بسمه تعالی

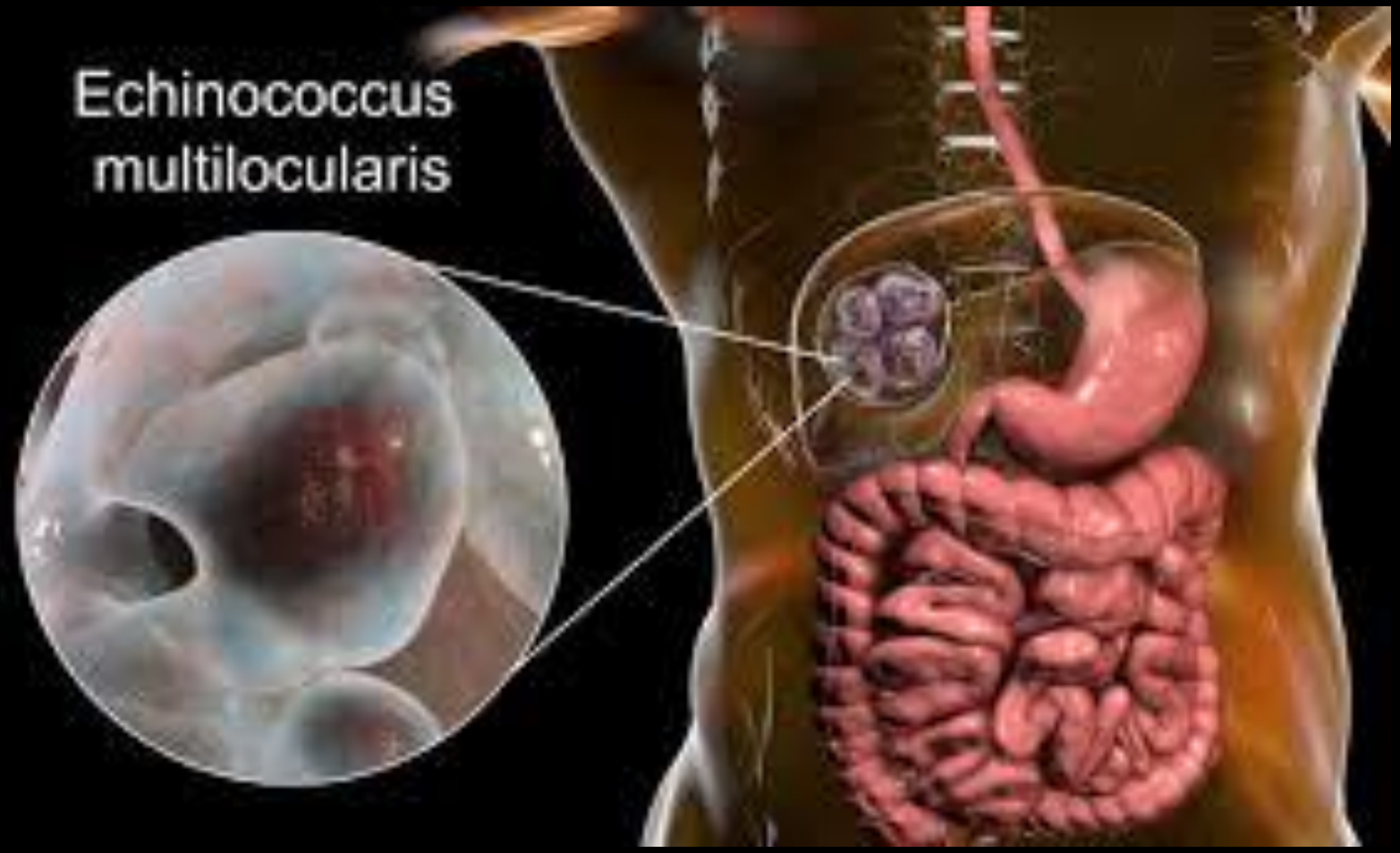
دانشگاه علوم پزشکی مازندران
مرکز آموزشی درمانی امام خمینی (ره) ساری
گروه آموزشی و درمانی جراحی عمومی

ECHINOCOCCOSIS TREATMENT

SOHRAB SAYYADI, M.D

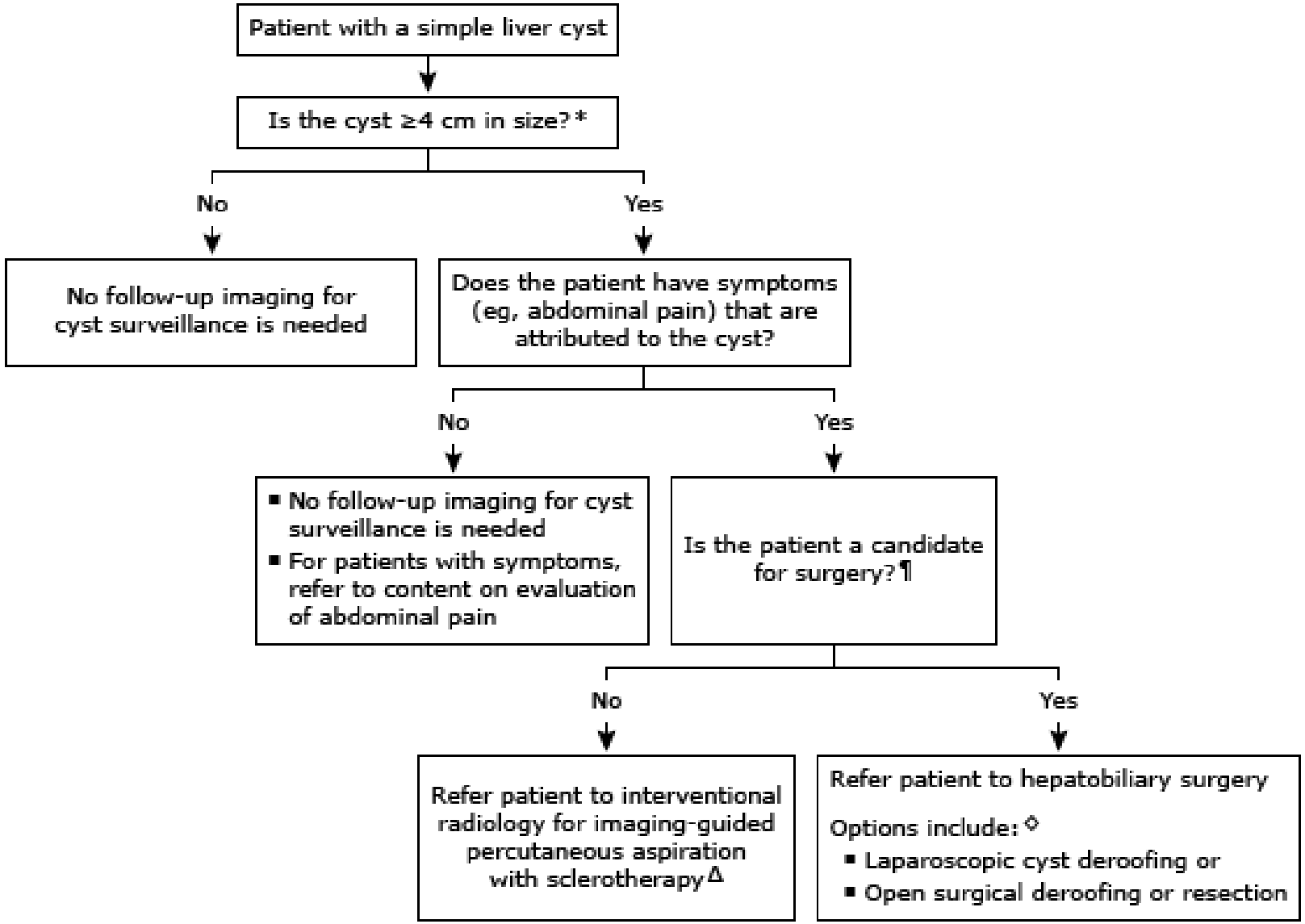
2024

- What's new in Echinococcosis Treatment



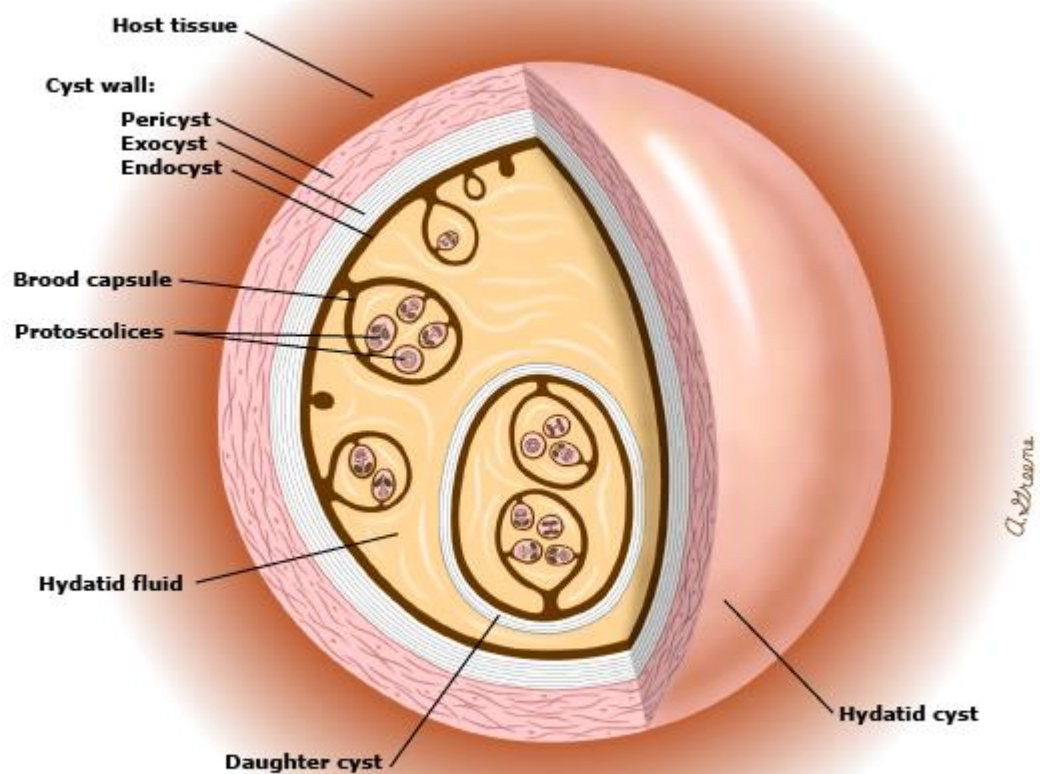
Cystic lesions of the liver represent a heterogeneous group of disorders, which differ in etiology, prevalence, and clinical manifestations. Most liver cysts represent true cysts that are found incidentally on imaging studies and tend to have a benign course. A minority of liver cysts can cause symptoms and rarely may be associated with serious morbidity and mortality. Larger cysts are more likely to be symptomatic and cause complications such as spontaneous hemorrhage, rupture into the peritoneal cavity or bile duct, infection, and compression of the biliary tree. Some cystic lesions of the liver may have unique complications such as malignant transformation in the case of a mucinous cystic neoplasm (cystadenoma) or a ciliated hepatic foregut cyst, or anaphylactic shock due to a hydatid cyst. Some of these complications may occasionally mandate surgical intervention.

An approach to managing the adult patient with a simple liver cyst



INTRODUCTION

Echinococcal disease is caused by infection with the metacestode stage of the tapeworm Echinococcus, which belongs to the family Taeniidae. Four species of Echinococcus produce infection in humans; E. granulosus and E. multilocularis are the most common, causing cystic echinococcosis (CE) and alveolar echinococcosis (AE), respectively. The two other species, E. vogeli and E. oligarthrus, cause polycystic echinococcosis but have only rarely been associated with human infection



Structure of the echinococcal cyst

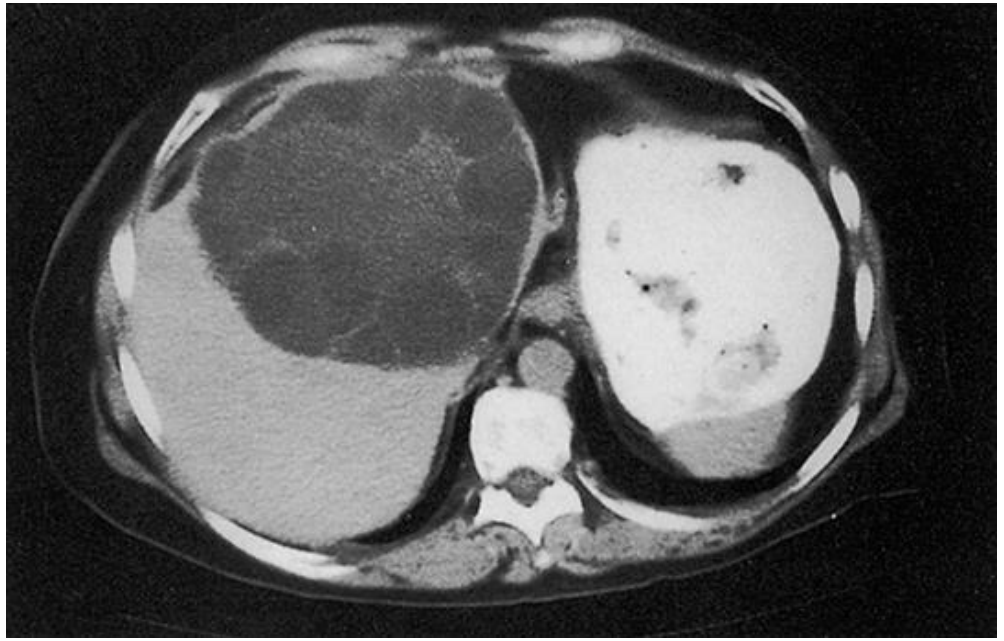
CLINICAL MANIFESTATIONS

- The initial phase of primary infection is always asymptomatic. Many infections are acquired in childhood but do not cause clinical manifestations until adulthood. Latent periods of more than 50 years before symptoms arise have been reported. While approximately 50 percent of detected cases occur in asymptomatic patients, many more cases remain undiagnosed or are found incidentally at autopsy.

- The clinical presentation of E. granulosus infection depends upon the site of the cysts and their size. Small and/or calcified cysts may remain asymptomatic indefinitely. However, symptoms due to mass effect within organs, obstruction of blood or lymphatic flow, or complications such as rupture or secondary bacterial infections can result.

LIVER INVOLVEMENT

- E. granulosus infection of the liver frequently produces no symptoms. The right lobe is affected in 60 to 85 percent of cases. Significant symptoms are unusual before the cyst has reached at least 10 cm in diameter. If the cysts become large, hepatomegaly with or without associated right upper quadrant pain, nausea, and vomiting can result.



- In approximately one-fourth of the cases, E. granulosus cysts rupture into the biliary tree, producing biliary colic, obstructive jaundice, cholangitis, and/or pancreatitis. Less commonly, cysts rupture into the peritoneal cavity or other organs, with potential for anaphylaxis and multiorgan failure.

- Pressure or mass effect on the bile ducts, portal and hepatic veins, or the inferior vena cava can result in cholestasis, portal hypertension, venous obstruction, or Budd-Chiari syndrome.
- Liver cysts can also rupture into the peritoneum, causing peritonitis, or transdiaphragmatically into the pleural space or bronchial tree, causing pulmonary hydatidosis or a bronchial fistula. Secondary bacterial infection of the cysts can result in liver abscesses.

LUNG INVOLVEMENT

- The most common symptoms of pulmonary cystic echinococcosis (CE) described in the literature include cough (53 to 62 percent), chest pain (49 to 91 percent), dyspnea (10 to 70 percent), and hemoptysis (12 to 21 percent). Less frequent symptoms include malaise, nausea and vomiting, and thoracic deformations. The majority of children and adolescents with lung lesions are asymptomatic despite having lesions of impressive size, assumedly because of a weaker immune response and the relatively higher elasticity of the lung parenchyma relative to older patients.

- Cysts can break or develop secondary bacterial infection. The presence of these complications changes the clinical presentation, either by causing new symptoms or by increasing the severity of existing symptoms. The principal complication is cyst rupture, with spilling of cyst material containing fragments of larval tissue and protoscolices into the bronchial tree or the pleural cavity. Bronchial tree involvement can lead to cough, chest pain, hemoptysis, or emesis; pleural cavity involvement can cause pneumothorax, pleural effusion, or empyema. Secondary bacterial infection of the cyst can manifest as a pulmonary abscess with poorly defined margins.
- Approximately 60 percent of pulmonary hydatid disease affects the right lung, and 50 to 60 percent of cases involve the lower lobes. Multiple cysts are common. Approximately 20 percent of patients with lung cysts also have liver cysts. The ratio of lung to liver involvement is higher in children than in adults

OTHER ORGANS

Involvement of organs outside of the liver or lung is unusual but can lead to significant morbidity and mortality.

- Infection of the heart can result in mechanical rupture with widespread dissemination or pericardial tamponade.
- Central nervous system involvement can lead to seizures or signs of raised intracranial pressure; infection of the spinal cord can result in spinal cord compression.
- Cysts in the kidney can cause hematuria or flank pain. Immune complex-mediated disease, glomerulonephritis leading to the nephrotic syndrome, and secondary amyloidosis have also been described.
- Bone cysts are usually asymptomatic until a pathologic fracture develops; growth of the parasite in the bone tissue is a very slow process; the spine, pelvis, and long bones are most frequently affected.
- Ocular cysts also occur.
- Subcutaneous cyst has been described

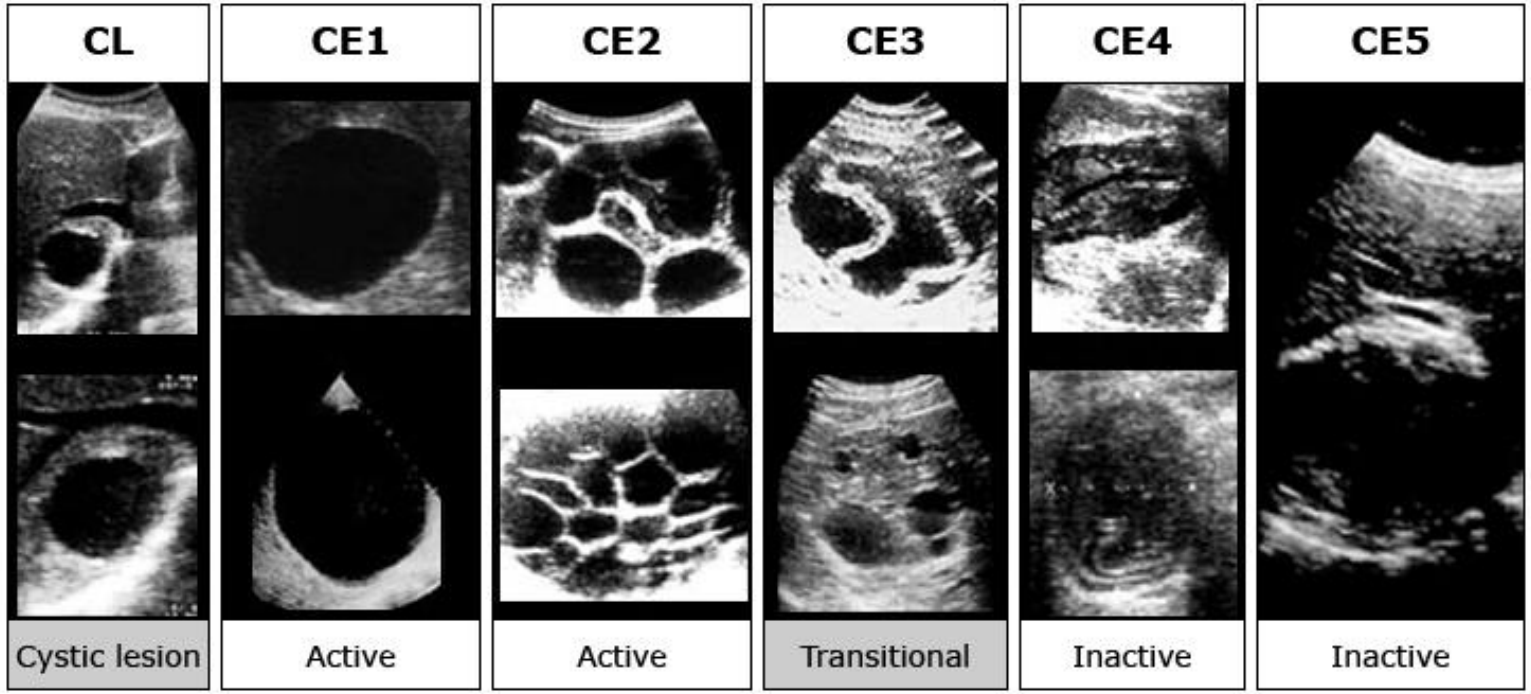
CYST RUPTURE

Fever and acute hypersensitivity reactions, including anaphylaxis, may be the principal manifestations of cyst rupture. Hypersensitivity reactions are related to the release of antigenic material and secondary immunologic reactions.

Diagnosis:

The diagnosis of E. granulosus is generally made by imaging techniques in conjunction with serology.

- Imaging
  - Ultrasonography
  - Computed tomography
  - Magnetic resonance imaging



Ultrasonographic classification of cysts due to cystic echinococcosis

- Several other classification systems are based upon ultrasound appearance
- The World Health Organization (WHO) classification characterizes cysts by type and size.
- The Gharbi classification divides cysts into five types. Type I cysts consist of pure fluid; type II have a fluid collection with a split wall; type III cysts contain daughter cysts (with or without degenerated solid material); type IV have a heterogeneous echo pattern; and type V have a calcified wall

Alternate treatment	Preferred treatment	Size	Stage	Description	WHO stage
PAIR	Albendazole alone	cm ۵>	Active	Unilocular unechoic cystic lesion with double line sign	CE١
PAIR	Albendazole + PAIR	cm ۵<			
Modified catheterization	Albendazole + either modified catheterization or surgery	Any	Active	Multiseptated, "rosette-like" "honeycomb" cyst	CE٢
PAIR	Albendazole alone	cm ۵>	Transitional	Cyst with detached membranes (water-lily sign)	CE٣a
PAIR	Albendazole + PAIR	cm ۵<			
Modified catheterization	Albendazole + either modified catheterization or surgery	Any	Transitional	Cyst with daughter cysts in solid matrix	CE٣b
-	Observation	Any	Inactive	Cyst with heterogenous hypoechoic/hyperechoic contents; no daughter cysts	CE٤
-	Observation	Any	Inactive	Solid plus calcified wall	CE۵

WORLD HEALTH ORGANIZATION CLASSIFICATION OF CYSTIC ECHINOCOCCOSIS AND TREATMENT STRATIFIED BY CYST STAGE

Diagnosis:

The diagnosis of E. granulosus is generally made by imaging techniques in conjunction with serology.

- Serologic tests
  - Complement fixation
  - Indirect hemagglutination (IHA)
  - Indirect immunofluorescence
  - Latex agglutination
  - Double diffusion immunoelectrophoresis
  - Counter-current immunoelectrophoresis
  - Radioimmunoassay
  - Enzyme-linked immunosorbent assay (ELISA)
  - Enzyme-linked immunoelectrodiffusion assay (ELIEDA)
  - Time-resolved fluoroimmunoassay
  - Immunoblot

Management approach:

Treatment of echinococcosis usually involves antiparasitic therapy combined with either surgical resection of the cyst or percutaneous aspiration and instillation of scolicidal agents.

Overview of approach:

Surgery has been the traditional approach for treatment of CE; subsequently, alternative approaches have been introduced and have replaced surgery as the treatment of choice in some cases .

In general, the clinical approach depends on the World Health Organization (WHO) diagnostic classification. Stage CE1 and CE3a cysts have a single compartment; such cysts that are <5 cm may be treated with albendazole alone. In settings where albendazole treatment with follow-up monitoring is not feasible, definitive management with percutaneous treatment via puncture, aspiration, injection, and reaspiration (PAIR) is an acceptable alternative approach. Stage CE1 and CE3a cysts that are >5 cm may be treated with albendazole in combination with PAIR. In situations where albendazole treatment is not feasible, percutaneous treatment with PAIR (in the absence of adjunctive drug therapy) is an acceptable alternative approach.

Stage CE2 and CE3b cysts have many compartments that require individual puncture; patients with such cysts commonly relapse after PAIR. Therefore, management of these cysts requires either modified catheterization technique (eg, non-PAIR percutaneous therapy) or surgery (with adjunctive drug therapy). The optimal choice between these approaches is uncertain and further study is needed.

Stages CE4 and CE5 are inactive cysts that may be managed with observation.

Surgery:

Surgery is the treatment of choice for management of complicated cysts (eg, rupture cyst, cysts with biliary fistulae, cysts compressing vital structures, cysts with secondary infection or hemorrhage). Surgery is also warranted for management of cysts with many daughter vesicles that are not suitable for percutaneous treatment (eg, WHO stage CE2 and CE3b). Other indications for surgery include cyst diameter >10 cm, superficial cyst at risk of rupture due to trauma, and extrahepatic disease (lung, bone, brain, kidney, or other site). Surgery is also appropriate in settings where percutaneous treatment is not available.

Adjunctive drug therapy should be administered to minimize risk of secondary echinococcosis from seeding of protoscolices in the abdominal cavity in the event of fluid spillage. Albendazole is generally administered beginning one week prior to surgery and continued for at least four weeks postoperatively. Some use praziquantel in addition to albendazole, although there is no clear evidence regarding its efficacy.

Surgery may cure the patient, but morbidity, mortality, and relapse rates can vary widely. Complications include secondary infection of cyst cavity, intraabdominal abscess, biliary fistula, sclerosing cholangitis, and spillage of cyst contents leading to secondary echinococcosis and/or anaphylaxis. Postoperative complications occur in less than 1 percent of cases; recurrent echinococcosis occurs in 2 to 25 percent of cases. These rates depend on the location and size of the cyst and the surgeon's experience.

Techniques:

- The goals of surgical therapy consist of evacuating the cyst and obliterating the residual cavity. Every effort should be made to avoid fluid spillage, which can lead to secondary seeding of infection and/or anaphylaxis. The safest and most effective surgical procedure is uncertain; the relative advantages of the different approaches have not been clearly established. Traditional approaches have included radical resection including pericystectomy or more conservative techniques. Laparoscopic surgery may be an alternative to open surgery in some cases.

- The surgical approach must be individualized depending on the cyst features. Removal of the intact cyst is preferred, if feasible. Alternatively, the cyst can be opened and sterilized with protoscolicidal agents, followed by evacuation of cyst contents and removal of the pericystic tissue. In one study including 132 patients with liver cysts treated with a variety of surgical procedures, cyst excision and omentoplasty were associated with the most favorable clinical results and lowest complication rates; a recurrence rate of 4.5 percent was observed with 4.5 years median follow-up.

- Every effort should be made to avoid fluid spillage, which can lead to secondary seeding of infection and/or anaphylaxis. For circumstances in which intact removal of the cyst is not feasible, a protoscolicidal agent such as hypertonic saline should be injected into the cyst prior to removing the contents. In addition, the surgical field should be protected with pads soaked in protoscolicidal agents. However, protoscolicidal agents should not be used in the setting of biliary communication, to minimize the risk of sclerosing cholangitis or pancreatitis. The anatomy of biliary communication should be defined intraoperatively (radio-opaque dye may be useful if available); any biliary leaks should be repaired surgically prior to application of the protoscolicidal agent.

- The most commonly used protoscolicidal agent is hypertonic saline (20 percent); the solution should be in contact with the germinal layer for at least 15 minutes. Albendazole, ivermectin, and praziquantel solutions have been used as protoscolicidal agents, although their efficacy and safety require further study. Formalin has been associated with sclerosing cholangitis and should not be used.

If spillage does occur, the peritoneum should be washed with hypertonic saline. The patient should be treated with albendazole (three to six months) and a brief course of praziquantel (seven days) should also be administered. The management of anaphylaxis is described separately.

Laparoscopic surgery has been described for treatment of Echinococcus, although no randomized trials comparing laparoscopy with open procedures have been performed. Laparoscopy may be associated with increased risk of spillage due to elevated intraabdominal pressures caused by pneumoperitoneum. Laparoscopy is most likely to be successful in the setting of anteriorly located hepatic cysts. Exclusion criteria for laparoscopy include deep intraparenchymal cysts, posterior cysts situated close to the vena cava, and presence of more than three cysts with calcified wall.

Surgical approaches for management of lung cysts include lobectomy, wedge resection, pericystectomy, intact endocystectomy, and capitonnage.

Complications

Postoperative complications may include:

- Obstructive jaundice (often attributable to echinococcal remnants in the biliary tree)
- Development of an external biliary fistula occurs in up to 2 percent of patients, typically two to four weeks postoperatively)
- Sphincter of Oddi stenosis, bile duct stricture, or sclerosing cholangitis − These are late complications most commonly observed in patients who underwent cyst sterilization with formalin.

Patients with one episode of recurrent bleeding following initially successful endoscopic therapy are typically treated with a second attempt at endoscopic therapy. Therapy may consist of the same therapy initially used or a different endoscopic modality (eg, if thermocoagulation therapy was used initially it may either be repeated or treatment with a hemostatic clip employed). If the bleeding was initially controlled with endoscopic clips, treating with thermal coagulation is an option, even if it is needed next to a clip or if there might be contact with the clip during treatment (however, thermal coagulation should not be applied to the clip intentionally with the goal of heating it up). Surgery or angiography-guided intervention may be indicated for patients who fail endoscopic therapy (persistent bleeding or recurrent bleeding after two therapeutic endoscopies).

Percutaneous management :

There are two categories of percutaneous techniques. The first approach aims to destroy the germinal layer with scolicidal agents. This is done via the PAIR technique. PAIR is usually effective for definitive treatment of cysts that do not have daughter cysts (eg, WHO stage CE1 and CE3a).

The second approach consists of evacuating the entire cyst with a large-bore catheter. This is generally done for management of cysts that are difficult to drain or tend to relapse after PAIR, such as WHO stage CE2 and CE3b cysts (which may contain daughter cysts). Establishing whether daughter cysts are present is important for guiding treatment, since the presence of daughter cysts reduces the likelihood of successful definitive treatment with PAIR.

Percutaneous treatment is associated with risk for anaphylaxis; in one review of treatment for nearly 6000 cysts, anaphylaxis occurred in 1.6 percent of patients. Albendazole should be administered for at least one month following percutaneous treatment.

PAIR should not be performed in the following circumstances:

- Cyst with nondrainable solid material or echogenic foci
- Superficial cyst at risk of rupture into the abdominal cavity
- Cyst that has ruptured into the peritoneum
- Cyst with biliary communication
- Inactive or calcified cyst

- Risks of PAIR include spillage of cyst contents into the peritoneum (which can lead to secondary echinococcosis, urticaria, and/or anaphylaxis), chemical sclerosing cholangitis, biliary fistula (6 percent), local recurrence (3 percent), and bleeding and infection (4 percent). Fever and urticaria occur in 11 to 13 percent of cases; the risk of anaphylaxis is 0.5 percent and has been reduced with development of fine needles and catheters and advances in imaging techniques .

Patients with biliary complications:

- Patients with biliary complications of echinococcosis may warrant endoscopic retrograde cholangiopancreatography (ERCP):
- Obstructive jaundice or cholangitis − Patients with obstructive jaundice or cholangitis (either prior to or following surgery) may warrant sphincterotomy, followed by removal of cysts and membranes with the help of a basket or an occlusion balloon.
- External biliary fistula − Management consists of external biliary fistula consists of endoscopic biliary stenting for approximately four to six weeks; sphincterotomy may also be effective.
- Sphincter of Oddi stenosis − Management of sphincter of Oddi stenosis consists of sphincterotomy.
- Bile duct stricture – For most patients with a biliary stricture associated with cholestasis, management consists of ERCP with balloon dilation and placement of a temporary biliary stent. Several endoscopic sessions may be required to achieve stricture resolution.

ALVEOLAR ECHINOCOCCOSIS (E. MULTILOCULARIS)

- The treatment of alveolar echinococcosis (AE) due to E. multilocularis is generally less effective than the treatment for cystic echinococcosis (CE) due to E. granulosus.
- In general, the approach to treatment of AE consists of surgery. Infected tissues should be removed as completely as possible, which requires complete excision of parasitic tissue and may also warrant radical resection of host tissue. The feasibility of radical resection depends on the site of the lesion, presence of metastases, patient comorbidities, and available surgical expertise.
- The benefit of routine preoperative albendazole administration is not known. Postoperatively, albendazole (10 to 15 mg/kg per day in two divided doses; usual adult dose 400 mg twice daily) should be administered to reduce the likelihood of relapse, even in cases of apparent cure. Alternative agents such as mebendazole, praziquantel, nitazoxanide, and amphotericin are less effective than albendazole.

- The optimal duration of albendazole is uncertain; in general, at least 2 years of therapy is advisable in conjunction with at least 10 years of follow-up monitoring for recurrence. Local complications may develop that warrant intervention such as stenting, drainage of necrotic liver lesions, or endoscopic sclerosing of esophageal varices.
- The role of palliative surgery is limited; in some cases, it may reduce the burden of infection and increase the benefit of adjunctive drug therapy.
- In cases that are not amenable to definitive surgery, albendazole should be administered indefinitely to suppress progression of infection. In such cases, albendazole is not curative but can improve quality of life and prolong survival. Survival rates at 15 years of 53 to 80 percent have been observed with palliative albendazole in the absence of surgery (versus 15 year mortality rate of 100 percent without treatment). Approximately half of patients respond with regression or lesion stabilization.
- As a last resort, liver transplantation may be a consideration

Thanks