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Ultrasound of Tropical Medicine
Parasitic diseases of the liver

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Amoebiasis

Amoebiasis is a parasitic infection caused by the protozoon *Entamoeba histolytica*. It is the third highest parasitic cause of death after malaria and schistosomiasis in developing countries, with an estimated 40,000 to 100,000 fatalities every year. Amoebic infection has been reported to affect approximately 12% of the world’s population and up to 50% of the population in tropical and subtropical regions, although the majority of these infections are caused by the non-pathogenic *E. dispar*, which is morphologically indistinguishable from *E. histolytica*.

Infection is acquired faecally or orally by ingestion of mature cysts passed in the faeces of infected individuals. This is made worse by poor sanitation, particularly in developing countries. After ingestion of mature cysts, excystation occurs in the small bowel. The trophozoites infect the large intestine and they remain confined (asymptomatic non-invasive infection), multiplying and producing cysts that are passed in the faeces. In some patients, the trophozoites invade the intestinal mucosa (intestinal invasive disease), which causes characteristic flask-shaped ulcers, and may disseminate through the bloodstream to other sites such as the liver, lungs and brain (extra-intestinal disease) to cause amoebic abscesses. These are usually located in the right lobe of the liver and are known as amoebic liver abscess (ALA).

ALA develops in less than 1% of *E. histolytica* infected patients. Adult males are affected 10 times more than women [(1)]. Abscesses form by the coalescence of initially small foci of hepatic necrosis, and are made up of a central area of colliquation (“amoebic pus”) surrounded by a rim of liver tissue and inflammatory cells in which the trophozoites feed and multiply. No capsule is present.

In non-endemic areas, symptoms of ALA typically begin a few months after the patient has travelled to an endemic region and include weight loss, high fever, chills and right upper quadrant abdominal pain or pleuritic pain.

Hepatomegaly and jaundice may be present, as well as atelectasis and pleural effusion. Rupture into the pleural cavity presents as a cough, pleuritic pain and dyspnoea. Occasionally, expectoration of brown amoebic material can occur if there is erosion of a bronchus. Abscesses located in the left hepatic lobe may rupture into the pericardium causing pericarditis or tamponade. In the abdominal cavity, rupture into the peritoneum occurs in 2–7% of cases, more often with abscesses located in the left lobe, but many other structures can be involved (bowel, large vessels, bile ducts and retroperitoneum). Finally, infection may spread to the skin and the central nervous system.

The diagnosis of ALA is based on clinical findings, laboratory tests and imaging techniques. Even if there is no history of diarrhoea this should not rule out ALA. Leukocytosis without eosinophilia, hypoalbuminemia and elevated alkaline phosphatase are common findings. Trophozoites are occasionally observed in abscess material, but the examination of the stool for ova and parasites is often negative in extra-intestinal amoebiasis. Serological tests are useful for the diagnosis of invasive amoebiasis. Antibodies are detectable 7–10 days after the onset of symptoms and gradually decrease in the 2 months following treatment; however, they persist for years, which limits the antibodies diagnostic value in patients from endemic areas.

Ultrasonography is reported to be as sensitive as CT and MRI, but very early pre-colliquative stages cannot be detected. On ultrasound, ALA lesions are typically single (in over 60% of cases), located in the right hepatic lobe near the surface of the organ, round or oval in shape. They appear hypoechogenic, with initially irregular and ill-defined margins (first 4–5 days), occasionally they are hyperechoic. Later, with the progressive colliquation of necrotic material, the lesion assumes a homogeneous hypoechoic pattern, with regular, well-defined
margins [Figure 1] [(2)]. This appearance typically occurs within 2 weeks. In immunocompromised patients, the amoebic abscess can assume a tumour-like or honeycomb appearance. In the healing phase, a slow progressive evolution can be observed with the lesion increasing in echogenicity and showing an irregular and ill-defined margin. Sometimes a sterile cystic cavity can persist for months or years [(3)].

Figure 1 Different sonographic appearance of ALAs. Large hypoechoigenic lesion with almost solid content (a) and hypoechogenic necrotic areas (b, c and d). Well-defined margins with slightly echogenic content in a quasi-cystic ALA.

The differential diagnosis includes pyogenic liver abscesses (PLA), echinococcal cysts and hepatic tumours. Patients with pyogenic liver abscess tend to have a more severe form of the disease; they have positive blood cultures, are probably older with significant co-morbidities such as diabetes and have a history of recent biliary disease or surgery. On ultrasound PLAs tend to be multiple with irregular and faded margins. Their echogenicity varies depending on the stage of the disease, from hypoechoic (pre-suppurative and resolution phase) to anechoic with floating or stratified echoes, or hyperechoic (suppurative phase). In the chronic phase, PLA walls may be hyperechoic with a thick fibrous capsule, they are sometimes surrounded by a thin hypoechoic halo. Echinococcal lesions are typically
asymptomatic. Their appearance on imaging is often unusual and rarely misleading (see Cystic Echinococcosis section). Malignant primitive or metastatic hepatic tumours can present as cystic lesions and should be considered in the differential diagnosis of ALA. Ultrasound-guided percutaneous drainage of abscesses followed by microscopic examination is a useful diagnostic tool. Amoebic “pus” has a typical “anchovy paste” appearance [Figure 2]. Ultrasound is useful in follow-up because the abscess resolution generally occurs between 2–20 months from the start of treatment.

Figure 2 “Anchovy paste” appearance of amoebic material drained from a liver abscess.

Besides ALA, amoebic colitis is also often found on ultrasound, the colon wall is typically thickened and hypoechoic. Typical ulcerative colitis is shown in Figure 3. Metronidazole is effective for the invasive forms, followed by either iodoquinol, paromomycin or diloxanide, which are active against the parasites in the gut lumen. Typical ulcerations are shown in Figure 3.

Figure 3 Amoebic colitis. Endoscopy reveals typical ulcerations (a). Ultrasound shows the signs of severe ulcerative colitis (b). Incidental finding of multiloculated liver abscess with liver like parenchyma echogenicity using panoramic imaging (c). Detail of the left liver lobe (d) and detail of the right liver lobe applying contrast enhanced ultrasound indicating non-enhancing abscess formation (e).
Ultrasound-guided percutaneous drainage, and less frequently surgical drainage, is indicated in cases of imminent rupture or risk of rupture in the pericardium, treatment failure, large cysts (>10 cm) or in pregnant women. Although size is often cited as the main reason to drain ALA percutaneously, the evidence on which this decision is made is still weak and prospective studies are needed [(4)].

**Ascariasis**

An estimated 1.2 billion people are infected by *Ascaris lumbricoides*, making ascariasis the most common human helminthic infection [(5)]. Although most infections are asymptomatic, over 250 million people are estimated to suffer from associated morbidity, and more than 200,000 deaths are attributed to ascariasis every year. It is also a significant cause of biliary disease in areas where the rate of *Ascaris* infection is high, representing 10–19% of all *Ascaris*-related hospital admissions. Ascariasis is found throughout the world, but it is more common in warm climates and overcrowded rural communities with inadequate sewage systems [(6)]. The infection is more common and severe among children, whereas biliary ascariasis is more common in adults.
Adult worms live in the small intestine, usually the jejunum in which the females produce eggs that are passed into the faeces. In the environment, the larva develops within fertile eggs in approximately 3 weeks. Infection occurs through ingestion of material (soil, food or water) contaminated with infective eggs. Once swallowed, the larvae hatch and invade the intestinal mucosa, they are then circulated through the liver to the lungs. Here the larvae penetrate the alveolar walls, ascend the bronchial tree to the throat and are swallowed again. On reaching the small intestine, they develop into adult worms [Figure 4] within 2–4 weeks. Although infection is commonly asymptomatic or oligo-symptomatic, actively motile adult worms can migrate to different segments of the gastrointestinal tract, into the oropharynx and the nose. The most common complication of ascariasis is mechanical bowel obstruction caused by a large number of worms, which may also cause volvulus, intussusception or intestinal perforation. They can enter the appendix and cause appendicular colic and gangrenous appendicitis.

Figure 4  Adult ascaris worms (Courtesy Prof. A. Kabaalioglu).

Severe pathology is associated with the migration of the worms through the duodenal papilla into the biliary system or the pancreatic duct, resulting in obstruction, perforation or pancreatitis. In addition, the intestinal bacteria carried by the worm can induce pyogenic cholangitis and empyema of the gallbladder. The adult worms usually migrate out of the biliary tract shortly after inducing symptoms; however, dead worms or their fragments in the bile duct can serve as a nidus for stone formation causing obstruction, and ongoing inflammation can result in the development of strictures.

Diagnosis of intestinal ascariasis is usually achieved by parasitological stool examinations. Whereas ascaris worms in the intestinal tract may be missed by ultrasound because of bowel gas, ultrasonography is a highly sensitive and specific non-invasive method for the detection of worms in the biliary tract [Figure 5], although the diagnosis of biliary ascariasis requires a high index of suspicion because the worms move in and out of the biliary tract and can be missed on biliary imaging. Adult A. lumbricoides are 15–35 cm long and 2–6 mm in diameter, with an unusual ultrasonographic appearance [(7)]. In longitudinal sections, they have an echogenic non-shadowing tubular structure with a hypo- or anechoic centre, and can be seen moving with a slow-waving pattern. Multiple worms in the bile duct produce a spaghetti-like image, with alternating echogenic and anechoic strips or, if densely packed in the bile duct,
can appear as a hyperechoic pseudotumour. On transverse sections, a “bull’s eye” echo can be seen owing to the presence of a worm in the dilated bile duct.

**Figure 5** Ascaris in the common bile duct (CBD) [Courtesy Dr. Fazal Karim, Dhaka, Bangladesh].

The management strategy for patients with biliary ascariasis depends on the clinical situation; it can include conservative management, endoscopic extraction or surgical intervention. In most cases, pathology resolves with pharmacological treatment and response to treatment can be monitored by ultrasound [(8)]. Conservative treatment includes the use of analgesics, antibiotics for pyogenic cholangitis and oral administration of albendazole, which paralyses the worms in the intestine so that they can be expelled. Symptoms usually resolve within 3 days in 60–80% of patients, shown by the disappearance of worms on ultrasound. Endoscopic intervention is indicated in cases of acute severe pyogenic cholangitis, recurrent biliary colic non-responsive to analgesics, high amylasaemia and when the worms persist in the bile duct for longer than 3 weeks probably because they are dead. Endoscopic extraction of worms across the papilla leads to rapid resolution of symptoms and can be performed using grasping forceps or a Dormia basket [(9)]. Surgical intervention is required when endoscopic treatment fails, or if the worms are located in the intrahepatic ducts or in the gallbladder.

**Toxocariasis (visceral larva migrans)**

*Toxocara spp* are nematodes that affect dogs and cats worldwide. In these definitive hosts, the adult worms reside in the small intestine in which the females produce eggs that are released with the faeces. These are infective in approximately 1 month by development of an infective larva, which can then be ingested by a definitive host or by other animals, including humans (parataenic hosts). In all cases, the eggs hatch in the intestine and the larvae penetrate the bowel wall and migrate through the liver to the lungs and other tissues. In young, pregnant and lactating dogs and cats, the worms complete the cycle and develop into adults. In older dogs and cats, and in the parataenic hosts, the larvae encyst in various organs and do not reach maturity. Dogs, cats and humans can also acquire the infection by ingestion of raw or undercooked meat, which contain the encysted larvae.
Human toxocariasis is caused by the larvae of the dog ascarid, *T. canis*, [Figure 6] or less commonly of the cat ascarid, *T. cati*. Their migration through, and encystation in host’s tissues can cause a severe local reaction, with eosinophilic infiltration and formation of granulomas or eosinophilic abscesses. The associated disease is referred to as visceral larva migrans (VLM) or ocular larva migrans in cases involving the eye. Clinically, most patients are asymptomatic and the infection is diagnosed during the investigation for peripheral eosinophilia. When symptoms are present, these are characteristic of self-limiting febrile eosinophilic syndrome with fever, peripheral eosinophilia, hepatomegaly, abdominal pain or discomfort and possibly cough and dyspnoea involving the lungs.

Figure 6 Adult *toxocara canis* ascarides (Courtesy Prof. C. Cretu and Dr.Mihaiescu, Bucharest, Romania).

The diagnosis of VLM is by serology, which detects antibodies specific for *Toxocara* excretory-secretory antigens. Serology can also differentiate VLM from eosinophilic syndromes caused by other tissue migrating larvae, such as *Fasciola* spp., *Paragonimus* spp., schistosomes, *Ascaris* spp, *Trichinella spiralis*, filariae, *Ancylostoma* spp, *Strongyloides stercoralis*, *Gnathostoma spinigerum*, *Balyascaris procionis* and *Capillaria* spp, which may have similar clinical and imaging features ([10;11]). Ultrasonographic abnormalities include non-specific hepatomegaly, lymphadenomegaly and pleuropericardial effusions. Hepatic granulomas appear as multiple small hypoechoic lesions with ill-defined margins, usually oval, angulated or trapezoid in shape and occasionally a central spot or line (“bean sign”) [Figure 7]. Sometimes lesions conglomerate to form a large area of mixed echogenicity.
The main differential diagnosis of VLM hepatic lesions is with hepatic metastases. Diagnostic clues include hepatic nodules in toxocariasis have ill-defined margins, they are uniform in size and are usually not spherical in shape [(12)]. Contrast CT and MRI can help in the differential diagnosis because *Toxocara* lesions are best seen or only seen in the portal venous phase [Figure 8]. A rim enhancement is frequently observed in liver metastasis, but seldom seen in toxocariasis [(13;14)].

Toxocariasis is mostly a self-limiting disease. On follow-up images, lesions usually improve and resolve spontaneously unless the patient is re-infected. The position and number of the lesions can change over time due to the migration of the larvae, which supports the diagnosis of VLM. Treatment includes the use of Albendazole and steroids for severe symptoms (15).
Fascioliasis

Fascioliasis is a zoonotic infection of the liver and the bile ducts caused by the trematodes *Fasciola hepatica* and *F. gigantica*, also called “flukes”. They infect approximately 17 million people worldwide. Ruminants are the natural hosts of *Fasciola* spp and infection is found in areas where ruminants are raised and the consumption of watercress is common [(16)].

Adult flukes reside in the intrahepatic bile ducts, where they release eggs that are passed in the stools. In freshwater, the eggs become embryonated and release the first stage larva “miracidium”, which invades a suitable snail. In this intermediate host, the parasite multiplies and develops through several stages. At the fourth stage cercariae abandon the snail and encyst as infective metacercariae on aquatic vegetation.

Ruminants and other mammals, including humans, acquire the infection through ingestion of aquatic plants or water contaminated with metacercariae. Once excysted in the small bowel, the metacercariae penetrate the gut wall and migrate through the peritoneal cavity to the liver. Here they perforate the capsule and start an intrahepatic migration. After 1–3 months, the worms finally enter the intrahepatic bile ducts and develop to adults in 2-3 months when they start to produce eggs. Occasionally, the larvae migrate to other organs or pass through the diaphragm and cause ectopic fascioliasis [(17)].

Clinically, an acute and a chronic-latent stage are distinguishable. During the acute stage, which is associated with the intrahepatic migration of the larvae, manifestations are typical of acute febrile eosinophilic syndrome, with abdominal and allergic symptoms. These can last several months and include fever, hepatosplenomegaly, upper-quadrant abdominal pain, gastrointestinal symptoms, urticaria, arthromyalgia and cough. Laboratory findings include eosinophilia, hypergammaglobulinaemia, increased liver enzymes and anaemia. The chronic-latent phase, caused by adult flukes in the bile ducts, occurs after approximately 3 months and can persist for years. The symptoms are generally more discrete and reflect biliary obstruction, inflammation and bacterial superinfection. They include upper abdominal discomfort, intermittent jaundice and fever. Elevated liver enzymes and bilirubin are common; however, eosinophilia is present in only half the cases.

Serological tests that detect *Fasciola* excretory-secretory antigens become positive after 2–4 weeks following infection and are consequently useful in the diagnosis of acute fascioliasis, when no eggs have been produced yet and during the chronic phase, because the shedding of eggs is intermittent and stool examination can give false-negative results. Antibody titres return to normal within 1 year of successful treatment. False-positive results can result from cross-reactivity with schistosomiasis.

In the acute stage, imaging techniques such as ultrasound and CT usually reveal a non-specific hepatosplenomegaly, which is sometimes accompanied by serosal effusions. Small necrotic lesions form along the migratory paths of juvenile flukes. These can be seen as hypoechoic or hypointense small lesions, which do not coalesce and are typically arranged along serpiginous tracts, from the surface of the organ to deep within the hepatic parenchyma [Figure 9]. They can change in quantity and location over time. This particular lesion arrangement can be helpful in the differential diagnosis of tumours, pyogenic abscesses and other visceral larva migrans [(18)]. Contrast enhanced ultrasound (CEUS) could better delineate the number, size and shape of the lesions [Figure 10].

**Figure 9** Ultrasound appearance of hepatic fasciolosis. Note the hypoechoic lesions with ill-defined margins, one of which is adjacent to the liver capsula (entry point of the
fluke) (Left) and the cyst-like nodules that progress from the liver capsule with a footprint-like pattern (Right). (Prof. Kabaalioglu).

Figure 10  Acute fascioliasis shown by B-mode imaging (a) and contrast enhanced ultrasound (b).

In the chronic stage, adult flukes are seen inside the biliary ducts as a few centimetres in length with single or multiple elongated filamentous echoic structures [Figure 11]. Spontaneous movement may be observed. Other ultrasound findings include thickening of
extra-hepatic bile ducts and gallbladder walls, common bile duct dilation, cholelithiasis, small calcifications of the liver parenchyma, liver abscesses, hepato-splenomegaly and ascites.

**Figure 11** Ultrasound scan of enlarged common bile duct with a Fasciola obstructing its lumen and another Fasciola floating in the gallbladder lumen (Left). A CT scan of a liver from a patient with fasciolosis. A subcapsular hypodense lesion and two other elongated lesions are seen in the right lobe (Right). (Prof. Kabaalioglu).

Fascioliasis is suspected by typical symptoms and diagnosis proved by serological testing (eventually over time). The treatment of Fascioliasis is relatively difficult, because the fluke has a thick cuticula which is not easily penetrated by any drug. Therefore, Praziquantel, otherwise the drug of choice in trematode infections, is of little use in Fascioliasis. Triclabendazole in a dose of 10 mg/kg body weight or bithionol are recommended [(19)]. It is usually given as single dose after meals. In severe infections, a second dose should be given after 12 hours. However, Triclabendazole is not licenced for use in humans in many countries, e.g., Germany. Endoscopic or surgical interventions may be necessary in complicated cases. Apart from the antiparasitic chemotherapy, patients sometimes suffer from cholangitis and liver abscesses. In these cases, antibiotics are required to prevent or treat bacterial superinfections, like Ceftriaxone and Metronidazole. If dead Fasciola worms obstruct the bile ducts, papillotomy and endoscopic drainage (ERCP) might be required.

**Small asian liver flukes: opistorchiasis and clonorchiasis**

*Clonorchis sinensis* and *Opisthorchis viverrini*, the “small Asian liver flukes”, together infect approximately 20 million people in Southeast Asia, Eastern Russia and China. Their definitive hosts include humans and other mammals including dogs, cats, pigs and wild animals. *O. felineus* is a zoonotic parasite of cats, which occasionally infects humans in Southeast and Eastern Europe and Eastern Russia.

Adult parasites reside in the intrahepatic and occasionally extrahepatic bile ducts, where they lay embryonated eggs that are passed in the faeces. In contact with fresh water, the eggs hatch and the first-stage larvae “miracidia”, are ingested by a suitable snail (first intermediate host) in which they multiply and develop through several stages. The fourth stage cercariae leave the snail and actively penetrate freshwater fishes (second intermediate hosts) in which they encyst as infective metacercariae in the muscles and under the scales. Humans and other definitive mammalian hosts acquire the infection through ingestion of raw or undercooked
infected fish, especially from the Cyprinidae family. After ingestion, the metacercariae excyst in the duodenum and reach the biliary tree where they ascend the ampulla of Vater. The adults mature and start to shed eggs approximately 1 month after infection [(16)].

Clinical manifestations of opistorchiasis and clonorchiasis depend on the intensity and duration of the infection and the species of liver fluke involved. These are caused by the obstruction and inflammation of the biliary ducts and occasionally the pancreatic ducts; the formation of intrahepatic calculi; and recurrent pyogenic cholangitis. Acute infections can be asymptomatic or oligosymptomatic with fever, abdominal pain or discomfort, nausea, jaundice (generally absent in O. viverrini infections) and hepatomegaly. Infections sustained by O. felineus can also present with allergy symptoms, such as arthralgia and a skin rash. Raised liver enzyme level and eosinophilia are common laboratory findings.

A progressive periductal fibrosis occurs as a consequence of chronic inflammation of the biliary tree. Small liver fluke infections have been associated with the development of cholangiocarcinoma, and in endemic areas C. sinensis infection is diagnosed in up to 95% of these tumours [(20)]. These are more often located peripherally, in second-order bile ducts, and infiltrate the hepatic parenchyma early with a generally poor prognosis [(21)]. Other complications include intrahepatic calculi, cirrhosis, liver abscesses, pyogenic cholangitis and pancreatitis.

The definitive diagnosis of opistorchiid infection is the demonstration of eggs in the stool; serological test are also useful.

Ultrasound and cholangiography are important diagnostic tools. Ultrasound findings reflect the pathology of the bile ducts, namely diffuse intrahepatic bile ducts dilation, truncation and increased periductal echogenicity, and infection complications, such as pyogenic cholangitis, liver abscesses, stones, pancreatitis and cholangiocarcinoma [(22)]. Occasionally flukes or aggregates of eggs are visualised as non-shadowing echogenic foci or casts within the bile ducts [Figure 12]. Ultrasound is less useful in therapy follow-up and in the differentiation between resolved and active infection, because the pathological changes of the bile ducts can persist for years even after the symptoms have resolved.

**Figure 12** Endoscopic ultrasound showing Opistorchis spp (between callipers) in a dilated common bile duct freeze – frame from a video recorded by Dr. William Brown and edited by Dr. Franklin Kasmin, Beth Israel Medical Center, New York City, NY.

Praziquantel is the drug of choice for treatment of opistorchiid infections, coupled with endoscopical or surgical interventions in complicated cases.
**Echinococcosis**

Human echinococcosis, or hydatidosis, is a zoonosis caused by larval forms (metacestodes) of *Echinococcus* spp tapeworms, which are found in the small intestine of carnivores. Four species of *Echinococcus* cause pathology in humans, of which *E. granulosus* is by far the most widespread. *E. multilocularis*, the second most frequent species, causes alveolar echinococcosis and its distribution is limited to the northern hemisphere. *E. vogeli* and *E. oligarthrus* cause polycystic echinococcosis and only a few human cases have been reported in Central and South America.

All *Echinococcus* species definitive host are carnivores (canids for *E. granulosus*, *E. multilocularis* and *E. vogeli*, and felids for *E. multilocularis* and *E. oligarthrus*), and have various mammals as the intermediate host (typically ruminants, but also horses and pigs for *E. granulosus* and rodents for the other species). The adult tapeworms reside in the small intestine of the definitive host. Mature eggs containing the infective larva (oncosphere) are released in the faeces and can be ingested by a suitable intermediate host. Here the eggs hatch and the oncospheres penetrate the intestinal wall and migrate through the bloodstream to various organs where they develop into cysts. These enlarge gradually to produce protoscolices (infective tapeworm heads) and daughter cysts. The definitive host becomes infected by ingesting the cyst-containing organs of the intermediate host. After ingestion, the protoscolices envaginate, attach to the intestinal mucosa and develop into the adult stage. Humans are dead-end intermediate hosts, who acquire the infection by ingestion of vegetables or water contaminated with infected eggs.

Here, we will focus on cystic echinococcosis (CE), caused by the metacestode of *E. granulosus*, which is the most geographically widespread and medically and economically important clinical disorder caused by this cestode. Human CE is highly endemic in pastoral communities worldwide, where there is close contact between humans, livestock and dogs. CE causes more than 95% of the 2–3 million estimated cases of echinococcosis worldwide. This is a yearly incidence of human infection of up to 50 cases per 100,000 inhabitants in highly endemic areas, where the prevalence can be up to 10% in humans and 50% in livestock. CE has a mortality rate of 2–4%, but this may increase considerably if medical treatment is inadequate.

The liver, followed by the lungs, is the organ most frequently infected. The metacestode develops into a single cyst that grows at a variable rate (on average 0.5–1.5 cm/year). Within the cyst, infective protoscolices and daughter cysts develop in approximately 3 months. Each protoscolex can, in cases of cyst rupture, generate a new cyst, in a process called “secondary infection”.

Approximately 60–75% of patients with CE are asymptomatic and the infection is usually discovered during an imaging exam carried out for other reasons. Morbidity depends on the number, size and developmental status of the cysts, the organ involved and the location within the organ. Clinical symptoms usually occur when the cyst compresses or ruptures into neighbouring structures. Patients with hepatic CE can present with upper-quadrant abdomen pain or discomfort and hepatomegaly. In the case of rupture or leakage of cystic material, recurrent allergic symptoms (rash, urticaria or bronchospasm) can appear, and in some cases an anaphylactic shock can occur. Other complications include rupture of the cyst into the biliary tract, with associated symptoms of cholangitis and biliary obstruction, or, less frequently, portal hypertension caused by compression of the caval vein or venous thrombosis. Mass effect, rupture and allergic reactions are the basis of the CE-related symptoms even in the case of thoracic localisation.

The diagnosis of CE is based on clinical findings, imaging techniques and serology. The presence of protoscolices may be seen on microscopic examination of the cystic fluid and
histology. Haematochemical parameters are generally unaltered, with the exception of increased cholestasis indices in case of biliary involvement. Eosinophilia is often mild or does not occur. Serology can be useful to confirm the diagnosis of CE made at imaging, but is hampered by its variable sensitivity (false-negative results are frequent in the case of young or inactive cysts, and cysts located in organs other than the liver) and by the persistence of the antibodies even after a complete cure. Ultrasound examination is the basis of CE diagnosis in abdominal localisation. Other radiological techniques are useful for the diagnosis of extrahepatic CE and to support the ultrasound diagnosis of hepatic infection.

The use of ultrasound for CE has revolutionised its diagnosis and treatment, along with the introduction of percutaneous procedures and follow-up. In 1995, the WHO-IWGE (Informal Working Group on Echinococcosis) developed a standardised classification that divided the cysts into three relevant groups according to their biological activity: active (CE1, uniloculated and CE2, with daughter cysts), transitional (CE3) and inactive (CE4, with solid content and CE5, solid content with calcifications) [(23)]. CE3 transitional cysts may be differentiated into CE3a (with detached endocyst) and CE3b (active, predominantly solid with daughter cysts) [(24)]. CE1 and CE3a are early stages, and CE4 and CE5 are late stages [Figure 13 and 14].

**Figure 13  WHO IWGE Ultrasound classification of echinococcal cysts.**

<table>
<thead>
<tr>
<th>WHO-IWGE</th>
<th>CL</th>
<th>CE1</th>
<th>CE2</th>
<th>CE3a</th>
<th>CE3b</th>
<th>CE4</th>
<th>CE5</th>
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Sonographic features along with serological results are important for the differential diagnosis of CE. A number of elements are important in the differentiation of parasitic from non-parasitic cysts. When they are not sufficient, ultrasound-guided aspiration of the cyst and search for protoscolices in the aspirate can be diagnostic. Generally, the visualisation of a double wall and regular, round and avascular “septations” (actually the walls of the daughter cysts) is pathognomonic of CE. In non-parasitic cysts, septations, if present, are grossly irregular, can have a fuzzy appearance due to the presence of fibrin [Figure 14], or may be vascularised in neoplasms.
The WHO-IWGE US classification is important for guiding the choice of treatment and in follow-up [Figure 15]. The characteristics of cysts and the patient, and the availability of resources, are all important parameters to take into consideration when choosing a therapeutic approach. In reference to the ultrasound classification only, hepatic CE1 and CE3a cysts may be treated with Albendazole (3–6 months) or percutaneous intervention with PAIR (puncture, aspiration, injection of a scolecidal agent, re-aspiration). Hepatic CE2 and CE3b cysts can be treated with Albendazole or PAIR, but in general they are less responsive to treatment. In selected cases, a “watch-and-wait” approach can be the best option [(25)]. Inactive cysts do not require treatment, and are only followed with ultrasound over time. Surgery, with radical or partial cystectomy, is the first therapeutic choice in complicated cysts, in case of resistance to other treatments or when these treatments are contraindicated.

Figure 15  Echinococcal cysts in various stages. CE1 with unspecific uniloculated (a) and CE2 with daughter cysts (b) are active forms, with CE1 being the early stage. Transitional CE3a cysts have a folded endocyst (also known as “waterlily sign”) floating within the cavity (c). The transitional CE3b stage is characterised by multiple daughter cysts within a solid matrix produced by the folded endocyst in a pseudocaseous inflammatory material (d). The contrast enhanced image (e) does not show any enhancement but artifacts. The surgical specimen is also shown (f, see also the liver chapter and EFSUMB cases of the month). The stages CE4 displays solid content (g). CE5 is characterised by solid content with calcifications (h), CEUS shows non-enhancement (i).
Ultrasound of parasitic disease ....

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b
c
d
Schistosomiasis

Human schistosomiasis, also known as “bilharziosis”, is a highly prevalent disease caused by the trematode worms of the genus *Schistosoma*. *S. mansoni*, *S. haematobium* and *S.*
and are the most common species affecting humans, whereas *S. mekongi* and *S. intercalatum* have been described more recently. More than 230 million people are currently infected with *Schistosoma* spp, and over 20 million suffer from severe disease, with an estimated mortality of 15,000–20,000 deaths per year.

85% of cases occur in Africa, where prevalence can exceed 50% in hyperendemic communities. *S. haematobium* is responsible for approximately 60% of all infections, with approximately 120 million people infected in Africa and the Middle East. *S. mansoni*, which is endemic in Africa, the Middle East, Latin America and the Caribbean, infects an estimated 67 million people. *S. japonicum* is present in China and Southeast Asia, where it infects 1 million people [26].

The other four species have a more localised distribution; *S. mekongi* in Cambodia and Laos, *S. intercalatum* in parts of Central and West Africa. Humans are the most important definitive hosts for *S. mansoni*, *S. haematobium* and *S. intercalatum*, but rodents, baboons and monkeys can be infected as well. *S. japonicum* and *S. mekongi* are the cause of zoonosists with various animals including rodents (*S. japonicum*), dogs (*S. mekongi* and *S. japonicum*) and cats, goats, horses, pigs and water buffalos (*S. japonicum*) are all possible definitive hosts [27].

Contamination of freshwater with faeces and urine containing worm eggs, and human skin contact with water contaminated by worm larvae can all result in infection. Adult worms reside in the mesenteric veins (*S. mansoni* and *S. japonicum*) and in the venules of the bladder (*S. haematobium*). Here the females release eggs that move progressively toward the lumen of the intestine or the bladder and urethers, and are eliminated with faeces or urine. In the water, the eggs hatch and release the first stage larva “miracidium”, which actively swim to and penetrate a suitable snail. In the intermediate host, the larva undergoes multiplication and maturation to the cercarial stage. The cercariae are then released from the snail and using their bifurcated tails swim until they reach the skin of the definitive host. Penetrating the skin, the larvae lose the tail to become schistosomulae. These juvenile worms then migrate through the host’s body until they reach their final destination in the portal and perivescical veins, depending on the species, and begin to produce eggs approximately 2 months after infection.

Travellers to endemic areas can present with infection as an acute cercarial dermatitis immediately after exposure (“swimmer’s itch”) and acute hypereosinophilic febrile syndrome after several weeks (“Katayama fever”), seen as fever, chills, gastrointestinal symptoms, hepatosplenomegaly and eosinophilia. In inhabitants of endemic foci, the acute stage is often asymptomatic or oligosymptomatic and patients are usually seen in the chronic stage of the disease.

Chronic pathology is caused by an inflammatory reaction to eggs that are trapped in the intestinal wall and in the liver (for *S. mansoni* and *S. japonicum*) or in the wall of the urether and bladder (for *S. haematobium*). This inflammation eventually leads to granulomas and fibrosis. Hepatosplenic schistosomiasis causes hepatic portal “pipe stem” fibrosis and intestinal wall thickening and stenosis.

Symptoms are non-specific, with abdominal discomfort, diarrhoea and sometimes blood in stools. Later, portal hypertension develops and sudden life-threatening haemorrhage can occur as a result of the rupture of gastro-oesophageal varices, which is the most common complication of portal fibrosis. Hepatic complications are especially severe in patients with associated liver damage due to hepatitis B, C and/or D virus co-infection or nutritional factors. Other complications include portal vein thrombosis, which in turn leads to the cavernous transformation of the collateral veins and cardiopulmonary schistosomiasis that occurs when ova reach the caval veins through collateral circulation. Ectopic schistosomiasis as a result of erroneous migration of worm pairs can occur in any location including the central nervous system, appendix or breast in females.
Generally, hepatic function is preserved. The most common sign of urogenital schistosomiasis is the presence of blood in urine. Renal impairment can follow hydronephrosis. Genital involvement can develop in both sexes, and bladder cancer has been related to urinary schistosomiasis. The effects of schistosomiasis are not well known but placenta involvement and anaemia due to chronic blood loss through urine or stool are thought to contribute to foetal prematurity and impaired growth.

Definitive diagnosis relies on serology and the presence of eggs in stool, urine, seminal fluid or cervical or rectal biopsies. However, this can give false-negative results during the pre-patent period. Moreover, antibodies persist for years following exposure, which is not helpful in follow-up or in patients from endemic areas [(26)]. Egg excretion does not directly correlate to the severity of organ involvement.

Ultrasonography is the first-line imaging technique used in the diagnosis and staging of schistosomiasis and, in the follow-up, to detect improvement following therapy or the onset of complications. During acute schistosomiasis, non-specific hepatosplenomegaly with enlargement of the hilar lymph nodes can be observed. These can show an unusual structure, with a hypoechoic halo surrounding a moderately hyperechoic centre.

Ultrasonography readily detects periportal fibrosis and thickening of the walls of portal branches, splenomegaly and portal hypertension in chronic hepatosplenic schistosomiasis. Portal vein thrombosis and echogenic foci in the spleen can also be observed. Portal fibrosis, also named “Symmer’s pipe-stem fibrosis” can be classified into six progressive patterns [(28)] [Figure 17].

These can progress from a “starry sky” appearance, with diffuse echogenic foci, to an increased wall thickness of the portal vein branches: ring-echoes and pipe-stem appearance, echogenic “ruff” around the main portal branches, up to patches and bands that extend from the main portal vein to the liver surface, which induce a retraction of the surface itself.

Ultrasound has made it possible to classify all these features, and can be used to stage liver involvement. This classification for S. Mansoni was proposed at a WHO conference in Niamey, Niger in 1996 and subsequently reviewed during a meeting held in Belo Horizonte, Brazil [(28)] [Figure 16].
Figure 16  Niamey Ultrasound classification for *S. Mansoni* liver involvement.

Patterns associated with schistosomiasis (A – F)

A: normal  
B: “starry sky”

C: “rings and pipe-stems”  
D: “ruff” around portal bifurcation

E: “patches”  
F: “bird’s claw”
The liver may be enlarged, normal or shrunken, depending on the stage of liver fibrosis. Signs of portal hypertension include an increased diameter of the portal vein, presence of varices of the collateral veins, recanalization of the paraumbilical vein and presence of ascites. The wall of the gallbladder can be thickened, with occasional external echogenic protrusions [(29;30)]. In *S. japonicum* infection, a peculiar fibrotic pattern is observed, with a “network”, “fish-scale” or “tortoise-shell” appearance [Figure 17].
In urinary schistosomiasis, ultrasound can show hydronephrosis, dilation of the urethers, bladder-shape abnormalities, thickening of the wall and presence of intravesical masses. Calcification of the bladder wall is almost pathognomonic, but rarely identified on ultrasound. Ultrasound findings of genital pathology include ulcerations, papillomata, salpingitis, adnexial and pelvic masses, vagino-vesical fistulae, increased uterus volume, hyperechoic patches and pelvic masses in females and scrotal fibrotic masses, fibrotic lesions of the prostate and seminal vesicles and hydrocoele in males. Schistosomiasis in mothers can result in impaired foetal growth [(31)].

**Figure 17** Network-like appearance of *S. japonicum* infection of the liver.
Praziquantel is the treatment of choice for schistosomiasis, but it is only effective on adult worms; therefore, the treatment should be repeated after 2–4 weeks to target juvenile forms that are not yet sensitive to the first dose. After therapy, antibodies remain detectable for years, but ultrasound can detect a slow improvement of the organ abnormalities over months, up to their complete resolution depending on the stage and whether re-infection has occurred [(32;33)].
References


