Cystic Echinococciosis

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Synonyms and related keywords: hydatidosis, CE

INTRODUCTION

Background: Cystic echinococcosis (CE) is the larval cystic stage (called echinococcal cysts) of a small taeniid-type tapeworm (*Echinococcus granulosus*) that may cause illness in normal, intermediate hosts, generally herbivorous animals, and people who are infected accidentally (see Picture 1).
Three other species are recognized within the genus *Echinococcus*, and they also may develop in the human host and cause various forms of echinococcosis (hydatidosis). *E. granulosus* is discussed separately from the other 3 species, notably from *E. multilocularis*, which causes alveolar echinococcosis, because of marked differences in epidemiology, clinical features, diagnosis, and treatment.

In the normal life cycle of *Echinococcus* species, adult tapeworms (3-6 mm long) inhabit the small intestine of carnivore definitive hosts, such as dogs, coyotes, or wolves, and echinococcal cyst stages occur in herbivore intermediate hosts, such as sheep, cattle, and goats. A number of other suitable intermediate hosts, such as camels, pigs, and horses, are involved in the life cycle in many parts of the world.

In the typical dog-sheep cycle, tapeworm eggs are passed in the feces of an infected dog and subsequently may be ingested by grazing sheep; they hatch into embryos in the intestine, penetrate the intestinal lining, and then are picked up and carried by blood throughout the body to major filtering organs (mainly liver and/or lungs). After the developing embryos localize in a specific organ or site, they transform and develop into larval echinococcal cysts in which numerous, tiny tapeworm heads (called protoscolices) are produced via asexual reproduction.

These protoscolices are infective to dogs that may ingest viscera containing echinococcal cysts (with protoscolices inside), mainly because of the habit in endemic countries of feeding dogs viscera of home-slaughtered sheep or other livestock. Protoscolices attach to the dog's intestinal lining and in approximately 40-50 days grow and develop into mature adult tapeworms, once again capable of producing infective eggs to be passed to the outside environment with the dog's feces.

Because humans play the same role of intermediate hosts in the tapeworm life cycle as sheep, humans also become infected by ingesting tapeworm eggs passed from an infected carnivore. This occurs most frequently when individuals handle or pet infected dogs or other infected carnivores or inadvertently ingest food or drink contaminated with fecal material containing tapeworm eggs.

**Pathophysiology:** In primary echinococcosis, metacestodes develop from oncospheres after peroral infection with *E. granulosus* eggs. In secondary echinococcosis, larval tissue proliferates after being spread from the primary site of the metacestode. This can occur by spontaneous trauma such as induced rupture or during medical interventions.

In primary echinococcosis, larval cysts may develop in every organ. Most patients (as many as 80%) have single organ involvement and harbor a solitary cyst. Approximately two thirds of patients suffer from liver echinococcosis. The second most common organ involved is the lung.

In each anatomic site, cysts are surrounded by the periparasitic host tissue (pericyst), encompassing the endocyst of larval origin. Inside the laminated layer, or hyaline membrane, the cyst is covered by a multipotential germinal layer, giving rise to the production of brood capsules and protoscolices. The central cavities of
cysts of *E. granulosus* are filled with clear fluid, numerous brood capsules, and protoscolices. In addition, daughter cysts of variable size often are detected. The growth rate of cysts is highly variable and may depend on strain differences. Estimates of the average increase of cyst diameter vary (approximately 1-1.5 cm/y).

The clinical features of CE are highly variable. The spectrum of symptoms depends on the following:

- Involved organs
- Size of cysts and their sites within the affected organ(s)
- Interaction between the expanding cysts and adjacent organ structures, particularly bile ducts and the vascular system of the liver
- Complications caused by rupture of cysts
- Bacterial infection of cysts and spread of protoscolices and larval material into bile ducts or blood vessels
- Immunologic reactions such as asthma, anaphylaxis, or membranous nephropathy secondary to release of antigenic material

**Frequency:**

- **In the US:** Unfortunately, realistic national or international figures do not exist for total numbers of cases of CE. The problem is that, until recently, the only basis for diagnosis was surgery, and few countries systematically reported cases. When they did report cases, uneven reporting occurred in different regions of countries. The groups most at risk of CE usually are underserved by medical services. Now that active diagnostic screening with ultrasound (US) and serology is available, such figures could be obtained if studies were performed on representative samples of the population.

  In the US, transmission of *E. granulosus* in the dog-sheep cycle is known to occur most frequently in several western states, including California, Arizona, New Mexico, and Utah. In Arizona and New Mexico, CE is known to occur in American Indians belonging to the Zuni, Navajo, and Santo Domingo tribes, whose members live in close proximity to their animals, kill many of their own animals each year, and generally have limited knowledge concerning the life cycle and transmissibility of the parasite. In the US, Utah has had the highest number of surgical cases of those states involved, with approximately 45 cases from 1944-1994.

- **Internationally:** *E. granulosus* is a cosmopolitan parasite, and endemic regions exist in each continent. Considerable public health problems occur in many areas, including countries of Central and Southern America, Western and Southern/Southeastern Europe, the Middle East and North Africa, some sub-Saharan countries, Russia and adjacent countries, and China. Annual incidence rates of diagnosed human cases per 100,000 inhabitants vary widely, from less than 1 per 100,000 to high levels. For example, rates are as follows:
Greece - 13 per 100,000 persons
Rural regions of Uruguay - 75 per 100,000 persons
Rural regions of Argentina - 143 per 100,000 persons in Rio Negro province
Parts of Xinjiang province of China - 197 per 100,000 persons
Parts of the Turkana district of Kenya - 220 per 100,000 persons

**Mortality/Morbidity:** CE is rarely fatal. Occasionally, deaths occur due to anaphylactic shock or cardiac tamponade in heart echinococcosis.

**Race:** No racial predilection exists.

**Sex:** In some endemic countries, females are affected more than males because their lifestyle habits and practices bring them into contact with the parasite.

**Age:** Individuals of all ages are affected. In some endemic countries, children have higher infection rates because they are most likely to play with dogs.

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**History:**

- Months or years may pass before an individual exhibits any signs or symptoms of infection with the cystic larval stages.

- During the natural course of infection, the fate of *E. granulosus* cysts is variable.
  - Some cysts may grow to a certain size and then persist without noticeable change for many years.
  - Other cysts may rupture spontaneously or collapse and completely disappear.

- Spontaneous or traumatic cyst rupture and spillage of viable parasitic tissue during interventional procedure may result in secondary echinococcosis. Cysts may rupture into the peritoneal or pleural cavity, into the pericardium, the bile ducts, the gastrointestinal tract, or even into blood vessels, leading to extraordinary manifestations and severe complications.

- Spontaneous cure of CE is possible.

- After a variable incubation period, infections may become symptomatic if cysts are growing and exerting pressure on adjacent tissue and inducing other pathologic findings.

- Sudden symptomatology usually is due to spontaneous or traumatic cyst rupture.
• Usually, cysts do not induce clinical symptoms before they have reached a size sufficient to exert pressure on adjacent organs.

**Physical:** The presentation of human echinococcosis is protean. Patients come to the clinician's attention for different reasons, such as when a large cyst has some mechanical effect on organ function or rupture of a cyst causes acute hypersensitivity reactions. The cyst also may be discovered accidentally during x-ray examination, body scanning, surgery, or for other clinical reasons. Common chief complaints are upper abdominal discomfort and pain, poor appetite, and a self-diagnosed mass in the abdomen. Physical findings are hepatomegaly, a palpable mass if on the surface of the liver or other organs, and abdominal distention. If cysts in the lung rupture into the bronchi, intense cough may develop, followed by vomiting of hydatid material and cystic membranes.

• **Liver**
  - Hepatomegaly
  - Jaundice
  - Biliary colic-like symptoms
  - Cholangitis
  - Pancreatitis
  - Liver abscess
  - Portal hypertension
  - Ascites
  - Inferior vena cava compression or thrombosis
  - Budd-Chiari syndrome
  - Cyst rupture, peritoneal spread, and peritonitis
  - Hemobilia
  - Biliary fistula to skin, bronchial system, or gastrointestinal tract

• **Lungs**
  - Tumor of chest
  - Chest pain
  - Chronic cough, expectoration, and dyspnea
  - Pneumothorax
  - Eosinophilic pneumonitis
- Pleural effusion
- Parasitic lung embolism
- Hemoptysis
- Biliptysis

- Heart
  - Tumor
  - Pericardial effusion

- Spine - Mass with neurologic symptoms

**Causes:**

- See [Introduction](#) for a brief discussion of infection routes.
- Susceptibility of humans to infection varies, presumably because of individual differences in nutritional, immunologic, and genetic factors.

**Differentials**

- Pyogenic Hepatic Abscesses
- Pyonephrosis

**Other Problems to be Considered:**

- Abscess
- Epidermoid cyst
- Neoplasm
- Simple cyst

**Workup**

- Lab Studies:
  - Generally, routine laboratory tests do not show specific results.
    - In patients with rupture of the cyst in the biliary tree, marked and transient elevations of cholestatic enzymes occur, often in association with hyperamylasemia and eosinophilia (up to as many as 60%).
    - In most cases eosinophilia is limited (<15%) or absent.
• CE is one of the few parasitic infections in which the basis for laboratory diagnosis is primarily serology.
  o Indirect hemagglutination test and enzyme-linked immunosorbent assay are the most widely used methods for detection of anti-Echinococcus antibodies (immunoglobulin G [IgG]).
  o Depending on the test system used and other parameters, approximately 10% of people with hepatic cysts and 40% with pulmonary cysts do not produce detectable serum antibodies and exhibit false-negative results.
  o Cysts of the brain or eye and calcified cysts often induce no or low antibody titers.
  o Children aged 3-15 years may produce minimal serologic reactions.

• No standard, highly sensitive, and specific serologic test exists for CE antibody detection. In specialized laboratories, the arc 5 test or detection of cestode-specific antibodies can be used to exclude cross-reactions caused by noncestode parasites.

Imaging Studies:

• X-ray examination is useful for cysts in the lungs, bone, and muscle and for detecting calcified cysts.

• US is the procedure of choice when making the diagnosis of asymptomatic CE because it is noninvasive, and relatively inexpensive. US is an imaging technique that uses the reflection of sound waves emitted by a probe on the bodily organs to build images of the organs explored.
  o Any abnormality can be viewed using US from an infinite number of angles and positions. Cysts in every part of the abdomen and in muscles can be imaged with US.
  o US is useful in longitudinal studies, such as monitoring the response of cysts to treatment and recording cyst growth rate.
  o US also has been used extensively in endemic areas for mass screening, often using portable machines that can work without an electrical distribution system by running on batteries or on a generator.
  o Many authors consider US mass surveys to be the best way to assess prevalence.

• Various classifications exist of the US picture in CE, the most widely used being the one proposed by Gharbi in the early 1980s, but a general consensus exists about the following:
  o Simple cysts with well-defined borders and uniform anechoic contents are not pathognomonic for echinococcal cysts (nonparasitic cysts have the same appearance).
  o Cysts with a visible split wall inside (floating membrane or "water lily" sign) are pathognomonic.
Septated cysts, or cysts with a "honeycomb" pattern, are likely to be echinococcal.

A solid, heterogeneous mass is difficult to differentiate from granulomas or tumors, although calcification suggests echinococcal cyst.

- Echocardiography may be used to detect cardiac lesions.

- CT scan has the advantage of inspecting any organ (lungs cannot be explored by US), detecting smaller cysts when located outside the liver, locating cysts precisely, and sometimes differentiating parasitic from nonparasitic cysts. Measurement of cyst density appears to be an additional tool to differentiate parasitic from nonparasitic cysts and for follow-up studies during chemotherapy. However, the cost of CT scan is prohibitive in several endemic countries.

- MRI may have some advantages over CT scan in the evaluation of postsurgical residual lesions, recurrences, and selected extrahepatic infections, such as cardiac infections. It is also superior in identifying changes of the intrahepatic and extrahepatic venous system.

Other Tests:

- Endoscopic retrograde cholangiopancreatography may be indicated in patients with cholestasis or jaundice. This technique also may be a therapeutic intervention when cysts communicating with the biliary tree can be basketed out.

Procedures:

- Fine-needle aspiration biopsy of the cyst performed under US guidance, by the transhepatic approach, and under anthelmintic coverage is generally safe and diagnostically useful for differentiation of CE, malignancy, and abscesses. It may be particularly helpful in cases with detectable anti-*Echinococcus* serum antibodies and inconclusive imaging appearance. These cysts are usually numerous and can be found even in bacteriologically infected and/or degenerate cysts (see Picture 2).

Medical Care:

- Two benzimidazolic drugs, mebendazole and albendazole, are the only anthelmintics effective against CE. Albendazole and mebendazole are well tolerated but show different efficacy.

  - Albendazole is significantly more effective than mebendazole in the treatment of liver cysts. Benzimidazole treatment alone requires prolonged administration over many weeks and an unpredictable outcome in terms of response rates in individuals.

  - Treatment with albendazole in *E granulosus* infection can result in an apparent cure in as many as 30% of patients, with a further 40-50% of patients showing objective evidence of response when observed short term. Patients who do not show obvious initial evidence of response may be found to be cured when observed over several years.
Duration of therapy and doses are also important. Albendazole efficacy increases with course up to 3 months in the more common cyst sites.

Usually, patients receive these drugs in cycles of 4 weeks separated by 1-2 weeks without treatment. With albendazole, many patients receive 3 treatment cycles. However, the issue of cyclic continuous treatment must be resolved.

The safety profile shows that liver function abnormalities are common, although they rarely occur during treatment, while occasional hematologic changes affecting white cells may be more serious. Safety data supply the rationale for monitoring patients during treatment.

Overall, albendazole has been demonstrated to be a useful advance in the management of echinococcosis, when used as sole treatment or as an adjunct to surgery or other treatments.

Praziquantel recently has been suggested, administered additionally once per week in a dose of 40 mg/kg during treatment with albendazole. However, available data are limited.

Surgical Care:

Surgery was the only treatment available before the introduction of anthelmintic drugs. It is considered the first choice treatment of echinococcosis but is associated with considerable mortality (up to 2% in some series, increasing with second and further operations), morbidity, and recurrence rates (2-25%). Given the more frequent detection of early and asymptomatic Echinococcus granulosus liver lesions, a widened indication for chemotherapy exists.

Several procedures have been described for the treatment of hepatic echinococcal cysts, ranging from simple puncture to liver resection and transplantation, although the most commonly used technique is total or partial cystopericystectomy.

Usually, radical surgery (total pericystectomy or partial hepatectomy) is indicated for liver lesions. Conservative surgery (open endocystectomy with or without omentoplasty) or palliative surgery (simple tube drainage of infected cysts or communicating cysts) is also an option. More radical interventions have higher intraoperative risks but less numerous relapses. With the inclusion of chemotherapy prior to or after surgery, being less aggressive may be possible.

Surgery for pulmonary cysts includes extrusion of cysts using Barrett technique (intact endocystectomy without preliminary aspiration), pericystectomy, and lobectomy.

Peripheral and unilobar echinococcal cysts, whether or not complicated, also can be treated laparoscopic surgery using partial cystopericystectomy and drainage. When surgery cannot be avoided, presurgical use of albendazole reduces risk of recurrence and facilitates surgery by reducing intracystic pressure.

Minimally invasive treatment involves the following:

- The puncture of echinococcal cysts long has been discouraged because of risks of anaphylactic shock and spillage of the fluid; however, as experience with US-guided interventional techniques has increased since the early 1980s, an increasing number of articles have reported its effectiveness and safety in treating abdominal, especially echinococcal cysts. At least 2309 cysts have been treated with this procedure, and cases of anaphylactic shock (1 lethal) have been reported. Peritoneal seeding never...
been reported.

- Under albendazole coverage, cysts are punctured under US or CT guidance either with a needle or with a catheter according to their size. The presence of an anesthesiologist intervenes in case of allergic manifestations or anaphylactic shock is mandatory. Usually, a small quantity of fluid first is aspirated to be examined by light microscope to observe the presence of viable protoscolices. If they are present, the cyst is aspirated completely.

- At this point, exclude possible connections of the cyst with the biliary tree by means of injection of contrast medium in the cavity. If no connections are evident, a scolecidial agent, usually hypertonic saline or ethanol, is injected and left for a variable period (usually 5-30 min) and then reaspirated. The destruction of protoscolices can be observed in fluid sample aspirated after the injection of a scolecidial agent. This sequence is called PAIR (puncture, aspiration, injection, reaspiration). As happens with drug therapy, PAIR responses include both a decrease in cyst size and a progressive change in echo pattern (generally solidification).

- From a diagnostic standpoint, PAIR is the only method that helps provide a direct diagnosis of the parasitic nature of the cysts. Neither imaging modalities nor serology are sufficient to exclude the diagnosis. PAIR is also an effective alternative to chemotherapy alone since it has a higher efficacy and avoids the problem of drug resistance. It also shortens the period of treatment and final recovery. PAIR is a valuable alternative to surgery in terms of cost containment and hospitalization time. In types I, II, and III (Gharbi classification) echinococcal cysts with no or incomplete response to therapy, PAIR is an effective therapeutic tool in the management of human CE.

- Reserve PAIR for use in highly specialized centers where teams are well prepared to deal with possible complications.

Consultations:

- Consult a surgeon to discuss the opportunity of surgical intervention.

- Consult a radiologist for injection of contrast medium in the cyst after fluid aspiration if PAIR is scheduled. Contrast injection in the cyst allows the physician to exclude connections of the cyst with the biliary tree. Contact of scolecidial agents, such as alcohol and hypertonic saline, with biliary epithelium may lead to cholangitis.

- Consult a gastroenterologist for ruling out connections with the biliary tree by endoscopic retrograde cholangiopancreatography if PAIR is scheduled. This step may be avoided if injection of contrast medium after aspiration and before injection is planned.

- Consult an anesthesiologist for assistance in case of anaphylactic shock or anaphylactoid reactions if PAIR is scheduled.
Albendazole and mebendazole are the only anthelmintics effective against CE. Albendazole is the drug of choice against this disease because its degree of systemic absorption and penetration into hydatid cysts is superior to that of mebendazole. Albendazole in combination with percutaneous aspiration (PAIR) therapy can lead to a reduction in cyst size, and in one study, it improved efficacy over albendazole alone against hepatic hydatid cysts. When surgery cannot be avoided, presurgical use of albendazole in echinococcus infestations reduced risk of recurrence and/or facilitated surgery by reducing intra-cyst pressure.

Treatment of echinococcosis for patients weighing more than 60 kg is albendazole administered with meals in a dose of 400 mg twice daily for 28 days. A dose of 15 mg/kg body weight daily in 2 divided doses (not to exceed total daily dose of 800 mg) has been suggested for patients weighing fewer than 60 kg. For CE, the 28-day course may be repeated after 14 days without treatment to a total of 3 treatment cycles.

**Drug Category:** Anthelmintics -- Parasite biochemical pathways are sufficiently different from human host to allow selective interference by chemotherapeutic agents in relatively small doses.

<table>
<thead>
<tr>
<th><strong>Drug Name</strong></th>
<th><strong>Albendazole (Albenza)</strong> -- Decreases ATP production in worm, causing energy depletion, immobilization, and finally, death. To avoid inflammatory response in CNS, patient also must be started on anticonvulsants and high-dose glucocorticoids.</th>
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<tbody>
<tr>
<td><strong>Adult Dose</strong></td>
<td>&gt;60 kg: 400 mg PO bid with meals for 28 d 14 d after receiving treatment, may repeat 28-d cycle for a total of 3 cycles Intracerebral echinococcal cysts: 200 mg PO tid for 90 d has been described in a single patient</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>Not established Suggested dose, &lt;60 kg: 15 mg/kg/d PO in 2 divided doses</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity; hepatic disease</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Coadministration with carbamazepine may decrease efficacy; dexamethasone, cimetidine, ritonavir, and praziquantel may increase toxicity</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Discontinue use if LFTs (transaminases) increase significantly (resume when levels decrease to pretest values); use only if constant medical supervision with regular monitoring of serum-transaminase concentrations and of leucocyte, RBC, and platelet counts (rare cases of bone marrow damage have been reported); treat in liver damage with reduced doses, if at all</td>
</tr>
<tr>
<td><strong>Drug Name</strong></td>
<td><strong>Mebendazole (Vermox)</strong> -- Causes worm death by</td>
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selectively and irreversibly blocking uptake of glucose and other nutrients in susceptible adult intestine where helminths dwell.

**Adult Dose**
50 mg/kg/d PO for at least 3 mo; not to exceed 4.5-6 g/d

**Pediatric Dose**
100-200 mg/kg suggested in pulmonary echinococcosis

**Contraindications**
Documented hypersensitivity

**Interactions**
Carbamazepine and phenytoin may decrease effects of mebendazole; cimetidine may increase mebendazole levels

**Pregnancy**
C - Safety for use during pregnancy has not been established.

**Precautions**
Coadministration with alcohol can cause disturbances of attention; adjust dose in hepatic impairment

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**Further Inpatient Care:**
- Reevaluate patients for symptom resolution and determination of cure.

**Further Outpatient Care:**
- During treatment of patients discharged on benzimidazoles, monitor aminotransferases, WBC, RBC, and hemoglobin monthly.
- Evaluate patients for US appearance modifications and changes in serology titers after 3 mo of treatment and then for several years (at least 5).

**Deterrence/Prevention:**
- In endemic areas, distribution of educational material in elementary schools regarding modes of transmission of the disease is helpful to increase knowledge about the nature and transmission of CE.
- Educational material should include information about proper disposal of sheep viscera in abattoirs and proximity to dogs and sources of transmission.

**Complications:**
- The cysts may rupture, and the cyst content may be released into biliary or bronchial systems. This may cause infection of the cyst and an obstruction of the biliary or bronchial tree with clinical consequences (eg, pneumonitis, pleural effusion, pneumothorax, secondary echinococciosis of the pleural and peritoneal cavity).
Prognosis:

- Prognosis is generally good.
- Sometimes after removal of a cyst, one or more new cysts may develop at a different site. A hypothesis for this is that the growth of some cysts may be inhibited by the presence of the thymus that has been removed.

Patient Education:

- See Deterrence/Prevention.

Medical/Legal Pitfalls:

- Failure to consider the possible echinococcal nature of a cyst found on an imaging exam and subsequent percutaneous puncture may lead to anaphylactic shock and possible death.
  - Always consider the possibility of an echinococcal cyst, especially with patients coming from endemic areas, and try to exclude it with serology.
  - If serology is inconclusive, diagnostic puncture may be indicated with the presence of an anesthesiologist; however, cases in which echinococcal cysts were misdiagnosed as simple cysts and punctured with no adverse effects are listed in the literature.

Special Concerns:

- Consider PAIR in pregnant patients with large liver cysts that are at risk of rupture due to increased intra-abdominal pressure during labor.

Caption: Picture 1. Ultrasound appearance of echinococcal cysts (Gharbi type I)