Echinococcosis

Echinococciasis,
Hydatidosis,
Hydatid Disease

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Importance

Echinococcosis is a zoonotic disease caused by *Echinococcus* spp. tapeworms. The definitive hosts, which include dogs, other canids, hyenas and cats, carry the adult tapeworms subclinically. Dogs are particularly important in zoonotic transmission due to their close relationships with humans. Intermediate hosts are initially asymptomatic; however, the growth of the larvae, which form cysts in vital organs such as the liver and lungs, can lead to illness and death. Echinococcosis is a major public health problem in some countries, and it may be emerging or re-emerging in some areas. Approximately 2-3 million human cases are thought to occur worldwide.

Cystic echinococcosis, the most common form of the disease in people and domesticated animals, is caused by *Echinococcus granulosus sensu lato* (*E. granulosus s. l.*). Because the larvae of this organism usually develop as discrete single cysts, it is the least severe and most treatable form. Nevertheless, large or multiple cysts may cause irreversible damage to organs, and the rupture or puncture of the cyst can seed multiple organs with larvae or cause anaphylactic reactions. Humans typically become symptomatic many years after infection. Most livestock are slaughtered before the cysts become large enough to cause clinical signs, but if their entrails are fed to dogs, it perpetuates the cycle. Animals that live long enough, such as horses, may become ill. In addition, cystic echinococcosis causes economic losses from the condemnation of internal organs at meat inspection. In some cases, it may also result in decreased meat and milk production or decreased value of the fleece due to debilitation.

Alveolar echinococcosis, caused by *E multilocularis*, is less common than cystic echinococcosis, but it is very serious and more difficult to treat. The larvae of this organism grow as multiple, budding cysts, which can infiltrate entire organs and disseminate to distant sites including the brain. As well as affecting people, alveolar echinococcosis is reported to cause serious disease in animal intermediate hosts including dogs. The occurrence of this organism in a wildlife cycle between foxes and small mammals makes it difficult to prevent. Polycystic echinococcosis, which is usually caused by *Echinococcus vogeli* in humans, is similar to alveolar echinococcosis in the growth of the larvae and its presence in wildlife hosts. Other *Echinococcus* species seem to be rare in people or domesticated animals, but may affect wildlife.

Etiology

Echinococcosis is caused by several species of *Echinococcus*, tiny cestode parasites in the family Taeniidae. Currently recognized species include *Echinococcus granulosus sensu lato, E. multilocularis, E. vogeli, E. oligarthrus* and possibly *E. shiquicus.*

E. granulosus s.l. causes a type of echinococcosis known as cystic echinococcosis, unilocular echinococcosis or cystic hydatid disease. This species has traditionally been divided into strains, named G1 to G10, which have a degree of host adaptation (see "species affected"), and may be maintained in distinct cycles. These strains have generally been named after the intermediate host thought to be most important in perpetuating the life cycle. In some cases, other species may also maintain the strain (see Transmission/ Life Cycle and Species Affected for details). Strains may differ in their morphology, rate of development, virulence, geographic range and other factors. Some strains have been proposed as species. Three strains, the G1 sheep strain, G2 Tasmanian sheep strain and G3 buffalo strain, are grouped together in the species *Echinococcus granulosus sensu stricto.* The G4 strain, which occurs in equid intermediate hosts, and does not mature in media that support the growth of the sheep strains, , is called *E. equinus*. The G5 cattle strain also appears to be distinct, and has been designated *E. ortleppi.* The G6 camel strain, G7 pig strain, a poorly characterized G9 strain, and two cervid strains, G8 and G10, might comprise another species called *E. canadensis*. The G8 and G10 strains may eventually be split from the G6 and G7 strains. The G9 strain has been reported only from human cases

in Poland, and some authors consider it to be a variant of the G7 pig strain. A lion strain, called *E. felidis*, has been reported from Africa. Unlike most *Echinococcus* species, which have canids as their primary definitive hosts, this strain mainly uses felids. Some strains are still poorly characterized, and additional strains probably exist. *E. granulosus sensu lato* can be used as a general term for all of these species and strains.

E. multilocularis causes a type of echinococcosis known as alveolar echinococcosis, alveolar hydatid disease, multilocular echinococcosis or multivesicular hydatidosis. It has been divided into Eurasian, North American and Chinese 'strains,' which are less distinct than those of *E. granulosus s.l.* One group of organisms has been proposed as a distinct species, *Echinococcus shiquicus*. *E. shiquicus* has been isolated only from small mammals and Tibetan foxes (*Vulpes ferrilata*) from the Tibetan Plateau region of China. Whether it should receive its own species designation is still uncertain.

Infections with *Echinococcus vogeli* and *Echinococcus oligarthrus* are usually known as polycystic echinococcosis (or neotropical polycystic echinococcosis), from the form of the disease in intermediate hosts. Because *E. oligarthrus* has been reported only as one or more discrete cysts in humans, this disease has also been called unicystic echinococcosis.

Zoonotic species

Some strains or species of *Echinococcus* affect people infrequently, or grow relatively slowly and are less likely to cause disease. *E. oligarthrus* seems to be extremely rare in people, and *E. equinus* (*E. granulosus* strain G4) has not been reported to be zoonotic in the literature. The G1 sheep strain of *E. granulosus s. l.*, which is particularly widespread, is the most frequent cause of disease in humans. Regionally, other *E. granulosus s. l.* strains/ species may be more important than G1.

Geographic Distribution

E. granulosus s. l. occurs worldwide, with the exception of a few countries such as Iceland and Greenland. Within an area, its distribution may be focal. Each strain/ species has a distinct geographic range. The G1 sheep strain is cosmopolitan; it has been reported in Europe, the Middle East, Africa, parts of Asia, Australian, New Zealand, and North and South America. In North America, this strain has mainly been reported from the western U.S. It also occurs in Mexico. The G2 Tasmanian sheep strain was once thought to be limited in its geographic range, but it has now been identified in Asia, South America, Africa and Europe, as well as in Tasmania. The G3 strain has been reported from Asia, Europe and South America, and the G4 strain (*E. equinus*) is known to occur in Europe, the Middle East and Africa. The G5 cattle strain (*E. ortleppi)* has been documented in Europe, Africa, parts of Asia, and South America, and the G6 camel strain is known to occur in the Middle East, Africa, Asia and South America. The G7 pig strain has been identified in Europe, Russia, South America and Mexico, while the closely related G9 strain has been reported only from Poland. The G8 and G10 cervid strains have been found in North America, mainly in Canada and some northern U.S. states, as well as in Eurasia. *E. felidis* (the "lion strain") is thought to occur only in Africa. Molecular techniques have recognized many strains/species in new areas during the last 5-10 years, and these geographic ranges are probably incomplete.

E. multilocularis is found primarily in the northern hemisphere. This parasite is either expanding its geographic range or it is being identified in new areas due to increased surveillance. *E. multilocularis* has been reported in much of northern and central Eurasia eastward to Japan. It is widely distributed in continental Europe. This organism also occurs in North America, where it is primarily found in Canada, Alaska and the north central U.S. from Montana to central Ohio.

E. vogeli and *E. oligarthrus* have been found only in Central and South America, and *E. shiquicus* has been identified on the Tibetan plateau in China.

Transmission and Life Cycle

Echinococcus species have an indirect life cycle, and must develop in both an intermediate and a definitive host. In many cases, the parasite cycles through specific predators or scavengers, and their prey.

Echinococcus granulosus s. l.

The definitive hosts for *E. granulosus s. l.* (canids, felids, and hyaenids) become infected when they ingest cysts (metacestodes) in the tissues of the intermediate hosts. Feeding the viscera of intermediate hosts to dogs perpetuates cycles in domesticated animals. The cysts develop into tapeworms, which mature in the host's small intestine. Gravid proglottids or eggs are shed in the feces, and are immediately infective. *Echinococcus* eggs have a sticky coat that will adhere to an animal's fur and other objects. Insects such as flies and beetles, or birds, can also act as mechanical vectors. In addition, the shed proglottids may perform rhythmic contractions that help to disperse the eggs widely on pastures.

Under ideal conditions, *E. granulosus s. l.* eggs remain viable for several weeks or months in pastures or gardens, and on fomites. They survive best under moist conditions and in moderate temperatures. Viable eggs have been found in water and damp sand for three weeks at 30°C, 225 days at 6°C and 32 days at 10-21°C. The eggs survive for only short periods of time if they are exposed to direct sunlight and dry conditions.

The intermediate hosts include a large number of domesticated and wild animals, particularly herbivores. Humans can also be infected. If an intermediate host ingests the eggs, the larvae are released, penetrate the intestinal wall, and are carried in blood or lymph to the target organs.

Parasites can develop into cysts in many different organs, but they are found most often in the liver and, less frequently, the lungs. The rate of development varies with the intermediate host and species of parasite, but the cysts usually grow slowly. Their diameter generally increases from less than 1 cm to 5 cm each year. Some cysts may persist unchanged for years. Most *E. granulosus s. l.* cysts are 1-7 cm in diameter when they are discovered, but some may eventually reach 20 cm. Each fluid-filled cyst is surrounded by a fibrous wall from the host and contains two walls derived from the parasite: an outer laminated membrane and an inner membrane called the germinal layer. Brood capsules develop from the germinal membrane. Each brood capsule contains one to several invaginated heads (protoscolices) that can develop into adult tapeworms if they are ingested by the definitive host. Capsules and protoscolices either float freely in the hydatid fluid or adhere to the wall with a peduncle; the capsules and protoscolices that float freely are known as "hydatid sand." If a cyst ruptures, the hydatid sand can develop into new cysts. Some cysts are sterile; they either never produce brood capsules, or they become sterile after bacterial infection or calcification. The percentage of sterile cysts varies with the intermediate host and its susceptibility to a particular strain/ species.

In some hosts, few or no cysts of a given parasite species/ strain appear to be fertile and viable. These hosts serve as indicators for the presence of that organism, but are unimportant in perpetuating it. The importance of a host species, and the proportion of sterile cysts, seems to vary with the geographic region in some cases. For example, sheep are the primary intermediate hosts for the G1 strains in some countries, and many or most cysts in cattle are not viable. In other locations, livestock such as cattle and/or camels have a high proportion of fertile cysts and participate in the G1 parasite's life cycle. In one study, the percentage of cattle with fertile and viable G1 cysts was considerably higher among cattle in Argentina than Spain. It has not been determined whether host immune responses, management factors or parasite genetic differences are responsible for this difference.

Echinococcus multilocularis

The life cycle and transmission of *E. multilocularis* is very similar to that of *E. granulosus s. l.*. Although this species usually cycles in wildlife, with a variety of carnivores serving as definitive hosts, the adult tapeworms can also mature in domesticated dogs and cats. Eggs can remain viable for up to a year in a moist environment at low temperatures. *E multilocularis* eggs are cold resistant to –50°C, but they are killed by desiccation, high temperatures, or sustained temperatures of –70°C or below. The intermediate hosts are usually small mammals, particularly rodents, but domesticated animals and humans can also be infected. Dogs can act as intermediate hosts, either by autoinfection or by ingesting eggs shed in the feces of another definitive host, such as a fox. Extraintestinal infections do not seem to occur in foxes.

In both animal and human intermediate hosts, the primary metacestodes are found almost exclusively in the liver. The germinal membrane of *E. multilocularis* proliferates externally, rather than internally, to form a multilocular structure with many small cysts. These vesicles are usually 1-10 mm in diameter, but occasionally grow as large as 20-30 mm, and are embedded in fibrous connective tissue or a semisolid matrix. Hundreds to thousands of protoscolices develop from the germinal membrane in some intermediate hosts. Protoscolices may be absent or rare in humans.

E. multilocularis cysts resemble tumors: they are not contained within a capsule and are very invasive. Eventually, they can completely infiltrate an organ, and spread to other organs and tissues nearby. The cysts can also metastasize to distant sites such as the central nervous system (CNS), lungs or bones.

Echinococcus vogeli

The definitive hosts for *E. vogeli* are bush dogs (*Speothos venaticus*) and the intermediate hosts are South American rodents, especially pacas (*Cuniculus paca*). Dogs, which may be given the entrails from pacas after a hunt, can also act as definitive hosts. The metacestode is found primarily in the liver of the intermediate host, but it can also occur in the lungs and other organs. In pacas, *E. vogeli* cysts are fluid-filled, usually 0.5 cm to 6 cm in diameter, and can occur singly or as aggregates. These cysts are often interconnected and can have multiple chambers. *E. vogeli* undergoes exogenous proliferation in accidental hosts such as primates, resulting in multichambered cysts as well as endogenous daughter cysts. These proliferating cysts, like those of *E. multilocularis*, are invasive. Exogenous proliferation does not seem to occur in the natural host.

Echinococcus oligarthrus

The definitive hosts for *E. oligarthrus* are wild felids, and the intermediate hosts are rodents. This species can mature in experimentally infected housecats. In the intermediate host, cysts develop in the muscles, subcutaneous tissues, and internal organs such as the heart and lungs. The cysts resemble those of *E. vogeli* and can reach up to 5 cm in diameter. Exogenous proliferation has not been reported. In the rare cases described in humans, unicystic single or multiple metacestodes were found behind the eye or in the heart.

Transmission to humans

Humans act as intermediate hosts for *Echinococcus* spp., and are infected when they ingest tapeworm eggs from the definitive host. The eggs may be eaten in foods such as vegetables, fruits or herbs, or drunk in contaminated water. They can also stick to the hands when a person pets an infected dog or cat, handles a wild animal or its carcass, or

touches contaminated soil and vegetation. Uninfected pets may carry the eggs on their fur if they contact the feces of infected wild hosts. This is probably more common in dogs, which may roll in feces.

Disinfection

Chemical disinfection is unreliable for clinical samples, but a percentage of the eggs may be destroyed by sodium hypochlorite. *Echinococcus* eggs are inactivated by heat (hot water of 85°C or above is effective) and desiccation. They can also be killed by freezing at –80°C for 48 hours or –70°C for 4 days.

Laboratories can be decontaminated by setting the environmental conditions to 40% humidity combined with 30°C room temperature for at least 48 hours.

Infections in Humans

Incubation Period

The incubation period for echinococcosis varies from months to years. It can be as long as 20-30 years, if the cyst grows slowly and is not in a critical location.

Clinical Signs

The symptoms of echinococcosis depend on the size, number and the location of the metacestodes. Until the cysts become large enough to damage adjacent tissues and organs, they are usually asymptomatic. The clinical signs are those of a mass lesion.

Cystic echinococcosis (Echinococcus granulosus s. l.)

E. granulosus s. l. cysts can remain asymptomatic for many years. They are usually well tolerated until they cause pressure on surrounding tissues. The symptoms resemble those of a slowly growing tumor. Although most people have only one cyst, multiple cysts can be found. Approximately 60-70% of *E. granulosus s. l.* cysts occur in the liver and 20-25% in the lungs. The remaining cysts can be found almost anywhere in the body including the bones, kidneys, spleen, muscles, CNS and behind the eye. Depending on the location, some cysts can become very large and may contain up to several liters of fluid. Others in critical locations such as the brain become symptomatic when they are still small. Nonspecific signs may include anorexia, weight loss and weakness. Secondary cystic echinococcosis occurs when a cyst leaks or ruptures; dissemination is seen mainly in the abdominal cavity. Leakage of the cyst fluid can also cause allergic reactions including shaking chills and/or fever, asthma, pruritus, urticaria or life-threatening anaphylaxis.

Other symptoms vary with the location(s) of the cysts. When the cyst occurs in the liver, common symptoms include abdominal pain, nausea, vomiting and indigestion. If the cyst obstructs the biliary system, it can mimic gallstones and cause pain or cholestatic jaundice. Hepatomegaly, anemia, pleural pain, ascites and portal hypertension can also be seen. Cysts in the lungs are more likely to be clinically apparent while they are still small, compared to those in the liver. In the lungs, cysts can cause respiratory signs including chronic cough, chest pain, dyspnea and hemoptysis, particularly if they rupture. Abscess formation (from secondary bacterial infection of the cyst) and pneumothorax can also occur, and fragments of the capsule may cause arterial embolism. Neurologic signs, including blindness and seizures, may be seen if the brain or spinal cord is affected. Cysts in the bones can destroy the structure of the bone and result in spontaneous fractures. In the heart, a cyst can result in pericardial effusion, heart block or other arrhythmias, and sudden death. Cysts in any location may become secondarily infected by bacteria.

E. granulosus s. l. cysts can also be asymptomatic throughout the individual's life, and may be incidental findings at surgery or autopsy. Some cysts may die and not develop further.

Alveolar echinococcosis - (Echinococcus multilocularis)

The primary lesion of *E. multilocularis* is almost always in the liver, and the course of the disease is slow. During the early stages, the infection is usually asymptomatic. Larger tumors cause hepatomegaly and epigastric pain. Ascites, malnutrition, jaundice and signs of hepatic failure may occur in later stages of disease. Splenomegaly can also be seen.

E. multilocularis cysts are very dangerous as they are not enclosed within a membrane and invade tissues by budding outward; alveolar hydatidosis is progressive and malignant. The cysts can spread to nearby organs and metastasize to the brain, lungs, mediastinum and other organs or tissues. Sometimes, the primary cyst dies early in its development, and remains asymptomatic.

Polycystic hydatidosis (E. vogeli and E. oligarthrus)

E. vogeli tends to occur initially in the liver; however, the cysts are invasive and can spread to nearby organs and tissues. The clinical signs resemble alveolar echinococcosis. Common symptoms with liver involvement include hepatomegaly, abdominal distension, weight loss, abdominal pain, jaundice and anemia. Palpable masses, which may or may not be painful, can be present in the liver or abdomen, and there may be signs of portal hypertension or biliary obstruction. Coughing, chest pain and hemoptysis can be seen if the lung in involved, and the rupture of esophageal varices can result in hematemesis. Congestive heart failure and acute pulmonary edema have been reported when the heart was involved. In some cases, cysts have been found only in the mesentery of the intestinal tract and/or the stomach. Calcified metacestodes have also been reported.

E. oligarthrus localizes in the internal organs, subcutaneous tissues and muscles of its normal intermediate hosts. Little is known about this organism in humans; only rare cases have been described. In two cases, a single cyst behind the eye caused irritation of the eye, exophthalmia and blindness. In another case, cysts were found in the heart of a person who had died of tetanus. The lesions included an enlarged heart, myocarditis, and excess pericardial fluid.

Communicability

Echinococcosis is not transmitted from person to person. Humans can transmit the infection to the definitive hosts if affected tissues are eaten, but this does not occur in most societies due to cultural practices.

Diagnostic Tests

In humans, echinococcosis is diagnosed mainly with imaging techniques such as ultrasonography, radiology, magnetic resonance imaging (MRI) or CT scanning, supported by serology. Serological tests used in humans include enzyme-linked immunosorbent assays (ELISAs), indirect immunofluorescence, indirect hemagglutination, immunoblotting and latex agglutination. Complement fixation is now rarely used. Some people with cysts do not develop detectable antibodies. False positives, which include cross-reactions with other taeniid cestodes, are also possible.

Biopsies can also be used in diagnosis, but there is risk of cyst leakage or rupture, and antiparasitic drugs must be given concurrently. Ultrasonography-guided fine-needle puncture can distinguish cysts from tumors, abscesses and other lesions. The cyst fluid recovered with this technique can be examined for protoscolices and other evidence of the parasites. It may also be tested for *Echinococcus* antigens with an antigen-detection ELISA, or for parasite DNA using polymerase chain reaction (PCR) assays. When the lungs are affected, protoscolices might be found in sputum or bronchial washings.

Histopathology is usually sufficient to diagnose echinococcosis in tissues, but antigen detection or PCR may be needed in some cases, such as when the cyst is calcified.

Echinococcus species can be distinguished by PCR followed by sequencing or restriction fragment length polymorphism analysis. Both nuclear and mitochondrial genes are used in differentiating species/ strains. Cysts from different species can also be distinguished by the morphology of the protoscolices, if they are present. In humans, some cysts are "sterile"; they do not produce protoscolices.

Treatment

Cysts are often removed surgically. The success rate varies with the species of *Echinococcus* and the location and size of the cyst(s). In some situations, particularly with *E. multilocularis* or *E. vogeli* infections, it may not be possible to remove the entire cyst. Long-term post-surgical treatment with antiparasitic drugs such as albendazole or mebendazole may shrink or destroy the organism, help prevent it from regrowing and/ or ameliorate the symptoms. Drug treatment is also an alternative to surgery in some cases. Another treatment option is the removal of most of the cyst contents and the introduction of an anthelminthic chemical into the cyst under ultrasonographic guidance (PAIR - puncture, aspiration, injection, and re-aspiration). Sometimes (e.g., small inactive cysts in certain locations) a "wait and see" approach might also be appropriate. In severe cases of alveolar echinococcosis, a liver transplant may be an option.

Prevention

Controlling *Echinococcus* spp. that occur in domesticated animal cycles reduces human exposure. In particular, dogs should not be fed the entrails from livestock at slaughter. Because dogs and cats can also be infected from parasites in wildlife cycles, they should not be allowed to hunt wild animals, or be fed any tissues from these species. In endemic areas, regular testing and/or treatment is advisable in animals allowed outside.

It is difficult to completely prevent exposure to *Echinococcus* spp. eggs from wild animals; however, food safety precautions, combined with good hygiene, can be helpful. All fruits and vegetables, particularly those picked in the wild, should be washed thoroughly to remove any eggs. Fences should be placed around vegetable gardens to keep animals, especially dogs and other canids, away. The hands should always be washed after handling pets, farming, gardening or preparing food, and before eating. Untreated water from sources such as lakes may also contain *Echinococcus* eggs, and should be avoided. Wild carnivores, especially canids and felids, should be discouraged from coming close to homes. If these animals or their carcasses must be handled, gloves should be used. In some areas, foxes have been treated with antiparasitic drugs in bait, to decrease the prevalence of *E. multilocularis*. Meat, particularly canine intestines, should be thoroughly cooked before eating.

Anyone who handles the definitive hosts or material that may be contaminated with eggs should use appropriate personal protective equipment. In some countries, *Echinococcus* spp. must be handled in a BSL-3 laboratory. Regular surveillance with serological tests can be helpful in high-risk populations such as laboratory personnel working with eggs, or children who have been exposed to the feces of infected foxes. The purpose of testing is to detect cysts in the early stages, when they are most treatable. Vaccines are not available for people.

Morbidity and Mortality

Most cases of echinococcosis are of the cystic form. The annual incidence of cystic echinococcosis in endemic regions usually varies from less than 1 to 200 cases per 100,000 population, while the annual incidence of alveolar

echinococcosis is 0.03 to 1.2 cases per 100,000 population. These numbers may be higher in some endemic foci. Although cysts have been diagnosed even in infants, most symptomatic infections are reported in adults due to the slow growth of the parasite.

Cystic echinococcosis is particularly common in rural areas, particularly sheep-raising regions where dogs are given the entrails of livestock to eat. It is also prevalent when canine intestines are part of the human diet (e.g., in parts of Kenya). Hunters, fur trappers, fur traders, wildlife veterinarians and wildlife biologists may have an increased risk of contracting alveolar echinococcosis due to increased exposure.

Although cystic echinococcosis is a potentially life-threatening disease, the cysts are usually well tolerated unless they damage adjacent tissues or rupture. Many cysts are asymptomatic throughout the individual's life, and may be incidental findings at surgery or autopsy. This form of echinococcosis is usually treatable; however, some infections can be fatal if the cyst ruptures and causes anaphylactic shock, or if it damages vital organs. The prognosis for symptomatic cysts located in the brain, kidney, heart or other vital organs is grave.

Alveolar echinococcosis is uncommon but very serious. Many infections are diagnosed late, when the risk of a serious or fatal outcome is increased. Treatment may be curative or it may prolong survival and ameliorate the symptoms. Improved survival has been reported with modern treatment methods. In Europe, the average life expectancy at diagnosis was only 3 years in the 1970s, but increased to 20 years by 2005. The 10-year survival rate of patients on long-term drug treatment is reported to be 80%. Because the multilocular cyst is very invasive and also metastasizes, a complete surgical cure is rare except in the early stages of infection. Without treatment, 70-100% of all cases are fatal.

Polycystic echinococcosis is also uncommon. Approximately 170 cases, mainly caused by *E. vogeli*, had been reported as of 2007. Like alveolar echinococcosis, polycystic echinococcosis caused by this organism can be a very serious, life-threatening disease. *E. oligarthrus* has been reported very rarely in people. The reason for this is uncertain; however, the definitive hosts are wild felids, and burial of the feces may decrease exposure.

Infections in Animals

Species Affected

Echinococcus granulosus s. l.

The definitive hosts for *E. granulosus s. l.* include many members of the Canidae, such as dogs, wolves, coyotes, foxes, jackals and dingoes, as well as some species of cats (Felidae) and hyenas (Hyaenidae). A wide variety of intermediate hosts, which are mainly herbivores or omnivores, can be affected.. The degree of host specificity seems to vary with the parasite strain/ species.

Sheep are important intermediate hosts for the G1 and G2 strains. The G1 strain also occurs in other livestock including cattle, pigs, camels, goats, horses, yaks and water buffalo, as well as in some wildlife intermediate hosts including wild boar. Cattle have been considered poor hosts for the G1 strain, with studies from some countries reporting that this parasite mainly cycles between sheep and dogs, and that few cysts in cattle are fertile. However, recent studies found that cattle, camels and other livestock may be important in maintaining this strain in some geographic areas. In addition to sheep, the G2 strain has been found in cattle and water buffalo. The G3 (water) buffalo strain is reported to produce fertile cysts in water buffalo, sheep, goats and pigs, and also occurs in cattle and camels. In the domestic cycle, dogs are usually the definitive hosts for all three strains of *E. granulosus s.s.* The G2 strain has also been reported in foxes, and the G3 strain might occur in this host. The G1 strain has many definitive hosts including dingoes (*Canis lupus dingo*), jackals (*Canis aureus*), wolves (*Canis lupus*), foxes and hyenas, which can maintain this parasite in wildlife cycles. In Australia, the G1 strain is reported to cycle between dingoes and (less often) red foxes (*Vulpes vulpes*) as definitive hosts, and wallabies (*Macropus* spp. and *Wallabia* spp.), kangaroos (*Macropus* spp.), feral pigs (*Sus scrofa*) and wombats (*Vombatus ursinus*) as intermediate hosts. In southern Argentina, a wildlife cycle between a native species of fox (*Pseudalopex culpaeus*) and introduced European hares (*Lepus europaeus*) has been reported.

Dogs are reported to be definitive hosts for the G4, G5, G6 and G7 strains. The G5 strain has also been found in jackals in Africa. The intermediate hosts for the G4 strain (*E. equinus*) are equids such as horses, donkeys and zebras. The G5 strain (*E. ortleppi*) infects cattle. It has also been reported in water buffalo, sheep, goats, pigs and a zebra, and it was reported to produce fertile cysts in pigs. In addition to camels, the G6 camel strain occurs in cattle, sheep and goats, and it may also affect pigs. The G7 strain is primarily a parasite of domesticated pigs and wild boar (*Sus scrofa*), but it has been described in goats and sheep. The intermediate and definitive hosts for the G9 strain (which might be a variant of G7) are unknown.

Two strains, G8 and G10, have been described in cervids. Important intermediate hosts include moose (*Alces alces*), elk (C*ervus elephas*) and reindeer/ caribou (*Rangifer tarandus*). Wolves and dogs can act as definitive hosts for both strains. In some areas, there may be a domestic cycle between dogs and domesticated reindeer.

Lions are thought to be the definitive hosts for *E. felidis*, which is also known as the "lion strain" of *E. granulosus.* Eggs from this species were documented in a spotted hyena (*Crocuta crocuta*), but the importance of definitive hosts other than lions is unknown. Reported

intermediate hosts include zebras (*Equus quagga*), wildebeest (*Connochaetes* spp.), warthogs (*Phacochoerus* spp.), bushpigs (*Potamochoerus larvatus, P. porcus)*, buffalo and various species of antelope. Zebras were confirmed as an intermediate host by experimental infection of lions, but some other intermediate hosts could have been carrying species other than *E. felidis*.

In some cases, the species/ strain of *E. granulosus s.l.* in a host was not identified. This is particularly common in older research. In the 1970s, *E. granulosus* was reported to occur among coyotes and deer in California. The parasite was thought to be the same organism found among sheep in the western U.S., i.e. G1; however, there are no published reports of surveys since the advent of genetic techniques. Recently, *E. granulosus s.l.* was reported in a cycle involving wolves, elk (*Cervus elaphus*) and mule deer (*Odocoileus hemionus*) in Montana and Idaho. Coyotes or other predators were not examined. The authors speculated that this organism belongs to the G8/G10 cervid strains (also known as the "Northern biotype"), which circulates in Canada. Definitive identification has not yet been published.

With the increased use of genetic techniques to identify *E. granulosus* species/ strains, the range of intermediate hosts that can maintain a given species/ strain seems likely to expand.

Echinococcus multilocularis

The definitive hosts for *E. multilocularis* are primarily foxes, particularly red foxes (*Vulpes vulpes*) and arctic foxes (*Alopex lagopus*). Tibetan foxes (*Vulpes ferrilata*), and sand foxes (*Vulpes corsac*) are regionally important. Additional definitive hosts include wolves, coyotes (*C. latrans*), raccoon dogs (*Nyctereutes procyonoides*), lynx (*Lynx* spp.), wild cats (*Felis silvestris*) and jackals; the importance of each species may vary with the geographic region. *E. multilocularis* can also mature in domesticated dogs and cats. Some studies have found that cats seem to be less susceptible than dogs and have lower tapeworm burdens; however, one recent study from Europe reported that a similar proportion of dogs and cats shed this organism.

The intermediate hosts for *E. multilocularis* are usually rodents and other small mammals such as voles (*Microtus* spp.), lemmings, shrews and mice. Infections have also been reported in other species including muskrats (*Ondatra zibethicus*) and lagomorphs. Humans and domesticated mammals occasionally act as intermediate or accidental hosts: cysts have been reported in dogs, domesticated and wild pigs , horses, nutrias (*Myocastor* spp.) and non-human primates. Some hosts, such as pigs and horses, are not thought to be involved in perpetuating the parasite, as cyst development seems to stop at an early stage. However, this might be influenced by how long the host lives, and fertile cysts might occur in older animals. A dog can be both a definitive host and an intermediate host at the same time. Foxes have never been reported to be intermediate hosts.

Echinococcus shiquicus

Echinococcus shiquicus has been described in plateau pika (*Ochotona curzoniae*), which serve as the intermediate host, and Tibetan foxes (*Vulpes ferrilata)*, which are the definitive hosts.

Echinococcus vogeli

The most important definitive host for *E. vogeli* is the bush dog (*Speothos venaticus*), a canid found in South America. *Cerdocyon thous*, the crab-eating fox, has been infected experimentally, and other wild canids might be susceptible. Domesticated dogs can also serve as definitive hosts. Pacas (*Cuniculus paca*) seem to be the most important intermediate hosts, but cysts have also been reported in agoutis (*Dasyprocta* spp.) and nutrias, as well as in humans and nonhuman primates including captive orangutans and gorillas.

Echinococcus oligarthrus

The definitive hosts for *E. oligarthrus* are wild felids including the pampas cat (*Felis colocolo*), Geoffroy's cat (*F. geoffroyi*), ocelot (*F. pardalis*), jaguarundi (*F. yagouaroundi*), jaguar (*Panthera onca*), and puma (*Puma concolor*). *E. oligarthrus* was also found in a bobcat (*Lynx rufus*) in northern Mexico, and it can mature in experimentally infected housecats. The intermediate hosts for *E. oligarthrus* are wild rodents including agoutis, spiny rats (*Proechimys* spp.) and pacas. Infections have also been reported in opossums (*Didelphis marsupialis*). Climbing rats (*Tylomys panamensis*), cotton rats (*Sigmodon hispidus*) and Mongolian gerbils have been infected experimentally. Humans can act as intermediate hosts but this is very rare.

Incubation Period

Echinococcus cysts grow slowly and do not usually become symptomatic until they damage adjacent tissues and organs. *E. multilocularis* can kill rodent intermediate hosts within weeks. The incubation period for *E. granulosus s. l., E. multilocularis* or *E. vogeli* in larger mammals is unknown. However, many asymptomatic *E. granulosus s. l.* cysts are found in livestock at slaughter, suggesting that this species may remain subclinical for years. In nonhuman primates infected by *E. vogeli* at a zoo, clinical signs developed over a period of approximately 10 years.

Clinical Signs

Definitive hosts

Echinococcus spp. are usually carried asymptomatically in their definitive hosts. Large numbers of parasites may be able to cause enteritis and diarrhea, but this seems to be rare; thousands of adult parasites have been found in asymptomatic dogs and foxes.

Intermediate hosts – Echinococcus granulosus s. l.

There is little information on natural infections with *E. granulosus s. l.* in domesticated animals. The cysts grow slowly and are usually asymptomatic until they are large enough to put pressure on adjacent tissues and organs. Livestock are often slaughtered before this occurs. If clinical signs are seen, they are those of a mass lesion and vary with the organ affected. Most cysts are found in the liver and lungs, but they may also occur in many other organs. Symptoms that have been reported occasionally in sheep include hepatic disorders with ascites and jaundice, as well as bronchopneumonia, heart failure, poor growth, weakness and lameness.

Intermediate hosts – Echinococcus multilocularis

E. multilocularis usually affects the liver, but, in more advanced cases, metastatic lesions may be found in other organs including the lungs and brain. The tumor-like cysts can kill rodents within a few weeks of infection. Symptomatic infections, associated primarily with lesions in the liver and abdominal cavity, have also been reported in dogs and nonhuman primates. In eleven dogs, progressive abdominal enlargement, without severe clinical signs, was the most consistent sign. Ascites, abdominal masses, hepatomegaly, dyspnea, intermittent diarrhea, nausea, vomiting and weight loss have also been reported. In advanced disease, cysts may seed multiple organs, causing severe illness and death within weeks. In one dog, a single cystic lesion was reported in the subcutaneous tissues.

Asymptomatic hepatic lesions have also been reported in pigs and horses, as an incidental finding at necropsy.

Intermediate hosts – Echinococcus vogeli and Echinococcus oligarthrus

E. oligarthrus has not been documented in domesticated animal intermediate hosts. Two outbreaks caused by *E. vogeli*, one affecting nutrias and the other in nonhuman primates, have been reported in zoos. Orangutans and gorillas developed severe clinical signs including very pendulous abdomens. A number of animals died or had to be euthanized. In pacas, *E. vogeli* does not seem to be symptomatic unless the cysts become very large.

Post Mortem Lesions

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There are no lesions in the definitive hosts. Adult *Echinococcus* tapeworms are tiny, usually vary from 1.2 mm to 7 mm in length, and are attached to the small intestine. Most species have five or fewer segments, although some individual specimens may have up to seven. In the intermediate hosts, the cysts are grossly apparent in tissues at necropsy.

E. granulosus s. l. metacestodes are usually individual fluid-filled cysts, surrounded by a fibrous wall. Most cysts are 1-7 cm in diameter, but some can become much bigger. Some cysts may be calcified, necrotic or infected. In general, multilocular cysts are rare; however, infertile, multilocular cysts were common in yaks infected with the G1 strain of *E. granulosus s.s.*. Although most cysts occur in the liver, some may be found only in the lungs or, less often, in other internal organs including the bones. Organs to be examined in large animals should be palpated or incised if cysts are not seen.

E. multilocularis metacestodes occur initially in the liver, but they can metastasize to other organs, particularly the lungs and CNS. These multilocular cysts have a semisolid matrix and resemble malignant tumors. They may be firm and lobulated or contain viscous fluid, and can contain many scattered transparent cysts of a few millimeters to centimeters in diameter. The center of the lesion may be necrotic. In pigs, *E. multilocularis* lesions may be sharply demarcated, dense white foci of approximately 1-20 mm in diameter.

In their natural hosts, the cysts of *E. vogeli* and *E. oligarthrus* can occur singly or as aggregates. Exogenous proliferation occurs in nonhuman primates and possibly in other aberrant hosts.

Communicability

Definitive hosts can transmit echinococcosis to susceptible intermediate hosts, via eggs shed in the feces. *E. granulosus s. l.* becomes prepatent in 32 to 80 days in the definitive host; this period varies with the species or strain. Although the parasites stop laying eggs after 6 to 10 months in dogs, the adult worms may survive for up to three years in some cases. *E. multilocularis* usually becomes prepatent in foxes or dogs in 28 to 35 days. Experimentally infected dogs and foxes have shed eggs for 1 day to 4 months, with shedding becoming more irregular during the later stages. The adult worms are estimated to survive in the definitive host for approximately five months.

Intermediate hosts can only transmit infections to definitive hosts if their tissues contain mature cysts with protoscolices, and these cysts are ingested. The percentage of viable cysts can vary with the host and the species or strain of *Echinococcus*. Most *E. granulosus s. l.* cysts in sheep are fully infectious. Feeding the viscera of intermediate hosts to dogs perpetuates cycles in domesticated animals Intermediate hosts cannot transmit echinococcosis by casual contact.

Diagnostic Tests

Echinococcosis in the definitive hosts

Infective material that may contain eggs should be decontaminated (e.g., by freezing carcasses, intestines or feces at ultra-low temperatures), and personal protective equipment should be used to reduce the risk of human exposure during diagnostic investigations.

Infected dogs and cats cannot be identified by routine fecal testing: *Echinococcus* eggs are morphologically indistinguishable from *Taenia* spp., and the tiny proglottids are rarely noticed in feces. ELISAs that detect *Echinococcus* antigens in fecal samples (coproantigen ELISA) can be used to screen definitive hosts. This assay can detect both prepatent and patent infections. A PCR assay designed for fecal samples (copro-DNA assay) is mainly used to confirm the infection or to identify eggs from the feces. *Echinococcus* adults or their proglottids can also be found in the definitive host after purgation with arecoline compounds.

Direct examination of the intestines at necropsy may be used in some circumstances (e.g., in research or if the animal has died). The small intestine is collected as soon as possible after death, and tied at both ends. If the intestines are not frozen or fixed with formalin, they should be inspected as soon as possible, because the adult tapeworms can be digested within 24 hours. *Echinococcus* spp. tapeworms can be examined and counted with a hand lens. Sedimentation and counting, intestinal scraping, or the 'shaking in a vessel' technique can be used for a quantitative analysis of the number of parasites.

Echinococcus species can be distinguished by PCR followed by sequencing or restriction fragment length polymorphism analysis. The parasites also differ in their morphology and can be identified by experts. *E. granulosus s. l.* adults usually have 3 to 4 segments and are 3-6 mm long. However, some individual worms may have as few as 2 or as many as 7 segments, and can be up to 11 mm in length. The scolex has four suckers and a double row of 28-50 hooks, and it is typically followed by a germinative neck region, one developing proglottid, one mature proglottid and one gravid proglottid. The last (gravid) segment is usually more than half as long as the worm. In dogs, this species is usually found in the first third of the small intestine. *E. multilocularis* adults have 2 to 6 (usually 4-5) segments and are 1.2-4.5 mm long. The scolex has 26-36 hooks in a double row. In dogs, this species usually occurs from the middle to the end of the small intestine. *E. oligarthrus* and *E. vogeli* adults usually have three segments. *E. oligarthrus* is approximately 2-3 mm long and . *E. vogeli* is 3.9-5.6 mm long. In addition to these characteristics, *Echinococcus* species have subtle differences in their mature proglottids.

Echinococcosis in the intermediate hosts

In animal intermediate hosts, echinococcosis is mainly diagnosed at necropsy, or occasionally at surgery. Fine needle biopsy might also be used in live animals, but the possibility of cyst leakage or rupture (similarly to humans) should be considered. Metacestodes and protoscolices in cyst fluid or tissues can be identified by histology. Antigen detection or PCR can also be done. DNA techniques are particularly useful for distinguishing *Echinococcus* species or strains (especially among *E. granulosus s.l.*), or for identifying small, degenerated or calcified lesions. Ultrasound and other imaging methods may be helpful in some species such as dogs, but a biopsy or exploratory laparotomy might be required for a definitive diagnosis.

Serological tests are not generally used for diagnosis in domesticated animals. A species of *Echinococcus* sometimes induces relatively poor serological responses in its usual intermediate hosts. ELISA tests may be useful for serological diagnosis in infected sheep flocks, but they are not reliable in individual animals. Serology might also be of some use, in conjunction with imaging techniques, in dogs with cysts; however, antibodies can be caused by previous infections with the adult tapeworms, and cross-reactions can occur with *Taenia* species.

Treatment

In the definitive host, *Echinococcus* spp. can be treated with anthelminthic drugs. Praziquantel, which is effective against both juvenile and adult *Echinococcus* parasites, is often used.

In intermediate hosts, surgery is often the treatment of choice. Long-term anthelminthic treatment may also suppress some cysts. Long term daily albendazole treatment, after surgical resection of the cyst masses, has suppressed parasite growth in some dogs with *E. multilocularis* cysts.

Prevention

Dogs may be treated with anthelminthic agents before they are allowed to enter *Echinococcus*-free areas. Praziquantel is often used. Infected intermediate hosts could also bring the parasite into a country if their tissues are fed to dogs or eaten by other definitive hosts.

In endemic areas, dogs and cats should not be allowed to eat the carcasses, particularly the viscera, of potential intermediate hosts. In areas where *E. multilocularis* is a problem, cats and dogs should also be kept from hunting wild rodents. Regular examination and treatment of dogs, particularly sheep dogs, can decrease echinococcosis in domesticated livestock. One-time treatment is not adequate; definitive hosts often become reinfected if they are re-exposed. Dogs that might be infected should not be allowed onto pastures where livestock may graze. In some countries, foxes have been treated with praziquantel in bait to decrease the incidence of *E. multilocularis*, and the risk to other species.

Eradication or control programs for the *E. granulosus* sheep/dog cycle have been successful in some areas, particularly on islands such as Iceland, New Zealand and Tasmania. These programs have targeted the parasite in domesticated dogs by regular surveillance, and if necessary, treatment. Education campaigns have also been used, either alone or in conjunction with programs aimed at dogs. The elimination of farm slaughter of sheep reduces the risk that dogs will be infected from this source.

A recombinant vaccine for *E. granulosus* in sheep has been successful in field trials. This vaccine has been licensed to a commercial group in the People's Republic of China. Models suggest that livestock vaccines would be most effective if combined with testing and treatment of dogs.

Morbidity and Mortality

Where *E. granulosus s. l.* is endemic and uncontrolled, this parasite may be common in dogs and livestock. More than 30% of the dogs and up to 80-100% of the sheep and/or cattle are infected in some severely affected areas. However, the incidence in many endemic areas is much lower. The prevalence of infection in livestock often increases with age. *Echinococcus* is also common among wildlife in some areas. In some parts of Australia, up to 100% of dingoes and dingo/domestic dog hybrids, and more than 60% of some wildlife intermediate hosts are infected with *E. granulosus* G1. Wildlife cycles might spill over into domesticated animals, or vice versa. However, this depends on the epidemiology of the organism.

E. multilocularis can be relatively common in wild animals in some areas. Adult tapeworms have been found in 1% to greater than 60% of foxes and coyotes, depending on the region, and cysts may occur in approximately 2-10% of rodents. This parasite is less common than *E. granulosus s. l.* in domesticated animals, although relatively high prevalences may be seen in localized areas. Currently, less than 1% of dogs and cats are infected overall, but as many as 12% of dogs carry this parasite in parts of China and Alaska, and up to 7% of dogs and 3% of cats may be infected in parts of rural Switzerland. Few symptomatic infections have been reported in domesticated animal intermediate hosts, and the prevalence in these species is poorly understood. In Switzerland, *E. multilocularis* lesions were found in 10% of feeder pigs kept outdoors. In eastern Switzerland, one study reported that 2.9% of breeding sows had antibodies to an *E. multilocularis* antigen; three of these sows were necropsied and had multiple *E. multilocularis* lesions in the liver. In Lithuania, lesions were reported in 0.5% of the pigs from family farms, and in one area of China, this parasite was found in 0.3% of yaks and sheep at slaughter.

The definitive host is rarely affected by infection with *Echinococcus* spp. Most *E. granulosus s. l.* cysts in livestock also seem to be asymptomatic, probably due to the relatively short lifespan of these animals. Fatal *E. multilocularis* infections have been reported in intermediate hosts including rodents, dogs and non-human primates, but the morbidity and mortality rates are unknown. In most susceptible hosts, these tumor-like metacestodes are probably very dangerous, as they are not confined by a fibrous capsule and can metastasize. In pigs, however, the growth of *E. multilocularis* metacestodes appears to be suppressed. Serious infections and fatal disease have also been reported in gorillas, orangutans and other nonhuman primates infected with *E. vogeli*.

Internet Resources

Centers for Disease Control and Prevention (CDC)
http://www.dpd.cdc.gov/dpdx/HTML/Echinococcosis.htm

eMedicine.com
http://emedicine.medscape.com/article/997714-overview

Food and Agriculture Organization of the United Nations (FAO). Manual for the Recognition of Exotic Diseases of Livestock
http://www.spc.int/rahs/

FAO Manual on Meat Inspection for Developing Countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

International Veterinary Information Service (IVIS)
http://www.ivis.org

Public Health Agency of Canada. Material Safety Data Sheets
http://www.phac-aspc.gc.ca/msds-ftss/index.html

Review of Echinococcosis/Hydatidosis: a Zoonotic Parasitic Disease
http://www.fao.org/docrep/t1300t/t1300T0m.htm

The Merck Manual
http://www.merckmanuals.com/professional/index.html

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

World Organization for Animal Health (OIE)
http://www.oie.int/

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

OIE Terrestrial Animal Health Code
http://www.oie.int/international-standard-setting/terrestrial-code/access-online/

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