

## HYDATID DISEASE: CURRENT STATUS AND RECENT ADVANCES

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Hydatid disease, also known as echinococcosis or hydatidosis, is caused by infection with larva (metacestode) of the tapeworms of the genus *Echinococcus*. Within the genus *Echinococcus*, four species are recognized: *E. granulosus* which causes cystic hydatid disease; *E. multilocularis* which causes alveolar hydatid disease; *E. vogeli* and *E. oligarthrus* both of which cause polycystic hydatid disease (Table 1).<sup>1,2</sup>

Hydatid disease is a public health problem in Asia, the Mediterranean, South America and Africa. With immigration, the prevalence of the disease has increased in Europe and North America in recent years.<sup>3-8</sup> There has been considerable recent progress in the diagnosis and surgical treatment of hydatid disease.<sup>2,9,10</sup> Drug therapy and percutaneous aspiration have been successfully used to treat hydatid disease, and long-term results have been encouraging.<sup>11,12</sup> In view of the above, clinicians need to be aware of the prevalence of hydatid disease and the recent advances on its treatment.

### Life Cycle

*Echinococcus* species require two hosts for completion of the life cycle. The definitive hosts are carnivores harboring mature tapeworms in the intestines. Metacestodes develop in the liver and other viscera of intermediate hosts, and under natural conditions, host assemblages are linked together in predator-prey relationship. Human beings become incidental intermediate hosts and do not complete the life cycle of the parasite.

Adult *Echinococcus* species are small tapeworms measuring 2-11 mm in length. Each adult worm consists of a protoscolex, the cephalic end for attachment and 2 to 5 segments, the proglottids. The scolex bears two rows of keratinized hooks and four suckers. The proglottids are produced continuously from the neck region immediately

behind the scolex. The terminal gravid proglottid contains several hundred fertilized eggs and is shed every 7 to 14 days. Ovoid eggs have a diameter of 30-36 µm and contain fully differentiated oncosphere. Eggs are shed with the feces of the infected definitive host. When ingested by a suitable intermediate host, the oncospheres hatch in the small intestines, become activated, penetrate the epithelial layer and migrate via blood or lymphatic vessels to the viscera. In the viscera, the oncosphere undergoes a series of reorganization events involving degeneration, cell proliferation, differentiation and vesiculation, resulting in the formation of primary vesicle (metacestode). Metacestode develop into hydatid cyst by a process unique for each species of *Echinococcus*. Scoleces are formed within the cysts which when ingested by the definitive host (eating offal of intermediate host) develop into adult tapeworms.

### Cystic Hydatid Disease

#### Geographic Distribution (Figure 1)

*E. granulosus* is a cosmopolitan parasite and has at least six genetically distinct strains, two of which are relevant to human infection. The sylvan strain is maintained in wolves and wild ungulates in Northern Alaska, Canada, Scandinavia and Eurasia. The pastoral strain is maintained in dogs and domestic ungulates throughout the world. Most of the human infections occur from pastoral strain maintained between dog and sheep. Endemic regions of human cystic hydatid disease include the southern parts of South America (Uruguay and Argentina), the Mediterranean region, the Middle East, many parts of Africa (especially Kenya), Southern and Central Russia, Central Asia and many regions in China (especially Xinjiang province). The majority of patients reported in Austria, Germany and Switzerland are immigrants from the Mediterranean region. The disease has been eradicated in Iceland and disease load significantly diminished in New Zealand, Tasmania and Cyprus by control measures. In the United States, most infections are seen in immigrants from endemic areas, but autochthonous transmission is currently recognized in Alaska, California, Utah, Arizona and New Mexico. The annual incidence of human infection in endemic areas varies widely (<1 to 220 per 100,000 per annum) from region to region.<sup>1-8,13</sup>

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FIGURE 1. Geographical distribution of cystic hydatid disease.

FIGURE 2. Life cycle of *Echinococcus granulosus*. The parasite completes the life cycle between dog, the definitive host and sheep, the intermediate host. Human beings become incidental intermediate hosts and do not complete the life cycle of the parasite.

FIGURE 3. Morphology of cystic hydatid disease. Panel A shows resected left upper lobe lung with a large hydatid cyst. Panel B shows detached ivory-white laminated membrane of the cyst. Panel C shows histological section of the laminated membrane. The inner dark staining layer is the germinal layer of the cyst. Panel D shows two evaginated protoscolices within brood capsules.

### Pathogenesis and Pathology

Dogs infected with the tapeworm, *E. granulosus*, pass eggs in their feces and the cestode eggs adhere to the hair, muzzle and paws of the animal. Humans become infected in the course of playful and/or intimate contact with the infected animal. The eggs hatch in the small intestine, liberate oncosphere that burrow the mucosa, migrate via vessels or lymphatics to distant sites, and develop into a metacestode. The metacestode develops into a unilocular fluid-filled cyst (Figure 2).<sup>2,10,13</sup>

*E. granulosus* cysts following primary infection may inhabit any anatomic site. The two most common organs involved are liver (65%) and lungs (25%). Cysts of the sylvan strain predominantly localize in the lungs. Other less common sites affected by cysts include the muscles (5%), spleen (1%), bones (3%), kidneys (2%), heart (1%), pancreas (1%) and central nervous system (1%). The majority of patients have single-organ involvement (87%) and harbor a solitary cyst (72%). Secondary infection follows cyst rupture and scolices can grow in the peritoneum, pleura, bronchial tree and bile ducts or be carried via blood stream to distant organs. Cyst size ranges from 1 to 15 cm and cyst growth varies from 1 to 30 mm per year.<sup>13,14</sup>

Hydatid cyst wall consists of inner germinal layer and outer laminated membrane (Figure 3). Surrounding the wall is the pericyst, which has an outer zone of compressed liver cells, middle zone of heavy lymphoplasmocytic infiltrate and inner tough zone formed of collagen. The cyst fluid is crystal clear with a specific gravity of 1.012 and contains salts, enzymes, proteins, and toxic substances, and is antigenic. The germinal layer forms small cellular masses projecting into the cyst cavity, which vesiculate to form brood capsules. In each brood capsule, multiple protoscolices (head of the future worm) develop on the inner surface of their walls by asexual budding. Brood capsules and protoscolices may be released into the cyst fluid to form hydatid sand. Protoscolices have a potential to develop into adult tapeworm within the gut of the definitive host, differentiate into secondary cysts when released following cyst rupture (ectogenic vesiculation), and form daughter cysts within the mother cyst by endogenic vesiculation. Each daughter cyst is a true replica of the mother cyst and has a germinal layer and laminated membrane and contains brood capsules and protoscolices. Daughter cysts may be packed together in the mother cyst (multivesicular cyst) or float freely in the mother cyst cavity. In older cysts, the contents degenerate forming a gelatinous amber-colored structure called the matrix. The matrix gives a pseudo-tumor appearance on imaging tools and can be confused with pus by the surgeon. Calcification can occur in the pericyst, mother cyst and daughter cyst. Calcification of endocyst indicates that the cyst is nonviable. However, calcification of the pericyst is found in one-third of cysts and occurs in all stages of cyst development.<sup>2</sup>

TABLE 1 *Human hydatid disease*

	Cystic	Alveolar	Polycystic	
<b>Agent</b>				
Species	<i>Echinococcus granulosus</i>	<i>Echinococcus multilocularis</i>	<i>Echinococcus vogeli</i>	<i>Echinococcus oligarthrus</i>
Adult size	2-7 mm	4-11 mm	1.9-3.7 mm	1.9-2.9 mm
Definitive host	Dog, wolf, jackal, lion	Foxes	Bush dogs	Wild felid
Intermediate host	Sheep, cattle	Rodents	Paca	Spiny rats
<b>Human disease</b>				
Occurrence	Common	Uncommon	Rare	Extremely rare
Mode of infection	Contact with infected dogs	Contact with fur from infected fox, ingestion of contaminated wild berries	Contact with hunting dogs	Contact with infected cats fed on paca
Lesion appearance	Fluid filled unilocular cyst	Solid mass	Polycystic fluid filled	Polycystic fluid filled
Calcification	Ring type (30%)	Microcalcification or plaque like foci (70%)	Annular, bizarre, amorphous (50%)	Not known
<b>Organs involved</b>				
Primary	Liver (65%), lung (25%), others	Liver (100%)	Liver (100%)	Extrahepatic (orbit others)
Spread	By rupture	Contiguous, metastatic to lung, brain	Contiguous	Contiguous
Presentation	No symptoms, mass effect, rupture, infection	Invasive liver mass, liver failure, cholestasis, Budd chiari, portal hypertension, lung and brain involvement	Liver masses, liver failure, cholestasis, Budd chiari syndrome, portal hypertension	Exophthalmos, soft tissue mass
Mortality untreated (10 years)	Unusual (<5%) (anaphylaxis/complicated cyst)	High (75-100%)	High (>75%)	Not known

### Clinical Manifestations

Infections are usually acquired during childhood, however, most cases of cystic hydatid disease present in adults in the third to fifth decades of life, with equal sex distribution. The clinical features depend upon the organ involved, site of organ involvement, stage of cyst development and viability of the cyst contents. The majority of the cysts produce no symptoms and are detected as incidental findings on routine imaging or at autopsy. Symptoms of the disease are related to expanding mass, pressure on adjacent structures, infection and rupture of cyst contents into surrounding body cavities.<sup>15</sup>

Uncomplicated liver cysts usually present with dull ache in the right upper quadrant or a feeling of abdominal swelling or distension. Clinical examination is unremarkable except for enlarged liver with a rounded mass felt on its surface. A hydatid thrill may be elicited on a large mass pointing to its fluid content. Rarely, the mass is calcified giving it a hard consistency, and needs to be differentiated from a primary or secondary liver tumor.<sup>13,15</sup> A large cyst in the hilar region can compress the common hepatic duct causing cholestasis.<sup>16</sup> Hepatic vein or inferior vena cava compression can cause Budd-Chiari syndrome.<sup>17</sup> Cyst rupture into the biliary tree causes obstruction of the ducts by daughter cysts and laminated membranes and presents as biliary colic, cholangitis and progressive cholestasis.<sup>18</sup> Cyst contents may block the ampullary orifice causing acute pancreatitis. Cyst rupture into the peritoneum causes immediate life-threatening anaphylaxis and if the person survives, the scoleces implant on the peritoneal surface resulting in extensive peritoneal hydatidosis.<sup>19,20</sup> A

cyst can rupture into the pleural cavity or lung and can establish cystobronchial fistula.<sup>15</sup> Rarely, cyst can grow on to the skin along a sinus tract following surgery or percutaneous drainage of the cyst.<sup>21</sup> Infection of the cyst follows tear in the laminated membrane and soilage of the cyst with bile or blood. Infected hydatid cyst has clinical features of a liver abscess.<sup>15</sup>

Intact hydatid cysts in the lungs often cause no symptoms. However, a large cyst may cause pressure symptoms and lead to cough and hemoptysis. Complications arise when the cyst ruptures either into the bronchial tree or pleura. Bronchial rupture manifests with cough, chest pain and dyspnea. Spontaneous cures are known, as laminated membranes may be coughed up leading to collapse and disappearance of the cyst cavity. Rupture of cyst contents into the pleural cavity may cause allergic reactions including anaphylaxis, pleural effusion, pleural implantation and empyema. Infection of the cyst follows leakage of the cyst and presents as lung abscess.<sup>13,15</sup>

Involvement of other organs can lead to varied manifestations, namely soft tissue fluctuant swelling (muscle cysts), raised intracranial pressure and focal epilepsy (cerebral cysts), segmental portal hypertension (splenic cysts), acute pancreatitis and obstructive jaundice (pancreatic cysts), bone pain, swelling and pathological fractures (bone cysts), paraplegia (vertebral body cysts), conduction defects, pericardial effusion and cardiac tympanade (cardiac cysts), loin pain and hematuria (kidney cysts), unilateral exophthalmos and blindness (orbital cyst).<sup>22-24</sup>

### Diagnosis

Routine hematological and biochemical tests do not help in diagnosis of cystic hydatid disease. Serology and imaging tools establish diagnosis.

### Serology

Serology detects specific serum antibodies or circulating antigen by a variety of immunodiagnostic methods. Of these, the enzyme immunoassay (ELISA) employing hydatid fluid antigen for detection of echinococcal antibodies (IgG) in the serum is the most widely used. This test has a sensitivity of 80% -100% and specificity of 88%-96% in hepatic cysts. However, the sensitivity of this test is around 50% -56% in pulmonary cysts and 25% -56% in cysts involving other organs. False-positive test can occur in normal persons from endemic areas and in those with other parasitic infections.<sup>25,26</sup> Positive test results need confirmation by the arc-5 immunoelectrophoretic (IEP) test, which detects antibodies against immunodominant and specific antigen (antigen 5) of the cestode. This test does not cross-react with noncestode parasites. Cross-reaction with *Taenia solium* cysticercosis does occur and need to be differentiated in regions where both infections are prevalent.<sup>27</sup> Serological tests have limitations in monitoring patients after surgery, percutaneous drainage or drug therapy. The antibody titers rise following surgery and percutaneous drainage. The titers start falling at 3 months and become negative in a period of 12-24 months.<sup>12</sup>

PCR using recombinant DNA antigens is valuable in defining particular species of *E. granulosus*. This has been effectively applied in the control of the disease and development of an animal vaccine.<sup>28</sup>

### Imaging

A number of imaging tools are available to define hydatid cysts and need to be utilized judiciously. The selection of these tools depend upon the organ to be imaged, the status of the cyst (intact, ruptured or infected) and adjacent structures which need to be assessed.<sup>2,18,29</sup> Plain radiography has a role in lung and bone cysts. A plain film of chest shows intact cyst as sharply demarcated round-to-oval homogenous mass of variable size. Pulmonary cysts do not calcify, and daughter cyst formation is rare. Rupture of the cyst wall may present as the air meniscus sign (radiolucent air shadow between pericyst and intact endocyst); the double arch sign (air delineating wall of the pericyst, the outer arch and detached wall of the endocyst, the inner arch); and the water lily sign (collapsed wavy endocyst membranes floating on the top of remaining cyst fluid). Bone cysts occur in the pelvis, vertebral column, long bones and skull, and cause expansion and destruction of the bone without attempt at repair. A true pericyst does not develop within the bone. The lesion often crosses the joints and involves adjacent bones. A plain film of abdomen may show liver cyst

calcification. This occurs in the ectocyst and is typically curvilinear (egg shell calcification). Endocyst calcification is spotty in nature and appears as speckled calcified densities. Cysts at other sites may calcify and are shown on plain films of the organs.<sup>30,31</sup>

Abdominal cysts, particularly in the liver and cysts in soft tissues, are well visualized by ultrasound. Cysts may appear univesicular, rounded with well-defined margins containing pure fluid, or multivesicular (daughter cysts) with pure fluid collection in each vesicle. Cysts may have hyperechoic solid pattern (pseudotumor appearance) or may have reflective wall suggestive of calcification. Rupture of liver cysts into the bile ducts can be suspected on ultrasound. Ultrasound appearances include dilated bile ducts, non-shadowing echogenic structures within the ducts and loss of continuity of the cyst wall adjacent to the bile duct representing site of communication. However, ERCP is the recommended tool and reveals filling defects of varying shape and size in the dilated bile ducts and leakage of contrast medium into the cyst cavity.<sup>26</sup>

Computed tomography is the method of choice for detecting lung, brain and bone cysts. It has an advantage over ultrasound for cysts at other sites for better documentation of site, size and structure of cyst and for monitoring of lesions during chemotherapy and following surgery, daughter cysts and detachment of membranes, if any. Magnetic resonance imaging may show a characteristic intense rim. Angiography and scintigraphy have no major advantage over above imaging tools and are rarely employed in this setting.<sup>24</sup>

Diagnostic puncture of cysts is only justified when imaging and serological tests do not permit discrimination between hydatid cyst and neoplasm. It carries risk of anaphylaxis and spillage of cyst contents with secondary echinococcosis.<sup>31,32</sup>

### Treatment

Treatment options for cystic hydatid disease are surgery, drug therapy and percutaneous drainage. Surgery has the potential to remove cysts and lead to complete cure. Surgical procedures of choice include cystectomy with removal of the germinal and laminated layers and preservation of pericyst. Cavity is either tightly drained, closed, or packed with omentum (omentoplasty). Occasionally, cyst is removed by total pericystectomy, partial hepatectomy or segmentectomy. Surgery is the treatment of choice in large hepatic cysts with multiple daughter cysts, subcapsular or pedunculated liver cysts, infected liver cysts, cysts communicating with bile ducts, and cysts in the lungs, brain, kidney, bones and other organs. Surgery is contraindicated in patients at extremes of age, pregnant women, patients with co-morbid diseases and in those with multiple cysts and cysts, which are difficult to access. Operative mortality varies from 0.5% -4.0% in centers with adequate medical and surgical facilities. Cyst fluid spillage can occur during surgery resulting in

anaphylaxis and/or secondary echinococcosis (2% -25% of cases).<sup>10,33-35</sup>

Two benzimidazoles (mebendazole and albendazole) and praziquantel, an isoquinolone derivative, have scolicidal activity and have been used in over 1000 well-documented patients with cystic hydatid disease.

Mebendazole is poorly absorbed, and scolicidal drug levels are achieved with a daily dose of 40-50 mg/kg administered orally in divided doses. Albendazole is better absorbed, and the usual daily dose is 10-15 mg per kg. Drug dosing with a fat-rich meal improves intestinal absorption. Cyclic treatment (three 1-month courses with intervals of 14 days) has been widely used. Recent data show that uninterrupted drug therapy for 3-6 months has better efficacy with no increase in adverse effects. Praziquantel is administered at a dose of 40 mg/kg once a week concomitantly with benzimidazoles, and has been shown to increase the scolicidal activity of the imidazoles. Chemotherapy achieves a cyst disappearance of 30%, partial response in another 30% and no response in 40%. It is effective in small cysts (<4 cm diameter), cysts with thin walls and in younger patients. It is indicated in patients who are high risks for surgery, in patients with multiple peritoneal cysts, to prevent secondary echinococcosis after spillage during surgery, and as a concomitant therapy with percutaneous drainage. Imidazoles are hepatotoxic, can cause neutropenia, thrombocytopenia, alopecia and are potentially embryotoxic and teratogenic.<sup>11,36-41</sup>

Recently, percutaneous drainage of hepatic hydatid cysts, popularly known in Europe as the PAIR (Puncture, Aspiration, Installation of scolicidal agent and Reaspiration) technique has gained acceptance.<sup>42-48</sup> The procedure is minimally invasive, cost-effective, involves reduced hospital stay and has less morbidity and mortality than surgery.<sup>12</sup> It is the treatment of choice in patients with hepatic hydatid cysts who either refuse surgery or have significant co-morbid diseases.<sup>36</sup> The procedure is highly effective in intact univesicular and multivesicular cysts with few large daughter cysts, cysts with diameters of over 5 cm and multiple cysts in different liver segments. Cysts relapsing after surgery or failed to regress following chemotherapy are amenable to percutaneous drainage. The procedure cannot be done in superficial or pedunculated cysts, small volume cysts, cysts with honeycomb appearance (multiple small daughter cysts), cysts with dominant solid component, and those with infection or communicating with bile ducts. The procedure is associated with possible complications of liver puncture (bleeding, bile peritonitis), anaphylaxis, allergic reactions and biliary communications.<sup>36</sup> Inadvertent installation of sclerosing agent into a cyst with biliary communication can cause sclerosing cholangitis.<sup>49,50</sup> Long-term follow up has shown that secondary echinococcosis does not occur following percutaneous drainage.<sup>21</sup>

Endoscopic therapy has been used in a small number of patients with hepatic cysts which have ruptured into bile

FIGURE 4. Geographical distribution of alveolar and polycystic hydatid disease.

FIGURE 5. Polycystic hydatid disease with cholestasis. Panel A shows contrast-enhanced CT scan of upper abdomen. Left lobe liver is replaced by large multicystic mass with involvement of surrounding structures. Panel B shows a cholangiogram obtained at ERCP. Common bile duct in its upper part revealed a complete obstruction by infiltrating cyst. Panel C shows resected left lobe liver revealing multicystic mass. Each cyst was fluid filled with surrounding laminated membrane. The hooklets from the fluid had characteristic morphology of *Echinococcus vogeli*.

ducts. At ERCP, endoscopic sphincterotomy is performed; laminated membranes and daughter cysts are extracted, and a nasobiliary drain is placed in the bile duct. The cyst regresses and disappears over the next 4-6 weeks.<sup>12,20,44,51</sup> Laparoscopic removal of hepatic cysts have been reported and liver transplant has been performed in extensive hepatic hydatidosis not amenable to surgical resection. None of these modalities have been evaluated in controlled trials.<sup>52,53</sup>

### Alveolar Hydatid Disease

#### Geographic Distribution (Figure 4)

*E. multilocularis* has limited distribution in the northern hemisphere, within a belt stretching from the Northern Tundra zone southward to some regions around the 40th to 45th degree of northern latitude.<sup>13</sup> Human alveolar hydatid disease has been reported in central parts of Europe (Southern Germany, Western Austria, Switzerland and Eastern France), some parts of Russia (Siberia), Eastern Azerbaijan, some parts of Turkey (Eastern Anatolia), Northern Iran, Northern Afghanistan, Northern India (Kashmir), Northwestern Canada, Western Alaska (St. Lawrence Island) and Northern Japan (Hokkaido). The annual incidence of human infection is low (0.03 to 1.2 per 100,000 per annum) in most of the areas where disease is reported.<sup>54-57</sup>

#### Pathogenesis and Pathology

Humans are exposed to *E. multilocularis* by direct handling of the infected fox carcass or through ingestion of berries contaminated with cestode eggs. The egg hatches in the small intestines, release the oncosphere which penetrates the mucosa and is carried via blood or lymphatics to the liver. In the liver, metacestode divides asexually by lateral budding of germinal tissue and the secondary vesicles invade and infiltrate the surrounding host tissue. Surrounding each vesicle, there is intense host cell response consisting of epithelioid cells, lymphocytes and thick collagen tissue. This gives rise to a tumor, which may cavitate in the center. Calcification of the lesion is seen in over 70% of the cases and occurs as clusters of micro-calcifications or plaque-like calcific foci, with irregular distribution in central or peripheral parts of the lesion. In humans, the parasite does not form protoscolices and is

made of a thin cuticle with non-germinative membrane demarcating a small cavity.

Primary infection occurs in the liver in all cases. The disease invades bile ducts, portal veins, hepatic veins and inferior vena cava and the adjacent structures beyond the organ borders. The disease metastasizes via the blood stream and lymphatics to distant organs namely lung, liver and bone. The growth of alveolar cysts in liver and other body organs is very slow and requires 5 to 15 years for the cyst to become symptomatic.<sup>54</sup>

#### *Clinical Manifestations*

The age of presentation of the alveolar disease is in 5th decade and beyond, with equal sex distribution. The disease has insidious onset and is detected as an incidental finding in over one-third of patients.<sup>13</sup> Hepatic disease presents as fatigue, epigastric pain, abdominal mass, and abnormal liver function tests. The disease has chronic progressive clinical course. Over the years, patients develop progressive hepatic failure (extensive hepatic infiltration), cholestatic jaundice (biliary obstruction), Budd-Chiari syndrome (hepatic venous outflow obstruction), portal hypertension (portal venous obstruction) and ascites (peritoneal involvement). Hepatic lesion can also grow into the pleura, lungs, inferior vena cava, right atrium, pericardium, retroperitoneum, kidneys and pancreas. This results in varied clinical manifestations depending on the organ involved. Apart from contiguous spread, the parasite metastasizes to the lungs, brain and bones resulting in multiple foci of *Echinococcus* infection. If untreated, the disease results in death in most of the patients in around 10-15 years.<sup>54-59</sup>

#### *Diagnosis*

The routine laboratory tests do not help in the diagnosis of alveolar hydatid disease. However, such tests help to assess the extent of hepatic involvement.

#### *Serology*

Serologic tests are very useful in diagnosis. Enzyme immunoassay using specific antigen Em2plus (mixture of purified metacestode antigen Em2 and a recombinant EmII/3-10 antigen) has a sensitivity of 97.1% and specificity of 98.9% in the diagnosis of alveolar hydatid disease.<sup>13</sup>

#### *Imaging*

The parasite liver lesions have varied ultrasound patterns: solid heterogeneous echo texture with multiple echogenic nodules (hailstorm pattern), echogenic area associated with cystic zones (geographical map pattern) and transonic pseudocystic necrotic zone with debris. CT scan reveals heterogeneous hypodense mass, which does not enhance with intravenous contrast. Clustered micro-calcification and characteristic perinecrotic plaque-like calcifications are detected in these lesions. Magnetic

resonance imaging is very useful in assessing the spread of disease to hepatic veins, portal veins and bile ducts. ERCP and hepatic venography may be needed to find the site and extent of bile duct and hepatic vein disease, and for possible dilation and stenting.<sup>56,57</sup>

#### *Treatment*

Treatment options include radical resection of the involved liver segments or other affected organs, long-term chemotherapy and liver transplantation. Radical liver resection is considered in patients with localized liver disease without involvement of major blood vessels and distant metastasis. Around 20% -40% of patients at presentation are amenable to radical liver resection. Hemihepatectomy or extended (trisegment) liver resection can be performed with operative mortality of 0% -5%. Following radical surgery, chemotherapy is recommended for two years and disease surveillance for 10 years. Long-term survival in patients with radical resection is nearly 100%.<sup>36,54</sup>

Long-term (life-long) chemotherapy is indicated in patients with inoperable disease or in those with incomplete surgical resection. *Benzimidazole* derivatives (mebendazole or albendazole) are generally well tolerated, and adverse reactions are usually mild and transient. These drugs suppress metacestode growth and stabilize tumor size. Tumor regression occurs in around 20% of patients. Surveillance of patients on chemotherapy has shown marked improvement (10-year survival of 80% -83% , and a

15-year survival of 53% -83% ) when compared to historical patients on no chemotherapy (10 year survival of 0% -25% and a 15-year survival of 0%).<sup>13,36</sup>

Liver transplantation has been performed in a small group of patients with extensive liver involvement and liver failure. Local disease recurrence or distant metastasis occurs in around half of patients within one year of transplant. Six-year survival of 66% has been reported. In view of disease recurrence, adjuvant post-transplant chemotherapy is recommended.<sup>60</sup>

#### **Polycystic Hydatid Disease**

Polycystic hydatid disease is the developed metacestode of *E. vogeli* or *E. oligarthrus* in humans. *E. vogeli* is a rare human disease, and sporadic human cases have been reported in neotropical America (Panama, Ecuador, Colombia, and Venezuela) and French Guiana (Suriname) (Figure 4). *E. oligarthrus* is an extremely rare human disease and only isolated case reports have been recorded from Venezuela, Brazil, India and Suriname.<sup>61-64</sup>

#### *Pathogenesis and Pathology*

Bush dogs, the definitive hosts, play little role in direct exposure in humans. In contrast, hunting dogs fed on the raw viscera of pacas get infected and then expose humans.

*E. vogeli* and *E. oligarthrus* metacestodes develop by endogenous proliferation of membranes in a unique fashion resulting in the formation of polycystic masses (Figures 5). Cysts of varying size are grouped together, each containing a yellowish fluid or gelatin-like substance. Cysts are often packed with proliferated laminated membranes that become convoluted giving a cerebroid configuration. Brood capsules and protoscolices are formed within the cavities. Cysts are surrounded by a chronic inflammatory foreign body granulomatous reaction similar to that observed in parasite-induced granulomas. The larval structures often degenerate with secondary calcification. Calcification is seen in around half of cysts and may be annular, bizarre or amorphous.<sup>61</sup>

Liver is the primary site of infection in *E. vogeli*. Surrounding structures, like diaphragm, lungs, pericardium, heart, mesentery and omentum, can be involved by contiguous spread. In contrast, *E. oligarthrus* produces polycystic disease in only extrahepatic tissues, namely orbit, lower jaw, heart and other sites without liver involvement.<sup>58-61</sup>

#### Clinical Manifestations

Polycystic hydatid disease of the liver presents in the fourth decade and beyond. The majority of patients present with abdominal pain, abdominal distension, fever and weight loss. Clinical examination reveals hepatomegaly and hard, round masses on the liver surface. The disease is slowly progressive and clinical course is complicated by progressive liver failure, cholestasis, portal hypertension and involvement of surrounding structures.<sup>58</sup>

#### Diagnosis

Serologic tests are positive in most of the patients, especially in those with hepatic involvement. *E. vogeli* and *E. oligarthrus* share antigens with other *Echinococcus* species, thus current immunodiagnostic tests do not permit specific diagnosis of polycystic disease. Ultrasound, CT scan and MRI are useful in defining polycystic large fluid-filled larval cestode lesions with diffuse calcification. However, specific or characteristic findings of these cysts have not been reported in detail. Aspiration of the cysts, especially in the extrahepatic sites, is recommended and shows scoleces. Species diagnosis and differentiation is possible by examining the size and shape of rostellar hooklets in the scoleces. Anaphylaxis has been reported with aspiration of soft-tissue cysts, and needs to be done under close patient monitoring.<sup>61-64</sup>

#### Treatment

Radical surgical excision of cysts in the soft tissue, if possible, is the ideal treatment. Albendazole therapy prior to and following excision is recommended, particularly if the excision is not complete. Liver cysts need radical excision if localized. Extensive disease can be treated by long-term albendazole and praziquantel therapy.<sup>61-64</sup>

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