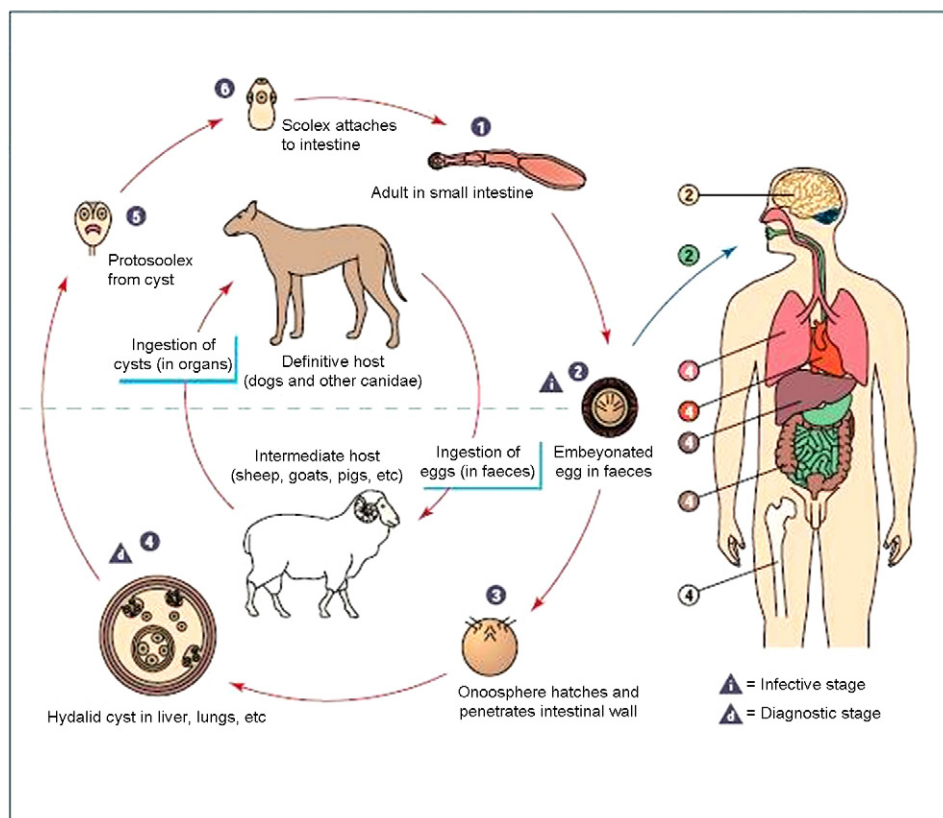

Figure 1   Life cycle of *Echinococcus granulosus* (Reproduced from the Centers for Disease Control and Prevention at http://www.dpd.cdc.gov/dpdx/html/Echinococcosis.htm). The adult *Echinococcus granulosus* (3—6 mm long) ❶ resides in the small bowel of the definitive hosts, dogs or other canids. Gravid proglottids release eggs ❷ that are passed in the feces. After ingestion by a suitable intermediate host (under natural conditions: sheep, goat, swine, cattle, horses, camel), the egg hatches in the small bowel and releases an oncosphere ❹ that penetrates the intestinal wall and migrates through the circulatory system into various organs, especially the liver and lungs. In these organs, the oncosphere develops into a cyst ❹ that enlarges gradually, producing protoscolices and daughter cysts that fill the cyst interior. The definitive host becomes infected by ingesting the cyst-containing organs of the infected intermediate host. After ingestion, the protoscolices ❺ evaginate, attach to the intestinal mucosa ❻, and develop into adult stages ❶ in 32 to 80 days. The same life cycle occurs with *Echinococcus multilocularis* (1.2—3.7 mm), with the following differences: the definitive hosts are foxes, and to a lesser extent dogs, cats, coyotes and wolves; the intermediate host are small rodents; and larval growth (in the liver) remains indefinitely in the proliferative stage, resulting in invasion of the surrounding tissues. With *Echinococcus vogeli* (up to 5.6 mm long), the definitive hosts are bush dogs and dogs; the intermediate hosts are rodents; and the larval stage (in the liver, lungs and other organs) develops both externally and internally, resulting in multiple vesicles. *Echinococcus oligarthrus* (up to 2.9 mm long) has a life cycle that involves wild felids as definitive hosts and rodents as intermediate hosts. Humans become infected by ingesting eggs ❷, with resulting release of oncospheres ❸ in the intestine and the development of cysts ❹, ❹, ❹, ❹, ❹, 4 in various organs. Image courtesy of the CDC-DPDx.

vatic genotype (G8), is maintained in cycles involving wolves and dogs and moose and reindeer in northern North America and Eurasia. Human infection with this strain is characterized by predominantly pulmonary localization, slower and more benign growth, and less frequent occurrence of clinical complications than reported for other forms.[2] The presence of distinct strains of *E. granulosus* has important implications for public health. The shortened maturation time of the adult form of the parasite in the intestine of dogs suggests that the interval period for administering anti-parasite drugs to infected dogs will have to be shortened in those areas where the G2, G5, and G6 strains occur.[4]

Certain human activities (e.g., the widespread rural practice of feeding dogs the viscera of home-butchered sheep) facilitate transmission of the sheep strain and consequently raise the risk that humans will become infected (Figure 2).[5] Dogs infected with Echinococcus tapeworms pass eggs in their feces, and humans become infected through fecal—oral contact, particularly in the course of playful and intimate contact between children and dogs. Eggs adhere to hairs around an infected dog's anus and also are found on the muzzle and paws. Indirect transfer of eggs, either through contaminated water and uncooked food or through the intermediary of flies and other arthropods, can also result in infection of humans.

The greatest prevalence of cystic echinococcosis in human and animal hosts is found in countries of the temperate zones, including southern South America, the entire Mediterranean littoral, southern and central parts of the former Soviet Union, central Asia, China, Australia, and parts of Africa.[6,7] In the USA, most infections are diagnosed in immigrants from countries in which echinococcosis disease is highly endemic. Sporadic autochthonous transmission is currently recognized in Alaska, California, Utah, Arizona, and New Mexico. *E. granulosus* infection has re-emerged in certain areas where it was once believed to be controlled. In Bulgaria the incidence of cystic echinococcosis in children increased from 0.7 to 5.4/100 000 between the 1970s and the mid-1990s, following the collapse of control efforts, and in

Figure 2   In endemic areas dogs often have ready access to viscera from slaughtered livestock as seen in this picture.

Wales the prevalence of infected dogs has more than doubled between 1993 (3.4%) and 2002 (8.1%), following policy changes favoring health education over weekly dosing of dogs with praziquantel.[8]

Clinical manifestations

After ingestion, Echinococcus eggs hatch and release embryos in the small intestine. Penetration through the mucosa leads to blood borne distribution to the liver and other sites, where development of cysts begins. Most primary infections in humans consist of a single cyst; however, 20—40% of individuals have multiple cysts or multiple organ involvement.[9] The liver is the most common site of the echinococcal cyst of the pastoral strains (>65%; Figure 3), followed by the lungs (25%; Figure 4); the cyst is seen less frequently in the spleen, kidneys, heart, bone, and central nervous system.

Even though infections may be acquired in childhood, most cases of liver and lung cysts become symptomatic and are diagnosed in adult patients because of the slowly
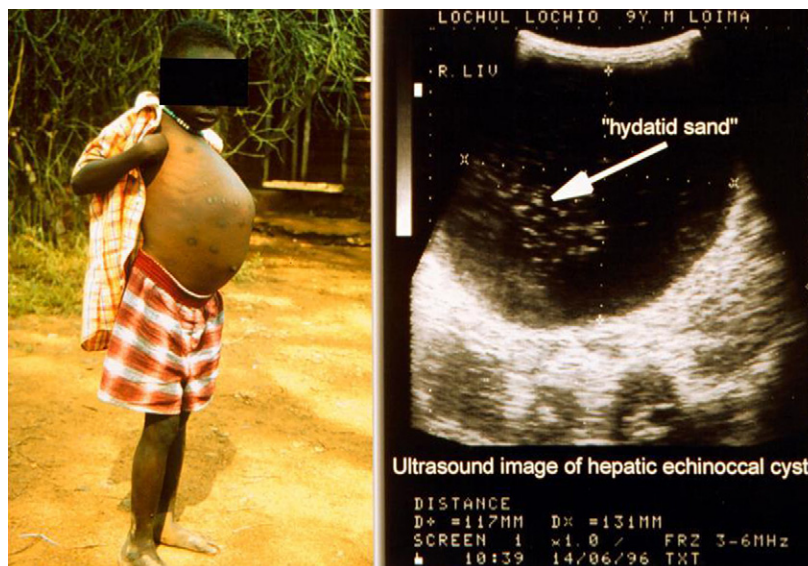

Figure 3   Boy with abdominal distention due to cystic echinococcosis of the liver as shown by ultrasound imaging.
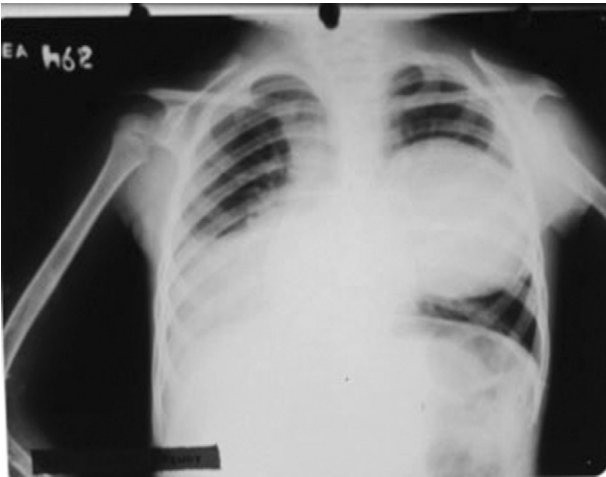
Figure 4 Chest radiograph of a 5-year old Peruvian girl with a hydatid cyst in the left lung field detected as part of an imaging survey in an endemic area. The child manifested some cough with occasional blood-streaked sputum and difficulty breathing.

growing nature of the echinococcal cyst. Only 10—20% of cases are diagnosed in patients younger than 16 years. However, cysts located in the brain or an eye can cause clinical symptoms even when small; thus, most cases of intracerebral echinococcosis are diagnosed in children.

The clinical manifestations of cystic echinococcosis are variable and are determined by the site, size, and condition of the cysts.[9] The rates of growth of cysts are variable, ranging from 1 to 5 cm in diameter per year. The slowly growing echinococcal cyst often is tolerated well until it causes dysfunction because of its size. The signs and symptoms of hepatic echinococcosis can include hepatic enlargement (with or without a palpable mass in the right upper quadrant), right epigastric pain, nausea, and vomiting. If a cyst ruptures, the sudden release of its contents can precipitate allergic reactions ranging from mild to fatal anaphylaxis. In the lungs, ruptured cyst membranes can be evacuated entirely through the bronchi or can be retained to serve as a nidus for bacterial or fungal infection. Dissemination of protoscolices can result in multiple secondary echinococcosis disease. Larval growth in bones is atypical; when it occurs, invasion of marrow cavities and spongiosa is common and causes extensive erosion of the bone.

Laboratory findings and diagnosis

The presence of a cyst-like mass in a person with a history of exposure to sheepdogs in areas where *E. granulosus* is endemic supports the diagnosis of cystic echinococcosis. However, echinococcal cysts must be differentiated from benign cysts, cavitary tuberculosis, mycoses, abscesses, and benign or malignant neoplasms. A non-invasive confirmation of the diagnosis can usually be accomplished with the combined use of radiologic imaging and immunodiagnostic techniques. Radiography permits detection of echinococcal cysts in the lungs; in other sites, however, calcification is necessary for radiographic visualization. Computed tomography, magnetic resonance imaging, and ultrasonography are useful for diagnosis of deep-seated lesions in all organs and also for determination of the extent and condition of the avascular

fluid-filled cysts. Abdominal ultrasonography has emerged as the most widely used imaging technique for echinococcosis because of its widespread availability and usefulness for defining number, site, dimensions, and vitality of cysts.[10] Portable ultrasonography machines have been applied for field surveys with excellent results.[11,12] A standardized classification system for hepatic cysts detected by ultrasonography has been developed by the World Health Organization (WHO).[13] This classification system includes the following categories: type CL, unilocular cystic lesion(s) with uniform anechoic content (but ultrasound does not detect any pathognomonic signs); type CE1, unilocular cysts with uniform anechoic content and with pathognomonic signs that include visible cyst wall and 'snowflake' signs; type CE2, multivesicular, multiseptated cysts; type CE3, anechoic content with detachment of laminated membrane from the cyst wall visible as floating membrane or as 'water-lily sign'; type CE4, heterogeneous hypoechoic or hyperechoic degenerative contents, no daughter cysts present; and type CE5, cysts characterized by thick calcified wall which is arch-shaped, producing a cone-shaped shadow, the degree of calcification may vary from partial to complete.

Antibody assays are useful to confirm presumptive radiologic diagnoses, although some patients with cystic echinococcosis do not demonstrate a detectable immune response.[14] Hepatic cysts are more likely to elicit an immune response than pulmonary cysts. Regardless of location, the sensitivity of serologic tests is inversely related to the degree of sequestration of the echinococcal antigens inside cysts; for example, healthy, intact cysts can elicit a minimally detectable response, whereas previously ruptured or leaking cysts are associated with strong responses. The indirect hemagglutination test is sensitive but has now been replaced by the enzyme immunoassay (ELISA) for initial screening of sera. Specific confirmation of reactivity can be obtained by demonstration of specific echinococcal antigens by immunoblot assays. Eosinophilia is present in <25% of infected persons.

In seronegative individuals, a presumptive diagnosis can be confirmed by the demonstration of protoscolices or hydatid membranes in the liquid obtained by percutaneous aspiration of the cyst. Ultrasonographic guidance of the puncture, anthelmintic coverage, and anticipation of the possible need to treat an allergic reaction minimize risks.[15] Protoscolices can sometimes be demonstrated in sputum or bronchial washings; identification of hooklets is facilitated by acid-fast stains.

Treatment

Until the 1980s, surgery was the only option for treatment of echinococcal cysts; however, chemotherapy with benzimidazole compounds and, more recently, treatment with cyst puncture, aspiration, injection of chemicals and re-aspiration have been introduced and, increasingly, have supplemented or even replaced surgery as the preferred treatment. The benefits and limitations of current treatment options have been reviewed by the WHO Informal Working Group on Echinococcosis.[10,16]

Surgery
Surgical removal of intact hydatid cysts, when possible, remains the treatment with the best potential to remove

cysts and lead immediately to complete cure. The aim of surgery is total removal of the cyst with avoidance of the adverse consequences of spilling the contents. Pericystectomy is the usual procedure, but simple drainage, capitonnage, marsupialization, and resection of the involved organ may be used, depending on the location and condition of the cyst.[16–21] The more radical the intervention, the higher the operative risk but the lower the likelihood of recurrence, and vice versa. Surgery is the preferred treatment when liver cysts are large (>10 cm in diameter), secondarily infected, or located in certain organs (i.e., brain, lung, or kidney).

Surgery is contraindicated in patients who refuse it, are pregnant, have preexisting medical conditions that put them at risk, or have multiple cysts that are difficult to access. Surgical risks include those associated with any surgical intervention (e.g., anesthesia, infections) as well as those unique to echinococcosis (e.g., anaphylaxis, secondary recurrence). Operative mortality varies from 0.5% to 4% but rises with repeated interventions and when surgery is performed in inadequate facilities.

Chemotherapy

Documentation of experience with chemotherapy using benzimidazole compounds is now extensive, and this medical approach can be recommended for many patients.[10] Approximately a third of patients treated with benzimidazole drugs have been cured (e.g., complete and permanent disappearance of cysts) and even higher proportions (30–50%) have demonstrated significant regression of cyst size and alleviation of symptoms.[22–26] However, 20–40% of cases do not respond favorably. In general, small (<7 mm in diameter), isolated cysts, surrounded by minimal adventitial reaction, respond best, whereas complicated cysts, with multiple compartments or daughter cysts or with thick or calcified surrounding adventitial reactions, are relatively refractory to treatment.

Both albendazole (10–15 mg/kg/day) and mebendazole (40–50 mg/kg/day) have demonstrated efficacy; however, the results for albendazole have been superior, probably because of its pharmacokinetic profile, which favors intestinal absorption and penetration into the cyst. The minimum duration of treatment is 3 months. Adverse reactions (neutropenia, liver toxicity, alopecia, and others), reversible upon cessation of treatment, have been noted in a minority of patients treated with both drugs. Contraindications to chemotherapy include pregnancy, chronic hepatic diseases, and bone marrow depression. The combination of praziquantel and albendazole has been used successfully in the treatment of hydatid disease.[27,28] Praziquantel used at 50 mg/kg in different regimens (once daily, once weekly, or once every two weeks) in combination with albendazole produced very effective and rapid results compared with albendazole therapy alone.[28]

Percutaneous aspiration, injection, re-aspiration

A third option for the treatment of hydatid cysts in the liver and some other locations consists of: (1) percutaneous puncture using sonographic guidance, (2) aspiration of substantial amounts of the liquid contents, (3) injection of a protoscolicidal agent (e.g., 95% ethanol or hypertonic saline) for at least 15 minutes, and (4) re-aspiration (PAIR, puncture, aspiration, injection, and re-aspiration).[29–32] PAIR is indicated for patients who cannot undergo surgery and for those who refuse surgery who have single or multiple cysts in the liver, abdominal cavity, spleen, kidney, and bones. PAIR is contraindicated for inaccessible or superficially located liver cysts and for inactive or calcified cystic lesions.

To avoid sclerosing cholangitis, PAIR must not be performed in patients whose cysts have biliary communication; the presence of the latter can be determined by testing the cyst fluid for presence of bilirubin or by intra-operative cholangiogram or endoscopic retrograde cholangiopancreatography. Complications of the procedure have included secondary infection of the cavity, acute allergic reactions, and recurrence; however, these have been rare. Application of PAIR to pulmonary cysts has been associated with frequent complications and is not recommended.

The physician using PAIR must be prepared to treat an allergic reaction. The possibility of secondary echinococcosis resulting from accidental spillage during this procedure can be minimized by concurrent treatment with benzimidazoles; indeed, combined treatment (PAIR with albendazole) may yield better results than those of either chemotherapy or PAIR alone.[29] The recommended treatment course is 1 month of albendazole after the PAIR procedure. Favorable results have been reported from more than 2000 PAIR interventions. A meta-analysis comparing the clinical outcomes for 769 patients with hepatic cystic echinococcosis treated with PAIR plus albendazole or mebendazole with 952 era-matched historical control subjects undergoing surgical intervention found greater clinical and parasitological efficacy, lower rates of morbidity and mortality and disease recurrence, and shorter hospital stays than surgical treatment.[32]

Monitoring results of treatment

The occult nature of the hydatid cyst confounds post-treatment evaluation. Objective response to treatment is best assessed with repeated evaluation of cyst size and consistency at 3-month intervals with ultrasonography, computed tomography, or magnetic resonance imaging. Since the time of the appearance of recurrence is extremely variable, such monitoring should be continued for at least 3 years. Change in titer of serologic antibody values is not reliable in itself to define the outcome of chemotherapy or PAIR.

Prevention and control

The earliest successful control program was that in Iceland initiated nearly 130 years ago, when cystic hydatid disease was recognized as affecting approximately one in every six Icelanders.[33] An extremely effective health education campaign sensitized the entire population to the disease, and subsequent measures virtually eliminated home slaughter of sheep resulting in the gradual elimination of transmission. By the 1950s echinococcosis was considered eradicated from Iceland. Programs initiated in New Zealand (1959) and in Tasmania (1965) were primarily based upon education of rural populations and motivating them to change their practices. Strict control and prohibition of farm slaughter were key features in those programs. The initially voluntary nature of the programs was reinforced by legislative acts and strengthened efforts at enforcement as the programs progressed. This policy proved highly successful: the number of infected dogs fell steadily throughout the campaigns. Decline in canine infection preceded drops in prevalence of infection in sheep and young cattle and a reduced number of cases in

humans diagnosed annually. In New Zealand the first year when no dogs were found infected was 1985—1986, and hydatid cysts in sheep are now rare. No new human cases of hydatid disease have been reported in children or adults under 19 years old since 1977. Cystic echinococcosis has been declared provisionally eradicated in both Tasmania and New Zealand. A program in Cyprus benefited from very aggressive stray dog elimination and strict control of working dogs and those kept as pets. All used diagnostic purging of dogs with arecoline as a surveillance technique for monitoring the effectiveness of the program and identifying problem farms. Tasmania quarantined infected dogs and infected sheep flocks. Regional programs in Argentina (1970), Chile (1978), and Uruguay benefited from the use of the highly effective echinococcicidal drug praziquantel. Surveillance data from all these programs documented the reduction of prevalence in dogs, animal intermediate hosts, and humans.[34] A promising advance has been the development of a recombinant vaccine (EG95), which seems to confer 96—98% protection against challenge infection. Recent trials in Australia and Argentina using EG95 have reported that 86% of vaccinated sheep were completely free of viable hydatid cysts when examined 1 year after immunization. Vaccination reduced the number of viable cysts by 99.3%.[35,36] A vaccine has also been developed against the dog tapeworm stage, which conferred 97—100% protection against worm growth and egg production.[37]

Mathematical modeling has revealed that the most effective intervention against echinococcosis is a combination of sheep vaccination and dog anthelmintic treatment.[38] According to this model, a vaccine coverage of 75% of the sheep population would only require 6-monthly anthelmintic treatments and would reduce echinococcosis in both intermediate and definitive hosts to very low levels. Important advantages of this less intensive strategy would be lower cost and possibly increased compliance.

It must be noted that the positive achievements of successful control programs, however significant at the local level, have not markedly changed the global distribution and public health importance of hydatid disease. In most endemic areas, effective control has not been achieved or even attempted. Much remains to be done. There is concern that echinococcosis may have become hyperendemic in areas where it was once endemic. For example, in the Peruvian central highlands, the sudden cessation of a control program at the end of the 1970s may have led to a marked increase in the prevalence of infection in intermediate and definitive hosts and in the human population.[39] There is evidence that suggests that the incidence of cystic echinococcosis may have increased in the newly independent central Asian states (Kazakhstan, Uzbekistan, Kyrgyzstan, Tajikistan, Turkmenistan) due to the major social and political changes that affected veterinary and public health services following the collapse of the former Soviet Union in 1992.[40]

Echinococcus multilocularis (alveolar echinococcosis)

Description of the pathogen

Alveolar echinococcosis results from infection by the metacestode (larval) form of Echinococcus multilocularis. In rodents, the natural intermediate hosts, the larval mass proliferates rapidly by exogenous budding of germinative tissue and produces an alveolar-like pattern of microvesicles filled with protoscolices.[1] In humans, the larval mass resembles a malignancy in appearance and behavior, because it proliferates indefinitely by exogenous budding and invades the surrounding tissues. Protoscolices are rarely observed in infections of humans.

Epidemiology

The life cycle of E. multilocularis involves foxes and their rodent prey in ecosystems generally separate from humans.[2] However, there is ecologic overlap to humans, because fox and coyote populations have increasingly encroached upon suburban and urban areas of many regions, and domestic dogs or cats may become infected when they eat infected wild rodents.[41] Alveolar echinococcosis has been reported in parts of central Europe, much of Russia, the Central Asian republics, and western China, the northwestern portion of Canada, and western Alaska. Data on E. multilocularis from human cases are difficult to evaluate because of low human prevalence levels of E. multilocularis infection, and the long asymptomatic period of alveolar echinococcosis makes identification of infection trends in time and place difficult to assess.[8] The annual incidence in endemic areas of Europe has increased from a mean of 0.10 per 100 000 during 1993—2000 to a mean of 0.26 per 100 000 during 2001—2005.[42] There is evidence of parasites spreading from endemic to previously non-endemic areas in North America and North Island, Hokkaido, Japan, due principally to the movement or relocation of foxes. Hunters, trappers, and persons who work with fox fur are often exposed to alveolar hydatid disease. Hyperendemic foci have been described in some Eskimo villages of the North American tundra and in western China, where local dogs regularly feed on infected commensal rodents.[6,43] The infection of humans by the larval E. multilocularis is often the result of association with dogs that have eaten infected rodents. Villages within the zone of tundra may constitute hyperendemic foci because of the interaction between dogs and wild rodents that live as commensals in and around dwellings. In central Europe, rodents inhabiting cultivated fields and gardens become infected by ingesting embryophores expelled by foxes and, in turn, may be a source of infection for dogs. A recent case—control study demonstrated a higher risk of alveolar echinococcosis among individuals who owned dogs that killed game, dogs that roamed outdoors unattended, individuals who were farmers, and individuals who owned cats.[44] However, the risk of human alveolar echinococcosis from owning cats reported in this study has to be taken with caution. The role of cats in the transmission of E. multilocularis may not be as significant as once believed, as studies have shown they are much less susceptible to infection with the parasite than canids.[45] In rural regions of central North America, the cycle involves foxes and rodents of the genera Peromyscus and Microtus. The role of foxes in the zoonotic transmission of alveolar echinococcosis appears to be important, as demonstrated by increases in the incidence of human alveolar echinococcosis following the increase in population of foxes in certain parts of Europe.[42]

Clinical manifestations

The liver is the primary location of the metacestode of *E. multilocularis* in humans as well as in natural intermediate hosts. Local extension of the lesion and metastases to lungs and brain may follow.[9] In chronic alveolar echinococcosis infections, the lesion consists of a central necrotic cavity filled with a white amorphous material that is covered with a thin peripheral layer of dense fibrous tissue.[46] Focal areas of calcification exist, as does extensive infiltration by proliferating vesicles. The initial symptoms of alveolar hydatid disease are usually vague. Mild upper quadrant and epigastric pain with hepatomegaly may progress to obstructive jaundice. Patients eventually succumb to hepatic failure, invasion of contiguous structures, or, less frequently, metastases to the brain.[43] The mortality in progressive, clinically manifest cases may be 50—75%.[43] However, instances of spontaneous death of the cyst during its early stage of development have been reported in people with asymptomatic infection.

Laboratory findings and diagnosis

Alveolar echinococcosis typically becomes symptomatic in persons of advanced age; it closely mimics hepatic carcinoma or cirrhosis. Plain radiographs show hepatomegaly and characteristic scattered areas of radiolucency outlined by calcific rings 2—4 mm in diameter. The usual computed tomographic image of *E. multilocularis* infection is that of indistinct solid tumors with central necrotic areas and perinecrotic, plaque-like calcifications.[46] Results of serologic tests are usually positive at high titers; purified *E. multilocularis* antigens are highly specific and permit serologic discrimination between infections with *E. multilocularis* and *E. granulosus*.[47,48] Needle biopsy of the liver can confirm the diagnosis if larval elements are demonstrated. Exploratory laparotomy is often performed for diagnosis as well as determination of the size and extent of invasion.

Treatment

In alveolar echinococcosis, surgical resection of the entire larval mass, usually by excision of the entire affected lobe of the liver, is the preferred treatment; when involvement is extensive, wedge resections of the lesion may be attempted.[43] Because alveolar echinococcosis is often not diagnosed until the disease is advanced, the lesion is commonly inoperable. Long-term treatment with mebendazole (50 mg/kg/day) or albendazole (15 mg/kg/day) inhibits growth of larval *E. multilocularis*, reduces metastasis, and enhances both the quality and length of survival; prolonged therapy can eventually be larvicidal in some patients.[49,50] Liver transplantation has been employed successfully in otherwise terminal cases.[51] In a Swiss study, therapy for non-resectable alveolar echinococcosis with mebendazole and albendazole resulted in an increased 10-year survival rate of approximately 80% (versus 29% in untreated historical controls) and a 16- to 20-year survival rate of approximately 70% (versus 0% in historical controls).[41]

Preliminary in vitro studies suggest nitazoxanide and albendazole may be parasiticidal against *E. multilocularis* larvae, but further efficacy trials in humans are warranted to assess efficacy.[52]

Prevention

Eliminating *E. multilocularis* from its wild animal hosts is impractical; therefore, contact with dogs and foxes in areas where the infection is endemic should be avoided. Preventing infection in humans depends on education to improve hygiene and sanitation.[41] Infection in dogs and cats prone to eat infected rodents can be prevented by monthly treatments with praziquantel.

Echinococcus vogeli (polycystic echinococcosis)

A polycystic form of echinococcosis is caused by *E. vogeli*, the life cycle of which involves the bush dog and possibly other wild canids; domestic dogs are also susceptible. Pacas, agoutis, and spiny rats are the principal intermediate hosts. *E. vogeli* is indigenous to the humid tropical forests in central and northern South America.[2,5] In endemic areas, hunting dogs are often fed the raw viscera of pacas; dogs thus infected may then expose humans. Polycystic echinococcosis has been recognized in humans in Panama, Peru, Ecuador, Colombia, Venezuela, and Brazil.[53,54] A small number of polycystic echinococcosis cases in these geographic areas are caused by *E. oligarthrus*.

The characteristics of polycystic echinococcosis are intermediate between those of the cystic and alveolar forms.[53] The relatively large cysts are filled with liquid and contain brood capsules with numerous protoscolices. The primary localization is the liver, but cysts may spread to contiguous sites. Techniques useful for diagnosis of cystic or alveolar hydatid disease are also of value in polycystic hydatid disease. Because *E. vogeli* shares antigens with the other *Echinococcus spp*, most currently available immunodiagnostic tests do not permit species diagnosis. However, the hydatid cysts of *E. vogeli* differ from those of other species in the dimensions of the hooks of the protoscolices.

Because the lesions in polycystic echinococcosis are so extensive, surgical resection is always difficult and usually incomplete.[53,55] A combination of surgery with albendazole therapy is most likely to be successful.[56] The principles of management for cystic and alveolar echinococcoses also apply to polycystic echinococcosis.

Echinococcus shiquicus

Mitochondrial DNA sequencing and morphological studies have identified *E. shiquicus* as a new species with distinct characteristics from those of *E. granulosus* or *E. multilocularis*.[57] The larval form of *E. shiquicus* occurs in the plateau pika, *Ochotona curzoniae*, found in Shiqu County, in the Qinghai-Tibet plateau region of western Sichuan, China. The adult stage has been isolated from the Tibetan fox, *Vulpes ferrilata*. The metacestode develops into a unilocular cyst mainly in the liver. Its zoonotic transmission potential is presently unknown.

Echinococcus felidis

Recent mitochondrial DNA studies have identified *E. felidis* as a distinct species from any other *Echinococcus spp*.[58] The

adult stage has been isolated in African lions, but it is unclear if other felids, canids, or hyaenids may also be involved in the lifecycle. The larval form, which develops into a unilocular cyst, is believed to occur in wild ungulates. However, the specific intermediate hosts susceptible to infection remain to be identified. There are no data available on the pathogenicity of *E. felidis* to humans, but its public health impact may be minimal, as lions are largely restricted to national parks and game reserves where there is little human activity. *E. felidis* may have an impact on pastoralists in East Africa who coexist with wildlife.

Conflict of interest: No conflict of interest to declare.

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